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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 23 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Robert J. Taylor, PM #25
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THRU: Gary J. Burin, Toxicologist
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SUBJECT: Metribuzin Registration Standard

Attached is the Toxicology Chapter for the Metribuzin Registration Standard. Included are the following:

1. Summary of toxicology data for Metribuzin.
2. Updated TOX "One-liners".
3. Data Summary Table A, which indicates TOX data gaps.
4. Tolerance reassessment.
5. Bibliography
6. Evaluations of all studies reviewed during the course of this standard.

Stephen C. Dapson 1/22/85

Stephen C. Dapson, Ph.D.
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TOXICOLOGY DATA SUMMARY

Acute Toxicity

An acute oral toxicity study (DuBois and Kinoshita, 1969) in the rat places this compound in Toxicity Category III with LD_{50} of 2,200 mg/kg reported for the male and 2,345 mg/kg for the female. Data submitted for the mouse, rabbit, cat and chicken (Kimmerle et al, 1969) also indicate acute oral LD_{50}s greater than 500 mg/kg for these species whereas the LD50 in the guinea pig was found to be 274.5 mg/kg. An acute inhalation toxicity study found an LC_{50} of >20mg/l (Toxicity Category IV). Eye irritation testing in the rabbit found this compound not to be an irritant (Toxicity Category IV) and a dermal irritation study found this compound to have little potential for dermal irritation (PIS= 0.33/8.0). Metribuzin technical should thus be considered Toxicity Category III for oral toxicity and Toxicity Category IV for all other forms of toxicity.

Teratology

One teratology in the rat and three teratology studies in rabbits have been submitted for metribuzin. A teratology study in rats (Machemer, 1972) was conducted using 4 dosages of SENCOR, 5, 15, 50 and 100 mg/kg/day with treatment of pregnant females from day 6 to 15 of gestation. There was evidence of minimal maternal toxicity at the high dose level in the form of reduced maternal body weight gain. No evidence of fetal toxicity or teratogenicity was noted at the dose levels used in this study. This study is classified as Core-Supplementary Data.

Three rabbit teratology studies were conducted at IBT (Ladd 1971, Ladd and Smith 1972a) and were found to be Invalid by the Canadian goverment. An additional study in the rabbit (Unger and Shellenberger, 1981) was a replacement for the IBT Study No. J-9027. This study indicated that SENCOR in the dosages tested caused maternal toxicity without significant fetal toxicity at the high dose (135 mg/kg/day) with no maternal or fetal effects evident at the low dose (15 mg/kg/day). No evidence of teratogenicity was observed at the dose levels tested. The NOEL for maternal and fetal toxicity is 15 mg/kg/day with a LOEL of 45 mg/kg/day for maternal toxicity. This study is classified as Core-Guidelines.

Reproduction

A multigeneration (3 generation) reproduction study in rats (Loser and Siegmund, 1974) employed three dosages of BAY

94 337 (35, 100 and 300 ppm, equivalent to 3.5, 10 and 30 mg/kg) mixed in the animal feed. There was no evidence of compound related reproductive or fertility effects in the three generations of rats examined. The high dose (300 ppm) did not induce any toxicity as is required by CORE, however the NOEL for reproductive effects can be set at 300 ppm (HDT). This study is classified as Core-Supplementary Data.

Chronic and Oncogenicity

Two mouse oncogenicity studies are available. The first study (Smith and Gordon, 1972 a and b) was conducted at IBT and was found to be Invalid in a review by the Canadian Government. The second study (Hayes et al, 1981), a replacement for IBT Study No. B-9069, was a two year feeding study in the mouse employing groups of 50 male and 50 female mice. They were given diets containing 0, 200, 800 or 3200 ppm Metribuzin (equivalent to 0, 28, 111 and 435 mg/kg/day for males and 0, 35, 139 and 567 mg/kg/day for females). Minimally toxic effects were observed at the high dose level in the form of increased liver weight and changes in the hematocrit and hemoglobin measurements. Although some increase in the number of tumor bearing animals was observed in low and mid dose females, significant increases in the incidence of specific tumor types were not observed at any dose level. It was concluded that under the conditions of the test, did not increase the incidence of tumors in mice. This study is classified as Core-Guidelines.

In a two year feeding study in rats (Loser and Mohr, 1974) 4 doses of BAY 94 337 were utilized (25, 35, 100 and 300 ppm, equivalent to 1.25, 1.75, 5, and 15 mg/kg/day) mixed in the animal feed. Analysis of the neoplastic histopathological observations indicated a statistically significant ($p<.05$) increase in the incidence of ademona of the liver bile duct and pituitary gland in the 300 ppm females. Non-neoplastic histopathological observations showed a statistically significant increase in liver "changes in the nucleus" in the females of the 300 ppm test group. However, not enough animals were examined histopathologically in the other 3 dosage groups to allow a judgement to be made in regard to a dose response effect of the chemical for either neoplastic or nonneoplastic lesions. Further data must be supplied by the registrant in the form of histopathological examinations of the animals not previously examined in the other 3 dosage groups along with historical control data on the incidence of these tumors in this particular strain of rat. No systemic NOEL can be determined without the additional histological data. This study is classified as Core-Supplementary Data.

A 2 year feeding study (Loser and Mirea, 1974) was conducted in groups of 4 male and 4 female beagle dogs using three dosage levels (25, 100 and 1500 ppm, equivalent to 5, 15, 50 and 150 mg/kg/day) of BAY 94 337. Decreased body weight of the animals at the high dose, increased relative liver weight along with the related clinical tests and the histopathological findings also indicate that a dose level of 1500 ppm is associated with toxicity. Histopathological observations included evidence of liver parenchymal necrosis, interstitial infiltration and other changes not observed in the control, 25 and 100 ppm test groups. The 2 lower doses did not show any compound related effect. The NOEL for this study is 100 ppm with a LOEL of 1500 ppm (HDT). This study is classified as Core-Minimum Data.

Subchronic

Two subchronic (90 day) feeding studies were conducted in rats. The first (Loser et al, 1969) used doses of 50, 150, 500 and 1500 ppm (equivalent to 5, 15, 50 and 150 mg/kg/day). Based on the data provided in this study the systemic NOEL is below 50 ppm since the increase in liver weight was statistically significant at all 4 dose levels in the females. This study is classified as Core-Supplementary Data since no NOEL could be established for this study, no protocol was provided for the pathological examinations and only limited organs and small numbers of animals were used for histopathological studies.

The second subchronic study in rats (Loser et al, 1970) used doses of BAY 94 337 of 10, 25 and 60 ppm. An increase in liver weight was observed in the females, statistically significant at the 60 ppm and a trend of an increase was observed in the males. Histopathology that was provided was unremarkable between test groups. A systemic NOEL of 25 ppm can be set as determined by the increase in liver weight in the 60 ppm females. The 60 ppm dose is the LOEL for this study. This study is classified as Core-Supplementary Data based on the limited organs and the small number of animals examined for histopathology and the limited clinical chemistry.

An IBT subchronic dog study (Lindberg and Richter, 1970) was found to be valid in a review by the Canadian Government. In a subsequent IBT Evaluation Report prepared for the Agency, it concluded that this study had been compromised because of the incomplete gross and histopathological data and the absence of clinical observations of signs of toxicity and that a NOEL for subchronic toxicity could not be determined based on this study. It was noted also that a dose-related increase in liver weight and the liver to body weight ratio was found in treated animals.

Mutagenicity

The selection of assays for a mutagenicity battery should consider the nature of the test chemical, and a justification for test selection should be provided.

Minimum requirements are:

1. Microbial point mutation tests
2. Mammalian point mutation tests in vitro
3. In vivo cytogenetics tests in mammals with either heritable translocation or dominant lethel studies.
4. Tests for primary DNA damage such as sister chromatid exchange or unscheduled DNA synthesis assays.

The mutagenicity studies submitted by the registrant (Machemer and Lorke, 1974a, 1974b, 1975, 1976; Inukai and Iyatomi, 1977; Shirasu et al, 1978). The first requirement is partially satisfied by the Inukai and Iyatomi (1977) and Shirasu et al (1978) reports. These microbial point mutation assays did not indicate a mutagenic potential for metribuzin in the test systems utilized. The other 4 studies done by Machemer and Lorke (1974a, 1974b, 1975 and 1976) ,although limited to only one dose level, indicated that SENCOR does not induce dominant lethal mutations in mice or chromosomal aberrations in hamster spermatogonia at dose levels of 300 mg/kg and 100 mg/kg, respectively. These studies satisfy the third requirement mentioned above. Additional mutagenicity testing is required to satisfy the other requirements in this area.

Metabolism

A metabolism study was conducted in rats with oral dosing of radiolabeled SENCOR (Flint et al, 1973) evaluating excretion and tissue residue levels as well as the pattern of metabolites. The excretion studies found sex related differences with the males excreting the radiolabel primarily in the feces and the females excreting the label primarily in the urine. However, an inadequate number of animals was used in this study (one male and one female in one study and two males in another study). Tissue distribution studies also suggest slight sex related differences in distribution up to the 28 hour interval (after administration) with similar patterns of reduction in residue levels after that time point (however, the females tended to present with higher overall levels at all time points measured). The investigators found a metabolic scheme for SENCOR in rats that was similar to what was found in to an earlier study in soybeans. The metabolites that were identified were the deaminated, diketo and deaminated diketo parent compound. Due to an inadequate number of animals and other deficiencies, these studies were classified as Supplementary Data.

A metabolism study was conducted in 4 dogs using oral dosing of radiolabeled SENCOR (Khsawinah et al, 1972) evaluating absorption, distribution and metabolites. Analysis of blood samples showed a peak level at 4 hours. The excretion study data indicated that 52 to 60% of the administered dose was eliminated in the urine and 30% in the feces. The true patterns of metabolites could not be accurately determined. However, it appeared that the same metabolites found in an earlier study in soybeans and a concurrent study in rats were found in this study. Due to deficiencies including the small number of animals and the use of only a single dose level, this study is classified as Supplementary Data.

Toxicology Data Gaps

The available studies satisfy data requirements for the mouse oncogenicity, chronic nonrodent study and rabbit teratology studies and partially satisfy the requirements for mutagenicity. The rat teratology, reproduction and chronic rat studies are not completely adequate for regulatory purposes and thus should be considered data gaps. The upgrading of one or more of these studies may be possible upon the submission of of additional data. Acceptable metabolism and acute inhalation studies must also be submitted.

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Teratology - rabbit; IBT; J-233; 11/12/71; MRID #	Technical		Teratogenic NOEL > 30 mg/kg (HDT) CANADA INVALID combined with IBT # J-1851		001151
Teratology - rabbit; IBT; J-1851; 11/21/72; Mobay # 35159; MRID # 00061256	Technical	112892	Maternal toxicity NOEL > 30 mg/kg (HDT) Terata NOEL > 30 mg/kg (HDT) CANADA INVALID		001148 001151
Teratology - rabbit; IBT;#J-9027; 5/18/71; Mobay # 30172; MRID # 00061254;	Technical; Batch # 9059332	112892	Maternal toxicity NOEL > 15 mg/kg (HDT) Terata NOEL > 15 mg/kg (HDT) CANADA INVALID		001148 001151
Teratology - rabbit; Mobay; MRI # 7212-B; 10/30/81; Mobay # 80051; MRID # 00087796	Technical; Purity= 93.0% Ref. # 77-297-50	246397	Teratogenic NOEL $\geq$ 135 mg/kg/day (HDT) Maternal Toxic NOEL = 15 mg/kg/day Maternal Toxic LOEL = 45 mg/kg/day Fetal Toxic NOEL = 15 mg/kg/day Fetal Toxic LOEL = 45 mg/kg/day		Guideline 001761
Teratology - rat; Bayer AG; #3678; 9/29/72 ; Mobay # 35073; MRID # 00061257	Technical; Consignment 1603/71, Batch 17, Rcd. 6/71 Purity= 99.5%	112892	Maternal toxicity NOEL > 100 mg/kg (HDT) Terata NOEL > 100 mg/kg (HDT)		001148 Supplementary
3 Generation reproduction - rat; Bayer AG; #4889; 9/24/74 ; Mobay # 41818; MRID # 00061262	Technical; Sdg. 1603/71 Purity= 99.5%	112891	Reproductive NOEL > 300 ppm (HDT) Maternal toxicity NOEL > 300 ppm (HDT)		001147 001148 Supplementary
90 Day feeding - rat; Bayer AG; #1719;11/20/69 ; Mobay # 26488; MRID # 00106161	Technical	112032	Systemic NOEL = 150 ppm Systemic LEL = 500 ppm Re-review: Systemic NOEL below 50 ppm (LDT), see next study		001146 Supplementary

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Study/Lab/Study #/Date	Material	Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
90 Day feeding - rat; Bayer AG; #2150; 7/6/70; Mobay # 27908; MRID #	Technical	112032	Systemic > 60 ppm (HDT) Re-review : Systemic NOEL = 25 ppm Systemic LOEL = 60 ppm (HDT)		001146
90 Day feeding - dog; IBT, #C-7760; 1/9/70; Mobay # 26488; MRID # 00106162	Technical Batch # 9050332		Systemic NOEL = 150 ppm Systemic LOEL = 500 ppm CANADA VALID		001146 001151 Supplementary
2 Year feeding - dog; Bayer AG; #4887; 9/24/74 ; Mobay # 41814; MRID # 00061260	Technical; Batch 1603/71 Purity= 99.5%	112892	Systemic NOEL = 100 ppm Systemic LOEL = 1,500 ppm (HDT); weight reduction, increased mortality, hematological changes, liver and kidney damage)		001147 001148 Supplementary
2 Year feeding - rat; Bayer AG; #4888; 9/25/74 ; Mobay # 41816; MRID # 00061261	Technical; Batch 1603/71 Purity= 99.5%	112891	Systemic NOEL > 300 ppm (HDT) Oncogenic NOEL > 300 ppm (HDT) Re-review: Systemic NOEL and oncogenic potential could not be determined	?	001147 001148 Supplementary
18 Month oncogenic-mice; IBT; #B-9069 ;8/15/72; Mobay # 34481; Pathology Addendum; 12/21/73; Mobay # 34481a; MRID # 00061256 and 00079527	Technical; Batch # 9050332 and 1050265	112892	Oncogenic NOEL > 2500 ppm CANADA INVALID		001147 001148 001151
Oncogenic - mice; Mobay ; # 218, #78CCM01; 10/30/81; Mobay # 80050; MRID # 00087795	Technical; Batch # 77-297-50 Purity= 92.9%	246397	Did not increase the incidence of tumors in test conditions. However apparent increases in tumor incidences noted must be evaluated with results from second species.		Guideline 001761 003911

Study/Lab/Study #/Date	Material	Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	Tox Category	Core Grade/ Doc. No.
Metabolism - rat; Chemagro; #33366; 7/5/73 ; Mobay # 33366; MRID # 00045265	14C and 3H SENCOR and 14C SENCOR		Excretion was essentially through the urine and feces. No radioactive material was detected in expired gases		001146 Supplementary
Metabolism - dog; Chemagro; #33361; 5/1/72 ; Mobay # 33361; MRID # 00045264	14C Sencor		60% excreted in urine 30% excreted in feces		001146 Supplementary
Mutagenic- dominant lethal - mice; IBT; #E-8922; 6/14/71; Mobay #; MRID #	Technical	112032	Not a mutagen at 20 mg/kg CANADA INVALID		001146 001151
Mutagenic - dominant lethal - mice; Bayer AG; #5523; 7/10/75 ; Mobay # 45023; MRID # 00086767	Technical; Batch 6/71 Consignment 1603/71 Purity= 99.5%	246226	Negative for dominant lethal effects in male treated mice at 300 mg/kg		Acceptable 001762
Mutagenic - dominant lethal - mice; Bayer AG; #6110; 5/19/76 ; Mobay # 49068; MRID # 00086768	Technical; Batch 6/71 Consignment 1603/71 Purity= 99.5%	246226	Negative for dominant lethal effects in male treated mice at 300 mg/kg		Acceptable 001762
Mutagenic - dominant lethal - mice; Bayer AG; #4942; 10/5/74 ; Mobay # 43068; MRID # 00086766	Technical; Batch 6/71 Consignment 1603/71 Purity= 99.5%	246226	Negative for dominant lethal effects in female treated mice at 300 mg/kg/day		Acceptable 001762

Study/Lab/Study #/Date	Material	No.	LD_{50}, LC_{50}, PIS, NOEL, LEL	Category	Doc. No.
Mutagenic - cytogenetic-chinese hamster; Bayer AG; #4961; 10/7/74 ; Mobay # 43067; MRID # 00086765	Technical; Batch 17 Consignment 1603/71 Purity= 99.5%	246226	Negative for chromosomal aberrations at 100 mg/kg in treated mice		Acceptable 001762
Mutagenic - S. typhimurium and B. subtilus; Nitokuno Agric Chem. Instit.; #67; 12/19/77; Mobay # 54127; MRID # 00086770	Technical; Purity= 93.7%	247885	The results should be considered with other rec assay and reversion assay data such as that provided in the 1978 study.		002778 Acceptable
Mutagenic - S. typhimurium, E. coli, and B. subtilis; Inst. Environ. Tox.; 8/17/78; Mobay # 66748; MRID # 00109254	Technical; Purity= 93.3%	247885	These results should be considered with those described in the 1977 mutagenic report. No mutagenic activity was observed.		002778 Acceptable
Mutagenic - mice; micronucleus test; Bayer AG Inst. of Toxicology; #10718; 10/3/82	DIC-1468 (Sencor Active ingredients)	251219	Negative response when the test compound was administered twice orally with a stomach tube at an interval of 24 hours. (Tested at 2 x 200 and 2 x 400 mg/kg dose levels) The assay was not performed properly in accordance with the accepted procedures.		Unacceptable 003865

Study/Lab/Study #/Date	Material	No.	LD_{50}, LC_{50}, PIS, NOEL, LEL	Category	Doc. No.
Mutagenic - mitotic gene conversion in Sacchramycees cerevisiae D. Siebert and E. Lemperle; Mutation Res. 22 (1974), 111-120	Sencor	251219	The test compound at 1000 ppm did not induce a significant increase in the conversion frequenc (convertants/10^6 survivals) neither in the ade 2 nor the trp 5 locus of the diplcid strain D 4 of of saccharamyces cerevisiae. (tested at a single dose of 1000 ppm without metabolic activation) The assay was not peformed properly in accordance with the accented procedures.		Unacceptable 003865
Dermal irritation - human	Technical		No irritation (24 hrs) (M)		
Acute oral LD_{50} - rat; 6/3/69; Mobay # 25118	Technical; in 20% ethanol and 80% PPG; Batch # 9050332		LD_{50} = 1985.9 mg/kg (male) LD_{50} = 1937.0 mg/kg (female)	III	001146
Acute oral LD_{50} - guinea pig; 6/3/69; Mobay # 25118	Technical; in 20% ethanol and 80% PPG; Batch # 9050332		LD_{50} = 198.3 mg/kg (male)		001146
Acute oral LD_{50} - rat; Bayer AG; #1574; 9/12/69; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} = 2200 mg/kg (male) LD_{50} = 2345 mg/kg (female)	III	001146
Acute oral LD_{50} - mice; Bayer AG; #1574; 9/12/69; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} = 698 mg/kg (male) LD_{50} = 711 mg/kg (female)		001146

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Study/Lab/Study #/Date	Material	No.	LD_{50}, LC_{50}, PIS, NOEL, LEL	Category	Doc. No.
Acute oral LD_{50} - guinea pig; Bayer AG; 1574; 9/12/69; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} > 250 mg/kg (approximately) (male)		001146
Acute oral LD_{50} - rabbit; Bayer AG; #1574; 9/12/69; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} > 500 mg/kg		001146
Acute oral LD_{50} - cat; Bayer AG; #1574; 9/12/69; Mobay # 25942 MRID # 00106158	Technical	112032	LD_{50} > 500 mg/kg		001146
Acute oral LD_{50} - chicken; Bayer AG; #1574; 9/12/69; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} > 1,000 mg/kg		001146
Acute oral LD_{50} - guinea pig; Chemagro; 3/20/72; Mobay # 33045	Technical	112032	LD_{50} = 274.5 mg/kg		001146
Acute dermal LD_{50} - rabbit; Chemagro; 4/10/72; Mobay # 33123	Technical	112032	LD_{50} > 20 gm/kg (male and female)		001146
Acute dermal LD_{50} - rat; Chemagro; 4/10/72; Mobay # 33123	Technical	112032	LD_{50} > 20 gm/kg (male and female)		001146

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Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Acute inhalation LC_{50} - rat; Chemagro; 1/19/72; Mobay # 31931	Technical	112032	LC_{50} > 20 mg/L/1 hour		001146
Acute intraperitoneal LD_{50} - rat; Bayer AG; #1574; 9/12/69 ; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} = 363 mg/kg (male and female)		001146
Acute intraperitoneal LD_{50} - mice; Bayer AG; #1574; 9/12/69 ; Mobay # 25942; MRID # 00106158	Technical	112032	LD_{50} = 247 (male) LD_{50} = 275 (female)		001146
Primary dermal irritation - rabbit; Chemagro; 3/21/72; Mobay # 32862	Technical	112032	PIS = 0.33/8.0		001146
Primary eye irritation - rabbit; Chemagro; 3/21/72; 3/21/72	Technical	112032	Not an eye irritant		001146
Acute oral LD_{50} - rat; Chemagro; #29347; 2/9/71	DADK Metabolite Control No. 70-109-22	112032	LD_{50} = 1,100 mg/kg (female)		001146
Acute oral LD_{50} - rat; Chemagro;#31656;12/21/71	DA Sencor 50% WP (metabolite)	112032	275 < LD_{50} < 300 mg/kg		001146
Acute oral LD_{50} - rat; Chemagro;#31656;12/21/71	DK Sencor (metabolite)	112032	600 < LD_{50} < 900 mg/kg		001146

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Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Primary eye irritation-rabbit	4-Amino-6-(1,1-dimethyl-ethyl)-3-(methylthio) -1,2,4-triozin-5 (4H)-one 75%	3125-325	No corneal opacity or iris irritation, discharge present in 4/6 animals, but all irritation had cleared by day 4.	III	Guideline
Acute oral LD_{50} - rat; Dupont Haskell Lab; HLR-315-78	Lexone DF (75% a.i.)		LD_{50} = 2795 mg/kg (male) dypsprea, weakness, weight loss	III	Minimum 001145
Acute dermal LD_{50} - rabbit; Dupont Haskell Lab; HLD-287-78; 6/2/78	Lexone 75 DF 84% technical		LD_{50} > 7500 mg/kg (male) mild to moderate skin irritation	III	Minimum 001145
Primary eye irritation - rabbit; Dupont Haskell Lab; HLR108-78; 3/17/78	Lexone 75 DF 84% technical		Keratitis and conjunctivitis persisting at 72 hours	I	Minimum 001145
Primary dermal irritation - guinea pig; Dupont Haskell Lab; HLR443-78; 8/4/78	Lexone 75 DF 84% technical		Mild irritation when tested as a 20% suspension		Guideline 001145
Dermal sensitization - guinea pig; Dupont Haskell Lab; HLR-443-78	Lexone DF (75% a.i.)		Not a sensitizer		Guideline 001145
Primary dermal irritation - rabbit; Dupont Haskell Lab; HLR-98-78; 3/17/78	Lexone 75 DF 84% technical		Not a skin irritant	IV	Minimum 001145

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Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Primary eye irritation - rabbit; Stanley Res; #68534; 2/22/80	Sencor 75%	3125325	No corneal opacity or iris irritation Discharge present in 4/6 animals with clearing by day 4	III	Guideline 001149
Primary eye irritation - rabbit; Stanley Res; #68535; 2/22/80	Sencor 75%	3125325	No corneal opacity or iris irritation Erythema and discharge with clearing by day 4	III	Guideline 001149
Acute oral LD_{50} - rat; Mobay;#78-R-020; 9/25/78; Mobay #66552	Sencor 75 WG 75% AI		LD_{50} = 2379 mg/kg (male) LD_{50} = 2794 mg/kg (female) Tremor, convulsion, tremor, lacrimation	III	Guideline 001150
Acute dermal LD_{50} - rabbit; Mobay;#78-R-020; 9/19/78; Mobay #66553	Sencor 75 WG 75% AI		LD_{50} > 5,000 mg/kg (male & female) Single dose tested	III	Guideline 001150
Primary eye irrit.- rabbit; Mobay;#78-R-020; 9/25/78; Mobay #66554	Sencor 75 WG 75% AI		Corneal opacity in 5/6 animals (unwashed eyes) with clearing by day 7 Irritation of the iris and conjunctivae persisted at 7 days	II	Minimum 001150
Primary dermal irritation - rabbit; Mobay;#78-R-020; 9/25/78 ; Mobay #66554	Sencor 75 WG 75% AI		PIS = 0.17/8.0 slight erythema	IV	Guideline 001150
Acute inhalation LC_{50} - rat; Mobay; # 68-22; 9/25/78; Mobay #66555	Sencor 75 WG 75% AI		LC_{50} > 20 mg/L/1 hour (male & female)	IV	Supple- mentary 001150
Acute oral LD_{50} - rat; Chemagro Lab	Lexone 4L		LD_{50} = 2890 mg/kg		001145
Acute dermal LD_{50} - rabbit; Chemagro Lab	Lexone 4L		LD_{50} > 7500 mg/kg		001145

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Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Primary dermal irritation - rabbit; Chemagro Lab	Lexone 4L		PIS = 3.2/8.0		001145
Primary eye irritation - rabbit; Chemagro Lab	Lexone 4L		Irritant to the eyes		001145
Acute oral LD_{50} - rat; Chemagro Lab	Sencor 4F		LD_{50} > 500 mg/kg		001145
Acute dermal LD_{50} - rabbit; Chemagro Lab	Sencor 4F		LD_{50} > 20 gm/kg		001145
Acute inhalation LC_{50} - rat; Chemagro Lab	Sencor 4F		LC_{50} > 1920 ug/L		001145
Primary dermal irritation - rabbit; Chemagro Lab	Sencor 4F		Not an irritant		001145
Primary eye irritation - rabbit; Chemagro Lab	Sencor 4F		Severe ulcerations of the conjunctivae		001145
Acute oral LD_{50} - rat; Chemagro Lab; Mobay #26014	70% WP		LD_{50} > 1,400 mg/kg (females)		001146
Acute oral LD_{50} - rat; Chemagro;#29987; 4/29/71	70% WP	112032	LD_{50} > 2,000 mg/kg(male)		001146
Acute dermal LD_{50} - rabbit; Chemagro #29987; 4/29/71	70% WP	112032	LD_{50} > 20 gm/kg		001146
Acute inhalation LC_{50} - rat; Chemago; #29987; 4/29/71	70% WP	112032	LD_{50} > 160 mg/l/1 hour		001146

Tox Chem No. 33D Metribuzin

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Acute oral LD_{50} - rat; Chemagro; #31936; 1/2/72	50% WP	112032	LD_{50} = 4,000 mg/kg (male) LD_{50} = 4,753 mg/kg (female)		001146
Acute dermal LD_{50} - rabbit; Chemagro; 4/10/72; Mobay #33123	50% WP	112032	LD_{50} > 20 gm/kg (male and female)		001146
Acute dermal LD_{50} - rat; Chemagro;#33123; 4/10/72	50% WP	112032	LD_{50} > 20 gm/kg (male and female)		001146
Acute inhalation LC_{50}- rat; Chemagro;# 31931; 1/19/72	50% WP	112032	LC 50 > 20 mg/L/1 hour		001146 001145
Primary dermal irritation - rabbit; Chemagro;#32862; 3/21/72	50% WP	112032	PIS = 0.33/8.0		001146
Primary eye irritation - rabbit; Chemagro;#32862; 3/21/72	50% WP	112032	Not an eye irritant		001146

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TABLE A

GENERIC DATA REQUIREMENTS FOR Metribuzin (BAY 94 337, SENCOR, LEXONE

Data Requirement	Composition[1/]	Use Patterns[2/]	Does EPA Have Data To Satisfy This Requirements? (Yes, No or Partially)	Bibliographic Citation MRID #	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?[3/]
158.135 Toxicology					
ACUTE TESTING:					
81-1 - Oral LD_{50} - Rat	TGAI	A,B	Yes	00106158	No
81-2 - Dermal LD_{50}	TGAI	A,B	Yes	GS0181-01	No
81-3 - Inhalation LC_{50} - Rat	TGAI	A,B	Partially*	GS0181-02	Yes
81-4 - Primary Eye Irritation	TGAI	A,B	Yes	GS0181-03	No
81-5 - Primary Skin Irritation	TGAI	A,B	Yes	GS0181-04	No
81-6 - Dermal Sensitization	MUP	A,B	Yes	GS0181-05	No
81-7 - Acute Delayed Neurotoxicity-Hen	—	—	No	—	No

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LEXONE)

Data Requirement	Composition[1/]	Use Patterns[2/]	Does EPA Have Data To Satisfy This Requirements? (Yes, No or Partially)	Bibliographic Citation MRID#	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)?
SUBCHRONIC TESTING:					
82-1 - 90-Day Feeding - Rat	TGAI	A, B	N/A	00106161 and GS0181-06	No
Dog	TGAI	A, B	N/A		
82-2 - 21-Day Dermal				00106162	No
82-3 - 90-Day Dermal	—	—	N/A	—	No
82-4 - 90-Day Inhalation - Rat	—	—	N/A	—	No
82-5 - 90-Day Neurotoxicity - Hen/Mammal	—	—	N/A	—	No
CHRONIC TESTING:					
83-1 - Chronic Toxicity - 2 species: Rat	TGAI	A, B	Partially *	00061261	Yes
Dog	TGAI	A, B	Yes	00061260	No

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Data Requirement	Composition[1]	Use Patterns[2]	Is Data Adequate to Satisfy Requirements? (Yes, No or Partially)	Bibliographic Citation MRID #	Data Be Submitted Under FIFRA Sec. 3(c)(2)(B)?
83-2 - Oncogenicity Study -					
Rat	-See chronic rat				
Mouse	TGAI	A, B	Yes	00061256 and 00079527	No
83-3 - Teratogenicity - Rat	TGAI	A, B	Partially*	00061257	Yes
Rabbit	TGAI	A, B	Yes	00087796	No
83-4 - Reproduction - 3 generation	TGAI	A, B	Partially*	00061262	Yes
MUTAGENICITY TESTING:					
84-2 - Gene Mutation	PAI	A, B	Partially*	00086770 00109254	Yes
84-2 - Chromosomal Aberration	PAI	A, B	Yes	00086766 00086765 00086767 00086768	Yes
84-2 - Other Mechanisms of Mutagenicity	PAI	A, B	No		Yes

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TABLE A

GENERIC DATA REQUIREMENTS FOR Metribuzin (BAY 94 337, SENCOR, LEXONE)

Data Requirement	Composition[1/]	Use Patterns[2/]	Does EPA Have Data To Satisfy This Requirements? (Yes, No or Partially)	Bibliographic Citation MRID#	Must Additional Data Be Submitted Under FIFRA Sect 3(c)(2)(B)?[3/]
SPECIAL TESTING:					
85-1 General Metabolism Rat	PAIRA	A,B	Partially*	00045265	Yes
85-1 General Metabolism Dog	PAIRA	A,B	Partially*	00045264	Yes
85-2 - Domestic Animal Safety	—	—	N/A		No

Composition: Material to be tested is technical grade unless otherwise specified in footnotes. PAI= Pure Active Ingredient. PAIRA= Pure Active Ingredient, Radio-Labeled.

The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-Food; C = Aquatic, Food Crop; D = Aquatic, Non-Food; E = Greenhouse, Food Crop; F = Greenhouse, Non-Food; G = Forestry; H = Domestic Outdoor; I = Indoor; IP = Industrial Preservative.

* This study was Core Classified as Supplementary Data.

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Metribuzin Tolerance Reassessment

A previous acceptable daily intake (ADI) for Metribuzin was based on a NOEL of 300 ppm in a 2 year chronic rat feeding study (Loser and Mohr, 1974). On 1/25/79, using a subsequent 2 year chronic dog feeding study (Loser and Mirea, 1974) which presented with a lower NOEL of 100 ppm, the ADI was recalculated. The ADI (with a safety factor of 100) was determined to be 0.025 mg/kg/day with a maximum permissable intake (MPI) of 1.5 mg/day for a 60 kg adult human. The current theoretical maximum residue concentration (TMRC) for Metribuzin based on established tolerances is 0.3508 mg/day for a 1.5 kg diet and the percent of the ADI currently utilized is 23.39 (see attached computer printout).

The previously mentioned 2 year chronic rat feeding study was re-reviewed under CORE and classified as Core-Supplementary Data since no systemic NOEL could be determined due to a lack of sufficient data. An increased incidence of liver histopathology ("changes in the nucleus") was observed in the high dose group. There also appeared to be an increase in the incidence of adenoma of the liver bile duct and pituitary gland in the 300 ppm females. However, not enough animals were examined in the other 3 dosage groups to allow an adequate determination of potential cancer risk or to establish a NOEL for nonneoplastic liver lesions.

The 2 year chronic dog feeding study was re-reviewed in this standard and the NOEL was found to be 100 ppm. The Agency recommends that the ADI continue to be based on this chronic dog study. Upon the submission of an additional chronic rat study (or the upgrading of the existing one), the ADI can then be re-evaluated.

CFR 180.332 Metribuzin/Sencor 8/[redacted]/84

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File last updated 6/25/82

ACCEPTABLE DAILY INTAKE DATA

Dog NOEL mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day(60kg)
2.500	100.00	100	0.0250	1.5000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Potatoes(127)	0.600	5.43	0.04884
Soybeans (oil)(148)	0.100	0.92	0.00138
Sugar,cane&beet(154)	0.100	3.64	0.00546
&Dairy Products(93)	0.050	28.62	0.02146
Eggs(54)	0.010	2.77	0.00042
Asparagus(5)	0.050	0.14	0.00011
Corn,all types(38)	0.050	2.51	0.00188
Peas(117)	0.100	0.69	0.00104
Tomatoes(163)	0.100	2.87	0.00431
Lentils(83)	0.050	0.04	0.00003
leat,inc poultry(89)	0.700	13.85	0.14540
Barley(8)	0.750	0.03	0.00034
Wheat(170)	0.750	10.36	0.11658

MPI	TMRC	% ADI
1.5000 mg/day(60kg)	0.3472 mg/day(1.5kg)	23.15

****

Current Action 4E3112

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Soybeans (oil)(148)	0.100	0.92	0.00138
Carrots(24)	0.300	0.48	0.00216

MPI	TMRC	% ADI
1.5000 mg/day(60kg)	0.3508 mg/day(1.5kg)	23.39

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Bibliography

DuBois, K.; Kinoshita, F. (1969) The Acute Mammalian Toxicity of Bay 94337: (Submitted 25118. (Unpublished study received Jul 3, 1971 under 0G0940; prepared by Univ. of Chicago, Toxicity Laboratory, submitted by Mobay Chemical Corp., Kansas City, MO; CDL:091606-E) MRID # 00106155.

Flint, D.R.; Gronberg, R.R.; Sandie, F.E. (1973) The Metabolism and Excretion of Sencor in Rats: Report No. 33366. Rev. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-K) MRID # 00045265.

Hayes, R.H.; Lamb, D.W.; Mallicoat, D.R.; et al. (1981) Metribuzin (=(R)= Sencor) Oncogenicity Study in Mice: 80050. (Unpublished study received Nov 23, 1981 under 3125-270; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246397-A) MRID # 00087795.

Inukai, H.; Iyatomi, A. (1977) Bay 94337: Mutagenicity Test on Bacterial Systems: Report No. 67; 54127. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Nitokuno Agricultural Chemicals Institute, Japan, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-F) MRID # 00086770.

Khasawinah, A.M.; Flint, D.R.; Shaw, H.R.; et al. (1972) The Metabolic Fate of Carbonyl 14C-Sencor in Dogs: Report No. 33361. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-J) MRID # 00045264.

Kimmerle, G.; Solecke, B.; Lorke (1969) Bay 94 337 Toxicological Studies from Dr. George Kimmerle, M.D. and Dr. Brigitte Solecke, M.D.: Report No. 1574; 25942. (Unpublished study received Jul 3, 1971 under 0G0940; prepared by Farbenfabriken Bayer, AG, W. Ger., submitted by Mobay Chemical Corp., Kansas City, MO; CDL: 091606-I) MRID # 00106158.

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Bibliography -2

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Lindberg, D.; Richter, W. (1970) Report to Chemagro Corporation: 90-day Subacute Oral Toxicity of Bay 94537 in Beagle Dogs: IBT No. C7760; 26488. (Unpublished study received Jul 3, 1971 under 0G0940; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, MO; CDL: 091606-M) MRID # 00106162.

Loser, E.; Lorke, D.; Mawdesley-Thomas, L. (1969) Bay 94337 Subchronical Toxicological Studies on Rats (3 Months Feeding test): Report No. 1719; 26469. (Unpublished study received Jul 3, 1971 under 0G0940; prepared by Farbenfabriken Bayer, AG, W. Ger., and Huntingdon Research Centre, Eng., submitted by Mobay Chemical Corp., Kansas City, MO; CDL:091606-L) MRID #00106161.

Loser, E.; Lorke, D.; Spicer, E.J.F. (1970) Bay 94 337 Sub-Chronic Toxicological Studies on Rats (3 month Feeding experiment): Report No. 2150; 27908 (prepared by Farbenfabriken Bayer AG, W. Germ. and Huntingdon Research Centre, Eng. submitted by Mobay Chemical Corp, Kansas City, Mo.) [redacted] Accession No. 112032.

Loser, E.; Mirea, D. (1974) Bay 94 337: Chronic Toxicity Studies on Dogs (Two-Year Feeding Experiment): Report No. 4887; Report No. 41814. (Unpublished study received on unknown date under 5F1559; prepared by Bayer, AG, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094258-J) MRID # 00061260

Loser, E.; Mohr, U. (1974) Bay 94337: Chronic Toxicity Studies on Rats (Two-Year Feeding Experiment): Report No. 4888; Report No. 41816. (Unpublished study received on unknown date under 5F1559; prepared by Bayer, AG and Medizinische Hoschule Hannover, submitted by Mobay Chemical Corp., Kansas City, Mo.; MRID # CDL:094259-A)

00061261

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Bibliography-3

Loser, E.; Siegmund, F. (1974) Bay 94337: Multigeneration Study on Rats: Report No. 4889; Report No. 41818. (Unpublished study received on unknown date under 5F1559; prepared by Bayer, AG, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094259-B) MRID # 00061262

Ladd, R. (1971) Report to Chemagro Corporation: Teratogenic Study with Bay 94337 Technical in Albino Rabbits: IBT No. J9027; Report No. 30172. (Unpublished study received on unknown date under 5F1559; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094258-B) MRID # 00061254

Ladd, R.; Smith, P.S. (1972a) Report to Chemagro, a Division of Baychem Corporation: Teratogenic Study with Sencor (Bay 94337) in Albino Rabbits: IBT No. J [redacted] 233

(was combined with IBT No. J 1851)

Ladd, R.; Smith, P.S. (1972b) Report to Chemagro, a Division of Baychem Corporation: Teratogenic Study with Sencor (Bay 94337) in Albino Rabbits: IBT No. J1851; Report No. 35159. (Unpublished study received on unknown date under 5F1559; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094258-G) MRID # 00061258

Machemer, L. (1972) Sencor (Bay 94 337): Studies for Possible Embryotoxic and Teratogenic Effects on Rats after Oral Administration: Report No. 3678; Report No. 35073. (Unpublished study received on unknown date under 5F1559; prepared by Bayer, AG, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094258-F) MRID # 00061257

Machemer, L.; Lorke, D. (1974a) Evaluation of ®(R)Sencor for Mutagenic Effects on the Mouse: Report No. 4942; 43068. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 246226-B) MRID # 00096766

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Bibliography - 4

Machemer, L.; Lorke, D. (1974) Evaluation of the Mutagenic Potential of ¬(R)¤Sencor in an in vivo Cytogenetic Study on Spermatogonia of Chinese Hamster: Report No. 4961; 43067. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-A) MRID # 00086766

Machemer
~~Demer~~, L.; Lorke, D. (1975) ¬(R)¤Sencor: Dominant Lethal Study on Male Mice To Test for Mutagenic Effects: Report No. 5523; 45023. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-C) MRID # 00086767

Machemer, L.; Lorke, D. (1976) ¬(R)¤Sencor: Additional Dominant Lethal Study on Male Mice To Test for Mutagenic Effects by an Improved Method: Report No. 6110; 49068. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-D) MRID # 00086768

Shirasu, Y.; Moriya, M.; Ohta, T. (1978) Metribuzin Mutagenicity Test on Bacterial Systems: ©Submitted 66748. (Unpublished study received Jul 14, 1982 under 3125-270; prepared by Institute of Environmental Toxicology, Dept. of Toxicology, submitted by Mobay Chemical Corp., Kansas City, MO; CDL: 247885-B) MRID # 00109254

Smith, P.S.; Gordon, D.E. (1972) Report to Chemagro, a Division of Baychem Corporation: 18-Month Carcinogenic Study with Sencor (Bay 94337) in Swiss White Mice: IBT No. B9069; Report No. 34481. (Unpublished study including report no. 34481a, received on unknown date under 5F1559; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094258-D) MRID # 00061256

↑ SAME ↓ (different MRID #'s / Submission #'s)

Smith, P.S.; Gordon, D.E. (1972) Report to Chemagro, a Division of Baychem Corporation: 18-month Carcinogenic Study with Sencor (Bay 94337) in Swiss White Mice: IBT No. B9069; Report No. 34481. (Unpublished study received Mar 13, 1973 under 3125-EX-120; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:120999-A)

MRID # 00079597

Bibliography -5

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Unger, T.M.; Shellenberger, T.E. (1981) A Teratological Evaluation of Sencor-(R)- in Mated Female Rabbits: 80651. Final rept. (Unpublished study received Nov 23, 1981 under 3125-270; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246397-B)

MRID # 00087796

The following have no bibliographic reference

Chemagro # 33045 [redacted] Acute Oral LD_{50} - Guinea Pig
3/20/72

Accession No. 112032

Chemagro # 32862 Primary eye irritation - Rabbit
3/21/72

Accession No. 112032

also Primary dermal irritation - Rabbit
under same numbers

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Data Review:

Study Identification:

Study Title: SENCOR (BAY 94 337) Studies for Possible Embryotoxic and Teratogenic Effects on Rats after Oral Administration (Bay Report No.: 3678)

EPA Identification Numbers: EPA Accession No. 112892

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: BAYER AG
Institut Fur Toxikologie
Wuppertal-Elberfeld

Study Number: 3678

Report Number: 35073

Date of Study: September 29, 1972

Study Directors: Dr. L. Machemer

Test Compound: SENCOR, BAY 94 337 (4-amino-6 tert.-butyl-3 (methylthio)-1,2,4-triazin-5-one) (also called Metribuzin)
Purity: 99.5%
Consignment 1603/71, Batch 17, Received 6/71

Vehicle: Cremophor EL, 1.5% aqueous emulsion

Dosage Used: 5, 15, 50 and 100 mg/kg/day

Test Animal: Rats, FB 30 Strain
Males: 3 to 6 months old, 350 to 500 gm.
Females: 2 1/2 to 3 1/2 months old, 200 to 250 gm.
No source of animals given.

Materials and Methods: A copy of the methods and materials section from the investigators report is appended.

The investigators stated that there were 21 to 22 "fertilized rats" in each study group. There was no mention of how many rats were used for mating at study initiation. Although elsewhere in the report they state in a table that 22 to 24 inseminated females were used, with 21 to 22 females considered fertilized and 20 to 22 females presenting as pregnant. There was no mention of the number of male rats used in this study.

Animals were housed singly except during the mating period. For the mating period 1 male rat was housed with 2 female rats.

Altromin R pelleted food and tap water were made available ab lib. There was no mention of analysis of food or water for contaminants, also no mention of collection of food consumption data.

Confirmation of copulation was by vaginal smear with positive confirmation of sperm considered as day 0.

Although there was no mention in this report if the technical grade of SENCOR was used, the consignment number and batch was the same as in other studies where it was stated that the compound was of technical grade.

Animals were treated on day 6 through 15 with doses of either the vehicle or prepared Sencor at a volume of 5 ml per kg body weight daily.

Ether was used to narcotize animals for cesarean section.

Only average weight of fetuses were given (both per litter and per study group), no individual fetal weight determinations were provided.

One-third of the fetuses were examined for soft-tissue anomalies and the other 2/3 were examined for skeletal anomalies.

Fetuses for soft-tissue evaluation were inspected by a modified Wilson technique for visceral malformation. There was no mention of the "method of modification".

The fetuses for skeletal examination were first eviscerated, the organs examined and then processed for staining of the skeletal system.

References given after statement "the method was published in:", make no reference to what method or procedure the references relate to.

Results:

Clinical Observations:

There was no maternal mortality in any of the study groups.

The investigators stated that no effect was seen in the dams at dosage of 15 mg/kg/day and below. One dam in the 50 mg/kg/day dosage group and 2 dams in the 100 mg/kg/day dosage group presented with ruffled coats, dyspnea and reduced activity, however this is limited evidence of any maternal toxicity. The other animals from each of those two group appeared unaffected. No individual clinical observation data was presented.

Necropsy observations for the dams were apparently not recorded.

Maternal Weight:

Maternal weight data was only provided in terms of weight gain during the treatment period and for the entire gestation period. Weight gain data during the treatment period was presented as individual numbers with no animal identification whereas the weight gain data for the entire gestation period provided animal identification numbers and therefore the data for individual animals could not be reliably compared. See Table 1 below:

Table 1. Maternal Weight Changes (gms ± S.D.) Sencor (mg/kg/day)

	Control*	5	15*	50	100
Number of Animals	20	22	21	22	21
Days 6 to 15	44.3±11.6	42.4±13.2	41.5±9.3	42.9±8.5	38.0±11.9
Days 0 to 20	118.1±19.2	121.1±21.1	117.5±22.7	119.7±18.6	109.8±17.1

*One dam from each group not included in calculation due to complete loss of embryos.

Data extracted from BAYER AG Report No. 3678 Results and Tables 1 through 5.

The dams of the high dose group on the average gained slightly less weight during the treatment period (days 6 to 15) and over the entire gestation period (days 0 to 20).

No other weight data was provided. There was no initial (start of study), weekly or terminal weights provided.

Cesarean Section Observations: (Table 2)

There was no difference in pregnancy rate between any of the 5 study groups (95.2 to 100%).

No significant differences were observed in the number of implantations per dam, fetuses per dam and mean fetal body weight. There appears to be an increase in the number of resorptions per dam at the high dose level, also when calculated as group mean post implantation loss, a similar increase is seen. There was also a dose-related decrease in mean placental weight (statistically significant from control at the high dose level).

No corpora lutea data was provided. This data would have allowed for determination of preimplantation loss.

There was no separation of resorption data into early and late observations.

Although not stated, one must assume from the data that all fetuses in the study were viable.

The sex of the fetuses was apparently not determined.

Table 2: Cesarean Section Data - Sencor (mg/kg/day)

	Control	5	15	50	100
Number of Animals	21	22	22	22	21
Pregnancy Rate	95.2%	100%	95.5%	100%	100%
Total Implantations	247	239	251	247	251
Implantations/Dam	11.8±2.3	10.9±3.2	11.4±2.7	11.2±1.9	12.0±1.9
Total Fetuses	217	214	231	221	215
Fetuses/Dam	10.3±2.9	9.7±3.4	10.5±3.3	10.1±2.4	10.2±1.7
Total Resorptions	30	25	20	26	36
Resorptions/Dam	1.4±2.4	1.1±1.4	0.9±1.2	1.2±1.9	1.7±1.8
Group Mean Post Implantation Loss	12.2%	10.5%	8.0%	10.5%	14.3%
Mean Fetal Weight (gms)	3.90±0.20†	4.15±0.30	3.98±0.25†	4.00±0.32	3.98±0.34
Mean Placental Weight (gms)	0.547±0.054	0.559±0.079	0.557±0.116	0.525±0.083	0.502±0.052*

Data presented as mean ± S.D. or as indicated

† - One dam left out of calculation due to complete loss of fetuses.

* - Statistically significantly different from control.

Data extracted from BAYER AG Report No. 3678 Tables 1 through 6.

Fetal Morphological Observations:

There were no observable differences between numbers of stunted fetuses in any of the study groups. See Table 3. However, fetal crown-rump data (this data was suggested as useful by CORE) would have been helpful in evaluation of these fetuses.

Only 2 incidences of malformations were observed, 1 fetus in the control group with micrognathia (mandible) and 1 fetus in the low dose group with hypoplasia of the mandible. No other malformations were observed. See Table 3 A.

There were no observable differences in incidence of "slight bone alterations" (this term must be defined by the registrant, other than the reference stated) between any of the study groups. See Table 3 B. However, no data was provided on individual fetal or litter expression of the separate bone alteration observations, the only data provided was for total number of fetuses showing bone alterations (of any kind) by litter and average by study group.

Table 3: Fetal Morphological Observations - Sencor (mg/kg/day)

	Control	5	15	50	100
Litters:	20	22	21	22	21
Fetuses:	217	214	231	221	215
division for examination:					
Soft Tissue (Wilson)	67	63	70	65	64
Skeletal	150	151	161	156	151
Stunted Fetuses (<3 g)	3(3)†	2(1)	3(2)	4(3)	0(0)
A. Malformations:					
Micrognathia	1(1)	0(0)	0(0)	0(0)	0(0)
Hypoplasia of the mandible	0(0)	1(1)	0(0)	0(0)	0(0)

continued

Table 3: continued

B. "Slight Bone Alterations":

Total incidence:	75(18)†	64(18)	68(18)	75(20)	76(19)
as % of fetusestt:	50.0%	42.4%	42.2%	48.1%	50.3%
# of fetuses showing the following "slight bone alterations"					
Sternum	6	1	5	6	5
Hyoid	14	3	14	11	11
Vertebrae	47	37	39	47	50
Ribs	21	32	30	24	14
Skull	13	4	7	1	11
Extremities	0	0	1	0	0

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† - Data presented as fetuses (litters).
†† - examined for skeletal abnormalities

Data extracted from BAYER AG Report No. 3678 Tables 1 through 5 and 7.

No historical control data of any kind was provided with this study.

Conclusions:

The dosage of Sencor used (5, 15, 50 and 100 mg/kg/day), based on the data presented, produced slight evidence of maternal toxicity at the 100 mg/kg/day dose level, in the form of reduced maternal weight gain. There was slight corroborative clinical observation data.

There was no evidence of fetal toxicity or teratogenicity at the dose levels used in this study.

This study lacked the following data:

1. Whether the test compound was of the technical grade.
2. Justification of the dose levels used in the study since there was only slight evidence of maternal toxicity.
3. Individual and study group maternal weight data, at initiation of study, weekly and at sacrifice.
4. Maternal necropsy observations.
5. Individual fetal and litter observation data for all parameters
6. The definition of the term "slight bone alterations".
7. Corpora lutea determinations.
8. Separation of resorptions into early and late.
9. Viability of fetuses.
10. Sex of the fetuses.
11. Individual fetal weight data.

Core Classification: Core-Supplementary Data based on inadequacy of data as stated above. This study may be updated if the deficiencies can be corrected.

METRIBUZIN

Page_____ is not included in this copy.

Pages 36 through 39 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

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004262

Data Review:

Study Identification:

Study Title: BAY 94 337, Multigeneration Study on Rats.

EPA Identification Numbers: EPA Accession No.: 112891

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: BAYER AG
Institut fur Toxikologie

Report Numbers: 4889
41818

Date of Study: September 24, 1974

Study Directors: Dr. rer. nat. Eckhard Loser
Dr. med. vet. Fred Siegmund

Test Compound: BAY 94 337, Technical Grade Compound (also called Metribuzin; SENCOR)
Purity: 99.5%
Sdg 1603/71

Dosage: 35, 100 and 300 ppm mixed in pulverized Altromin R laboratory feed.

Test Animal: Rats, FB 30 strain
Elberfeld breed
33 days old at beginning of study
Average body weight 45 to 55 gms.

Materials and Methods: A copy of the materials and methods section from the investigators report is appended.

Comment: The confidential stamp used by MOBAY should not be placed over critical material in the text and tables, it obscures data and important words. This reviewer requested an umarked copy from the registrant, however the copy obtained had numerous illegible entries in the individual animal data addendum.

There was no rationale given for the selection of the dosage levels used in the study (the results revealed that the high dose level did not produce any sort of maternal toxicity).

The test material was mixed with pulverized Altromin R feed, first as a stock and then extended to proper dietary concentrations. The food mixtures were prepared twice a week.

A more frequent weighing of pups (than just at birth, 5 days after birth, one week after birth and then weekly) would be advantageous for growth rate determination, especially in the earlier days. Also the growth rates should be reported by sex (as required by CORE).

Culling of the pups 5 days after birth to standardize litter size can lead to bias by removing the smallest pups. There was no indication in the Materials and Methods section that the pups were randomly culled.

In the selection of pups for the F_{1b} and F_{2b} generation mating, there was no indication if the selection was such that pups of the same litter (siblings) were not mated.

There was no indication as to whether the animals were checked once daily for mortality, adverse effects on lactation, nursing instinct, and adverse effects on the newborn.

Apparently a full examination of the litters was not performed. According to CORE, the necessary determinations are number of offspring per litter, number of live and dead offspring by litter, fecundity, length of the gestation period and general condition of the offspring (especially gross anomalies) and mother through weaning. There was no indication of the parameters considered for gross examination of the pups.

Representative numbers of weanlings in each treatment group should have been necropsied and the second litter of the third generation should have been subjected to a complete necropsy rather than just one male and one female from each of 5 dams per study group (Materials and Methods section of the final report stated 4 dams, results indicated 5 dams).

Results:

I. Parental Data

A. Physical Signs

The investigators stated that for the F_0 generation, "during the study periods, the rats of the 35 to 300 ppm groups did not differ in appearance and behavior from its controls". However, no clinical observation data was presented to support this statement.

There was no mention of appearance or behavioral changes in the F_{1b} or F_{2b} rats.

B. Mortality

F_0 generation: One female in the 100 ppm dose group died after the 2nd mating. This animal was pregnant and no cause of death was determined. One female in the 300 ppm dose group was found to have severe inflammation of the middle ear and was sacrificed.

F_{1b} generation: One female control animal died during the 1st mating. This animal was not pregnant and no cause of death was determined. One female in the 300 ppm dose group died after the 1st mating. This animal was not pregnant and no cause of death was determined.

F_{2b} generation: One male in the control group died after 2nd mating due to massive pneumonia. One male in the 35 ppm dose group died before the 1st mating also of massive pneumonia. One female in the 35 ppm dose group died before the first mating. The cause of death could not determined because of "decay". Two females in the 300 ppm dose group died before the first mating. One animal died of pneumonia and the cause of death in the other animal could not be determined.

C. Weight Changes

F_0 generation: From the plotted averages (graphs) provided there appears to be no dose-dependent differences in weight between treated and control animals up to the first mating in the females. After the 1st and after the 2nd mating there were slight fluctuations in the females but apparently the differences were not significant. In the males there were slight, non-significant fluctuation throughout the treatment period.

The individual data provided by the registrant is illegible and therefore could not be compared to the graphs provided, however in the future a table of mean weekly animal body weights would be helpful for evaluation.

F_{1b} generation: Again from the graphs, apparently there were no differences in the weights of the females throughout the treatment period. For the males, there were no differences up to the second mating. After the second mating the treated groups were slightly lower in weight than the controls.

F_{2b} generation: From the graphs, there were no differences in the weights of the females throughout the treatment period. For the males, between day 10 and 15, the treated animals gained less weight than the controls (the graphs indicated 20 to 30 grams less).

D. Length of Gestation

Not reported.

E. Fertility (Table 1)

First mating of the F_0 generation: There were essentially no differences in gestation rate between any of the 4 study groups.

Second mating of the F_0 generation: There was a slight reduction in gestation rate in all study groups as compared to first mating with a slightly greater reduction in the high dose group.

First mating of the F_{1b} generation: There were no significant differences in fertility noted between the study groups.

Second mating of the F_{1b} generation: The gestation rate was slightly lower than the first mating but no significant differences between study groups was noted.

First mating of the F_{2b} generation: There were lower gestation rates especially in the control group as compared to previous matings (see Table 1).

Second mating of the F_{2b} generation: Much lower gestation rates were seen in all study groups as compared to the 1st mating. The gestation rate in the control group was very low (20%), no explanation was provided by the registrant, except for the statement that the difference was "by chance", (see Table 1).

These lower fertility rates of the control groups of the F_{2a} and F_{2b} do not provide a valid control for comparison of the other groups.

Table 1: Fertility (Gestation Rate) BAY 94 337 Technical (ppm)
Number pregnant/number mated

	Control	35	100	300
1st Mating F_0	20/20 100%	20/20 100%	19/20 95%	20/20 100%
2nd Mating F_0	18/20 90%	18/20 90%	18/19 94.7%	15/19 78.9%
1st Mating F_{1b}	17/19 89.5%	20/20 100%	20/20 100%	19/20 95%
2nd Mating F_{1b}	16/19 84.2%	20/20 100%	18/20 90%	18/19 94.7%
1st Mating F_{2b}	8/20 40%	15/19 78.9%	18/20 90%	16/18 88.9%
2nd Mating F_{2b}	4/20 20%	11/19 57.9%	16/20 80%	11/18 61.1%

Data extracted from Report No. 4889 Tables 1, 5, 9a, 9b, 13a and 13b.

II. Litter Data

A. Litter size (Table 2)

F_{1a} litter: No significant differences between study groups.

F_{1b} litter: No significant differences between study groups.

F_{2a} litter: Slight larger litter size compared to previous and subsequent matings, but no treatment related effects could be discerned.

F_{2b} litter: No significant differences between study groups.

F_{3a} litter: No significant differences between study groups.

F_{3b} litter: Slightly smaller litter size overall, but no significant differences between study groups.

Table 2: Number of Fetuses per litter at birth - BAY 94 337 Technical (ppm)

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	Control	35	100	300
F_{1a}	11.4	10.8	11.9	11.9
F_{1b}	9.2	9.6	11.7	10.1
F_{2a}	11.5	12.0	12.5	12.1
F_{2b}	11.9	11.9	11.1	10.6
F_{3a}	11.4	9.6	10.5	9.9
F_{3b}	9.8	8.4	9.7	8.5

Data extracted from Report No. 4889 Tables 2, 6, 10a, 10b, 14a and 14b.

B. Survival of pups (Table 3)

There were no significant differences in percent survival of pups to day 5 between any of the study groups. The F_{3b} generation had a slightly lower overall survival as compared to the other generations.

Table 3: Percent Survival of Pups to Day 5 - BAY 94 337 Technical (ppm)

	Number of pups alive on day 5/number of pups at birth			
	Control	35	100	300
F_{1a}	9.1/11.4 (79.8)*	9.4/10.8 (87.0)	9.2/11.9 (77.3)	9.8/11.9 (82.4)
F_{1b}	7.4/9.2 (80.4)	7.9/9.6) (82.3)	10.8/11.7 (92.3)	9.7/10.1 (96.0)
F_{2a}	10.8/11.5 (93.9)	10.8/12.0 (90.0)	12.0/12.5 (96.0)	9.2/12.1 (76.0)
F_{2b}	10.3/11.9 (86.6)	9.4/11.9 (79.0)	10.7/11.1 (96.4)	8.2/10.6 (77.4)
F_{3a}	8.9/11.4 (78.1)	8.0/9.6 (83.3)	8.2/10.5 (78.1)	9.1/9.9 (91.9)
F_{3b}	7.8/9.8 (79.6)	6.4/8.4 (76.2)	6.9/9.7 (71.1)	7.3/8.5 (85.9)

*Numbers in parentheses are percentages.

Data extracted from Report No. 4889 Tables 2, 6, 10a, 10b, 14a and 14b.

After culling of the animals there were still no significant differences in litter size between any of the study groups in the various generations.

C. Survival to Weaning (Lactation Rate) (Table 4)

F_{1a} generation: There was a slight (not statistically significant) dose related decrease in lactation rate.

F_{1b} generation: There were no differences in survival between any of the 4 study groups.

F_{2a} generation: The lactation rates were comparable.

F_{2b} generation: The survival to weaning was comparable between all study groups. The low dose survival was slightly less than the other 3 groups.

F_{3a} generation: The total number of pups in all study groups was reduced overall, especially in the control group, but there were no differences observed in lactation rates.

F_{3b} generation: There was a further reduction in total numbers of pups, especially in the control group. The lactation rates were less than the previous F_{3a} generation and a slight, but not significant, dose related decrease was observed.

Table 4: Survival to Weaning (Lactation Rate) - BAY 94 337 Technical (ppm)

pups after reduction of litter size/# pups alive after 4 weeks

	Control	35	100	300
F_{1a}	165/146 (88.5)*	170/149 (87.6)	160/138 (86.3)	171/142 (83.0)
F_{1b}	121/112 (92.6)	135/122 (90.4)	164/155 (94.5)	127/114 (89.8)
F_{2a}	164/155 (94.5)	183/170 (92.9)	192/187 (97.4)	148/131 (88.4)
F_{2b}	144/129 (89.6)	166/139 (83.7)	159/155 (97.5)	131/115 (87.8)
F_{3a}	64/61 (95.3)	117/107 (91.5)	133/119 (89.5)	133/130 (97.7)
F_{3b} (3 weeks)	31/31 (100)	68/59 (86.8)	101/88 (87.1)	77/63 (81.8)

*Numbers in parentheses are percentages.

Data extracted from Report No. 4889 Tables 3, 7, 11a, 11b, 15a and 15b.

D. Pup Body Weights (Table 5)

F_{1a} generation: There were slight differences in mean birth body weights between control and high dose groups but the differences were not statistically significant. From graphs of pup body weights over the 4 week period, there appeared to be no significant differences between any of the 4 study groups. The data on the graphs combined both males and females.

F_{1b} generation: There were no real differences between birth weights of any of the 4 study groups over the 4 week period (from graph).

F_{2a} generation: There were slightly reduced mean body weights at birth compared to control in all 3 treatment groups. However, over the 4 week weaning period no differences between study groups was apparent (from graph).

F_{2b} generation: The body weights at birth of the low dose group was slightly lower (not statistically significant) than control. Over the 4 week period, a slight, but not statistically significant, difference continued to be observed (from graph).

F_{3a} generation: The mean body weights at birth of the 3 treatment groups were slightly lower (dose related) than control The 4 week weaning period showed slight variations, but not significant (from graph).

F_{3b} generation: The 3 treatment groups had lower mean body weights at birth than that of control, especially the mid dose group. The differences were not significant, possibly due to reduced numbers of animals in the control group. Over the 3 week period there were slight, not significant, variations (from graph).

Table 5: Mean Body Weights (gm) of Young at Birth
BAY 94 337 Technical (ppm)

	Control	35	100	300
F_{1a}	6.38	6.32	6.38	6.28
F_{1b}	6.34	6.21	6.42	6.88
F_{2a}	6.54	6.08	6.22	6.01
F_{2b}	6.69	5.90	7.03	6.36
F_{2a}	6.75	6.55	6.24	6.18
F_{3b}	7.08	6.46	5.99	6.40

Data extracted from Report No. 4889 Tables 4, 8, 12a, 12b, 16a and 16b.

E. Malformations

The investigators stated that there was no evidence of gross malformations in the F_{1a}, F_{1b}, F_{2a}, F_{2b}, F_{3a} or F_{3b} generations. However, no data was presented to substantiate this statement.

III. Necropsy Data

A. Parents

No necropsy data was reported.

B. Pups

1. Autopsies of the F_{3b} generation.

Three weeks after birth, one male and 1 female of each of 5 dams in every dose group were narcotized with ether, sacrificed by exsanguination and then examined grossly. According to the investigators no gross alterations attributable to BAY 94 337 was seen, however, no data was presented to substantiate this claim.

2. Histopathological Examinations.

Histopathological examinations were carried out on the thyroid, heart, thymus, lung, liver, spleen, kidneys, adrenals and gonads. The following are summary of the findings:

a. Lungs:

Minimal to medium grade focal interstitial pneumonia with peribronchial, peribronchiolar and perivascular lymphocytic infiltrates (includes infiltrate only findings) in the following incidences:

Control:	6/10
35 ppm :	8/10
100 ppm:	9/10
300 ppm:	10/10

Low grade hemorrhage in the alveolar space in the following incidence:

Control:	0/10
35 ppm :	1/10
100 ppm:	0/10
300 ppm:	1/10

Congestion in the following incidence:

Control:	0/10
35 ppm :	0/10
100 ppm:	3/10
300 ppm:	0/10

b. Liver:

Low grade interstitial lymphocytic and/or lympho-histiocytic infiltrates, particularly within the region of the Glisson trigonals in the following incidence:

Control:	5/10
35 ppm :	10/10
100 ppm:	5/10
300 ppm:	10/10

c. Heart:

Minimal to low-grade mesenchymal activation in the form of minute lympho-histiocytic infiltrates in the following incidence:

Control:	3/10
35 ppm :	1/10
100 ppm:	2/10
300 ppm:	0/10

d. Kidney:

Focal interstitial lympho-histiocytic infiltrates in the cortical area and a focal dilation of the tubui contori in the following incidence:

Control:	1/10
35 ppm :	1/10
100 ppm:	0/10
300 ppm:	0/10

Dilation of the Bowman's capsule spaces in the following incidence:

Control:	0/10
35 ppm :	1/10
100 ppm:	1/10
300 ppm:	0/10

e. Adrenal:

Minute focal leucocyte infiltrates in the following incidence:

Control:	2/10
35 ppm :	0/10
100 ppm:	1/10
300 ppm:	2/10

f. Thymus:

Hemorrage within the cortical substance (1 lobule) in the following incidence:

Control:	0/10
35 ppm :	1/10
100 ppm:	0/10
300 ppm:	0/10

g. Thyroid:

Epithelial desquamination within one follicle in the following incidence:

Control:	0/10
35 ppm :	0/10
100 ppm:	0/10
300 ppm:	1/10

There were no observed changes in the spleen or gonads. The above findings do not indicate any dose related effect of BAY 94 337. The incidences of inflammatory changes in the lung were attributed by the investigators to "rat-specific pneumonia" (historical data may have been helpful), there were no dose-dependent changes between any 4 of the study groups.

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Conclusions:

The dosages of BAY 94 337 tested (35, 100 and 300 ppm) induced no compound related reproductive or fertility related effects in the 3 generations of rats tested. The No Observed Effect Level (NOEL) for reproductive effects appeared to be 300 ppm (HDT).

Deficiencies of this study include:

1. The rationale for selection of dosage levels was not provided since the high dose level used did not induce any toxicity in parental animals as required by CORE.

2. Representative numbers of weanlings from each treatment group were not necropsied.

3. The entire F_{3b} litter was not subjected to a complete histological examination.

4. There was no indication if selection of pups for the F_{1b} and F_{2b} generation mating provided that pups from same litter (siblings) were not mated.

5. The litters were not examined fully as recommended by CORE for general condition especially for gross anomalies.

6. There was a lack of maternal clinical observation data.

7. The individual weight data provided by the registrant was illegible.

8. There was not a valid control group for either the F_{2a} and F_{2b} (in terms of the fertility index), there may have been a problem with the animal husbandry.

Core Classification: Core-Supplementary Data based on the above mentioned deficiencies.

METRIBUZIN

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Pages 52 through 57 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

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Data Review:

Study Identification:

Study Title: BAY 94 337 Chronic Toxicity Studies on Rats (2-year feeding experiment)

EPA Identification Numbers: EPA Accession No. 112891

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: BAYER AG
Institut fur Toxikologie
Wuppertal-Elberfeld

Report Numbers: 4888 & 41816

Date of Study: September 25, 1974

Study Director: Dr. rer. nat. Eckhard Loser

Histopathological Examination: Prof. Dr. med. U. Mohr

Test Compound: BAY 94 337 (Metribuzin) Technical (also called SENCOR)
Purity: 99.5%
Batch No.: 1603/71

Dosage: 25, 35, 100 and 300 ppm mixed with pulverized Altromin R feed (from Altrogge, Lage/Lippe).

Test Animal: SPF Rats (Wistar Strain) bred by Winkelmann, Kirchborchen, Kreis Paderborn. At start of experiment rats were about 28 to 32 days old with males having a mean body weight of 51.4 gm. and females with a 52.1 gm mean body weight.

Materials and Methods: A copy of the materials and methods section from the investigators report is appended.

Hematology examinations were performed on 5 rats per sex at 3, 6 and 12 month intervals (although Core recommends 4 month intervals). At 24 months the test were conducted on 10 rats per sex.

The hematology examination protocol was adequate and included reticulocyte counts.

The blood chemistry determination did not include Ca, PO_4, fasting glucos urea nitrogen but did include blood sugar (not fasting) and cho.esterol determinations.

Urinalysis tests were conducted on urine collected for 16 hours at 3, 6, and 12 months on 5 rats per sex and at 24 months on 10 rats per sex.

Thyroid function tests utilized 20 rats per sex for temperature studies at 6, 12 and 24 months and 5 rats per sex at 6 and 12 months and 10 rats per sex at 24 months for protein bound iodine determinations.

The investigators examined all tissues that are required by CORE, however histopathology was performed on all animals only in control and the high dose group. In the other three dose groups only selected tissues in selected animals (10 per group) were examined (see page 7, this review).

Results:

I. Clinical Observations:

The investigators observed no differences in "physical appearance and behavior from the control rats" in any of the test groups. No data was provided for these observations.

II. Clinical Data:

A. Food Consumption:

Although not stated in the table provided, the data presented for "average food consumption" is for 24 months. The "average quantity of active ingredient ingested" is stated as being "related to the animal body weight after 12 months of feeding". There was no statistical difference between groups in the amount of total food consumed, however as would be expected the males consumed more total food than the females (mean food consumption by males was 19.03 $\pm$ 0.59 g/animal/day and mean food consumption by females was 15.12 $\pm$ 0.50 g/animal/day, based on all groups combined).

When "average quantity of active ingredient ingested" is calculated, it was found that the female received more active ingredient than the male. See Table I below:

Table I: Active Ingredient (mg/kg body weight/day)

Dose (ppm)	Male	Female
Control	0	0
25	1.30	1.68
35	1.87	2.28
100	5.27	6.53
300	14.36	20.38

Data Extracted from BAYER AG Report No. 4888 Table 1.

B. Body Weight:

The investigators found no significant difference between control and the 25 to 100 ppm test groups through the 24 month test period. The males of the 300 ppm test group (from body weight curves) showed significant differences at weeks 70 to 80 and 90 to 100 while the females showed significant differences (according to the investigators: $p < 0.05$) from weeks 20 to 100, but at the end of the test period there was only a slight difference from control (for the females).

The registrants provided graphed mean data (curves) and individual weekly weight data for the animals. Numerous entries on the individual animal weekly weight data that were provided was illegible (including the "new" copy provided by the registrant).

C. Mortality:

At 12 months there was no significant mortality noted by the investigators. Survival to study termination was excellent, see Table II below. There was no apparent difference in mortality between any of the treatment groups and control.

Table II: Mortality Rates (in percent)

DOSE (ppm)	After 1 year	At study termination
Males		
Control	2.5	17.5
25	0	22.5
35	2.5	20.0
100	0	25.0
300	0	27.5
Females		
Control	0	10.0
25	2.5	12.5
35	0	22.5
100	0	17.5
300	2.5	12.5

Data extracted from BAYER AG Report No. 4888 Table 2.

D. Hematology:

At 3 months there were no significant differences in hematological parameters.

At 6 months there appears to be a slight dose related decrease in reticulocyte count in both males and females and a slight decrease in leucocytes in the male rats.

However, at the 12 and 24 month intervals there were no apparent differences in reticulocyte or leucocyte counts or other hematological parameters.

E. Liver Function Tests:

There were no significant differences between test groups at 3, 6, 12 or 24 months for male and female plasma enzyme alkaline phosphotase or the transaminases (GOT and GPT) or total protein levels.

F. Urinalysis and Kidney Function Tests:

At 3 months there was a slight increase in protein in the urine in both male and female animals of the test groups as compared to control. This was not apparent at the 6 month interval in the males, but slight increases were still seen in the females (dose related). At the 12 month interval there were no apparent differences noted and at 24 months the controls had higher levels of protein in the urine than the test groups.

G. Blood Sugar and Cholestrol Determinations:

There were no significant differences between control and test groups at the 3, 6, 12 and 24 month intervals.

1. Body temperature: There were no meaningful differences seen between control and test groups at 6, 12 and 24 months.

2. Protein-bound iodine: There were no significant differences seen between control and test groups at 6, 12 and 24 months.

III. Necropsy Data:

The investigators stated that examination of all rats that died during the study and were autopsied showed "No pathological changes atttributable to administration of the test compound". However, for many of the animals which died during the course of the study, the comment in the table under the causes of death was stated as "not determinable due to decay of animal", see Table III below. Many of the animals showed evidence of "massive pneumonia" as the cause of death.

The investigators further state, that the animals grossly examined at final sacrifice "showed no signs of any specific damage".

Table III: Number of Animals Lost to "Decay"

DOSE (ppm)	Males	Females
Control	5/14 (36%)	4/8 (50%)
25	1/9 (11%)	2/5 (40%)
35	2/8 (25%)	4/9 (44%)
100	2/10 (20%)	0/7 (0%)
300	2/11 (18%)	1/5 (20%)

Demoninators refer to animals dying prior to end of experiment.

Data extracted from BAYER AG Report No. 4888 Tables 15a and 15b.

A. Organ Weights:

The absolute weights of female rat heart (significant at 100 and 300 ppm) and lung (significant at 300 ppm) showed a dose related decrease. The absolute kidney weight in males showed a dose-related decrease with the 300 ppm level being statistically significant. See Table IV below:

Table IV: Absolute Organ Weight (in mg)

Male Rats

Dose(ppm)	Thyroid	Heart	Lung	Liver	Spleen	Kidney
0	24.7	1012	1902	10191	842	2602
25	26.2	1058*	1809	11547**	921*	2510
35	26.9*	1009	1863	10880*	804	2497
100	28.6**	1029	1913	10521	915	2491
300	27.4	979	1867	9711	781	2362**

Female Rats

Dose(ppm)	Thyroid	Heart	Lung	Liver	Spleen	Kidney
0	21.9	772	1319	8610	669	1761
25	21.5	754	1332	8411	649	1676
35	24.5	766	1483	8156	725	1767
100	20.2	715**	1231	7605**	663	1656**
300	20.9	721**	1199**	7762	613*	1705

*$p < 0.05$
**$p < 0.01$

Data extracted from BAYER AG Report No. 4888 Table 16a.

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The average relative organ weights show a similar pattern except that liver weight is reduced over control in the 35, 100 and 300 ppm dosage levels. See Table V below:

Table V: Relative Organ Weights (in mg/100 gm body weight)

Male Rats

Dose(ppm)	Thyroid	Heart	Lung	Liver	Spleen	Kidney
0	6.2	255	408	2553	211	654
25	6.0	246	424**	2683*	215	584**
35	6.8*	250	466	2702	198	620
100	6.8*	247	458	2511	217	595**
300	6.8	243	466	2416	193	588**

Female Rats

Dose(ppm)	Thyroid	Heart	Lung	Liver	Spleen	Kidney
0	8.7	301	519	3336	260	685
25	8.2	290	514	3236	250	646
35	9.1	285	548	3031**	270	660
100	7.9	283*	483	2999**	264	656
300	8.3	283*	471*	3028**	238*	668

*p < 0.05
**p < 0.01

Data extracted from BAYER AG Report No. 4888 Table 16a.

B. Histopathology:

The investigators evaluated the following organs from 66 males and 72 females in the control group and 29 males and 35 females in the high dose group: brain; pituitary gland; eyes; cervical lymph nodes; aorta; trachea; sternum including bone marrow; mammary gland; esophagus; stomach; 4 intestinal segments; pancreas; epidydimus; prostate; seminal vesicle; urinary bladder; uterus; thyroid; heart; lung; liver; spleen; kidneys; adrenal glands; testicles or ovaries; skeletal muscle with femur and sciatic nerve; salivary glands.

For the other treatment groups, the following organs of 10 animals per sex were examined: thyroid; heart; liver; spleen, kidney; adrenal gland; testicles or ovaries.

The "main" organs of animals which died during the study were also examined.

The pathologist stated that the "histological findings of the present compound investigation in Wistar rats cannot be proven to be treatment or dose dependent and it must be assumed that the found tumors lie within the range of the normal spontaneous tumor rate for this species".

The investigators supplied a summary table of "histological findings of suspected tumor material" without any reference (in the majority of the observations presented) to the organ in which the tumor was found. This reviewer utilized the provided individual histopathological findings and produced a summary table with organ by organ incidence of "suspected tumor" findings (see Table VI). As can be seen on Table VI, the females of the 300 ppm test group showed a statistically significant increase ($p < 0.01$ done by independent chi square method) over the control group for liver bile duct adenoma. A statistically significant increase ($p < 0.05$ done by independent chi square method) was also observed for pituitary ademona and a slight, but not statistically significant, increase in ovarian adenoma (23% as compared to 13% in control) was observed. Further data is required on the animals from the other 3 dosage groups along with historical control data on the incidence of these tumors in this breed of rat before evaluation of this study can be completed.

No tumors were found by the investigators in the (both sexes) aorta, bone marrow (sternum), brain, cervical lymph glands, epididymus, esophagus, eyes, heart, kidneys, lungs, skeletal muscle with femur, nerve, prostate gland, salivary gland, seminal vesicle, spleen (male), stomach (female), trachea and urinary bladder of the animals examined at final sacrifice.

Table VI: Histopathological Findings of Suspected Tumor Material
(rat sacrificied at the end of the study)

Dose (ppm):		Control	25	35	100	300
Adrenal gland- adenoma	M	8/66	1/10	1/10	0/10	1/29
	F	0/72	0/10	0/10	0/10	0/35
"Tumor"†	M	0/66	0/10	0/10	0/10	0/29
	F	0/72	0/10	2/10	0/10	0/35
Intestine- "Tumor"†	M	1/66	-††	-††	-††	0/29
	F	0/72	-	-	-	0/35
Liver-bile duct adenoma	M	19/66	10/10	8/10	5/10	9/29
	F	13/71	4/10	5/10	1/10	19/35**
Pancreas- adenoma	M	1/65	-	-	-	0/29
	F	1/71	-	-	-	1/35
Pituitary- adenoma	M	10/62	-	-	-	6/29
	F	27/71	-	-	-	21/35*
carcinoma	M	2/62	-	-	-	1/29
	F	11/71	-	-	-	5/35
Spleen- lymphoma	M	0/66	0/10	0/10	0/10	0/29
	F	0/72	0/10	(1/5)†††	0/10	(1/4)†††
Stomach- carcinoma	M	1/66	-	-	-	0/29
	F	0/72	-	-	-	0/35
Thyroid gland- adenoma	M	0/65	2/10	1/10	0/10	1/29
	F	2/72	0/10	0/10	2/10	0/35
papilloma	M	0/65	0/10	0/10	0/10	0/29
	F	3/72	0/10	1/10	1/10	0/35
Testes- interstitial cell tumor		3/66	1/10	0/10	0/10	0/29
"Tumor"†		0/66	0/10	1/10	0/10	0/29
Mammary gland- adenoma		5/72	-	-	-	0/35
Ovaries- adenoma		9/72	1/10	1/10	1/10(1/3)	8/35(2/4)
Uterus- adenoma		1/72	-	-	-	0/35
"Tumor"†		0/72	-	-	-	1/35
polyps		5/72	-	-	-	3/35

continued

Table VI continued:

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* $p < 0.05$
** $p < 0.01$

† - unspecified tumor (must be explained further by the registrant).
†† - tissue not examined.
††† - number in parenthesis, animals died prior to end of experiment.

Data extracted from addendum to BAYER AG Report No. 4888.

The investigators also did not supply a summary table of non-neoplastic histopathological findings. This review again utilized the provided individual animal histopathological findings to produce a summary table (see Table VII). As can be seen in Table VII there were numerous observations of inflammatory cellular infiltration (ICI) in the heart, kidneys and trachea as well as the presence of lymphocytes in the kidneys, liver and trachea. The liver showed the most significant observation of "changes in the nucleus" with a slight increase in the males and a statistically significant increase ($p < 0.01$ done by independent chi square method) in the females of the 300 ppm test group. This observation of "charges in the nucleus" in the liver must be further defined by the registrant as must the observation listed as "tumor" (unspecified) in the table. There also was a statistically significant increase ($p < 0.05$ done by independent chi square method) in parasitic (stated as "possible" by the registrant) cellular granuloma observed in the 300 ppm males. The 300 ppm females presented with a slight, but not statistically significant, increase in incidence of cysts and of uterine hypertrophy/hyperplasia. The lungs showed evidence of emphysema, pneumonia, bronchitis, blockages, peribronchial lymphocyte infiltration and occasional hyperplasia of the bronchial mucous membrane.

004262

Table VII: Non-neoplastic Histopathological Findings
(rats sacrificied at the end of the study)

Dose (ppm):		Control	25	35	100	300
Heart- ICI†	M	15/66(2/9)††	5/10	4/10(1/6)	4/10(1/8)	11/29
	F	22/72	1/10	1/10	4/10(1/7)	4/35(1/4)
Kidneys- ICI	M	3/66(3/6)	0/10	0/10	1/10(1/8)	0/29
	F	1/72	2/10	(1/5)	1/10	2/35
Lymphocytes	M	39/66	3/10(2/8)	4/10(2/6)	6/10	9/29
	F	15/72	2/10	3/10	0/10	2/35
Glomerular Damage	M	0/66	0/10	0/10	0/10	0/29
	F	1/72	2/10	3/10	0/10	4/35
Liver-"Changes in the nucleus"	M	6/66	3/10	3/10	3/10	4/29
	F	10/71	0/10	1/10	6/10	18/35**
Lymphocytes	M	18/66	2/10	2/10	2/10	9/29
	F	11/71	3/10	3/10(1/5)	1/10	4/35
Parasitic cellular granuloma (pcg)	M	7/66	0/10	0/10	5/10	8/29*
	F	0/72	1/10	0/10	0/10	0/35
Spleen- Mega-karyocytes	M	0/66	0/10	0/10	0/10	1/29
	F	1/72	0/10	0/10	0/10	2/35
Trachea- ICI	M	2/66	-†††	-	-	2/29
	F	2/71	-	-	-	1/35
Lymphocytes	M	4/66	-	-	-	0/29
	F	1/71	-	-	-	2/35
Mammary glands- Cysts		9/72	-	-	-	9/35
Uterus- Hypertrophy/ Hyperplasia		7/72	-	-	-	7/35

Lungs - see text for description of findings

* $p < 0.05$
** $p < 0.01$

† - ICI = Inflammatory cellular infiltration.
†† - number in parenthesis, animals died prior to end of experiment.
††† - tissue not examined.

Data extracted from addendum to BAYER AG Study No. 4888.

Conclusions:

There was no evidence of a compound related effect on hematological, clinical-chemical, urinalysis, kidney function, liver function and thyroid function test parameters. There also was no compound related effect on mortality or food consumption. However there was a statistically significant reduction of weight gain seen in the high dose (a table of weekly body weight gain data must be supplied by the registrant). Relative organ weights showed a significant decrease in heart (100 and 300 ppm females), lungs (300 ppm females), liver (35 to 300 ppm females), spleen (300 ppm females) and kidney (25, 100 and 300 ppm males), however there is a lack of dose response in these findings and there are no histopathological observations that correspond with these findings. The neoplastic histopathological observations consisted of a statistically significant increase in the incidence of adenoma of the liver bile duct and the pituitary gland in the 300 ppm females. However, not enough animals were examined histopathologically in the other 3 dosage groups to allow a judgement to be made with respect to a dose response effect of the chemical. Further data must be supplied in the form of histopathological examinations of the animals not previously examined in the other 3 dosage groups along with historical control data on the incidence of these tumors in this particular rat strain. The registrant must also explain the observation of "tumor" in certain tissues. Non-neoplastic observations showed a statistically significant increase in liver "changes in the nucleus" in the females of the 300 ppm test group. The registrant will also have to provide the non-neoplastic observations in the animals of the other 3 dosage groups that were not previously examined. No systemic No Observed Effect Level (NOEL) can be determined without this data.

The registrant is directed to provide summary tables of the neoplastic and non-neoplastic findings as produced in this review (see Tables VI and VII).

Certain biochemical parameters were not determined (Ca, PO_4, fasting glucose and urea nitrogen) and data for clinical observations was lacking.

Core Classification: Core-Supplementary Data since the oncogenic potential of the test compound cannot be fully ascertained without the above mentioned neoplastic histopathologic observations on animals of the 25, 35 and 100 ppm dosage groups. The non-neoplastic histopathologic observations are also lacking for the same group of animals. Historical control data of the incidence of neoplastic and non-neoplastic histopathological findings of the rat strain used in this study must be supplied by the registrant. The registrant must also explain the terms "changes in nucleus" and the observation of "tumor" (unspecified) seen in certain tissues on the individual animal pathology findings sheets. A table of mean weekly body weight data divided by sex for each study group must also be supplied. This study may be upgraded if the requested data is submitted and eliminates the deficiencies.

METRIBUZIN

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Pages 69 through 74 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

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Most of the tissues recommended by CORE were examined in all animals at the end of the experiment except for spinal cord, trachea, skin and sections of the sternebrae, vertebrae or tibio-femoral joint. However, the investigators included in the examinations the following tissues not recommended by CORE: tonsils, aorta and diaphragm.

Results:

I. Clinical Observations:

The investigators stated that the dogs of the 25 and 100 ppm test groups did not differ in appearance from those of the control group relative to such parameters as "activity, condition of coat, appetite or thirst", however no clinical observation data was presented.

It was noted after 2 weeks of feeding that the 1500 ppm test group animals "appeared weakened, their coats were dull and bristly and feed was frequently refused".

Three dogs were found to have severe Candida infection after 12 months, one male in the 100 ppm test group and one male and one female of the 1500 ppm test group.

The investigators stated that the eye examinations found "no dullness on the cornea or lenses" and "no changes in the fundus occuli" in any of the animals of the study.

Mortality was high in the 1500 ppm test group, while only one other death occured (in the 25 ppm test group), see Section II C.

II. Clinical Data

A. Food Consumption:

The animals in the control, 25 and 100 ppm groups consumed nearly equal mean amounts of food. The 1500 ppm test group, however, showed slightly reduced food intake. See Table 1 below.

Table I: Mean Food Consumption (g/animal/day)

Dose (ppm)	Male	Female
Control	298.10	297.91
25	298.10	298.10
100	298.10	296.39
1500	279.01	283.86

Data extracted from BAYER AG Report No. 4887 Table 1.

There were no sex related differences in the mean quantity of test compound ingested. See Table II below:

Table II: Mean Quantity of Test Compound Ingested (mg/kg body weight/day)

Dose (ppm)	Male	Female
Control	0	0
25	0.82	0.84
100	3.44	3.56
1500	55.65	55.30

Data extracted from BAYER AG Report No. 4887 Table 1.

B. Body Weight:

No differences were observed in weight gain between control and the 25 and 100 ppm dose groups. However, animals of the 1500 ppm test group gained significantly less weight than the control animals, but after approximately 65 weeks only 1 male and 1 female survived in the 1500 ppm test group and the female showed normal weight gain. The investigators only provided data in the form of graphs (curves) and individual animal data, no mean weekly animal body weight by group was provided. Some of the animals in the mid dose group may have reduced weight gain but the small numbers of animals used in the study groups preclude any statistical significance. In addition it is noted that there may not have been enough food provided to the animals to allow normal growth especially during the winter months.

C. Mortality:

There was one death noted after 1 year in the 25 ppm test group (a female) and 4 deaths in the 1500 ppm test group (2 males and 2 females) with 2 more deaths in this group after 2 years (1 male and 1 female).

D. Hematology:

Hematological tests were conducted prior to the start of the experiment and no unusual findings were observed.

At 2 months the 1500 ppm test group showed significant differences in test results seen as an increase in sedimentation rate and reticulocyte count, a decrease in thrombocyte and erythrocyte counts, medium cell volume (males) hemoglobin (as percent), hematocrit, medium cell hemoglobin, prothrombin time with only small changes in the differential blood counts such as a decrease in eosinophils, large lymphocytes, mature polymorphonuclear neutrophils (females) and an increase in monomorphonuclear neutrophils as well as evidence of immature polymorphonuclear neutrophils. The hematological changes were greatest in males.

At 4 months the 1500 ppm test group showed significant effects on nearly all the measured parameters. A similar pattern was seen at 6, 12, 23 and 24 months in the 1500 ppm test group with the females showing greater changes than were seen at 4 months. An increase in leucocyte counts were seen and differential blood counts at 23 and 24 months showed variability but no specific pattern.

E. Liver Function Tests:

Liver function tests were also conducted prior to the initiation of the study.

At 2 months there were slight decreases in plasma alkaline phosphatase (ALP) levels in the male and ornithine-carbamyl transferase (OCT) levels in both males and females of the 1500 ppm test group.

At 4 months the 1500 ppm test group showed increased ALP levels in the males and decreased OCT levels in both sexes.

At 6 months there were increased plasma glutamate-pyruvate transaminase (GPT) levels in all 3 test group males and a slight increase in 1500 ppm females. An increase in total bilirubin of the 1500 ppm males was observed. The investigators state that after 6 months, GPT and bilirubin levels "reached pathological values" in the males of the 1500 ppm test group.

At 12 months there were increased GOT levels in the 1500 ppm males and females, decreased ALP levels in all 3 test group females, increased GPT levels in all 3 treatment group male and female (dose related), a large increase in OCT levels in the 1500 ppm males and females, increased BSP retention in 1500 ppm males and decreased BSP retention in 1500 ppm females, increased total bilirubin in the 1500 ppm males and increased total protein in both males and females of the 1500 ppm test group. The investigators state that at 12 months there was increased GOT, GPT, OCT and BSP retention in the 1500 ppm male dogs and that the GOT in the 1500 ppm females was on the "borderline of normality". However, the GPT, OCT and total protein levels were increased over the other test groups in the 1500 ppm females.

At the 24 month period, only one male and one female survived in the 1500 ppm test group. The male showed slight increases in ALP, OCT and BSP retention and the female showed a slight increase in GOT. There were no apparent effects on these parameters at the lower dose levels.

F. Urinalysis and Kidney Function Tests:

The investigators stated that no differences were seen in sugar, albumin, blood and bile pigment measurements in the urine "between treated groups and the controls", both "before the start of the feeding experiment and after 2, 4, 6, 12 and 24 months of feeding". However no values were provided for the examinations (certain tests were done on "clinical sticks"). They further stated that the urine sediments "exhibited the usual constituents". However, no data was presented for any of these parameters.

Kidney function tests conducted prior to the study initiation showed no real differences in urea, creatinine or total protein measurements in the urine between any of the study groups, except for a very slightly elevated protein in the urine in the 25 ppm test group male. The investigators state that this is within "the physiological range".

No differences were seen at the 2 month interval in any of the parameters and at 4 months only a doubling of measured protein in the urine (compared to control) of the 1500 ppm test group females was seen.

At the 6 month interval a slight decrease in creatinine was seen in males and females of the 1500 ppm test group. This was also seen at the 12 month interval. At the 12 month period a doubling of the measured urea (compared to control) was seen in the males of the 1500 ppm test group along with a doubling in measured total protein (compared to control) in the urine of the females in the same test group.

At 24 months no real differences could be seen between control and the low and mid dose groups. However, too few animals remained in the 1500 ppm test group for purposes of comparison to the control group.

G. Blood Sugar and Cholesterol Determinations:

No real differences were seen between study groups on tests conducted prior to initiation of the study.

At 2 months there were no differences except for an elevation of the cholesterol of the 1500 ppm test group males which persisted to the 4 month interval at which time the females of the same group exhibited slightly elevated cholesterol levels (persisting to 6 months.

At the 6 month time point there was a slight dose-response elevation in blood sugar in the males of the treated groups, however the females did not show any differences.

At 12 months both males and females of the 1500 ppm test group showed an increase in blood sugar and a slight elevation in cholesterol.

At 24 months there was a dose-related increase in blood sugar in the males of all the treated groups with females only showing a slight increase in all 3 treatment groups. The cholesterol levels showed no real differences.

The investigators stated that the elevation of blood sugar was at the "upper end of the normal range" and the the cholesterol was only "temporarily increased".

The transient increase in cholesterol levels could be due to a toxic effect of the test compound on the liver.

4. Thyroid Function Tests:

Body temperature and protein-bound iodine studies showed no change throughout the duration of the experiment.

III. Necropsy Data:

The autopsies conducted on the animals which died during the study revealed that one female of the 25 ppm dose group died of severe pneumonia (present for 220 days) and at least 3 out of the 6 animals that died in the 1500 ppm dose group also died of severe pneumonia. One male and 2 females of the 1500 ppm test group were sacrificed due to "severe malnutrition".

The investigators stated, relating to the autopsies of all the animals sacrificed at the end of the experiment, that "no specific changes were seen which could be considered with certainty to be due to administration of the test compound", however no data was presented to substantiate this statement (assuming the investigators are referring to gross necropsy observations which were not provided).

A. Organ Weights:

It is best to consider mean relative organ weights when considering the difference in dog body weights at terminal sacrifice. Also consideration must be made for the fact that only one male and one female survived to sacrifice in the high dose group and the small number of animals on test at each dose level.

An apparent increase in relative thyroid weight was noted in both of the animals of the 1500 ppm dose group, also a very slight increase in the relative heart weight of the male dog. Seen also in the 1500 ppm male was an increase in liver and pancreas relative organ weight.

An increase in the relative spleen weight occurred in all males of the 3 test groups over control and the females showed an increase in the relative weight of the pancreas while there was a very slight dose related decrease in relative kidney weight. See Table III below.

Table III: Mean Relative Organ Weights (g/kg body weight except thyroid where mg/kg body weight)

Dose(ppm)	Thyroid	Heart	Liver	Spleem	Pancreas	Kidneys
Males						
0	85.11	9.09	34.84	1.96	2.70	5.28
25	74.39	8.14	29.59	2.90	2.51	4.35
100	67.98	8.70	33.38	2.59	2.55	4.68
1500	138.36	9.45	46.44	4.52	4.11	5.62
Females						
0	89.14	9.10	32.54	3.67	2.70	5.03
25	70.78	7.68	32.26	2.55	3.15	4.87
100	87.17	8.52	34.21	3.23	3.48	4.53
1500	111.54	9.13	32.79	3.46	2.88	4.13

Data extracted from BAYER AG Report No. 4887 Table 24b.

B. Histopathology:

Those animals which died early in the study and the cause of death diagnosed as severe pneumonia exhibited the expected histological signs (small foci of lympho-histocytic infiltrates, perivascular and focal lympho-histocytic infiltrates).

Relating histological findings to hematological observations, the changes observed in hematological tests may be related to changes in blood forming organs as evidenced by the increase in megakaryocytes observed in the bone marrow and spleen of the high dose group.

The results of the clinical tests along with the increase in liver weights of the 1500 ppm test group may indicate liver damage. Further evidence is the observation of parenchymal necrosis, interstitial infiltration and other changes not observed in the control or the 25 and 100 ppm test groups. The investigators believe that these changes are caused by "the increased destruction of ethythrocytes caused by hypoxaemia " and based on this they further state that "BAY 94 337 does not have a primary hepatoxic action". However, this must be considered as speculative since there is no evidence of activity that would reduce oxygen to the tissue and any subsequent destruction of red blood cells.

The other histological findings were either singular in nature or occured in equal incidence in all treatment groups and consisted mostly of lymphocytic infiltration due to inflammation ("non-specific") involving the heart, lungs, liver, lymph nodes, kidneys, testes, prostate, adrenals and thyroid gland.

Conclusions:

The choice of dosage levels utilized in this study was questionable since 75% of the high dose animals died during the study (3 out of 4 animals of each sex). The clinical tests and histopathological examinations revealed an effect of the test compound at this dose. Decreased body weight of the animals at the high dose level, increased relative liver weight along with the related clinical tests and the liver and kidney damage that was noted by histopathology indicate that a dose level of 1500 ppm is associated with toxicity. The 2 lower doses did not show any compound related effect. A more conservative approach to choice of dosage would have produced a better study, possibly with less mortality at the high dose.

The systemic No Observed Effect Level (NOEL) for this study is 100 ppm.

Certain biochemical parameter recommended by CORE were not examined: calcium, phosphorus, fasting glucose and urea nitrogen.

Core Classification: Core-Minimum Data.

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Data Review:

Study Information;

Study Title: BAY 94 337 Subchronic Toxicological Studies on Rats (Three-month feeding experiment)
Includes: Pathology Report of BAY 94 337 Three-Months Feeding Study in Rats

EPA Identification Numbers: EPA Accession No. 112032

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: Farbenfabriken BAYER AG
Institut fur Toxikologie
Wuppertal-Elberfeld

Study Numbers: 1719 & 26469

Date: November 20, 1969
Pathology Report: December 31, 1969

Study Authors: Dr. rer. nat. Eckhard Loser
Pathology Report: Dr. Lionel E. Mawdesley-Thomas
(Study Director: Dr. med. Dietrich Lorke)

Test Compound: BAY 94 337, Technical (also called Metribuzin, SENCOR)
Purity: not specified
Mixed in Altromin R powder feed

Dosage: 50, 150, 500 and 1500 ppm.

Test Animal: SPF Rats (Wistar Strain)
Bred by Winkelmann of Kirchborchen
At beginning of study rats 28 to 32 days old, mean body weight approximately 57 gms.

Materials and Methods: A copy of the materials and methods section from the investigators report is appended.

The purity of the test compound was not provided.

There was no mention of criteria for daily clinical observations, although the results section mentions some observations ("appearance, behavior, activity and mobility").

Blood examinations, liver function tests, urinalysis, kidney function tests, blood sugar and cholesterol determinations were carried out on 5 animals per sex of each study group whereas Core recommends 8 animals per sex. Urinalysis and the other tests were carried out at 4 weeks and 3 months, the Core recommendation is every 30 days.

Complete hematological evaluations (including reticulocyte counts) were performed at 4 weeks and 3 months, another evaluation at 2 months should have been done, as per CORE recommendations of every 30 days.

The blood chemistry determinations of calcium, phosphorus, fasting glucose (although non-fasting blood sugar was measured) and urea nitrogen were not done. However, blood sugar, cholesterol and other blood tests for specific organ function were performed during the course of the study. These tests should also have been carried out prior to initiation of the study.

At post mortem all the organs recommended by Core were weighed except for the brain and pituitary. The investigators included the thymus in the examination.

A pathological examination report was provided as an addendum, however no protocol was provided. They presented observations in the liver, lungs, thyroid gland, pituitary gland, uterus and spleen in 5 animals per sex per group. Core recommends that all animals in the control and high dosage groups be examined with limited organ evaluation in the intermediate and low dosage groups.

Results:

I. Clinical Examinations:

The investigators stated that none of the treated animals differed from control in terms of "appearance, behavior, activity and mobility" or "with respect to consumption of feed or water", however no data was provided for these parameters.

II. Clinical Data:

A. Food Consumption:

Those animals receiving test compound in the diet consumed slightly less (not statistically significant) than that of the control group. See Table I below.

Table I: Mean Food Consumption

	Dose (ppm)	kg/animal	g/animal/day
MALES	Control	1.93	21.19
	50	1.66	18.27
	150	1.82	20.02
	500	1.77	19.49
	1500	1.71	18.76
FEMALES			
	Control	1.64	17.97
	50	1.38	15.12
	150	1.41	15.51
	500	1.33	14.66
	1500	1.34	14.73

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 1.

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In terms of ingestion of active ingredient, the females consistently received less (mg/kg b.w./day). See Table II below.

Table II: Mean Quantity of Active Ingredient Ingested (mg/kg body weight/day)

Dose (ppm)	Male	Female
Control	0	0
50	0.91	0.76
150	3.00	2.33
500	9.75	7.33
1500	28.13	22.09

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 1.

B. Body Weight:

Based on data presented, the animals of the 50, 150 and 500 ppm test groups gained approximately the same amount of weight as the controls over the 90 day period, however both sexes of the 1500 ppm test group gained significantly less weight during the entire experimental period (females $p<0.01$, males $p<0.05$). See Table III below.

Table III: Mean Animal Body Weights (grams) at 3 Months

Dose (ppm)	Control	50	150	500	1500
Males	348.0	337.5	340.1	345.5	326.0*
Females	218.9	213.0	212.9	214.1	197.6**

*$p < 0.05$
**$p < 0.01$
Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 9a.

C. Mortality:

One male rat died in the control group (no cause of death provided) and one female rat was accidentally killed during a blood sampling.

D. Hematology.

At 4 weeks slightly decreased levels of hemoglobin were seen in 500 and 1500 ppm males and 150, 500 and 1500 females, also slight decreases in erythrocytes were seen in 500 and 1500 ppm animals of both sexes, reticulocytes were increased in a dose-related manner in 500 to 1500 ppm males and increased in all treated females, thrombocytes were decreased in 1500 ppm males. See Table IV.

At 4 weeks differential blood studies found that mature polymorphonuclear neutrophils appeared to be increased in 1500 ppm males and 50 to 1500 ppm females, also large lymphocytes were increased in all treated males and females. See Table IV.

Table IV: Hematological Parameters at 4 Weeks

Dose (ppm)	HB†	ERY††	RETI†††	THROM††††	MPN†††††
MALES					
Control	16.6	8.41	8.8	610	7.8
50	15.8	8.51	6.8	684	7.0
150	16.3	8.12	8.6	579	5.4
500	15.5	7.39	14.6	580	6.2
1500	14.6	7.29	21.4	447	9.2
FEMALES					
Control	16.0	8.07	8.8	541	4.6
50	16.0	8.88	12.0	529	6.8
150	14.9	8.30	11.2	646	4.2
500	15.1	7.22	16.2	498	5.4
1500	14.7	7.69	13.2	596	6.2

† - HB = hemoglobin as g%
†† - ERY = erythrocytes x 10^6
††† - RETI = reticulocytes in 0/00
†††† - THROM = thrombocytes x 10^3
††††† - MPN = mature polymorphonuclear neutrophils in %

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Tables 2a and 2b.

The investigators state that these values are "within the normal range for the dosed rats", but no data were submitted to support this contention. There is no indication of any pathological condition.

At 3 months an increase in reticulocytes was seen in the 50 to 1500 ppm males and 500 and 1500 females, also an increase in leucocytes was seen in 500 and 1500 ppm males with a dose-response decrease in 50 to 1500 ppm females, thrombocytes were seen to have a dose related increase in 500 and 1500 ppm males and also an increase in 500 and 1500 ppm females. See Table V.

The differential blood count saw an increase in mature polymorphonuclear neutrophils in 500 and 1500 ppm males and 50 to 1500 ppm females with a decrease in large lymphocytes in 50 to 1500 ppm males and 150 to 1500 ppm females. See Table V.

Table V: Hematological Parameters at 3 Months

Dose (ppm)	RETI†	LEUC††	THROM†††	MPN††††	L.L.†††††
MALES					
Control	15.0	5.1	606	4.2	6.2
50	19.8	6.5	520	4.0	4.6
150	17.2	6.1	503	3.4	4.4
500	19.0	8.3	637	9.0	2.2
1500	19.0	7.6	672	4.8	3.4

continued

Table V: continued

FEMALES					
Control	19.6	6.7	534	3.8	3.4
50	20.2	6.4	535	8.8	3.0
150	15.2	5.4	557	4.8	1.4
500	24.4	4.7	630	8.4	2.8
1500	22.4	4.1	620	8.2	2.8

† - RETI = reticulocytes in 0/00
†† - LEUC = leucocytes x 10^3
††† - THROM = thrombocytes x 10^3
†††† - MPN = mature polymorphonuclear neutrophils in %
††††† - L.L. = large lymphocytes in %

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Tables 3a and 3b.

The investigators stated that "the treated rats of all dose groups did not significantly differ from the control animals with respect to any of the examined parameters".

E. Liver Function Tests:

Studies at 4 weeks revealed slightly elevated alkaline phosphatase (ALP) levels in 150 and 1500 ppm males and 1500 ppm females, also an increase in glutamate-oxalacetate transaminase (GOT) levels in 150 to 1500 ppm males and 50 to 1500 ppm females, an increase in glutamate-pyruvate transaminase (GPT) levels in 150 to 1500 ppm females, there was an increase in total bilirubin levels in 1500 ppm animals of both sexes and an increase in total protein levels in 50 to 1500 ppm males and a dose-related increase seen in 50 to 1500 ppm females. See Table VI.

Table VI: Liver Function Tests at 1 Month

Dose (ppm)	ALP†	GOT††	GPT†††	BILI††††	PROT†††††
MALES					
Control	177.3	36.9	19.2	0.08	5.7
50	161.0	36.1	16.0	0.08	6.2
150	191.5	43.9	19.1	0.08	6.5
500	175.2	45.0	16.4	0.07	6.6
1500	204.3	53.2	20.3	0.15	7.7
FEMALES					
Control	147.6	52.2	14.8	0.07	5.0
50	134.7	64.9	14.8	0.06	6.0
150	127.6	70.6	17.7	0.07	6.3
500	148.1	55.4	16.1	0.06	6.4
1500	171.5	62.8	17.3	0.12	7.5

† - ALP = alkaline phosphatase in mU/ml
†† - GOT = glutamate-oxalacetate transaminase in mU/ml
††† - GPT = glutamate-pyruvate transaminase in mU/ml
†††† - BILI = total bilirubin in mg/100 ml
††††† - PROT = total protein in g/100 ml

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 4.

At 3 months an elevation in ALP levels was seen in 1500 ppm males, increased GOT levels in 50 to 1500 ppm rats of both sexes, elevated GPT levels in 150 to 1500 ppm females and increased sorbital dehydrogenase (SDH) levels in 50 to 1500 ppm females and dose related in 50 to 1500 ppm males. See Table VII.

Table VII: Liver Function Tests at 3 Months

Dose (ppm)	ALP†	GOT†	GPT†	SDH°
MALES				
Control	86.2	25.0	17.4	2.3
50	85.0	28.5	17.2	2.6
150	82.7	28.7	19.4	3.0
500	83.8	30.4	17.5	3.6
1500	94.2	32.8	16.0	4.1
FEMALES				
Control	71.5	30.6	16.8	2.2
50	66.9	29.7	15.9	2.8
150	82.7	28.7	19.4	3.0
500	70.0	39.4	21.9	4.0
1500	73.2	33.7	20.0	3.3

† for definitions see Table VI
° - SDH = sorbital dehydrogenase in mU/ml

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 5.

The investigators stated that all the levels seen "in male and female rats of all dose groups were within the physiological range for young rats".

F. Urinalysis and Kidney Function Tests:

The investigators stated that the urinalysis at 4 weeks and 3 months revealed no significant difference between control and treated animals. The utilized the "clinical stick" method for analysis. They further stated that those samples which were "slightly positive when tested for protein were about just as frequent among the treated rats as among the untreated ones". No data was provided for these parameters.

The urea determinations made at 4 weeks showed a dose related increase in male rats with an increase in females. The creatinine at 4 weeks showed an increase in 1500 ppm males. See Table VIII.

At 3 months essentially no differences were seen in urea or creatine levels. See Table VIII.

Table VIII: Urea and Creatinine Levels at 4 Weeks and 3 Months in mg/100 ml.

Dose (ppm)	Urea at 4 weeks	Creatinine at 4 weeks	Urea at 3 months	Creatinine at 3 months
MALES				
Control	25.3	0.83	27.1	1.05
50	29.4	0.87	29.5	1.12
150	31.0	0.85	32.9	1.18
500	30.8	0.86	32.0	1.17
1500	34.0	1.07	28.4	1.20
FEMALES				
Control	30.8	0.88	27.8	0.96
50	35.4	0.96	31.6	0.99
150	34.3	0.93	30.5	0.89
500	31.0	0.97	30.6	1.00
1500	33.2	0.99	30.1	0.99

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 6.

Protein determinations were unremarkable at the end of the study. Levels in males were variable while females were less variable. No set pattern was seen. See Table IX.

Table IX: Total Protein in the Urine (mg/100 ml.)

Dose (ppm)	MALES	FEMALES
Control	71.3	24.2
50	57.6	35.8
150	79.0	17.7
500	32.0	25.9
1500	57.8	28.8

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 7.

The investigators stated that all "levels were within the physiological range for rats".

G. Blood Sugar and Cholesterol Determinations:

Blood sugar determinations at 4 weeks showed a reduction in males (dose related at 150 to 1500 ppm) with females showing a dose related increase at 50 to 1500 ppm while at 3 months no real differences in blood sugar were seen. See Table X.

Cholesterol levels at 4 weeks showed an increase in 1500 ppm males and 500 to 1500 ppm females and at 3 months there were increases in cholesterol of males and females of the 500 and 1500 ppm groups. See Table X.

Table X: Blood Sugar and Cholesterol Levels at 1 and 3 Months in mg/100 ml.

Dose (ppm)	Blood Sugar	Cholesterol	Blood Sugar	Cholesterol
MALES	1 Month		3 Months	
Control	81	83.7	85	104.3
50	72	75.8	86	106.6
150	77	84.4	81	107.9
500	68	87.6	80	119.0
1500	63	100.3	93	121.4
FEMALES				
Control	69	94.1	98	111.2
50	66	91.5	88	111.8
150	76	95.6	88	104.3
500	74	100.2	93	128.3
1500	75	131.4	98	134.8

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 8.

The investigators state that the results of the tests are not "within the pathological range".

III. Necropsy Data:

The investigators stated that "none of the autopsied rats showed any macroscopic changes of the inner organs attributable to the inclusion of the active ingredient in the diet". No data was provided to substantiate this.

A. Organ Weight:

An increase was observed in thyroid weight significant in 1500 ppm males and 500 to 1500 ppm females. The heart showed a significant decrease in weight in the 1500 ppm rats of both sexes. The lungs showed an increase in weight significant in females at 1500 ppm. The liver showed the greatest effects with an increase in weight, seen especially in females, dose related, significant at all 4 dose levels in females and at 1500 ppm in males. Spleen weight was significantly increased in females at 1500 ppm with males showing a trend towards an increase. The kidney weight showed a dose related trend of increase in females, significant at 1500 ppm, males were increased over control. Ovaries in the females were significantly increased at 1500 ppm. The thymus and adrenals showed no remarkable differences. See Table XI.

Table XI: Mean Absolute and Relative Organ Weights (mg)

Dose (ppm)	Thyroids	Heart	Lung	Liver	Spleen	Kidneys(2)	Gonads
Absolute Organ Weights							
MALES							
Control	21.2	1050.6	1204.2	12578.4	563.8	2367.5	3248.9
50	22.1	978.5	1094.8	11452.8	555.9	2170.4	3123.7
150	21.3	1004.4	1122.3	11617.6	547.4	2231.9	3123.7
500	20.5	981.7	1112.5	11944.3	536.9	2396.3	3128.0
1500	27.8**	913.7**	1106.7	13371.1	597.6	2264.3	3113.7
FEMALES							
Control	17.0	718.5	860.0	7285.1	422.4	1448.2	121.8
50	19.4	707.1	917.8	7791.5	396.9	1444.9	119.1
150	18.6	717.6	890.4	8058.9*	408.6	1494.9	128.4
500	19.8*	704.8	896.6	8221.5*	435.8	1470.3	132.3
1500	27.5**	658.7**	875.2	8199.2*	411.9	1452.6	128.7
Relative Organ Weights (per 100 gm body weight)							
MALES							
Control	6.1	302.0	346.2	3618.9	161.8	631.4	935.9
50	6.5	291.2	325.7	3399.4	164.5	645.8	932.9
150	6.2	295.5	330.5	3406.9	161.4	657.0	919.8
500	5.9	284.2	323.1	3450.4	155.3	697.6	909.1
1500	8.5**	279.6*	339.7	4083.6**	183.1	693.8	956.4
FEMALES							
Control	7.8	328.8	393.2	3332.1	192.9	661.0	55.7
50	9.2	333.0	431.3	3662.4*	186.2	679.1	56.1
150	8.9	337.9	420.2	3796.9*	192.8	705.5	60.9
500	9.2	329.0	418.8	3839.9**	203.3	686.7	61.7
1500	13.9**	334.6	444.2**	4156.8**	208.7*	735.7**	65.3**

*$p < 0.05$
**$p < 0.01$

Data extracted from Farbenfabriken BAYER AG Report No. 1719 Table 9a and 9b.

B. Pathological Examination:

This was included as an addendum to the report.

The pathologist found evidence of chronic interstitial pneumonitis (not graded, described as "evidence of some" or "minimal degree"). The liver had small changes in "hepatocyte size" (not specified) along with occasional lymphocytic infiltration. The thyroid gland showed evidence of hyperactivity (eg. changes in follicular size). The investigators stated that this occured in the 1500 ppm animals with some minimal changes seen in the 500 ppm group, however, there is evidence in all dose groups (4/10 in control, 8/10 in 50 ppm, 10/10 in 150, 9/10 in 500 and 8/10 in 1500 ppm). Occasional pituitary cysts and hydrometria of the uterus were noted in both control and treated groups. The data provided did not include grading of lesions.

Conclusions: The investigators found no effects on "appearance, behavior, activity and mobility" or "with respect to consumption of feed or water". However there was a slight non-significant reduction in food intake in the treated groups. Body weight was found to be significantly reduced in the 1500 ppm group animals of both sexes.

Increases in weight in the 1500 ppm group thyroid, lung, liver, spleen, kidneys and gonads along with a reduction in heart weight were observed. The increase in liver weight was significant in all 4 dose groups in the females and at 1500 ppm in the males.

Pathological examinations revealed changes in lung and liver in relatively equal incidence in all groups.

Based on data presented the systemic No Observed Effect Level (NOEL) is below 50 ppm, since the increase in liver weight was statistically significant at all 4 dose levels in the females.

Core-Classification: Core-Supplementary Data since no NOEL could be established for this study, no protocol was provided for the pathological examinations and only limited organs and small numbers of animals were used for the histopathological studies. Another study was conducted subsequent to this one (BAYER AG Report Number 2150).

METRIBUZIN

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004262

Data Review:

Study Information:

Study Title: BAY 94 337 Subchronic Toxicological Studies on Rats (Three-Month feeding experiment)
Includes: Pathology Report of BAY 94 337 Three-Months Rat Study (Addendum to Report No. 2150)

EPA Identification Numbers: EPA Accession No. 112032

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: Farbenfabriken BAYER AG
Institut fur Toxikologie
Wuppertal-Elberfeld

Report Numbers: 2150 & 27908
Pathology Addendum: 3777/70/599 & 27908a

Date: July 6, 1970
Pathology Report: October 30, 1970

Authors: Dr. rer. nat. Eckhard Loser
Pathology Report: Eric J.F. Spicer
Study Director: Dr. med. Dietrich Lorke

Test Compound: BAY 94 337, Technical (also called Metribuzin, SENCOR)
Purity: not specified
mixed in Altromin R powder feed

Dosage: 10, 25 and 60 ppm.

Test Animal: SPF Rats (Wistar Strain)
Bred by Winkelmann of Kirchborchen
At the beginning of study rats were 28 to 32 days old, average body weight: 52.7 gms for males; 53.9 gms for females.

Materials and Methods: A copy of the materials and methods section from the investigators report is appended.

The purity of the test compound is not stated.

Clinical laboratory examinations were made on 5 rats per sex at 4 weeks and 3 months, whereas Core recommends 8 animals per sex every 30 days and should have been done on day 0 of study.

Hematology examinations (including reticulocyte counts) and urinalysis were done only at 4 weeks and 3 months whereas Core recommends every 30 days. The urinalysis studies utilized "clinical sticks" for sugar, protein and blood. Bile pigment content and microscopic examination of sediment were also analyzed

Kidney function tests involved measurement of urea and creatinine in the serum along with blood sugar (not fasting) and cholesterol levels, however calcium, phosphorus, fasting glucose and urea nitrogen determinations were not performed.

Liver function tests involved alkaline phosphatase, glutamateoxalacetate transaminase, glutamate-pyruvate transaminase, sorbitol dehydrogenase, bilirubin content and total protein content in heparin plasma.

Post-mortems were conducted on all animals surviving to the end of the study. Thyroids, thymus, heart, lung, liver, spleen, kidneys, adrenals and gonads were weighed and macroscopically examined.

This study report included a pathology report (with protocol) as an addendum. The tissues that were examined are as follows: heart; kidney; lung; pituitary; testes; ovaries; uterus; cervix; liver; spleen; thymus; stomach; duodenum; adrenal; thyroid; cerebral cortex; thalamic nuclei; midbrain; cerebellum. Tissues that were not examined but recommended for examination by Core are as follows: spinal cord; eye; salivary gland; trachea; esophagus; large intestine; pancreas; urinary bladder; aorta; prostate; lymph nodes; bone with marrow; skeletal muscle; skin; sciatic nerve; mammary gland; skeletal joint.

The histological examinations were conducted for only 5 rats per sex in each group whereas Core recommends all animals in control and high dosage groups with limited organ evaluation in intermediate and low dosage groups.

Results:

I. Clinical Examinations:

The investigators stated that the test groups, "did not differ from the control animals in appearance, behavior, activity and mobility" also no differences were found "with respect to consumption of feed or water", however no data was provided for these observations.

II. Clinical Data:

A. Food Consumption:

There were no differences seen in food consumption. In reference to the average quantity of active ingredient ingested, the males received slightly more at the high dose (1.31 mg/animal/day) than the females (1.06 mg/animal/day).

B. Body Weight:

There was no significant difference in body weight gain in either males or females between the 3 study groups and control.

C. Mortality:

One male and one female of the control group were sacrificed due to poor condition, another male of the control group injured itself and another female control was killed by accident during blood sampling. One male of the 10 ppm group and one female from the 25 ppm group died, the cause of death diagnosed as pneumonia.

No compound related deaths were noted.

D. Hematology:

Althougth, at 4 weeks decreases in the reticulocytes and medium cell volume of 60 ppm females, increases in leucocytes in the 10 to 60 ppm males, increases in thrombocytes, in 25 to 60 ppm males and decreases in 10 to 60 ppm females were observed, along with differential blood counts at 4 weeks showing an increase in mature polymorphonuclear neutrophils in 10 to 60 ppm males and 25 to 60 ppm females, the effects on these parameters were not compound related. The changes were not seen in the earlier study (BAYER AG Study # 1719) at the higher dosage levels used. The investigators stated that the values "were within the normal range for the dosed rats of all groups", including the differential counts. See Table I.

Table I: Hematological Parameters at 4 Weeks

Dose (ppm)	RETI†	MCV††	LEUC†††	THROM††††	MPN†††††
MALES					
Control	19.2	63	5.6	698	5.0
10	22.4	67	6.3	627	7.2
25	16.6	65	6.0	710	8.2
60	24.2	62	6.6	782	5.6
FEMALES					
Control	21.0	66	6.5	774	5.6
10	20.4	65	5.5	725	2.6
25	19.8	63	6.5	713	9.2
60	13.4	56	5.7	642	8.0

† - RETI = reticulocytes in 0/00
†† - MCV = medium cell volume in um^3
††† - LEUC = leucocytes x 10^3
†††† - THROM = thrombocytes x 10^3
††††† - MPN = mature polymorphonuclear neutrophils in %

Data extracted from Farbenfabriken BAYER AG Report No. 2150 Tables 3a and 3b.

At 3 months increased erythrocytes in 10 to 60 ppm males, increased reticulocytes in 10 to 60 ppm animals of both sexes and decreased thrombocytes of 60 ppm females were observed. See Table II.

The differential blood counts at 3 months showed variable counts mature polymorphonuclear neutrophils and large lymphocyes in both sexes. See Table II.

Table II: Hematological Parameters at 3 Months

Dose (ppm)	ERY†	RETI††	THROM†††	MPN††††	L.L.†††††
MALES					
Control	6.77	9.8	406	6.8	2.4
10	7.42	11.8	543	9.4	1.2
25	7.94	15.4	458	9.4	1.6
60	7.31	15.2	418	3.6	1.8
FEMALES					
Control	6.68	13.0	605	12.8	0.8
10	6.75	16.8	688	10.0	0.6
25	6.31	28.0	602	12.0	2.2
60	6.28	25.6	572	9.0	0.4

† - ERY = erythrocytes x 10^6
†† - RETI = reticulocytes in 0/00
††† - THROM = thrombocytes x 10^3
†††† - MPN = mature polymorphonuclear neutrophils in %
††††† - L.L. = large lymphocytes in %

Data extracted from Farbenfabriken BAYER AG Report No. 2150 Tables 4a and 4b.

There was no biological trend apparent from these data.

E. Liver Function Tests:

At 4 weeks increased levels of glutamate-oxaloacetate transaminase (GOT) in 10 to 60 ppm males and 25 to 60 ppm females, also increased levels of glutamate-pyruvate transaminase (GPT) in 25 to 60 ppm male and, dose related, 25 to 60 ppm females were noted. See Table III.

The investigators stated that the "levels in the rats of all dose groups were within the normal range".

At 3 months increased GOT levels in 25 to 60 ppm males, variable GPT levels in males, decreased GPT levels, in a dose-related manner, in females and increased sorbital dehydrogenase (SDH) levels in all treated animals (dose related in males) were observed. See Table III.

Table III: Liver Function Tests at 1 and 3 Months in mU/ml.

Dose (ppm)	GOT† at 1 month	GPT†† at 1 month	GOT at three months	GPT at three months	SDH†††
MALES					
Control	32.0	14.1	31.3	13.0	1.5
10	39.7	14.2	31.4	7.1	1.6
25	42.0	17.6	45.7	16.6	2.3
60	41.6	18.9	40.0	9.9	2.2
FEMALES					
Control	40.4	14.4	28.5	13.2	1.2
10	35.7	13.9	21.1	11.1	1.9
25	45.2	16.0	26.9	10.7	2.6
60	42.4	18.4	30.3	8.8	2.3

† - GOT = glutamate-oxaloacetate transaminase
†† - GPT = glutamate-pyruvate transaminase
††† - SDH = sorbital dehydrogenase

Data extracted from Farbenfabriken BAYER AG Report No. 2150 Tables 5 and 6.

The investigators stated that they did not see "any dose-dependent" changes.

F. Urinalysis and Kidney Function Tests:

According to the investigators, there was no sugar or blood, as analyzed by "clinical sticks" in the urine and no evidence of urobilinogen or differences in the evidence of protein between any of the study groups. No data was provided for any of these parameters.

At 4 weeks and 3 months there were no remarkable differences noted in urea or creatinine levels.

The investigators stated that levels were "within the normal range".

Protein determinations conducted at the end of the study found increases in 60 ppm males and 10 to 60 ppm females but the investigators stated that all findings were "within the physiological range". See Table IV.

Table IV: Protein Levels in Urine (24 hour) in mg/100ml.

Dose (ppm)	MALES	FEMALES
Control	31.5	22.5
10	25.0	25.1
25	31.7	29.3
60	41.5	28.8

Data extracted from Farbenfabriken BAYER AG Report No. 2150 Table 8.

G. Blood Sugar and Cholesterol:

At 4 weeks and 3 months there were no remarkable differences seen in measured blood sugar. Although, at 4 weeks a dose-related increase in cholesterol in 10 to 60 ppm animals of both sexes were noted and at 3 months the increase in cholesterol, in 10 to 60 ppm males was still observed, however the female levels were less consistent. See Table V.

Table V: Cholesterol Levels at 1 and 3 Months in mg/100 ml.

Dose (ppm)	MALES	FEMALES	MALES	FEMALES
	1 month		3 months	
Control	75	72	64	58
10	77	81	68	69
25	82	84	79	63
60	90	93	71	57

Data extracted from Farbenfabriken BAYER AG Report No. 2150 Table 9.

According to the investigators the blood sugar and cholesterol levels were "not within the pathological range".

III. Necropsy Data:

The investigators stated that "none of the autopsied rats showed any macroscopic changes of the inner organs attributable to inclusion of the active ingredient in the diet", however no data was provided to support this statement.

A. Organ Weights:

In a previous study (Farbenfabriken BAYER AG Report No. 1719), the liver, thyroid glands, heart, lungs, spleen, kidneys and gonads showed changes in weight, relative to this study only the liver showed an increase in weight in both sexes with 60 ppm females statistically significant at .05 level. See Table VI below.

Table VI: Mean Absolute and Relative Organ Weights

Dose (ppm)	Absolute Organ Weights (mg) Thyroids	Thymus	Lung	Liver	Spleen	Kidneys
MALES						
Control	22.5	312	1198	10844	664	2206
10	25.5	334	1159	12387	680	1976
25	25.1	295	1154	11462	613	2091
60	24.9	273	1106	11337	640	2160
FEMALES						
Control	17.9	307	919	7552	473	1362
10	18.7	269	889	7581	476	1376
25	16.9	272	888	7527	460	1338
60	19.7	306	871	7928*	453	1294

continued

Table VI continued

	Relative Organ Weights (per 100 gm body weight)					
	Thyroids	Thymus	Lung	Liver	Spleen	Kidneys
MALES						
Control	6.4	89	342	3073	189	631
10	7.2	94	327	3485	192	557
25	7.3	86	335	3325	178	607
60	7.1	79	319	3272	185	623
FEMALES						
Control	8.5	147	438	3590	226	649
10	9.0	130	429	3671	231	665
25	8.2	132	431	3655	223	650
60	9.3	145	411	3750*	214	612

*$p < 0.05$

Data extracted from Farbenfabriken BAYER AG Report No. 2150 Tables 10a and 10b.

B. Histological Evaluation

This study included a histological evaluation of certain organs (see page 2, this review) of 5 rats per sex per study group.

The pathologists found evidence in the respiratory tract of chronic interstitial pneumonitis (not graded, only "minimal degree" or "moderate degree") also parasite granuloma in one male of the 25 ppm test group. Lymphocytic aggregation in the portal tracts of the liver were reported in all test groups. In the kidneys minimal dystrophic mineralization (in all groups), 2 animals with calculi (both 25 ppm females) and occasional small aggregations of lymphocytes were reported. Slight congestion in the adrenals (a 25 ppm male), one female control with lymphocytic aggregation in the pons and occasional hydrometia (one incidence each in the 10, 25 and 50 ppm groups) were also reported.

The increase in the 25 and 60 ppm group of the pigment containing macrophages in the spleen should have been addressed.

Conclusions:

The investigators found no differences between groups "in appearance, behavior, activity and mobility" and also no differences "with respect to consumption of feed and water". There were also no differences in respect to body weight gain and mortality.

The observations in hematological parameters, liver function tests, urinalysis, kidney function tests, blood sugar levels and cholesterol levels were not compound related and were not noted in the earlier study (BAYER AG Study # 1719) at the higher dose levels examined. The investigators did not conduct these measurements on the first day of the study (day 0) and there was a lack of historical control data for comparison.

Necropsy examinations found an increase in liver weight in the females, statistically significant at 60 ppm and a trend in males. Histopathology was unremarkable between groups.

A systemic No Observed Effect Level (NOEL) of 25 ppm can be set as determined by the increase in liver weight at 60 ppm, which is the Lowest Observed Effect Level (LOEL) for this study. The previous subchronic study (BAYER AG Study # 1719) could not establish a NOEL for the study (NOEL < 50 ppm) due to an increase in liver weight that was statistically significant at all 4 dose levels in the females.

Core Classification: Core-Supplementary Data based on the limited organs, the small number of animals examined for histopathology and the limited clinical chemistry that was conducted.

METRIBUZIN

Page_____ is not included in this copy.

Pages 108 through 110 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Data Review:

Study Identification:

Study Title: The Metabolism and Excretion of SENCOR in Rats.

EPA Identification Numbers:

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: Chemagro Division of Baychem Corporation
Research and Development Department

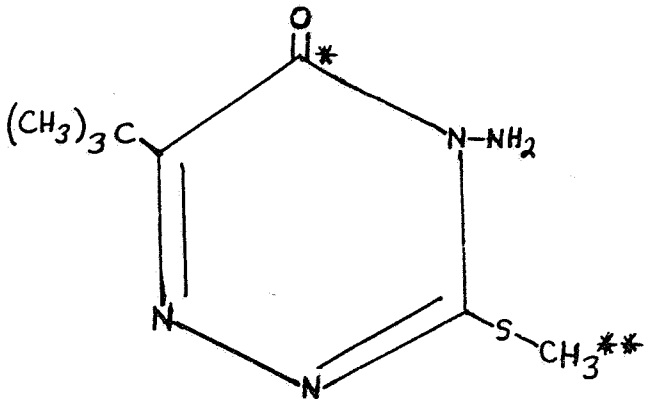
Report Number: 33366

Date of Study: May 1, 1972
Revised July 5, 1973 (to add additional information)

Study Authors: D.R. Flint
R.R. Gronberg
F.E. Sandie

Study Director: T.B. Waggoner

Test Compound: SENCOR [4-Amino-6-t-butyl-3-(methylthio)-1-2,4-triazin-5(4H)-one] (below) initially labeled with carbon-14 in the carbonyl group* and with tritium in the s-methyl group**.



Radiolabelled SENCOR

Dosages: First excretion study: 4 mg SENCOR - ^{14}C, ^{3}H in 0.8 ml 50% aqueous ethanol for a dose rate of 20 mg/kg in a 200 gm rat given orally by gavage (stomach tube).

Second excretion study and tissue residue studies: SENCOR (presumably ^{14}C labelled only , although not clearly stated) administered orally as a suspension in 0.5% aqueous gum tragacanth For animals weighing 150 to 165 gm, dosage volumes of 0.75 to 1.00 ml per animal were administered (presumably by gavage). The dose rates were calculated as 100 and 50 mg/kg for these studies.

Test Animals: Rats, Sprague-Dawley strain
Sprague-Dawley Company

Experimental: A copy of the experimental section from the investigators report is appended.

There was no clear indication as to how many animals were used at study initiation, however the results section states that one male and one female rat were used for the first excretion study, 2 males for the second excretion study and from the tables, 2 males and 2 females for the tissue residue studies. Also the age and sex of the animals was not given (although the results sections mentions male and female).

Apparently 2 excretion studies were conducted, one using glass metabolism cages with collection of respiratory gases and the other study using plastic with no collection of gases.

There was no mention of the purity of the test compound (a statement was made: "All equipment was standard except as listed and all chemicals were reagent grade or better.").

There was no indication of the time period for observation of animals (Guidelines state 7 days or until 90+% of the administered dose is excreted, with the animals in individual metabolism cages), although the individual tables in the final report state collection times.

The investigators examined expired air (only in the initial study for both ^{3}H and $^{14}CO_2$), urine, feces, blood, plasma, liver, kidney, heart, brain, muscle, testes, ovaries and fat. There was apparently no analysis of bone, lungs, spleen or residual carcass.

Results:

Excretion Studies:

The first study (using ^{14}C, ^{3}H labelled SENCOR) involved only 2 animals, one male and one female. The investigators reported sex related differences in excretion where in the male, 60.7% of the recovered radioactivity was found in the feces and in the female, 57.4% of the recovered radioactivity was found in the urine (over 90% of ^{14}C was recovered in urine and feces of both animals over a 16 day period). These values probably include measured ^{3}H levels as the total values on Table I do not totally agree. They further stated that no ^{14}C was recovered in the expired air. Sex related differences were also seen in the blood and tissue studies (to be discussed later).

The second study used 2 male rats (using only ^{14}C labelled SENCOR). The investigators found 45.89% of the radioactivity in the feces and 56.27% in the urine, from these finding they justified their reason for not collecting expired air, since the total was 102.16% of the administered radioactivity. See Table I. The excretion peak levels from this study were generally in agreement with the earlier study.

Table I: Excretion of Radioactivity (% of administered radioactivity)

Hours Post-Administration	Male		Female		2 Males	
	Urine	Feces	Urine	Feces	Urine	Feces
6.0	-	-	-	-	7.86	-
7.0	8.21	0.08	7.27	0.06	-	-
7.5	-	-	-	-	-	0.75
9.0	-	-	-	-	3.24	-
12.0	4.78	9.21	10.23	0.93	5.09	-
18.0	13.51	4.77	17.70	9.08	-	-
24.0	4.59	6.43	8.50	6.73	18.90	-
30.0	2.42	25.23	2.85	12.73	-	29.80
48.0	1.25	6.38	3.02	7.04	9.52	21.76
72.0	0.52	2.60	1.10	1.78	0.45	2.74
96.0	-	-	-	-	0.47	0.36
100.0	0.26	0.39	0.41	0.05	-	-
120.0	-	-	-	-	0.36	0.87
124.0	0.11	0.10	0.20	0.05	-	-
16 days	0.36	0.34	0.57	0.14	-	-
TOTAL	36.00	55.53	51.85	38.59	45.89	56.27

Data extracted from CHEMAGRO Report No. 33366 Tables I and II.

Tissue Residue Studies:

These determinations reportedly involved 2 male and 2 female rats. The investigators stated that the residue levels were "generally similar" between the male and female rats except at 28 hour (after administration) interval which showed the females retaining more of the radioactivity in all tissues examined. After this time point the decline is similar, however the females still show slightly higher levels. There were not enough animals for statistical evaluation. The investigators further state that this was due to "sex-related differences in rates of absorption, metabolism, distribution and/or excretion". The table which they present for "half-lives" compares different interval measurements. See Table II.

Table II: Radioactive Residues in Rat Tissues (estimated "half-lives" of total ^{14}C in hours)

Tissue	Male†	Female††
Brain	21.1	22.4
Heart	26.4	33.6
Liver	30.4	33.6
Kidney	26.9	31.2
Muscle	21.3	24.5
Testes or Ovaries	18.4	30.4
Fat	25.0†††	24.8
Blood Plasma	19.1	27.2

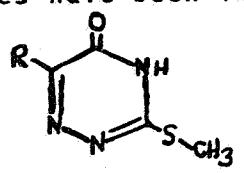
† - determined over a 24 to 96 hour interval.
†† - determined over a 48 to 96 hour interval.
††† - apparent biphasic decay curve after 24 hours.

Data extracted from CHEMAGRO Report No. 33366 Table III.

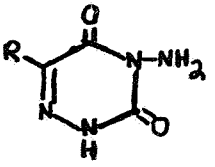
The investigators noted high tissue residue levels in liver and kidney (stated "presumably due to concentration in these organs for detoxification and elimination"). As can be seen in Table II the female rat presented with higher residue levels in heart, kidney, sex organs and blood plasma than the male rat.

Metabolite Identification:

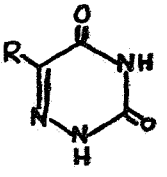
From earlier metabolism studies in the soybean plant, three metabolites have been identified.



A



B



C

R = tertiary butyl

A - DA, deaminated SENCOR, also called BAY Dic 2058
B - DK, diketo SENCOR
C - DADK, deaminated diketo SENCOR, also called BAY Dic 2164

These metabolites were also identified in the animal studies. However, not all the residues were accounted for in the present study and many of the methods employed by the investigators destroyed much of the primary metabolites; this was especially true for the conjugate hydrolysis methods. The investigators should have employed non-harsh methods which could have involved the pre-separation of the metabolites prior to analysis and then study each metabolite separately.

Urine:

The investigators employed thin-layer chromotography (TLC) methods for urine studies. They observed that very polar solvent systems were needed to separate the samples and stated that this indicated that there were "either highly polar metabolites or, more likely, conjugated metabolites".

Enzyme incubation did not substantially change the pattern urine metabolites. The investigators then employed acid hydrolysis and found that one third of the radioactivity in the urine was rendered organoextractable. The organoextractable fraction was submitted to gas chromotographic analysis and SENCOR, DA, DK and DADK metabolites were found.

From other experiments the investigators stated that they found that the conditions of hydrolysis (not given) can affect a near complete de-thiomethylation of SENCOR and the DA metabolite to produce the DK and DADK metabolites, therefore the procedure of using acid hydrolysis after enzyme treatment was not an accurate determination of urine metabolic distribution.

Studies with potatoes found that incubation in buffers of near neutral pH at 37°C could release significant amounts of SENCOR without other treatment.

A pooled 24 hour rat urine specimen was first deproteinized with perchloric acid and then extracted twice with isopropyl ether (IPE). The IPE extracts were analyzed by gas chromatography revealing small amounts of SENCOR and the 3 metabolites. The water soluble portion was analyzed by gel filtration. Two large fractions were found and were further treated by hydrolysis and ion-exchange chromatography. Although the investigators state that work in the area is not complete, they feel that significant amounts of the fractions they found from gel filtration are conjugates of SENCOR and its metabolites.

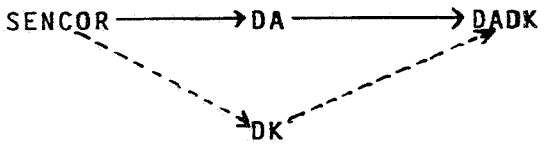
Tissues:

Liver and muscle tissues from male and female rats were homogenized in a two-phase water-chloroform system and each phase was assayed. They found slight differences in liver distribution of the compound between the male and female rats, whereas muscle distribution showed no sex related differences. The insoluble residue from the 28 hour female rat liver tissue extraction was also assayed using various enzymatic and hydrolytic methods (below).

The investigators evaluated several procedures and decided to employ a pepsin digestion followed by an acid hydrolysis of the aqueous phase. They were able to render 94-96% of the activity in the muscle, 55-78% of the activity in the liver and 43-58% of the activity in the kidney organosoluble. They could also render 63-96% of the activity of the brain and heart organosoluble without acid hydrolysis.

Tissues from male and female rats, collected at 4 and 28 hours after ^{14}C-SENCOR administration showed similar patterns of metabolites (no sex related differences). They determined that the DA metabolite appears early with the DK and DADK metabolite being produced at later intervals.

The scheme is as follows:



The investigators state that "the solid line indicates the more active pathway". However it is noted that on page 15 of the report both dotted lines point to "DK" and on page 16 one dotted line points to "DK" and the other to "DADK". The latter is consistent with the findings of the report.

Feces:

In a preliminary investigation the investigators tried organic extraction with acetone, methanol and then water. They were unable to extract the isotopes. TLC analysis yielded little information. No other procedures were tried.

Conclusions:

The excretion studies found sex related differences with the males excreting the radiolabel primarily in the feces and the females excreting the label primarily in the urine, however this reviewer feels that an inadequate number of animals was used in this study (one male and one female in one study and two males in another study). Tissue distribution studies also suggested slight sex related differences in distribution up to the 28 hour interval (after administration) with similar patterns of reduction in residue levels after that time point (however the females tended to present with higher overall levels at all time points measured). These studies also used an inadequate number of animals.

The investigators found a metabolic scheme for SENCOR in rats that was similar to what was found in an earlier study in soybeans. The metabolites that were identified are:

deaminated SENCOR (DA), also called BAY Dic 2058
diketo SENCOR (DK)
deaminated diketo SENCOR (DADK), also called BAY Dic 2164

Additional metabolites were not identified.

The following are the study deficiencies:

1. The numbers of animals used was inadequate.
2. The age of the animals was not provided.
3. The purity and clear isotope identification of the test compound was not given.
4. Rationale for time frame used for collection of urine, feces and expired air since there should have been some time points earlier than the 7.0 hour in one study and 6.5 in the other.
5. There was no tissue analysis of bone, lungs, spleen and residual carcass.

Core Classification: Core-Supplementary Data based on above deficiencies.

METRIBUZIN

Page_____ is not included in this copy.

Pages 118 through 124 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label. _____.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

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004262

Data Review:

Study Identification:

Study Title: The Metabolic Fate of Carbonyl ^{14}C-SENCOR in Dogs.

EPA Identification Numbers:

Sponsor: Mobay Chemical Corporation
Chemagro Agricultural Division
Kansas City, Missouri 64120

Testing Laboratory: Chemagro
Division of Baychem Corporation
Research and Development Department

Report Number: 33361

Date of Study: May 1, 1972

Study Authors: A.M. Khasawinah
D.R. Flint
H.R. Shaw
D.D. Cox

Study Director: T.B. Waggoner

Test Compound: Carbonyl carbon-14 label SENCOR with a specific activity of 1.45 mC/mM.
Radiochemical purity >99% (determined by thin-layer chromatography).
This chemical was diluted with unlabeled pure crystalline SENCOR to give a specific activity of 2273 dpm/ug (0.22 mC/mM).

Dosage: 200 mg oral dose of the labeled material in a gelatin capsule (#000), giving an approximate 10 mg/kg (body weight) dose.

Test Animal: Adult male dogs (3 hounds and 1 mongrel)
Supplier: Mr. George C. Lindquist
Hallsville, Missouri 65255

Experimental: A copy of the experimental section from the investigators report is appended.

No justification/reasoning was provided for the use of dogs in this study (unless this is a preliminary study for developing information on comparative metabolism).

The age of the animals was not provided.

Only one dose level was employed in this study. According to the Guidelines "at least two dose levels should be used, the low dose level should correspond to the no-effect level and the upper dose should produce toxic or pharmacologic signs, but should not produce severe effects or a high incidence of mortality which would prevent a meaningful evaluation."

The 4 dogs were sacrificed at different time periods (4, 24, 72 and 120 hours), these points did not provide much overlap in time periods especially in terms of collection of excretion products.

The expired air from the dogs was not collected. However in a study in rats conducted concurrently with this study, the investigators determined that no radiolabel (^{14}C) was excreted in the expired air.

The following tissue samples were collected: liver; heart; kidney; muscle; fat; brain; skin. There was no evidence that samples of bone, sex organs, lung, spleen or residual carcass were collected.

Results:

Absorption and Distribution in Tissues:

The investigators state that there was rapid absorption of the ^{14}C label from the gastrointestinal (GI) tract. They claim that maximum absorption from the GI tract occurs at 4 hours after administration of radiolabeled SENCOR. Blood samples were taken at 1, 2, 4 hours and greater intervals and the peak levels were found at the 4 hour period. However, the investigators also state this time point for maximum tissue levels, this claim cannot be made for the tissue levels since the first tissue samples were checked at 4 hours and only in one animal with the next animal sacrificed at 24 hours post administration.

They found 40-99% of the radioactivity as free SENCOR and its metabolites (specifically the deaminated (DA) metabolite). Fat tissue contained mostly non-metabolized SENCOR while liver tissue presented with a greater quantity of metabolites.

The investigators found that radioactive tissue residues declined after 4 hours, again assessed by individual time points in a single dog. They state that the $T_{1/2}$ of the tissue residues was less than 24 hours. However, it appears that the $T_{1/2}$ in the tissues could not be precisely determined due to an inadequate number of animals and time points for collection of tissues.

The investigators reported that the radioactivity in blood was first primarily found in the plasma and later in the red blood cells.

Excretion Studies:

A rapid excretion of metabolites in the urine was not found, however, this conclusion is limited by the small number of animals Combined urine and fecal radioactivity was 89.4% for animal # 2 (72 hour) and 85.9% for animal # 4 (120 hours). When combined with tissue residue levels, recovered radioactivity for animal # 2 is 94.2% and animal # 4 is 88.0%.

Tissue Metabolite Studies:

The investigators determined that the radioactivity in the tissues could not be extracted by organic solvents after 24 hours, therefore they tried enzymatic and chemical hydrolysis.

Papain and trypsin treatment of tissue from a 24 hour liver helped solubilize the radioactivity in water (66-88%) but no increase in the organoextractable fraction (4-5%) was seen.

Acid hydrolysis of a 24 hour liver sample yielded 92% of the radioactivity in the tissue organosoluble.

Steam autoclaving combined with acid hydrolysis of liver and kidney tissue samples was found to render nearly all the radioactivity organosoluble (liver - 86 to 120%, kidney - 65 to 96%), but the investigators found it did not yield a true pattern of metabolites. One-hundred twenty percent of the radioactivity of the 120 hour liver sample was found to be organoextractible.

Urine Metabolite Studies:

According to the investigators, thin-layer chromatography (TLC) studies at 4, 24 and 48 hours were not successful since they observed no movement of the sample on the plates. Also, since the investigators could not find any organoextractable radioactivity, they concluded that no free SENCOR or metabolites were eliminated in the urine.

Gel permeation chromatography studies yielded 2 peaks. From this finding the investigators then subjected the 24 hour urine samples to "specific enzymatic chemical and general enzymatic (bacterial) hydrolysis". Very little of the radioactivity was found to be organoextractable and they concluded that the metabolites were not o-glucuronide or aryl-sulfate conjugates.

Acid hydrolysis in combination with autoclaving was more successful in releasing radioactivity while incubation of the urine with E. coli was not helpful.

Fecal Metabolite Studies:

The investigators determined by TLC that 81% of the fecal radioactivity through 24 hours was unchanged SENCOR, while studies on samples from longer than 24 hours found that little radioactivity was organosoluble. Acid hydrolysis in an autoclave could release 80% of this radioactivity.

Conclusions:

Analysis of blood samples showed a peak level at 4 hours. However due to the small number of animals used, the time of the peak level in the tissues could not be determined. The excretion study data indicated that 52 to 60% of the administered dose was eliminated in the urine and 30% in the feces. The true patterns of metabolites could not be accurately determined. However, it appeared that the same metabolites found in an earlier study in soybeans and a concurrent study in rats were present in this study. They are as follows:

DA - deaminated SENCOR
DK - diketo SENCOR
DADK - deaminated, diketo SENCOR

The deficiencies of this study are as follows:

1. Inadequate number of animals (especially for the tissue distribution studies).

2. At least two dose levels are required (see page 2 of this review).

3. The justification for the use of dogs for this study.

4. The age of the animals in the study was not reported.

5. There was no analysis of bone, sex organs, lung, spleen or residual carcass.

Core Classification: Core-Supplementary Data based on above deficiencies.

METRIBUZIN

Page_____ is not included in this copy.

Pages 129 through 132 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

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United States
Environmental Protection
Agency

Office of
Pesticides and Toxic Substances
Washington DC 20460

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#033D

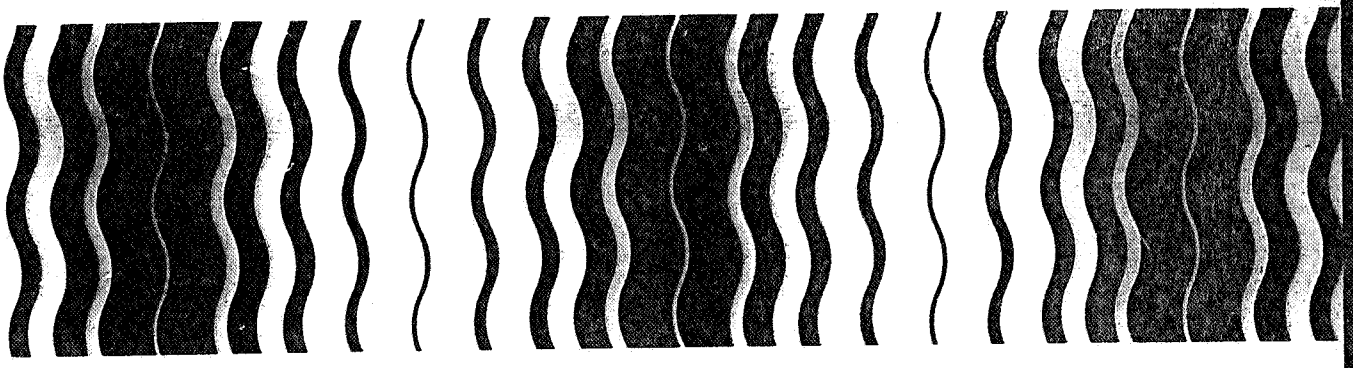
Pesticides

EPA

Guidance for the Reregistration of Pesticide Products Containing Metribuzin

Doc# 004262

(1) DOUGLAS CAMPT
REGISTRATION DIVISION TS-767



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004262

GUIDANCE FOR THE REREGISTRATION OF PESTICIDE PRODUCTS CONTAINING METRIBUZIN AS THE ACTIVE INGREDIENT

EPA CASE NUMBER 181

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
WASHINGTON, D.C. 20460

June 1985

004262

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APPENDICES

INTRODUCTION

004262

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA sec. 3(g)) directs EPA to reregister all pesticides as expeditiously as possible.

To carry out this task, EPA has established the Registration Standards program, which will review all pesticide products containing active ingredients first registered before January 1, 1977. Pesticides will be reviewed in use clusters which have been ranked to give earliest review to pesticides used on food and feed crops.

The Registration Standards program involves a thorough review of the scientific data base underlying pesticide registrations and an identification of essential but missing studies which may not have been required when the product was initially registered or studies that are now considered insufficient. EPA's reassessment results in the development of a regulatory position, contained in a Registration Standard, on each pesticide and its uses. The Agency may require the registrant to modify product labels to provide additional precautionary statements, restrict the use of the pesticide to certified applicators, provide reentry intervals, modify uses or formulation types, specify certain packaging limitations, or other requirements to assure that proper use of the pesticide will not result in adverse effects on the environment.

The scientific review, which is not contained in this Guidance Package but is available upon request, concentrates on the technical grade of the active ingredient and identifies missing generic data. However, during the review of these data we are also looking for potential hazards that may be associated with the end use (formulated) products that contain the active ingredient. If we have serious concerns, we will address end use products as part of the Registration Standards program and will propose regulatory actions to the extent necessary to protect the public.

EPA has the authority under FIFRA sec. 3(c)(2)(B) to require registrants to submit data that will answer our questions regarding the hazard that may result from the intended use of a pesticide. Although sec. 3(c)(2)(B) provides that all registrants are responsible for these data, the Agency generally imposes generic data requirements only on the registrants of the manufacturing use products (basic suppliers

of the active ingredient) and other producers who do not qualify for the formulator's exemption.*

A producer who wishes to qualify for the formulator's exemption may change his source of supply to a registered source, provided the source does not share ownership in common with the registrant's firm. A registrant may do so by submitting a new Confidential Statement of Formula, EPA Form 8570-4, identifying the registered source of the active ingredient, to the appropriate Product Manager within 90 days of receipt of this Guidance Document. The chart on the following page shows what is generally required of those who do and do not qualify for the formulator's exemption in the Registration Standards program.

If you decide to request the Agency to cancel the registration of any of your products subject to the requirements of this Guidance Document, please notify the Product Manager named in the cover letter, within 90 days from the receipt of this document. If you decide to maintain your product registration(s), you must provide the information described in the following pages within the timeframes outlined. EPA will issue a notice of intent to cancel or suspend the registration of any currently registered product which does not comply with the requirements set forth in this Guidance Document.

You are reminded that FIFRA sec. 6(a)(2) requires you to submit factual information raising concerns of possible unreasonable adverse effects of a pesticide. You should notify the Agency of interim results of studies in progress if those results show possible adverse effects.

*The formulator's exemption applies to a registrant of an product if the source of his active ingredient(s): (1) is a registered product and (2) is purchased from a source which does not have ownership in common with the registrant's firm.

PRODUCTS SUBJECT TO THE REGISTRATION STANDARDS PROGRAM	ACTION(S) REQUIRED TO MAINTAIN REGISTRATION
I. Products That Do Not Qualify For The Formulator's Exemption A. Single Active Ingredient Products*	These products must be reregistered. To obtain reregistration, labeling, packaging and data requirements must be satisfied in accordance with the Registration Standards Guidance Document.
B. Multiple Active Ingredient Products	These products will not be reregistered at this time. However, generic data required to continue the registration of the active ingredient under review, as described in the Registration Standards Guidance Document, will be required and some labeling precautions may also be required.
II. Products That Do Qualify For The Formulator's Exemption	Only when additional restrictions or labeling are needed to protect man or the environment will these products be subject to the Registration Standard requirements. Affected products will be dealt with in a variety of ways, including but not limited to the Label Improvement Program and special intent to cancel notices.

* End use products of registrants who also produce a manufacturing use product will not be required to be reregistered provided that registrant fulfills the requirements specified in the Guidance Document for manufacturing use product(s). Such end use products will be subject to the labeling changes required for products in "II" above. If there are no manufacturing use products registered by any company end use products will be required to be reregistered.

NOTE: If all registrants in "I" above fail to meet the requirements in I-A and B above, then the registrants in "II" lose their right to qualify for the formulator's exemption and become subject to the requirements in I-A and B.

II. REGULATORY POSITION AND RATIONALE

A. INTRODUCTION

This Registration Standard describes the regulatory position and rationale of the Environmental Protection Agency ("The Agency") for all registered manufacturing-use products (MP's) and end-use products (EP's) containing metribuzin as the sole active ingredient. The Agency bases its position and rationale on an evaluation of all MP's, and FIFRA sections 3 and 24(c) and intrastate uses registered for metribuzin. EP's are reviewed only when there are no MP's registered or when the label has been changed significantly from the current accepted label. Mixtures are included only when there is a significant change in the label. After briefly describing the chemical and its uses, this chapter presents the Agency's regulatory position and rationale, the criteria for registration, acceptable ranges and limits, labeling requirements, and the tolerance reassessments.

B. DESCRIPTION OF CHEMICAL

Metribuzin is the acceptable common name for the compound: 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H) one as determined by the British Standards Institution, International Organization for Standardization, and Weed Science Society of America. Other names include Lexone, Sencor, Sencoral, Sencorex, 4-amino-6-tert-butyl-3-(methylthio)-1,2,4-triazin-5(4H)-one, 4-amino-6-tert-butyl-4,5-dihydro-3-methythio-1,2,4-triazin-5-one, 4-amino-6-tert-butyl-3-(methylthio)-triazin-5(4H)-one, metribuzin, Bayer 94337, Bayer 6159H, Bayer 6443H, and DIC 1468. The Chemical Abstracts Service (CAS) Registery number is 21087-64-9. The Office of Pesticide Program's EPA Chemical Code Number is 101101.

Metribuzin is a white crystalline solid at room temperature and has a sulfurous odor. The empirical formula is $C_8H_{14}N_4OS$, and its molecular weight is 214.28. The melting point is 125.5-126-5 °C. Metribuzin is soluble in aromatic and chlorinated hydrocarbon solvents, and in water (at 20 °C) to 1220 ppm.

Metribuzin is a triazine herbicide which selectively controls certain broadleaf weeds and grassy weed species on field crops, vegetable crops, bermuda grass (turf) and noncrop areas. Metribuzin may be soil incorporated, surface applied or applied foliarly, broadcast or banded using ground equipment. It can be applied by aerial equipment or sprinkler irrigation (potatoes). Of the total amount of metribuzin used in the United States 94 percent is on soybeans, $\sim$ 1.8 percent on potatoes, $\sim$ 1.5 percent on wheat, and $\sim$ 1.2 percent on sugarcane.

Metribuzin is a systemic herbicide which is absorbed by the root system and then travels through the plant causing chlorosis, growth inhibition and necrosis. Metribuzin is a photosynthetic inhibitor. Metribuzin was first registered for use in 1973. Technical metribuzin is produced in the United States by Mobay Chemical Corporation of Kansas City, Missouri.

Metribuzin is available as a 50 percent formulation intermediate (FI) and 94 percent technical for formulation of metribuzin end-use products. Metribuzin is available as a wettable powder (WP), flowable concentrate (FlC), and dry flowable (DF) formulations.

C. REGULATORY POSITION AND RATIONALE

Based on the review and evaluation of all available data and other relevant information on metribuzin, the Agency has made the following determinations:

1. The available data do not indicate that any of the risk criteria listed in 162.11(a) of Title 40 of the U.S. Code of Federal Regulations have been met or exceeded for the uses of metribuzin at the present time.

Rationale: Only minor or no discernible toxicity by the oral, dermal, inhalation and ocular routes of exposure was observed. The 2-year dog study satisfied the requirement for a chronic and subchronic dog study. This study indicated that dogs dosed with 1500 ppm (37.5 mg/kg) had reduced weight gain, increased mortality, hematological changes and liver and kidney damage. These observations were not seen at lower dosages, and the Acceptable Daily Intake (ADI) was based on the NOEL of 100 ppm (2.5 mg/kg) as shown in section G. The oncogenic potential of metribuzin is unclear at this time. Although the chronic mouse study study is negative for oncogenic effects, the chronic rat study (currently classified as "supplementary data") indicates a statistically significant ($p < 0.05$) increase in the incidence of adenoma of the liver bile duct and pituitary gland in females at the 300 ppm dose level. However, only a small number of animals were examined histopathologically from other dose levels and at this point it is not clear whether the apparent increase is related to compound administration. Additional data must be supplied in the form of histopathological examinations in the animals not previously examined in the other three dosage groups along with historical control data on the on the incidence of these tumors in this particular rat strain. Exact nomenclature (terminology used) used for neoplastic and non-neoplastic findings, specifically live bile duct adenoma, "changes in nucleus" in the liver and "tumor" must be defined. A teratology study in rabbits indicated no evidence of teratogenic effects at 135 mg/kg/day, the highest dose tested (HDT) and a NOEL of 15 mg/kg/day for maternal and fetal toxicity. The available data indicate no mutagenic effects.

In addition to a repeat of the rat chronic study, other data gaps include rat teratology, multigeneration reproduction study, two categories of mutagenicity testing, specifically gene mutatuion testing, studies in mammalian cells and tests for primary DNA damage such as sister chromatid exchange or unscheduled DNA synthesis assay.

2. Products which are substantially similar to the registered products may be considered for registration subject to the terms and conditions of this document. However, the Agency will not allow any significant new uses* to be established for metribuzin until the toxicology and residue chemistry data deficiencies identified in Table A have been satisfied.

Rationale: The Agency does not think new registrations of uses already on the market will increase the risks to the public from exposure to metribuzin because the total amount of product used will not increase. The Agency is unable to complete a tolerance reassessment of metribuzin because of extensive residue chemistry data gaps including additional metabolism data in plants, poultry, ruminants and additional data on crop and processed commodities. Toxicology data gaps include rat chronic, rat teratology and a multigeneration reproduction study. If additional metabolites of toxicological concern are found in the requested metabolism studies, the tolerance expression will have to be changed to include the additional metabolite(s) of concern.

3. The Agency will require MP's containing metribuzin to bear Category III hazard statements and other warning statements as required in the precautionary labeling under 40 CFR 162.10.

Rationale: Acute toxicity studies for metribuzin showed the following: Toxicity Category III for oral toxicity and Toxicity Category IV for acute inhalation and for dermal and primary eye irritation.

4. The Agency is requesting information on presence of N-nitroso contaminants in the 94 percent T and 50 percent FI, but is not taking action at this time.

Rationale: Compounds of similar structure including cyanazine, atrazine, simazine, pendimethalin, and parathion have been shown to contain N-nitroso contaminants. Available data, although incomplete, do not provide grounds for concern at this time. Action is reserved pending submission and review of the requested data.

* "Significant New Use" is defined in 44 FR 27934, May 11, 1979. In case of new food or feed use, the Agency will consider as significant an increase in the Theoretical Maximum Residue Contribution of greater than 1 percent.

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5. The Agency is requiring acute testing of metribuzin on a marine/estuarine fish species and an oyster species, and an acute dietary study on an upland gamebird species. No additional precautionary labeling or field testing is being required at this time. For the present, the Agency is requiring MP's and EP's containing metribuzin to bear revised environmental hazard statements (Refer to Section F, REQUIRED LABELING).

Rationale: Ecological effects studies indicate that available data on metribuzin are adequate to fulfill regulatory requirements in most areas and that metribuzin was moderately toxic to upland bird species on an acute oral basis, no more than slightly toxic to birds in the diet, moderately toxic to Daphnia magna and slightly toxic to freshwater fish. Marine/estuarine species may be exposed to metribuzin used on sugarcane and soybeans. Available data indicate that metribuzin is slightly toxic to shrimp. Data on acute toxicity to a marine/estuarine fish species and an oyster species are needed. Directions for some use patterns indicate that applications can be repeated. Available information indicates that metribuzin is very persistent in the soil. Multiple treatments could increase dietary risk and a long soil half-life may indicate a significant chronic exposure. Environmental fate information is needed to determine the potential for chronic exposure. A detailed ecological hazard assessment cannot be made until the acute dietary study on an upland gamebird, acute toxicity studies on a marine/estuarine fish species and an oyster species, and appropriate environmental fate data are submitted. All other testing is reserved pending submission and review of these data.

6. The Agency is requiring a statement on the label concerning endangered plants on all EP's for use of metribuzin on non-cropland (specifically, rights-of-way). Refer to Section F, REQUIRED LABELING.

Rationale: Consultation with Office of Endangered Species (OES) on another chemical, sulfometuron methyl (Oust Herbicide) indicates that several species of endangered plants including Brady pincushion eactus (Pediocactus bradyi), Mesa Verde cactus (Sclerocactus mesae-verdae), Peebles Navajo cactus (Pediocactus peeblesianus var. peeblesianus), Wright fishhook cactus (Sclerocactus wrightiae), Kuenzler hedgehog cactus (Echinocereus kuenzleri), Lloyd's hedgehog cactus (Echinocereus lloydii), Sneed pincushion cactus (Coryphantha sneedii var. sneedii), Chapman rhododendron (Rhododendron chapmanii), Rydbergy milk-vetch (Astragalus perianus), Harper's beauty (Harperocallis flava), dwarf bear-poppy (Arctomecon humilis), MacFarlane's four-o'clock (Mirabilis macfarlanie), northern wild monkshood

(Aconitum noveboracense), gypsum wild buckwheat (Eriogonum gypsophilum), Texas poppy-mallow (Callirhoe scabriuscula), hairy rattleweed (Baptisia arachnifera), Malheur wire-lettuce (Stephanomeria malheurensis), phacelia (Phacelia argillacea), bunched arrowhead (Sagittaria fasciculata), San Diego mesa mint (Pogogyne abramsii), Solano grass (Orcuttia mucronata), salt marsh bird's beak (Cordylanthus maritimus ssp. maritimus), Uinta Basin hookless cactus (Sclerocactus glaucus), Contra Costa wallflower (Erysimum capitatum var. angustatum), and Antioch Dunes evening-primrose (Oenothera deltoides ssp. howelli), which occur on or adjacent to rights-of-way may be potentially exposed to metribuzin, when used in rights-of-way, and this exposure would cause mortality to contacted plants. Because of the limited population size of many of these species a local spraying program could virtually destroy the entire species. Exposure to metribuzin is likely to result in the destruction or adverse modification of the critical habitat of gypsum wild buckwheat, Malheur wire-lettuce, Contra Costa wallflower, and Antioch Dunes evening-primrose.

7. The Agency is imposing restrictions on rotational crops. The extent of these restrictions will be reconsidered when additional data are received (Refer to Section F, REQUIRED LABELING).

Rationale: It is the policy of the Agency to impose restrictions on planting rotational crops when data are insufficient to allow an assessment of the impact of planting subsequent crops. This serves to protect the public from impermissable residues in food and feed and to protect subsequent planted crops from adverse effects due to persisent residues.

8. The Agency will require ground water monitoring studies for metribuzin. The registrants will be notified of types of studies required and sites to be tested (the Agency is in the process of determining the types of studies and sites to be tested), by means of an amendment to the Standard three months after issuance of the Standard. The Agency is requireing that a ground water advisory appear on the label of all EP's (Refer to Section F, REVISIED LABELING).

Rationale: Metribuzin was detected in the low parts-per-billion range in Ohio rivers and Iowa wells. Although there are several data gaps in the area of environmental fate, the available data indicate metribuzin has a potential to contaminate ground water in soils lower in organic matter and clay content. Both the soil absorption and column studies reviewed indicate that metribuzin has considerable potential to leach in a number of soil types. Metribuzin dissipates in the field with half-lives of < 1 to about 6 months. Data gaps in the area of environmental

fate include hydrolysis, photodegradation, aerobic and anaerobic soil metabolism, leaching, absorption/desorption studies, field dissipation and accumulation studies in crops and fish.

However, hydrolysis, photodegradation in water and on soil, aerobic and anaerobic soil metabolism, mobility and field dissipation were requested on July 25, 1984 for ground water contamination assessment through the Data Call-in process. The data were received on November 1984. These studies have been screened and support the Agency's concern over the potential for ground water contamination and the need for the ground water monitoring.

9. The Agency has determined that all uses of metribuzin should be classified for "RESTRICTED USE" with appropriate labeling (Refer to Section F, REQUIRED LABELING and SECTION IV of the Guidance Document).

Rationale: Metribuzin has been detected in the low parts per billion range in Ohio rivers and Iowa wells. The chronic rat study indicates a significant ($p<0.05$) increase in the incidence of adenoma of the liver bile duct and pituitary gland in females of the 300 ppm dose level. In addition to a repeat of this study data gaps include rat teratology, multigeneration rat reproduction study and mutagenicity testing.

10. The Agency is not requiring a re-entry interval for currently registered uses of metribuzin at this time.

Rationale: Metribuzin has low acute toxicity (Category III) for oral and Category IV for all other forms of acute toxicity.

D. CRITERIA FOR REGISTRATION UNDER THIS DOCUMENT

To be subject to this guidance document, MP's must meet the following conditions:

1. Contain metribuzin as the sole active ingredient and,

2. Conform to the acute toxicity limits, production composition, and use pattern requirements listed in Section F of this document.

Registration of products subject to this document must comply with all terms and conditions described in it, including commitment to fill data gaps on a schedule acceptable to EPA and consistent with that required of the present registrant. All registrants and applicants for registration under this document must follow the instructions contained in this document and complete and submit the appropriate forms within the specified time.

E. ACCEPTABLE RANGES AND LIMITS

1. Product Composition Standard

Technical grade products must contain at least 94.0 percent metribuzin as the sole active ingredient. MP's must contain 50 percent metribuzin as the sole active ingredient. Each MP formulation proposed for registration must be fully described active ingredient found in MP's must be substantially similar to that in currently registered technical products or manufacturing-use products. An MP not meeting these requirements will be considered a new product and will not be registerable under this guidance document.

2. Acute Toxicity Limits

The Agency will reconsider registrations of products containing metribuzin, provided that the product labeling bears appropriate precautionary statements for the acute toxicity category in which each product is placed.

3. Use Patterns

To be registered under this standard, MP's containing metribuzin must be labeled for formulation only into end-use herbicide products for commodities listed below. The attached index entry lists all registered uses, as well as approved maximum application rates and frequencies of application.

Metribuzin, a selective herbicide is registered for control of broadleaf and grassy weed species on the following sites: soybeans, potatoes, alfalfa, sainfoin, asparagus, barley, field corn, sugarcane, tomatoes, wheat, turf (bermuda grass), peas, lentils, and noncrop sites.

F. REQUIRED LABELING

All technical grade products, MPs and EPs containing metribuzin must bear appropriate labeling as specified in 40 CFR Section 162.10. Other portions of this guidance package contain information regarding label requirements.

In addition to the requirements stated in 40 CFR Section 162.10, the following information must appear on the labeling of products released for shipment after December 31, 1985, and on products in the channels of trade after June 30, 1986.

1. Ingredient Statement

The ingredient statement for MPs must list the active ingredient as:

Metribuzin, 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)one

2. Manufacturing-Use Product Statements

All products intended for formulation into end-use products must bear the following statement:

"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or public water unless this product is specifically identified and addressed in an NPDES* permit. Do not discharge effluent containing this product to sewer systems without previously notifying in writing the sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of EPA."

* National Pollution Discharge Elimination System.

3. End-Use Products

Restricted Use

All products must be classified at "RESTRICTED USE" with appropriate language (Refer to 40 CFR 160.10(j)(2)(B).

Ground Water Advisory

"Metribuzin is a chemical which can travel (seep or leach) through soil and can contaminate ground water which may be used as drinking water. Metribuzin has been found in ground water as a result of agricultural use. Users are advised not to apply metribuzin where the water table (ground water) is close to the surface and where the soils are very permeable, i.e., well drained soils such as loamy sands. Your local agricultural agencies can provide further information on the type of soil in your area and the location of ground water."

Outdoor Uses

"Do not apply directly to water or wetlands. Do not contaminate water by cleaning of equipment or disposal of waste."

Endangered Species - Noncropland (Rights-of-Way)

Notice: The use(s) of this product on rights-of-way may pose a hazard to certain Federally designated endangered plant species. They are known to be found in specific areas within the locations noted below. Prior to making applications, the user of this product must determine that no such species are located in or immediately adjacent to the area to be treated. For information on protected species contact the Endangered Species Specialist of the appropriate Regional Office of the U.S. Fish and Wildlife Service listed below:

Region 1-Portland, Oregon
California counties of Contra Costa, Solano, San Diego, Santa Barbara, Ventura, Los Angeles and Orange.
Idaho, Idaho county.
Oregon, Harney county.
Region 2-Albequerque, New Mexico
Arizona counties of Coconino and Navajo.
New Mexico counties of San Juan, Otero, Chaves, Lincoln, Eddy and Dona Ana.
Texas counties of El Paso, Pecos and Runnels.
Region 3-Twin Cities, Minnesota
Iowa counties of Allamakee, Clayton, and Jackson.
Region 4-Atlanta, Georgia
Florida counties of Wayne and Brantley.
North Carolina, Henderson county.
South Carolina, Greenville county.
Region 5-Newton Corner, Massachusetts
New York, Ulster county.
Region 6-Denver, Colorado
Utah counties of Emery, Piute, Garfield, Washington, Utah and Wayne.
Colorado counties of Montezuma, Delta and Montrose.

Restrictions on Rotational Crops

"Do not plant food or feed crops other than those which are registered for use on metribuzin treated soils."

G. TOLERANCE REASSESSMENT

The Acceptable Daily Intake (ADI) for metribuzin was originally based on a 2-year feeding study in rats. The ADI was subsequently recalculated using a 2-year chronic dog feeding study because it resulted in a lower no-observable effect level (NOEL) of 100 parts per million (ppm).

The 2-year chronic rat feeding study was rereviewed and classified as supplementary data for the reasons stated in Section c(1). The 2-year chronic dog study was rereviewed and found adequate for regulatory purposes. It is recommended that the ADI continue to be based on this chronic dog study.

Using a 100-fold safety factor and the 100 ppm (2.5 mg/kg) NOEL from the dog study, the ADI was determined to be 0.025 mg/kg/day with a Maximum Permissible Intake (MPI) of 1.5 mg/kg for a 60 kg adult human. Theoretical maximum residue contribution (TMRC) for metribuzin based on established tolerances is 0.3508 mg/day for a 1.5 kg diet. Currently, the permanent tolerances utilize 23.39 percent of the ADI.

The Agency is unable to complete a full tolerance reassessment because the available metribuzin toxicology and residue data do not fully support the established tolerances listed below. The metabolism of metribuzin in animals is not fully understood. Therefore, the Agency is requiring data on metabolism of metribuzin and related metabolites in ruminants, poultry and several crops. An acceptable long-term rat study is required. The additional data will be used to assess dietary exposure to metribuzin and may lead to revisions in the existing tolerances. Therefore, the Agency will not grant any pending significant or new tolerances for metribuzin until the data are submitted.

In the United States, tolerances are currently established in 40 CFR Section 180.332 for the combined residues of the herbicide, 4-amino-6-(1,1-dimethylethyl)-3-(methythio)-1,2,4-triazin-5(4H)-one and its triazinone metabolites in or on the raw agricultural commodities listed below:

Commodities	Parts Per Million
Alfalfa, green	2.0
Alfalfa, hay	7.0
Asparagus	0.05
Barley grain	0.75
Barley, straw	1.0
Cattle, fat	0.7
Cattle, mbyp	0.7
Cattle, meat	0.7
Corn, fodder	0.1
Corn, forage	0.1
Corn, fresh (inc. sweet k +CWHR)	0.05
Corn, grain (inc. popcorn)	0.05
Eggs	0.01
Goats, fat	0.7
Goats, mbyp	0.7
Goats, meat	0.7

Grass	2.0
Grass, hay	7.0
Hogs, fat	0.7
Hogs, mbyp	0.7
Hogs, meat	0.7
Horses, fat	0.7
Horses, mbyp	0.7
Horses, meat	0.7
Lentils (dried)	0.05
Lentils, forage	0.5
Lentils, vine hay	0.05
Milk	0.05
Peas	0.1
Peas (dried)	0.05
Peas, forage	0.5
Peas, vine hay	0.05
Potatoes	0.6
Poultry, fat	0.7
Poultry, mbyp	0.7
Poultry, meat	0.7
Sainfoin	2.0
Sainfoin, hay	7.0
Sheep, fat	0.7
Sheep, mbyp	0.7
Sheep, meat	0.7
Soybeans	0.1
Soybeans, forage	4.0
Soybeans, hay	4.0
Sugarcane	0.1
Tomatoes	0.1
Wheat, forage	2.0
Wheat, grain	0.75
Wheat, straw	1.0

In the United States tolerances are currently established in 21 CFR 193.25 for the combined residues of the herbicide 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one and its triazinone metabolites in or on the following processed foods when present therein as a result of application of this herbicide to growing crops:

Food	Parts Per Million
Barley, milled fractions (except flour)	3.0
Potatoes, processed (inc. potato chips)	3.0
Sugarcane molasses	2.0
Wheat, milled fractions (except flour)	3.0

In the United States tolerances are currently established in 21 CFR 561.41 for combined residues of the herbicide 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one and its triazinone metabolites in the following processed feeds when present therein as a result of application of this herbicide to growing crops:

Feed	Parts Per Million
Barley, milled fractions (except flour)	3.0
Potato waste, processed (dried)	3.0
Sugarcane bagasse	0.5
Sugarcane molasses	0.3
Tomato pomace, dried	2.0
Wheat, milled fractions (except flour)	3.0

International Tolerances

Canadian Tolerances

Tolerances for residues of metribuzin are established in Canada for asparagus at 0.1 ppm, barley grain at 0.1 ppm, lentils at 0.1 ppm, peas at 0.1 ppm, potatoes at 0.5 ppm, soybeans at 0.1 ppm, tomatoes at 0.1 ppm and wheat grain at 0.1 ppm. Although these tolerances differ from those in the United States, it is inappropriate for the Agency to harmonize these tolerances at the present time because of the extensive toxicology and residue chemistry data gaps. At the time the indicated data gaps for residue chemistry and toxicology are filled we will reassess harmonizing these tolerances.

There are no tolerances for residues of metribuzin in Mexico or Codex Alimentarius.

h101101 4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE*

TYPE PESTICIDE: Herbicide

FORMULATIONS:
FI (50%)
WP (50%, 70%, 75%)
FlC (4 lb/gal)

GENERAL WARNINGS AND LIMITATIONS: A selective herbicide used for preemergence or early postemergence control of certain grasses and broadleaf weeds. Moisture is necessary to activate the chemical; for best results apply to moist soil. Rainfall or sprinkler irrigation within 2 weeks after application will improve effectiveness. Degree and duration of control will vary with dosage, soil type, soil texture, rainfall and other conditions. Heavy rains soon after application will cause injury to the crop. For best results, postemergence applications should be made when weeds are less than 1.5 inches tall. Where a dosage range is given, use the lower dosage on coarse and medium textured soils or soils with lower organic matter content (0.5 to 2 percent); use the higher dosage on fine soils or soils with higher organic matter content (more than 2 percent). Silty clay loams are transitional soils which may be classified as medium soils in some regions of the United States, and as fine soils in other regions. Do not use on sandy soils. When tank mixes are used, observe all cautions and limitations given on the labeling of tank mix chemicals. Apply in 10 to 40 gallons of water per acre by ground or 2 to 10 gallons by air, unless otherwise noted. Tolerances have been established for the combined residues of metribuzin and its triazinone metabolites.

Livestock Tolerances:

Cattle (fat, meat, mbyp)	0.7 ppm
Eggs	0.01 ppm
Goats (fat, meat, mbyp)	0.7 ppm
Hogs (fat, meat, mbyp)	0.7 ppm
Horses (fat, meat, mbyp)	0.7 ppm
Milk	0.7 ppm
Poultry (fat, meat, mbyp)	0.7 ppm
Sheep (fat, meat, mbyp)	0.7 ppm

DEFINITION OF TERMS:
K+CWHR = kernel plus cob with husk removed
mbyp = meat byproducts
lb = pounds
a.i. = active ingredient

*Metribuzin
Lexone
Sencor
4-amino-6-tert-butyl-3-(methylthio)-as-triazin-5(4H)-one

TIME REQUIRED FOR CONTROL: Not located.

PHYTOTOXICITY TO TARGET WEEDS: Not located.

PHYTOTOXICITY TO CROPS: Not located.

MODE OF ACTION: Inhibits photosynthesis.

BROADLEAF WEEDS CONTROLLED:

PBFADAA	Ageratum	(a)
PCQAUAA	Beggarweed	(a)
PBKAKBA	Blue mustard	
PEWAIBF	Buffalobur	
PZAAABW	Bur buttercup	
PFFAFBA	Bur beakchervil	
PADABBA	Carpetweed	(a)(c)
PAZAAAC	Chickweed	
PBFDQAA	Cocklebur	(a)(b)(c)
PCQATBA	Coffeeweed	(a)
PAZAOBB	Common chickweed	(a)
PBFDQBD	Common cocklebur	
PEDADBA	Common purslane	(a)(b)(c)
PBFAEBA	Common ragweed	(a)(c)
PBFBUBA	Common sunflower	
PAZALBB	Conical catchfly	
PAZABBA	Corn cockle	
PEUAPBB	Corn speedwell	
PAZAPBA	Cow cockle	
PEAAHBE	Curly dock	(b)(c)
PBFDHAA	Dandelion	(b)(c)
PBEABAA	Dayflower	
PBFBIBB	Dogfennel	
PBKAGAA	Falseflax	
PARABAA	Fiddleneck	
PBGACBB	Field bindweed	
PBKBFBA	Field penneycress	
PBZABAA	Filaree	
PDNABBA	Fireweed	
PBKANBE	Flixweed	(a)
PCQAUBC	Florida beggarweed	(c)
PEMAEBB	Florida pusley	(a)(b)(c)
PEYACBA	Florida waltheria	
PBXABBA	Fumitory	(c)
PBFBOAA	Galinsoga	
PBVAGBH	Garden spurge	
PBFAEBE	Giant ragweed	(b)
PBDAEAA	Goosefoot	
PBVAGBW	Graceful spurge	
PARAJAA	Gromwell	
PEWAIBG	Hairy nightshade	(d)

BROADLEAF WEEDS CONTROLLED (continued)

PCQBFBB	Haole koa	
PCQBSBB	Hemp sesbania	(a)(c)
PCOAFBA	Henbit	(a)
PCQAUBA	Hoary tickclover	
PBVABBB	Hophornbeam copperleaf	(a)
PEWAIBB	Horsenettle	(b)(c)
PEUAPBE	Ivyleaf speedwell	
PAAAABK	Jacob's ladder	
PAZAGBJ	Jagged chickweed	
PEWADBD	Jimsonweed	(a)(c)
PEAAGAC	Knotweed	
PBDAIBA	Kochia	(a)(b)(c)
PEAAGBP	Ladysthumb	(c)
PBDAEAB	Lambsquarters	(a)(c)
PBKBDBB	London rocket	
PARADBA	Madwort	
PDAAHAA	Mallow	
PBFAYBA	Marestail	
PBFAHBB	Mayweed	
PBFDKBC	Meadow salsify	(a)
PEMAEAA	Mexican clover	
PBVACBA	Mexicanweed	(c)
PEDACBA	Minerslettuce	
PBGAAAB	Morningglory	(b)(c)
PAZADBC	Mouseear chickweed	
PBKAAAC	Mustard	(c)
PELAZBA	Parsley-piert	
PEAAGBO	Pennsylvania smartweed	(a)(c)
PBKAWAA	Pepperweed	(a)
PAAAABI	Pigweed	
PBFCKBB	Pineappleweed	
PDAAJBF	Prickly sida	(a)(c)
PBFCEBF	Prickly lettuce	
PEAAGBD	Prostrate knotweed	
PAFACBC	Prostrate pigweed	(a)(c)
PBKAAAD	Purple mustard	
PCQARBE	Rattlebox	
PEAAHBB	Red sorrel	
PBFBFBA	Red tassleflower	
PAFACBI	Redroot pigweed	(a)(c)
PBZABBB	Redstem filaree	
PBFBHBF	Rough fleabane	
PBFARBI	Russian knapweed	
PBDAKBA	Russian thistle	(c)
PCQBKBC	Sensitiveplant	
PBKAHBA	Shepherdspurse	(a)
PCQAMBF	Sicklepod	(a)(c)
PEAAGAD	Smartweed	(c)
PAFACBE	Smooth pigweed	(a)(c)
PBFDCAA	Sowthistle	
PEUAPAA	Speedwell	

BROADLEAF WEEDS CONTROLLED (continued)

PAFACBJ	Spiny amaranth	
PAFACBD	Spleen amaranth	(a)(b)(c)
PBVAGBK	Spotted spurge	
PBVAGAA	Spurge	(a)
PDAACBA	Spurred anoda	
PZAAAGJ	Spurweed	
PFGAEBA	Stinging nettle	(a)(c)
PBFBUAA	Sunflower	(a)
PBKANBB	Tansymustard	
PAAAACD	Tarweed	
PARABBC	Tarweed fiddleneck	(c)
PEUAIAA	Toadflax	
PBKASAA	Treacle mustard	
PBKBDBA	Tumble mustard	(a)(c)
PDAABBB	Velvetleaf	(a)
PDAAEBC	Venice mallow	(a)
PAZAHBA	White cockle	(a)
PEAAGBH	Wild buckwheat	(a)
PBKAFBE	Wild mustard	(b)(c)
PBVAGAB	Wild poinsettia	(a)
PBKADBB	Yellow rocket	

(a) Control achieved by preemergence use.
(b) Partial control only.
(c) Control achieved by postemergence use.
(d) Suppression only; apply before plants are 1 inch tall.

GRASSES AND OTHER MONOCOTS CONTROLLED:

PCAARBC	Alexandergrass	
PCACKBA	Annual bluegrass	(a)(b)(c)
PCABHBB	Barnyardgrass	(c)
PCACKAA	Bluegrass	
PCACUBE	Bristly foxtail	
PCACEBA	Broadleaf panicum	(b)(c)
PCAARBD	Broadleaf signalgrass	
PCACKBB	Bulbous bluegrass	
PCAATBK	Cheat	(b)(c)
PCABFAA	Crabgrass	(a)
PCABCBA	Crowfootgrass	(c)
PBEABAA	Dayflower	(a)
PCAATBM	Downy brome	(a)
PCACEBD	Fall panicum	
PCAAWBB	Field sandbur	(b)(c)
PCACUAA	Foxtail	
PCABSBC	Foxtail barley	(c)
PCACUBA	Giant foxtail	(c)
PCABIBA	Goosegrass	(c)
PCACUBF	Green foxtail	
PCACEBH	Guineagrass	

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GRASSES AND OTHER MONOCOTS CONTROLLED (continued)

PCABZBA	Italian ryegrass	
PCAATBF	Japanese brome	
PCACWBG	Johnsongrass (seedling)	(c)
PCABFBF	Large crabgrass	(a)(c)
PCABSBF	Little barley	
PCAAOAA	Oat	
PCAAFBC	Pacific meadow foxtail	
PCAACBA	Quackgrass	(b)(c)
PCAAXBD	Radiate fingergrass	
PCAATBN	Rescuegrass	
PCACDAA	Ricegrass	
PCAATBI	Ripgut brome	
PCAARAA	Signalgrass	(a)
PCAATBE	Smooth brome	(a)
PCABFBD	Smooth crabgrass	(a)(c)
PCADFBA	Wheat (volunteer)	
PCABSBD	Wild barley	
PCAAOBB	Wild oat	(a)
PCAAJBA	Windgrass	
PAAAABC	Wiregrass	
PCACUBD	Yellow foxtail	(c)
PBMADBI	Yellow nutsedge	(a)(b)

(a) Control achieved by preemergence use.
(b) Partial control only.
(c) Control acheived by postemergence use.

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations

TERRESTRIAL FOOD CROP

(Agricultural Crops)

General Warnings and Limitations: Potatoes, soybeans, sugarcane, and tomatoes may be planted in treated areas 4 months after application of metribuzin. Barley and winter wheat may also be planted in treated areas 4 months after application to lentils, peas or soybeans. Alfalfa, asparagus, barley, corn, cotton, forage grasses, lentils, peas, rice and wheat may be planted in treated areas 8 months after application. All other crops may be planted 18 months after application. Do not apply to rotational crops during the same year as the first application. Cover crops may be planted any time after application, but treated areas should not be grazed, or the cover crop harvested for food or feed. Stand reduction of these crops may occur in some areas.

/28069AA Alfalfa

2 ppm (green alfalfa and grasses)
7 ppm (alfalfa and grass hay)
Twenty-eight day preharvest interval. Do not graze treated areas within 28 days after application.

General Information: Use only on a dormant established crop. Do not apply after growth begins in spring or before growth ceases in fall. May be applied to stands of alfalfa mixed with grasses; the higher dosages will result in reduction of forage grass stands. Do not use on sand or on soils with less than 0.5 percent organic matter content. In areas west of the Rocky Mountains, avoid using on soils with calcareous surface layer, high levels of lime or sodium and a pH greater than 7.5. May be applied to alfalfa in conjunction with a fluid fertilizer or impregnated on dry bulk fertilizer.

0.38-1 (50% WP) (75% WP) (4 lb/gal FlC)	Dormant application. Broadcast. Make a single application in the fall after plants become dormant or in the spring before new growth starts. Use the lower dosage on sandy loam, or loamy sand soils in areas other than ID, OR and WA.
0.75-1 (50% WP) (75% WP) (4 lb/gal FlC)	Dormant application. Broadcast. Apply to reduce stands of forage grasses, to prevent crowding out of alfalfa.

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
	Alfalfa (continued)	
	0.25-0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to ID, OR and WA. Dormant application. Broadcast. For the control of common chickweed. Apply to sandy loam or loamy sand soils.
	0.25-0.75 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to WA. Dormant application. Broadcast. Make a single application to established alfalfa during the dormant season. Tank mix with paraquat.
/16002AA	**Asparagus**	0.05 ppm Fourteen day preharvest interval. Do not exceed 2 lb a.i./A per crop season. General Information: Do not use on newly seeded asparagus or on young plants from crowns during the first growing season. Do not make postharvest applications until all spears have been harvested.
	1-2 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence. Broadcast. Make a single application in the early spring before spears or ferns emerge.
	0.5-1 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence. Broadcast. Split application. Apply before spears or ferns emerge, and follow with postharvest treatment. AND
	1-1.5 (50% WP) (75% WP) (4 lb/gal FlC)	Postharvest. Broadcast. Split application to follow preemergence treatment. Apply after last harvest of the season, but prior to fern emergence.

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
/28063AA	Barley	0.75 ppm (grain) 1 ppm (straw) 3 ppm (milled fractions (except flour) of processed food and feed) Do not graze or harvest treated barley for feed before crop maturity. Do not graze treated fields after a fallow application. General Information: Do not apply more than once per crop season. Do not apply in the spring if a fall fallow application was made. Do not plant spring cereals following fall fallow applications.
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas east of the Cascade Mountains in ID, OR, UT, MO and WA on the varieties Compana, Hannchen, Hector, Hudson, Luther, Kamiak, Klages, Olympic, Piroline and Steptoe. Postemergence. Broadcast. Apply after barley has fully tillered and developed secondary roots, but before jointing. Do not apply on any soil containing less than 1 percent organic matter. Do not use if soils are high in lime or sodium or have a pH greater than 7.7. Temporary chlorosis may occur especially if the crop is under stress or if application is made in fluid fertilizer. May be tank mixed with dicamba, dimethylamine salt; 2,4-D; bromoxynil; terbutryn; chlorsulfuron; or bromoxynil and MCPA.
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to KS, OK and TX. Postemergence. Broadcast. Apply prior to jointing when crop is well tillered (at least 3 tillers) and has developed 2 inch secondary roots throughout the field. Do not use on coarse textured soils with less than 2 percent organic matter. May be tank mixed with dicamba, dimethylamine salt; 2,4-D; bromoxynil; terbutryn; chlorsulfuron; or bromoxynil and MCPA.
	0.34-0.75 (50% WP) (75% WP) (4 lb/gal FlC)	Postharvest. Broadcast. For use on fallow land to be planted to winter wheat. Apply after weed emergence. Tank mix with propham; paraquat; glyphosate; or chlorsulfuron if large weeds are present.

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
	Barley (continued)	
	0.5-0.75 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to CO, ID, KS, MT, NE, ND, OK, OR, SD, TX, UT and WA. Postharvest. Broadcast. Apply to actively growing weeds in fall fallow. Tank mix with propham; paraquat; glyphosate; or chlorsulfuron, if large weeds are present.
	0.34-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to CO, ID, KS, MT, NE, ND, OK, OR, SD, TX, UT and WA. Postharvest. Broadcast. Apply to actively growing weeds in spring fallow. Tank mix with propham; paraquat; glyphosate; or chlorsulfuron, if large weeds are present.
	0.63-0.75 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to CO, KS, MT, NE and WY. Postharvest application in fall fallow. Broadcast. Apply prior to weed emergence. Do not plant crops in treated areas earlier than 10 months following fall applications. Do not make another application in spring. Tank mix with paraquat; glyphosate; or other contact herbicide if weed growth is present.
	0.38-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to CO, KS, MT, NE and WY. Spring application in summer fallow. Broadcast. Apply prior to weed emergence. Barley can be seeded 120 days after spring application. Tank mix with paraquat; glyphosate; or other contact herbicide if weed growth is present.
/28005AA	Corn	0.1 ppm (forage, fodder) 0.05 ppm (grain and fresh (including sweet K+CWHR))
	0.25-0.5 (50% WP)	Use limited to IA, KS, MN, MO and NE. Preemergence. Broadcast. Plant corn 1.5 inches deep. Do not use on inbred parent seed corn. Do not use on corn planted in deep furrows. Tank mix with alachlor.

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	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
/28006AA	Corn, Field	0.1 ppm (forage, fodder) 0.05 ppm (grain and fresh (including sweet K+CWHR))
	0.25 (75% WP) (4 lb/gal FlC)	Use limited to IL, IN, IA, KS, KY, MI, MO, NE, OH, SD and WI. Preemergence. Broadcast. Plant corn 1.5 inches deep. Use on hybrid seed corn only if both parent corn varieties are known to be tolerant to metribuzin and other tank mix chemicals. Tank mix with atrazine and alachlor; atrazine and metolachlor; alachlor and bladex; or bladex and metolachlor.
/14013AA	Potato	0.6 ppm 3 ppm (processed foci (including potato chips)) 3 ppm (processed feed (dried potato waste)) Sixty day preharvest interval. Do not apply more than 1 lb a.i./A per crop season. General Information: Do not use on early maturing smooth-skinned white or red-skinned varieties when applying postemergence. Apply only to those varieties that are known to be tolerant to metribuzin. Crop injury may result when used on sands or loamy sands containing 0.5 to 1 percent organic matter. Do not use on any soil containing less than 0.5 percent organic matter. Preemergence use on soils containing more than 10 percent organic matter may result in only partial weed control. Do not use on potatoes grown under rill/furrow irrigation.
	0.5-1 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence. Broadcast. Apply as a single application after planting or after drag-off but before crop emergence. May be tank mixed with alachlor or pendimethalin. Do not tank mix with pendimethalin in CA.
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Postemergence. Broadcast. Apply as a single application. Three successive days of sunny weather are necessary prior to application. Some chlorosis or minor necrosis may occur to crop plants. Application may follow a preemergence application provided no more than 1 lb a.i./A per season is applied.

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Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Potato (continued)	
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Postemergence application via sprinkler irrigation systems. Apply uniformly in 0.25 to 0.75 inches of water per acre. On sandy soil, apply in 0.25 to 0.5 inch of water. Make a single postemergence or a split postemergence application. Application may follow a preemergence application provided no more than 1 lb a.i./A per season is applied.
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to ID, OR and WA. Postemergence. Broadcast. Make 2 applications, but use only if a preemergence application was not made. Make the first application early in the season and allow at least 14 days between applications. Do not apply within 24 hours of application of other pesticides. On coarse soils containing 0.5 to 1 percent organic matter do not exceed 0.25 lb a.i./A per application in OR and WA. Do not apply after June 30 if treated field is to be planted to crops other than potatoes.
0.13-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to ID. Postemergence. Broadcast. Make 2 applications, but use only if a preemergence application was not made. On coarse soils containing 0.5 to 1 percent organic matter, do not exceed 0.38 lb a.i./A per application. Allow 14 days between applications, and do not apply within 24 hours of application of other pesticides.
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to OR and WA. Postemergence. Broadcast. Make 2 applications, but use only if a preemergence application was not made. Do not exceed the lower dosage on coarse soils containing 0.5 to 1 percent organic matter. Allow 14 days between applications, and do not apply within 24 hours of application of other pesticides.

004262

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
/28077AA **Sainfoin**	2 ppm (sainfoin and grasses) 7 ppm (sainfoin and grass hay) Twenty-eight day preharvest interval. Do not graze within 28 days after application. General Information: Use only on a dormant established crop. Do not apply after growth begins in spring or before growth ceases in fall. May be applied to stands of sainfoin mixed with grasses; the higher dosages will result in reduction of forage grass stands. Do not use on sand or on soils with less than 0.5 percent organic matter content. In areas west of the Rocky Mountains, avoid using on soils with calcareous surface layer, high levels of lime or sodium and a pH greater than 7.5.
0.38–1 (50% WP) (75% WP) (4 lb/gal FlC)	Dormant application. Broadcast. Make a single application in the fall after plants become dormant or in the spring before new growth starts. Use the lower dosage on sandy loam, or loamy sand soils in areas other than ID, OR and WA. When application is made to mixed stands with forage grasses, the higher rates may provide partial reduction of forage grass stands. Dosage rates of 0.75 to 1 lb a.i./A may severly reduce stands of forage grass.
0.25–0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to ID, OR and WA. Dormant application. Broadcast. For the control of common chickweed. Apply to sandy loam or loamy sand soils.

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
L5010AA	Soybeans	0.1 ppm (soybeans) 4 ppm (forage, hay) Do not use treated vines for feed or forage for 40 days after application. General Information: Altona, Coker 102 and 156, Govan, Semmes, Tracy and Vansoy are sensitive to metribuzin and injury may occur if used on these varieties. Determine tolerance to other varieties before implementing as a field practice. Injury may occur if used on soils having a calcareous surface layer or a pH of 7.5 or higher, if used in conjunction with soil applied organic phosphate pesticides, or if atrazine was applied on the soil the previous year. If initial seeding fails to produce a stand, treated fields may be replanted to soybeans, but do not rework soil, or retreat field with a second application. Do not replant treated areas to any crop other than soybeans within 4 months after application as injury to subsequent crops may result. For crop rotations in fields treated with chloramben, trifluralin, glyphosate, oryzalin, profluralin, fluchloralin, or metolachlor, follow instructions on individual product labels. When applying preemergence, use the higher dosage for minimum till or no-till soybeans, and in the States of GA and SC. May be applied in conjunction with fluid fertilizers, or may be impregnated on dry bulk fertilizer. Plant seeds at least 1.5 inches deep. Do not use on coarse textured soils with less than 2 percent organic matter, or on sandy soils when applying preemergent broadcast applications. Guidelines for preplant incorporated, tank mixed applications that are followed by a preemergence surface application are: On coarse textured soils, do not use on sand soils with less than 1 percent organic matter, or on loamy sand or sandy loam soils with less than 0.5 percent organic matter; On coarse textured soils with a calcareous surface layer or a pH of 7.5 or higher, do not use on sand soils with less than 2 percent organic matter, or on loamy sand or sandy loam soils with less than 1 percent organic matter; On medium and fine textured soils, do not use when the organic matter content is less than 0.5 percent.

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

00426

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	
0.25–0.5 (4 lb/gal FlC)	Preplant. Broadcast. Apply within 4 weeks of planting. Tank mix with oryzalin.
0.25–0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. Apply within 2 weeks of planting. Tank mix with trifluralin; alachlor; fluchloralin; or metolachlor.
0.25–0.5 (4 lb/gal FlC)	Preplant. Soil incorporation. Apply within 7 days of planting. Tank mix with alachlor.
0.25–0.5 (50% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. Apply within 10 days of planting. Tank mix with profluralin.
0.13–0.5 (4 lb/gal FlC)	Preplant. Soil incorporation. Apply within 2 weeks of planting. Tank mix with chloramben and trifluralin.
0.75 (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils in the Mississippi Delta. Preplant. Soil incorporation. Apply within 7 days of planting. Tank mix with alachlor.
0.5–0.63 (75% WP) 0.75 (4 lb/gal FlC)	Use limited to silty clay to clay soils of the Mississippi Delta. Preplant. Soil incorporation. Apply within 2 weeks of planting. Tank mix with alachlor or metolachlor.
0.5–0.63 (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils in the Mississippi Delta. Preplant. Broadcast. Apply within 4 weeks of planting. Tank mix with oryzalin.
0.25–0.5 (4 lb/gal FlC)	Preplant. Soil incorporation. Follow with preemergence surface application. Tank mix with trifluralin; alachlor; pendimethalin; or metolachlor. AND Preemergence. Broadcast.
0.13–0.5 (4 lb/gal FlC)	

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	
0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. Broadcast. For use on fine textured soils. Tank mix with alachlor; fluchloralin; metolachlor; pendimethalin; or trifluralin.
	AND
0.13-0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence. Broadcast.
0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. For use on fine textured soils having a calcareous surface layer or a pH of 7.5 or higher, and in areas where soils within a field vary extremely in texture or organic matter content. Tank mix with trifluralin; alachlor; pendimethalin; fluchloralin; or metolachlor.
	AND
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence. Reduce dosage by 0.13 lb a.i./A when applying on soils with over 4 percent organic matter and having a calcareous surface layer or a pH of 7.5 or higher.
0.25 (50% WP) (75% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. For use on coarse textured soils. Tank mix with trifluralin; alachlor; pendimethalin; fluchloralin; or metolachlor.
	AND
0.13-0.25 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence.

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	
0.25 (50% WP) (75% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. For use on medium textured soils having a calcareous surface layer or a pH of 7.5 or higher, and in areas where soils within a field vary extremely in texture or organic matter content. Tank mix with trifluralin; alachlor; pendimethalin; fluchloralin; or metolachlor.
	AND
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence. Reduce dosage by 0.13 lb a.i./A when applying on soils with over 4 percent organic matter and having a calcareous surface layer or a pH of 7.5 or higher.
0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Preplant. Soil incorporation. For use on medium textured soils. Tank mix with trifluralin; alachlor; pendimethalin; fluchloralin; or metolachlor.
	AND
0.13-0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Preemergence.
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to the Southern States and Eastern Coastal Plains (AL, AR, FL, GA, LA, MS, NC, OK, SC, TN, TX, Southeastern MO (Bootheel Region), and Coastal Plains of DE, MD, NJ and VA). Preplant. Soil incorporation. Incorporate and plant within 7 days after application. Tank mix with pendimethalin.
	AND
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to the Southern States and Eastern Coastal Plains (AL, AR, FL, GA, LA, MS, NC, OK, SC, TN, TX, Southeastern MO (Bootheel Region), and Coastal Plains of DE, MD, NJ and VA). Preemergence. May be preceded by preplant soil incorporation of pendimethalin alone.

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4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	
0.38-0.5 (50% WP) (4 lb/gal FlC)	Use limited to the Northeastern and Northcentral States (IL, IN, IA, KS, KY, MI, MN, NE, NY, ND, OH, PA, SD, WI, MO (except Bootheel Region), and except for the Coastal Plain, DE, MD, NJ and VA).
0.25-0.63 (75% WP)	Preplant. Soil incorporation. Incorporate and plant within 7 days after application. Tank mix with pendimethalin.
	AND
0.38-0.5 (50% WP) (4 lb/gal FlC)	Use limited to the Northeastern and Northcentral States (IL, IN, IA, KS, KY, MI, MN, NE, NY, ND, OH, PA, SD, WI, MO (except Bootheel Region), and except for the Coastal Plain, DE, MD, NJ and VA).
0.25-0.63 (75% WP)	Preemergence. May be preceded by preplant soil incorporation of pendimethalin alone.
0.38-0.88 (75% WP)	Preemergence. Broadcast or band.
0.38-0.5 (4 lb/gal FlC)	Use limited to AL, LA, MS and TN. Preemergence. Broadcast. For use on medium textured soils.
0.5-0.63 (4 lb/gal FlC)	Use limited to AL, LA, MS and TN. Preemergence. Broadcast. For use on fine textured soils.
0.75-1 (75% WP)	Use limited to the Mississippi Delta. Preemergence. Broadcast or band.
0.25-0.38 (4 lb/gal FlC)	Preemergence. Broadcast. For use on alkaline soils. Use the lower dosage on medium textured soils and the higher dosage on fine textured soils containing more than 0.5 percent organic matter. Use the higher dosage where soil pH is less than 7.5 and weed pressure is heavy. The lower dosage may be used as a preemergence surface application following preplant soil incorporation of trifluralin or profluralin.

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	004262
0.25-0.38 (75% WP)	Use limited to calcareous soils of MN and ND. Preemergence. Broadcast or band. Apply the lower dosage on medium textured soils, and the higher dosage on fine textured soils regardless of soil organic matter content, and where soil pH is less than 7.5 and weed pressure is heavy. The lower dosage may be applied alone or as a preemergence surface application following a preplant application of trifluralin.
0.38-0.75 (4 lb/gal FlC)	Use limited to the Midsouth. For the control of hophornbeam copperleaf. Preemergence. Broadcast.
0.38-1 (75% WP)	Preemergence. Broadcast. For use in areas where soybeans will be planted in preformed beds, cover crops or in previous crop residues. Apply with a nonionic surfactant. Tank mix with paraquat.
0.25-1 (75% WP)	Preemergence. Broadcast. For use in areas where soybeans will be planted in preformed beds, cover crops or in previous crop residues. Apply with a nonionic surfactant. Tank mix with paraquat and alachlor.
0.25-0.5 (75% WP)	Preemergence. Broadcast. For use in areas where soybeans will be planted in preformed beds, cover crops or in previous crop residues. Apply with a nonionic surfactant within 2 days after planting. Tank mix with paraquat and oryzalin.
0.13-0.5 (50% WP) (4 lb/gal FlC)	Preemergence. Broadcast. Plant seed 1.5 to 2 inches deep on flat or raised seedbeds. Tank mix with alachlor.
0.13-0.5 (75% WP) (4 lb/gal FlC)	Preemergence. Broadcast. Apply within 2 days after planting. Tank mix with oryzalin.
0.25-0.63 (75% WP)	Preemergence. Broadcast. Tank mix with chloramben.
0.13-0.5 (4 lb/gal FlC)	

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Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	
0.38-0.5 (50% WP) (4 lb/gal FlC)	Preemergence. Broadcast or band. May be preceded by a preplant soil incorporation of trifluralin; profluralin; pendimethalin; fluchloralin; or metolachlor.
0.25-0.62 (75% WP)	
0.13-0.5 (75% WP) (4 lb/gal FlC)	Preemergence. Broadcast. Tank mix with linuron and alachlor; linuron and metolachlor; or alachlor, sodium naptalam and sodium dinoseb.
0.25-0.62 (75% WP)	Preemergence. Broadcast or band. Tank mix with alachlor.
0.25-0.5 (4 lb/gal FlC)	Preemergence. Broadcast. Sequential application. Apply after a preplant soil incorporation of fluchloralin.
	OR
0.25-0.5 (4 lb/gal FlC)	Preplant. Soil incorporation. Tank mix with fluchloralin.
0.13-0.5 (4 lb/gal FlC)	Preemergence. Broadcast. Tank mix with chloramben and alachlor; chloramben and pendimethalin; chloramben and metolachlor; or alachlor, sodium naptalam and sodium dinoseb.
	OR
0.13-0.5 (4 lb/gal FlC)	Preplant. Soil incorporation. Tank mix with chloramben and alachlor; chloramben and pendimethalin; chloramben and metolachlor; or alachlor, sodium naptalam and sodium dinoseb.
1 (75% WP)	Use limited to silty clay to heavy clay soils of the Mississippi Delta. Preemergence. Broadcast or band. Tank mix with alachlor.

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Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Soybeans (continued)	
0.5-0.75 (50% WP) (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils of the Mississippi Delta. Preemergence. Broadcast. Plant seed 1.5 to 2 inches deep on flat or raised seedbeds. Tank mix with alachlor.
0.13-0.5 (4 lb/gal FlC)	Use limited to the Southern States and Eastern Coastal Plains. Preemergence. Broadcast. Tank mix with pendimethalin.
0.25-0.5 (4 lb/gal FlC)	Use limited to Northeastern and Northcentral States. Preemergence. Broadcast. Tank mix with pendimethalin.
0.5-0.63 (75% WP) (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils of the Mississippi Delta. Preemergence. Broadcast. Apply within 2 days after planting. Tank mix with oryzalin.
0.5-0.75 (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils of the Mississippi Delta. Preemergence. Broadcast. Tank mix with chloramben.
1 (75% WP)	
0.75 (75% WP) 0.5-0.75 (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils of the Mississippi Delta. Preemergence. Broadcast or band. May be preceded by a preplant soil incorporation of trifluralin; profluralin; pendimethalin; fluchloralin; or metolachlor.
0.38-0.75 (4 lb/gal FlC)	Use limited to OH. Preemergence. Broadcast or band. For use on medium and fine textured soils. Tank mix with alachlor.
0.25-0.5 (4 lb/gal FlC)	For use in minimum till or no-till soybeans. Preemergence. Broadcast. Tank mix with paraquat and glyphosate; or alachlor and glyphosate.
0.38-0.5 (4 lb/gal FlC)	For use in minimum till or no-till soybeans. Preemergence. Broadcast. Apply with ground equipment. Tank mix with paraquat; paraquat and alachlor; paraquat and oryzalin; or alachlor and glyphosate.

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
	Soybeans (continued)	
	0.5-0.75 (4 lb/gal FlC)	Use limited to silty clay to heavy clay soils of the Mississippi Delta. For use in minimum till or no-till soybeans. Preemergence. Broadcast. Apply with ground equipment. Tank mix with paraquat; paraquat and alachlor; paraquat and oryzalin; or alachlor and glyphosate.
	0.25-0.5 (75% WP) (4 lb/gal FlC)	Use limited to the Southern and Southeastern States (AL, AR, FL, GA, KY, CA, MS, MO, NC, OK, SC, TN and TX). Postemergence. Directed spray. Apply when soybeans are at least 8 to 12 inches tall. Do not spray higher than 2 inches on soybean stem. Apply with a nonionic surfactant. If needed, a second application may be made after 7 days. May be tank mixed with 2,4-DB.
/25003AA	Sugarcane	0.1 ppm 0.3 ppm (molasses, processed feed) 0.5 ppm (bagasse, processed feed) 2 ppm (molasses, processed food) Sixty day preharvest interval in FL, LA and TX. Seventeen month preharvest interval in HI. Do not use treated crop for feed or forage in FL, LA and TX. Do not apply more than 8 lb a.i./A per crop cycle in HI. General Information: Do not use on sugarcane grown on sand in FL, LA and TX.
	2-4 (50% WP) (70% WP) (75% WP) (4 lb/gal FlC)	Use limited to HI. Preemergence or very early postemergence. Broadcast. Apply within 2 weeks after planting, prior to cane emergence or shortly after emergence (spike stage).
		OR
	2-4 (50% WP) (70% WP) (75% WP) (4 lb/gal FlC)	Use limited to HI. Early postemergence. Broadcast. Apply over cane before weeds are 3 inches tall. Application may be delayed 4 to 6 weeks provided weeds are less than 3 inches tall.
		OR

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Sugarcane (continued)	
2-4 (50% WP) (70% WP) (75% WP) (4 lb/gal FlC)	Use limited to HI. Postemergence. Broadcast. Apply prior to close-in and before weeds are 3 inches tall.
4-6 (70% WP) (75% WP) (4 lb/gal FlC)	Use limited to HI. Preemergence. Aerial application. Apply to irrigated cane within 2 weeks after planting.
	OR
4-6 (70% WP) (75% WP) (4 lb/gal FlC)	Use limited to HI. Early postemergence. Aerial application. Apply over irrigated cane before weeds are 3 inches tall. Application may be delayed 4 to 6 weeks provided weeds are less than 3 inches tall.
	OR
2-4 (70% WP) (4 lb/gal FlC)	Use limited to HI. Postemergence. Aerial application. Apply to irrigated cane prior to close-in and before weeds are 3 inches tall.
2.5-5 (50% WP) (70% WP) (75% WP) (4 lb/gal FlC)	Use limited to HI. Spot treatment. Dilute the product in sufficient water to prepare 30 to 50 gallons of finished spray, and spot spray on missed areas or hard to control weeds.
1.5-3 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to LA and TX. Preemergence or postharvest. Broadcast. Apply in the fall after planting but before cane emergence, or to the stubble after harvest. Make a second application in early spring prior to new cane growth. If necessary, a third application may be made in the late spring at layby.
1-2 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to FL. Postemergence. Directed spray. Apply after sugarcane is 12 inches tall but before row crossing. Do not apply more than 2 lb a.i./A per crop season.

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
/11005AA	Tomato	0.1 ppm 2 ppm (dried tomato pomace, processed feed) Seven day preharvest interval. Do not forage or feed treated foliage to livestock. Do not apply more than 1 lb a.i./A within a 35 day period per crop season except in the case of directed sprays. General Information: Do not treat seeded or transplanted tomatoes until plants have reached the 5- to 6-leaf stage, or until transplants have recovered from transplant shock and new growth has started. Apply only if there have been at least 3 successive days of sunny weather prior to application, or crop injury may occur when applying postemergent. Do not apply within 24 hours of treatment with other pesticides. When applying postemergent to established tomatoes, do not tank mix with other pesticides. Tomato varieties vary in their resistance to metribuzin; therefore, determine varietal tolerance prior to large scale use. Do not use hot caps within 7 days before or at any time after application. Directed sprays should be used in fields with severe weed pressure or in fields with hard to control weeds. Do not apply to soils containing a calcareous surface layer or a pH of 7.5 or higher. Allow a minimum of 14 days between applications. Do not apply within 14 days of transplanting.
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas east of the Rocky Mountains (except FL). Pretransplant. Broadcast. Incorporate to a depth of 2 to 4 inches. Use the higher dosage for heavy weed pressure or hard-to-control weeds. May be tank mixed with trifluralin.
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas other than CA. Pretransplant. Broadcast. Incorporate to a depth of 2 to 4 inches. May be tank mixed with trifluralin.
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas east of the Rocky Mountains (except FL). Postemergence. Broadcast. For use on established tomatoes. Make 1 or more applications per crop season. Use the higher dosage for heavy weed pressure or hard-to-control weeds.

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Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Tomato (continued)	
0.5-1 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas east of the Rocky Mountains (except FL). Postemergence. Directed spray. Do not allow spray to contact tomato foliage. For use on established tomatoes. Make 1 or more applications per crop season. Use the higher dosage for heavy weed pressure or hard-to-control weeds.
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas other than FL. Postemergence. Broadcast. Apply to established tomatoes as a single or split application. For split applications, apply 0.25 to 0.38 lb a.i./A per application. Do not exceed 2 treatments per crop season.
0.25-0.38 (50% WP) (75% WP) (4 lb/gal FlC)	Postemergence. Broadcast. For use on established tomatoes. Make 1 or more applications per crop season. Use the higher dosage for heavy weed pressure or hard-to-control weeds.
0.5-1 (50% WP) (75% WP) (4 lb/gal FlC)	Postemergence. Directed spray. Do not allow spray to contact tomato foliage. For use on established tomatoes. Make 1 or more applications per crop season. Use the higher dosage for heavy weeds pressure or hard-to-control weeds.

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	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
/28065AA	Wheat	0.75 ppm (grain) 1 ppm (straw) 2 ppm (forage) 3 ppm (milled fractions (except flour) of processed food and feed) Do not graze treated fields for 14 days following application. Do not graze treated fields after a fallow application. General Information: Do not apply more than once per crop. Do not use on any soils containing less than 1 percent organic matter. Do not use on irrigated wheat or crop injury may occur. Temporary chlorosis may occur after application especially if frost occurs. Not recommended for use if soils are high in lime or sodium or have a pH greater than 7.7. Crop injury may occur if secondary roots have not developed at time of application. Do not plant spring seeded cereals following fall fallow applications. Do not apply in the spring if an application was made in the fall. Do not use on the winter wheat varieties Morex, Glenn or Morvain 3.
	(dryland winter)	
	0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to areas east of the Cascades in ID, OR, UT and WA on varieties Daws, Gaines, Hyslop, Luke, McDermid, Moro, Nugaines, Paha, Peck, Stevens and Wanser, and in MT on the varieties Centurk, Cheyenne and Winalta. Postemergence. Broadcast. Apply after wheat has fully tillered and developed secondary roots, but before jointing. Do not use on any soils containing less than 1 percent organic matter. Do not use if soils are high in lime or sodium or have a pH greater than 7.7. Temporary chlorosis may occur, especially if the crop is under stress or if application is made in fluid fertilizers. May be tank mixed with dicamba, dimethylamine salt; 2,4-D; terbutryn; or bromoxynil and MCPA.

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Wheat (continued)	
0.19-0.25 (75% WP)	Use limited to areas east of the Cascades in ID, OR, UT and WA on varieties Daws, Gaines, Hyslop, Luke, McDermid, Moro, Nugaines, Paha, Peck, Stevens and Wanser, and in MT on the varieties Centurk, Cheyenne and Winalta. Postemergence. Broadcast. Broadleaf weed control. Apply only in the spring after wheat has started to grow and has a well established secondary root system with at least 3 to 4 tillers. Tank mix with bromoxynil; or bromoxynil and MCPA.
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to KS, OK and TX on the varieties Tam W101, Tam 105, and Newton. Postemergence. Broadcast. Apply in the fall after wheat has a minimum of 3 tillers and 4 secondary roots at least 2 inches in length, but before winter dormancy. May be tank mixed with dicamba, dimethylamine salt; 2,4-D; bromoxynil; or bromoxynil and MCPA.
0.25-0.75 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to KS, OK and TX on the varieties Tam W101, Tam 105, and Newton. Postemergence. Broadcast. Apply in the spring after wheat has fully tillered and has developed secondary roots at least 2 inches in length. May be tank mixed with dicamba, dimethylamine salt; 2,4-D; bromoxynil; or bromoxynil and MCPA.
0.25-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to KS, OK and TX. Postemergence. Broadcast. Apply prior to jointing when crop is well tillered (at least 3 tillers) and has developed 2 inch secondary roots throughout the field. Do not use on coarse textured soils with less than 2 percent organic matter. May be tank mixed with dicamba, dimethylamine salt; 2,4-D; bromoxynil; terbutryn; chlorsulfuron; or bromoxynil and MCPA.
0.34-0.75 (4 lb/gal FlC)	Postharvest. Broadcast. For use on fallow land to be planted to winter wheat. Apply after weed emergence. Tank mix with propham; paraquat; glyphosate; or chlorsulfuron if large weeds are present.

Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
Wheat (continued)	
0.5-0.75 (4 lb/gal FlC)	Use limited to CO, ID, KS, MT, NE, ND, OK, OR, SD, TX, UT and WA. Postharvest. Broadcast. Apply to actively growing weeds in fall fallow. Tank mix with propham; paraquat; glyphosate; or chlorsulfuron if large weeds are present.
0.34-0.5 (4 lb/gal FlC)	Use limited to CO, ID, KS, MT, NE, ND, OK, OR, SD, TX, UT and WA. Postharvest. Broadcast. Apply to actively growing weeds in spring fallow. Tank mix with propham; paraquat; glyphosate; or chlorsulfuron if large weeds are present.
0.63-0.75 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to CO, KS, MT, NE and WY. Postharvest application in fall fallow. Broadcast. apply prior to weed emergence. Do not plant crops in treated areas earlier than 10 months following fall applications. Do not make another application in the spring. Tank mix with paraquat; glyphosate or other contact herbicide if weed growth is present.
0.38-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to CO, KS, MT, NE and WY. Spring application in summer fallow. Broadcast. Apply prior to weed emergence. Wheat can be seeded 120 days after spring application. Tank mix with paraquat; glyphosate or other contact herbicide if weed growth is present.
(wheat, fallow)	
0.5-0.63 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to ID, OR, UT and WA. Postharvest application in fall fallow. Broadcast. Apply prior to weed emergence. Do not plant crops in treated areas earlier than 10 months following fall applications. May be tank mixed with propham. Tank mix with paraquat or other contact herbicide if weed growth is present.
0.38-0.5 (50% WP) (75% WP) (4 lb/gal FlC)	Use limited to ID, OR, UT and WA. Spring application in summer fallow. Broadcast. Apply prior to weed emergence. Wheat can be seeded 120 days after spring application. May be tank mixed with propham after January 1 and before March 1.

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-O

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
	TERRESTRIAL NON-FOOD CROP	
	(Ornamental Plants and Forest Trees)	
/33017AA	**Bermudagrass**	General Information: For use on established mon bermudagrass growing on golf course fairw and commercial sod farms. Apply in 40 gallon water per acre. Do not apply more than 1.5 l a.i./A in a single growing season. Do not ap more than once to dormant turf, or more than to actively growing turf in a single growing son. Do not apply to greens, tees, aprons or other closely mowed turf. Do not mow for 3 d following treatment for maximum weed control.
	0.5 (50% WP) (75% WP)	Use limited to AL, AR, FL, GA, LA, MS, NC, SC TN, TX and VA. Broadcast. Apply to actively growing weeds in dormant turf prior to green
	0.25-0.5 (50% WP) (75% WP)	Use limited to AL, AR, FL, GA, LA, MS, NC, SC TN, TX and VA. Broadcast. Apply to actively growing turf. Repeat application if necessa with a minimum of 1 week between application Temporary discoloration may occur.
	(Noncrop, Wide Area, and General Outdoor Treatments)	
/67000OA	**Noncrop Areas**	
	1-6 (50% WP) (75% WP) (4 lb/gal F1C)	Broadcast. Apply to emerged weeds. May be tank mixed with paraquat or glyphosat
/67050OA	**Railroad Rights-of-Way**	
	6-7.5 (75% WP)	Broadcast. Apply to bare soil.

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

	Site, Dosage and Formulation (lb a.i./A)	Tolerance, Use, Limitations
	AERIAL AND TANK MIX APPLICATIONS	
90001500 AAAAAAA	Aerial Application	
	--	Refer to TERRESTRIAL FOOD CROP (Agricultural Crops) Alfalfa, Asparagus, Barley, Corn, Corn (Field), Potato, Sainfoin, Soybeans, Sugarcane, Wheat
99000300 AAAAAAA	Tank Mix	
	--	Refer to TERRESTRIAL FOOD CROP (Agricultural Crops) Barley, Corn, Corn (Field), Potato, Soybeans, Tomato, Wheat TERRESTRIAL NON-FOOD CROP (Noncrop, Wide Area, and General Outdoor Treatments) Noncrop Areas

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ON

Listing of Registered Pesticide Products by Site and Formulation

004262

&050.0002 50% formulation intermediate
4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one (101101)
003125-00305

&050.0006 50% wettable powder
4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one (101101)
000352-00375 003125-00277 039926-00002

&070.0006 70% wettable powder
4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one (101101)
003125-00294

&075.0006 75% wettable powder
4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one (101101)
000352-00390 000352-00407 003125-00325

&104.0014 4 lb/gal flowable concentrate
4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one (101101)
000352-00382 003125-00314 039926-00001

9999999 State Label Registration

LA Reg. No.
037820-08433

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4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

Appendix A

Listing of Common Chemical Names Used on the Entry

Chemical Code	Common Name (source)	EPA Acceptable Common/Chemical Name
030001	2,4-D	2,4-dichlorophenoxyacetic acid
030501	MCPA	2-methyl-4-chlorophenoxyacetic acid
030703	sodium naptalam	N-1-naphthylphthalamic acid, sodium salt
030801	2,4-DB	4-(2,4-dichlorophenoxy)butyric acid
047601	propham	isopropyl carbanilate
061601	paraquat	paraquat dichloride
100101	bladex	2-[[4-chloro-6-(ethylamino)-5-triazin-2-yl]amino]-2-methyl propionitrile
103601	glyphosate	glyphosate, isopropylamine salt
118601	chlorsulfuron	2-chloro-N-[((4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino)carbonyl]benzenesulfonamide

4-AMINO-6-(1,1-DIMETHYLETHYL)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE

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Appendix B

Listing of Registration Numbers by Site and Formulation

TERRESTRIAL FOOD CROP

(Agricultural Crops)

/28069AA Alfalfa

(50% WP)
000352-00375 003125-00277

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

/16002AA Asparagus

(50% WP)
000352-00375 003125-00277

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
003125-00314

/28063AA Barley

(50% WP)
000352-00375

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

/28005AA Corn

(50% WP)
003125-00277

/28006AA Corn, Field

(75% WP)
003125-00325

(4 lb/gal FlC)
003125-00314

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Appendix B

Listing of Registration Numbers by Site and Formulation (continued)

/14013AA **Potato**

(50% WP)
000352-00375 003125-00277 039926-00002

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314 039926-00001

/28077AA **Sainfoin**

(50% WP)
000352-00375 003125-00277

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

/15010AA **Soybeans**

(50% WP)
000352-00375 003125-00277 039926-00002

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314 039926-00001

/25003AA **Sugarcane**

(50% WP)
000352-00375 003125-00277

(70% WP)
003125-00294

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

Appendix B

Listing of Registration Numbers by Site and Formulation (continued)

/11005AA Tomato

(50% WP)
000352-00375 003125-00277

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

/28065AA Wheat

(dryland winter)
(50% WP)
000352-00375

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

(wheat, fallow)
(50% WP)
000352-00375

(75% WP)
000352-00390 003125-00325

(4 lb/gal FlC)
000352-00382 003125-00314

TERRESTRIAL NON-FOOD CROP

(Ornamental Plants and Forest Trees)

/33017AA Bermudagrass

(50% WP)
003125-00277

(75% WP)
003125-00325

Appendix B

Listing of Registration Numbers by Site and Formulation (continued)

(Noncrop, Wide Area, and General Outdoor Treatments)

/670000A Noncrop Areas

(50% WP)
000352-00375

(75% WP)
000352-00390

(4 lb/gal FlC)
000352-00382

/670050A Railroad Rights-of-Way

(75% WP)
000352-00407

REQUIREMENT FOR SUBMISSION OF GENERIC DATA

004262

A. This portion of the guidance document is a Notice issued under the authority of FIFRA sec. 3(c)(2)(B). The tables following this section list the data required for maintaining the registrability of each product.

EPA has determined that additional generic data described in Table A must be submitted to EPA for evaluation in order to maintain in effect the registration(s) of your product(s) identified as an attachment to the cover letter accompanying this guidance document. As required by FIFRA sec. 3(c)(2)(B), you are required to take appropriate steps to comply with this Notice.

EPA may suspend the registration of each of those products unless, within the specified time, you have informed EPA how you will satisfy the requirements of this Notice. Any such suspension will remain in effect until you have complied with the terms of this Notice.

B. What Generic Data[1/] Must be Submitted. You may determine which generic data you must submit by consulting Table A at the end of this chapter. That table lists the generic data needed to evaluate the continued registrability of all products, and the dates by which the data must be submitted. The required studies must be conducted in accordance with EPA approved protocols (such as those contained in the Pesticide Assessment Guidelines [2/] or data collected under the approved protocols of the Organization for Economic Cooperation and Development (OECD). If you do not wish to develop data in support of certain uses appearing in your labeling, you may delete those uses at the time you submit your revised labeling.

For certain kinds of testing (generally ecological effects), EPA requires the test substance to be a "typical formulation," and in those cases EPA needs data of that type

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1/ Generic data pertain to the properties or effects of a particular ingredient, and thus are relevant to an evaluation of the risks of all products containing that ingredient, regardless of the product's unique composition or specific use. Product-specific data relate only to the properties or effects of a product with a particular composition (or a group of products with closely similar composition).

2/ The Pesticide Assessment Guidelines are available in hard copy or microfiche from the National Technical Information Service, 5285 Port Royal Road, Springfield, Va. 22161.

for each major formulation category (e.g., emulsifiable concentrates, wettable powders, granulars, etc.) These are classified as generic data and when needed are specified in Table A. EPA may possess data on certain "typical formulations" but not others. Note: "Typical formulation" data should not be confused with product-specific data (Table B) which are required on each formulation. Product-specific data are further explained in Chapter III of this document.

C. Options Available for Complying With Requirements to Submit Data

Within 90 days of your receipt of this Notice you must submit to EPA a completed copy of the form entitled "FIFRA Section 3(c)(2)(B) Summary Sheet" [EPA Form 8580-1, Appendix II-3] for each of your products. On that form you must state which of the following methods you will use to comply with the requirements of this Notice:

1. (a) Notify EPA that you will submit the data, and

(b) either submit the existing data you believe will satisfy the requirement, or state that you will generate the data by conducting testing. If the test procedures you will use deviate from (or are not specified in) the Pesticide Assessment Guidelines or protocols contained in the Reports of Expert Groups to the Chemicals Group, Organization for Economic Cooperation and Development (OECD) Chemicals Testing Programme, you must enclose the protocols you will use.

OR

2. Notify EPA that you have entered into an agreement with one or more other registrants to jointly develop (or share in the cost of developing) the data. If you elect this option, you must notify EPA which registrant(s) are parties to the agreement.

OR

3. File with EPA a completed "Certification of Attempt to Enter Into an Agreement With Other Registrants for Development of Data" (EPA Form 8580-6, Appendix II-4)*/

*/ FIFRA sec. 3(c)(2)(B) authorizes joint development of data by two or more registrants, and provides a mechanism by which parties can obtain an arbitrator's decision if they agree to jointly develop data but fail to agree on all the terms of the agreement. The statute does not compel any registrant to agree to develop data jointly.

(Footnote continued on next page)

OR

4. Request that EPA amend your registration by deleting the uses for which the data are needed. (This option is not available to applicants for new products.)

OR

5. Request voluntary cancellation of the registration(s) of your products for which the data are needed. (This option is not available to applicants for new products.)

D. Procedures for Requesting Changes in Testing Methodology and Extensions of Time

EPA recognizes that you may disagree with our conclusions regarding the appropriate ways to develop the required data or how quickly the data must be submitted. If the test procedures you plan to use deviate from (or are not specified in) the registration guidelines or protocols contained in the reports of the Expert Groups to the Chemical Groups, Organization for Economic Cooperation and Development (OECD) Chemicals Testing Programme, you must submit the protocol for Agency review prior to the initiation of the test.

If you think that you will need more time to generate the required data than is allowed by EPA's schedule, you may submit a request for an extension of time. The extension request must be submitted in writing to the Product Manager.

(Footnote continued from previous page)
In EPA's opinion, joint data development by all registrants subject to a data requirement or a cost-sharing agreement among all such registrants is clearly in the public interest. Duplication of testing could increase costs, tie up testing facilities, and subject an unnecessarily large number of animals to testing.

As noted earlier, EPA has discretion to suspend the registration of a product when a registrant fails to submit data required under FIFRA Section 3(c)(2)(B). EPA has concluded that it should encourage joint testing rather than duplicative testing, and that suspension should be withheld in certain cases. to further this goal. Accordingly, if (1) a registrant has informed us of his intent to develop and submit data required by this Notice; and (2) a second registrant informs EPA that it has made a bona fide offer to the first registrant to share in the expenses of the testing [on terms to be agreed upon or determined by arbitration under FIFRA Section 3(c)(2)(B)(iii)]; and (3) the first registrant has declined to agree to enter into a cost-sharing agreement, EPA will not suspend the second firm's registration.

The extension request should state the reasons why you believe that an extension is appropriate. While EPA considers your request, you must strive to meet the deadline for submitting the required data.

III. REQUIREMENT FOR SUBMISSION OF PRODUCT-SPECIFIC DATA

Note: Unless stated otherwise in Section I, Regulatory Position and Rationale, this Section applies only to manufacturing use products, not to end use products.

A necessary first step in determining which statements must appear on your product's label is the completion and submission to EPA of product-specific data* listed on the form entitled "Product Specific Data Report" (EPA Form 8580-4, Appendix III-1) to fill gaps identified by EPA concerning your product. Under the authority of FIFRA sec. 3(c)(2)(B), EPA has determined that you must submit these data to EPA in order to reregister your product(s). All of these data must be submitted not later than six months after you receive this guidance document.

Table B--Product-Specific Data Requirements for Manufacturing Use Products--lists the product specific data you must submit. Data that are required to be submitted are identified in the column of those tables entitled "Must Data By Submitted Under §3(c)(2)(B)."

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*/ Product specific data pertain to data that support the formulation which is marketed; it usually includes product chemistry data and acute toxicity data.

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Guideline Citation and Name of Test	Test Substance	Guidelines Status	Are Data Required Yes	Are Data Required No	Footnote Number	Data Must Be Submitted Within Timeframes Listed Below 1/
§158.120 Product Chemistry						
Product Identity:						
61-2 - Product Identity and Disclosure of Ingredients	TGAI	R	[X]	[ ]		6 Months
61-3- Discussion of Formation of Impurities	TGAI	R	[X]	[ ]	2	6 Months
Analysis and Certification of Product Ingredients						
62-1 - Preliminary Analysis	TGAI	CR	[X]	[ ]	3	12 Months
Physical and Chemical Characteristics						
63-2 - Color	TGAI	R	[ ]	[X]		
63-3 - Physical State	TGAI	R	[ ]	[X]		
63-4 - Odor	TGAI	R	[X]	[ ]		6 Months
63-5 - Melting Point	TGAI	R	[X]	[ ]		6 Months
63-6 - Boiling Point	TGAI	R	[ ]	[X]		
63-7 - Density, Bulk Density, or Specific Gravity	TGAI	R	[X]	[ ]	4	6 Months
63-8 - Solubility	TGAI or PAI	R	[X]	[ ]	5	6 Months

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Guideline Citation and Name of Test	Test Substance	Guidelines Status	Are Data Required Yes	Are Data Required No	Footnote Number	Data Must Be Submitted Within Timeframes Listed Below 1/
§158.120 Product Chemistry (Continued)						
Physical and Chemical Characteristics (Continued)						
63-9 - Vapor Pressure	PAI	R	[ ]	[X]		
63-10 - Dissociation constant	PAI	R	[X]	[ ]		6 Months
63-11 - Octanol/water partition coefficient	PAI	R	[X]	[ ]		6 Months
63-12 - pH	TGAI	R	[X]	[ ]		6 Months
63-13 - Stability	TGAI	R	[X]	[ ]	6	6 Months
Other Requirements:						
64-1 - Submittal of samples	TGAI, PAI	CR	[ ]	[X]		

TGAI = Technical Grade of the Active Ingredient; PAI = Pure Active Ingredient; R = Required; CR = Conditionally Required

1/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
- 6 Month Due Date is December 31, 1985.
- 12 Month Due Date is June 30, 1985.

2/ A discussion of each impurity believed to be present at >0.1% based on knowledge of beginning materials, all possible chemical reactions and any contamination.

3/ Five or more representative samples should be analyzed for the amount of active ingredient and each impurity present for which a certified limit is required.

4/ The temperature at which the determination is made must be submitted.

5/ The solubility must be determined at 20 or 25° in distilled water and in representative polar and non-polar solvents.

6/ Information must be provided as to sensitivity to sunlight, metals and metal ions as well as temperature and pH.

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation		Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)?	Timeframes For Data Submission[2]/
§158.125 Residue Chemistry						
171-2 - Chemical Identity	TGAI	Partially	00056362 00093409	00106207	Yes	6 Months
171-3 - Directions for Use	—	Yes			No	
171-4 - Nature of Residue (Metabolism)						
- Plants	PAIRA	Partially	00024737 00036112 00036219 00036220 00045257 00045258 00045260 00045275	00045278 00045279 00045280 00106168 00106189 00106199 00106189 GS0181-003	Yes	24 Months[4]/[5]/
- Livestock	PAIRA and Plant Metabolites	Partially	00036105 00036106 00036107	00045263 00045262 00106164	Yes	18 Months[6]/[7]/
171-4 - Residue Analytical Method - Plant residues	TGAI and Metabolites	Yes	00015412 00015414 00029800 00036427 00032428 00032429 00036216 00036432 00036433	00087926 00106163 00106164 00106165 00106168 00106169 00106173 00106179 00106180	No[8]/	

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation		Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/
§158.125 Residue Chemistry - Continued					
			00036776	00106182	
			00036782	00106183	
			00039530	00106185	
			00045256	00106193	
			00054354	00106199	
			00054369	00106203	
			00069067	00106205	
			00087925	00106211	
				GS0181-006	
				GS0181-007	
- Animal residues	TGAI and Metabolites	Yes	00036431	GS0181-004	No
			00045282	GS0181-005	
171-4 - Storage Stability	PAI	Yes	00036441	00054358	No
			00036777	00054360	
			00036778	00054363	
			00054355	00054366	
			00054356	GS0181-002	
171-4 - Magnitude of the Residue-Residue Studies for each food use					
- Root and Tuber Vegetables Group[9]/					
- Potatoes	TEP	Yes	00039525	00078436	No
			00106199	00078438	
			00106203	00105212	
			00026411	00106191	
			00039531	00106797	

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GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation		Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/	
§158.125 Residue Chemistry - Continued						
- Potato Chips	EP	Yes	00036110 00026612		No	
- Processed potato waste	EP	Yes	00036110 00036112		No	
- Legume Vegetables Group[10]/						
- Lentils	TEP	Yes	00106179		No	
- Peas (dried and succulent)	TEP	Partially	00106179		Yes	24 Months[11]/
- Soybeans	TEP	Partially	00015773 00024503 00064797	00101537 00106215 GS0181-003	Yes	24 Months[12]/
Foliage of Legume Vegetables Group[13]/						
Lentil forage and hay	TEP	Yes[14]/	00106179		No	
Peas vines and straw	TEP	Yes[15]/	00106179		No	
Soybean forage, hay and straw	TEP	Partially[16]/	00015773 00015949 00067433 00086681	00087925 00101537 00106183 00106215	Yes	24 Months
Fruiting Vegetables (Except Cucurbits) Group[17]/						
Tomatoes	TEP	Yes	00106180 00106212		No	

TABLE A
GENERIC DATA REQUIREMENTS FOR CHEMICAL: METRIBUZIN

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/
§158.125 Residue Chemistry - Continued				
Tomato products (catsup puree)	EP	Yes	00106180 06106212	No[3]/[18]/
Cereal Grains Group[19]/				
Barley	TEP	Yes	00036428 00106185 00036444 00106182 00087926	No
Barley milling fractions	EP	Partially	00036428 00106185 00036444 00106182 00087926	No[20]/
Corn grain (including popcorn and fresh)	TEP	Partially	00036429 00078942 00036443 00078943 00106173	Yes[21]/ 24 Months
Fresh corn canning waste	EP	Yes	00036429 00078942 00036443 00078943 00106173	No[3]/[22]/
Wheat	TEP	Yes	00036426 00087926 00036435 00106173 00036439 00106182 00036445 00106184 00067425 00106185	No
Wheat milled fractions	EP	Partially	00036426 00087926 00036435 00106173 00036439 00106182 00036445 00106184 00067425 00106185	Yes[23]/ 24 Months

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TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/
§158.125 Residue Chemistry - Continued				
Forage, Fodder, Hay and Straw of Cereal Grains Group[24]/				
Barley forage, hay and straw	TEP	Partially	00036434 00087926 00036440 00106185 00045255 00106182	No[3]/[25]/
Corn forage, silage and fodder	TEP	Partially	00036429 00036443 00078942 00078943 00106173	Yes 24 Months[26]/
Wheat forage, hay and straw	TEP	Partially	00036426 00087926 00036435 00106173 00036439 00106182 00036445 00106185 00067425	Yes 24 Months[27]/
Grass Forage, Fodder and Hay Group[28]/				
Grass forage and hay	TEP	Yes	00036438 00036770 00036780	No
Non-grass Animal Feed Group[29]/				
Alfalfa forage, hay and seed	TEP	Partially	00036437 00106182 00036769 00106185 00036779	Yes 24 Months[3]/[30]
Sainfoin forage and hay	TEP	Yes	00036436 00036781	No

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/
§158.125 Residue Chemistry - Continued				
Miscellaneous Commodities				
Asparagus	TEP	Yes	00037841 00106173 00106211	No[3]/[31]/
- Sugarcane	TEP	Yes	00106168 00106190 00106202	No
Sugarcane forage	TEP	No	—	Yes 24 Months[32]/
Sugarcane bagasse, molasses, refined sugar	EP	Partially	00106168 00106190 00106202	Yes 24 Months[3]/[33]
171-4 Magnitude of the Residues in Meat, Milk, Poultry and Eggs				
Milk	TGAI or Plant Metabolites	Partially	00036772 00106199	Reserved[34]/
Meat, fat and meat byproducts of cattle, goats, hogs, horses and sheep	TGAI or Plant Metabolites	Partially	00045283	Reserved[34]/
Poultry and Eggs	TGAI or Plant Metabolites	Partially	00045284 00045286	Reserved[34]/

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TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

§158.125 Residue Chemistry - Continued

1/ Composition: TGAI = Technical grade of the active ingredient; PAIRA = Pure active ingredient, radiolabeled; TEP = Typical end-use product; EP = End-use product.

2/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
- 6 Month Due Date is December 31, 1985.
- 18 Month Due Date is December 31, 1986.
- 24 Month Due Date is June 30, 1987.

3/ Includes filing fee (establishing or changing a tolerance(s) requires a fee).

4/ Data reflecting the distribution and metabolism of ring-labeled [^{14}C] metribuzin in mature soybeans (foliage and beans) following preemergent soil application at 0.5 lb ai/A. Analysis should include hydrolysis and reextraction of plant residues and aqueous fractions to determine conjugated ^{14}C residues of metribuzin.

5/ Data reflecting the distribution and metabolism of ring-labeled [^{14}C] metribuzin in mature wheat (foliage and grain) following postemergence broadcast application at 0.75 lb ai/A. Analysis should include hydrolysis and reextraction of plant residues and aqueous fractions to determine conjugated ^{14}C-residues of metribuzin.

6/ Metabolism studies are required utilizing ruminants. Animals must be dosed for 3 days with ring-labeled [^{14}C] metribuzin at a level sufficient to make residue identification possible. Milk must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose. This distribution and characterization of residues (free and conjugated) must be determined in milk, liver, kidney, muscle and fat.

7/ Metabolism studies are required utilizing poultry. Hens must be dosed with ring labeled [^{14}C] metribuzin for 3 days at a level sufficient to permit residue identification. Eggs must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose and residues characterized in eggs, muscle, liver, kidney and fat.

8/ The conclusions stated here are tentative. Should the data requested in the "Nature of Residues in Plants" and "Nature of Residue in Animals" indicate additional metabolites of toxicological concern or that the methods do not adequately determine all conjugated residues of concern then submission of additional validated methods for data collection and tolerance enforcement will be required.

9/ A crop group tolerance is not appropriate at this time for the following reason: Residue data are required for two additional members of this group (radish and sugar beet), currently a tolerance exists for residues in or on potatoes only. The available data in support of a proposed tolerance for metribuzin residues in or on carrots are currently under review.

10/ A crop group tolerance is not appropriate at the present time for the following reasons:
a. Additional data are needed to support the established tolerances for residues in or on soybeans and dried peas.
b. Residue data are needed for one additional member of this crop group (succulent beans); presently, metribuzin is registered for use on lentils, peas, and soybeans.

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

§158.125 Residue Chemistry - Continued

11/ Data is required deplicting combined residues of metribuzin, DADK, DA, and DK in or on dried pea seed 50 days after postemergence application of the 50% WP formulation at 0.38 lbs ai/A. Test must be conducted in the Northwest.

12/ Data reflecting residues in or on soybeans harvested at normal maturity following two postemergence applications made at 7-day intervals of the 75% WP or 4 lb/gallon FLC formulation at 0.5 lbs ai/A application which were preceded by a preemergence application at 1 lb ai/A and a preplant application at 0.75 lb ai/A. Tests must be conducted in the MS delta region.

13/ A crop group tolerance is not appropriate at this time for the following reasons:
a. Additional data are required to support the established tolerances for residues in soybean forage and hay.
b. Pregrazing intervals must be proposed for lentil forage and pea vines.
c. The established tolerances for residues in or on pea and lentil forage (0.5 ppm) and in or on soybean forage (4 ppm) differ by more than a factor of five. Also, the established tolerances for residues in or on pea and lentil vine hay (0.05 ppm) and soybean hay (4 ppm) differ by more than a factor of five.

14/ The data to support the tolerances for lentil hay are adequate. The data to support tolerances for lentil forage will be adequate provided a pregrazing interval of 40 days is proposed for lentil forage.

15/ The data to support the tolerances for lentil hay and forage are translatable to support the tolerances for pea vines and straw. The data is adequate to support these tolerances provided a pregrazing interval of 40 days is proposed.

16/ Data reflecting combined residues of metribuzin, DADK, DA, and DK in or on soybean forage and hay harvested 40 days after the last of two postemergence applications of a WP or 4 lb/gal FLC formulation at 0.5 lb ai/A preceded by a preemergence application at 1 lb ai/A and a preplant application at 0.75 lb ai/A. Tests must be conducted in the MS delta region.

17/ A crop group tolerance is not appropriate at this time for the following reasons: Residue data are required for one additional member of this group (peppers); currently, a tolerance exists for residues in or on tomatoes only.

18/ A food additive tolerance of 0.2 part per million must be proposed for the combined residues of metribuzin and its triazinone metabolites in concentrated tomato products.

19/ A crop group tolerance is not appropriate at this time for the following reasons:
a. Residue data are required for two additional members of this group (rice and sorghum); metribuzin formulations are currently registered for use only on barley, corn and wheat.
b. The established tolerances for metribuzin residues in or on fresh corn (including kernels plus cobs with husks removed) and corn grain (including popcorn) for 0.05 ppm and the established tolerances (0.75 ppm) for residues in or on barley and wheat grain differ by more than a factor of five.
c. Additional residue data are required to support the currently established tolerance for residues in or on field corn grain.

§158.125 Residue Chemistry - Continued

20/ Additional data are not required for this topic because similar data requirements exist for wheat milled products which, upon their receipt, will be translated to barley milled products.

21/ The following data are required to support the tolerance on corn grain:
- a. Residue data for field corn grain harvested at normal maturity (~70-89% dry matter) after a single preemergence application with the 50% WP or the 4 lb/gal FLC formulation at 0.5 lb ai/A. Tests should be conducted in IA, MN, and NE as these states represent the major US corn production areas in which use of metribuzin on field corn is permitted.
- b. Field corn grain bearing detectable weathered residues of metribuzin must be processed into oil (crude and refined) and milled products; residues of metribuzin per se, DA, DK and DADK in these products must be sought. Exaggerated rates may be necessary to obtain detectable residues in or on grain. If residues concentrate in any of these products, appropriate food additive tolerances must be proposed.

22/ A feed additive tolerance of 0.1 ppm must be proposed for metribuzin residues for fresh corn cannery waste.

23/ Wheat grain bearing detectable weathered residues of metribuzin must be processed into germ and milled products and combined residues of metribuzin per se, DA, DK and DADK in these items must be determined. Exaggerated rates may be necessary to obtain residues in or on grain.

24/ A crop group tolerance is not appropriate at the present time for the following reasons:
- a. Additional residue data are required to support the currently established tolerance for residues in or on corn fodder.
- b. The established tolerances for metribuzin residues in or on corn forage (0.1 ppm) and wheat forage (2 ppm) differ by a factor >5X.
- c. Data and tolerance proposals must be submitted for residues in or on barley forage and hay, corn silage, and wheat hay; in the case of barley, grazing and feeding restrictions may be proposed in lieu of additional data.

25/ The available data are adequate to support tolerances on barley straw. Tolerances of 2 ppm for residues of metribuzin must be proposed for barley forage and straw. Alternatively, the present restriction against feeding or grazing barley prior to maturity may be amended to prohibit grazing or feeding treated barley, in any stage of maturity, to livestock. If tolerances are sought no additional data are required because data on wheat forage and data requested for wheat hay will be translated to barley forage and hay.

26/ Data are adequate to support the corn forage tolerance but not the corn fodder data. Data should be submitted and a tolerance proposed for corn silage. The following data are required:
- a. Data concerning residues in or on corn fodder harvested at normal maturity following a single preemergence broadcast application with either the 50 WP or 4 lbs/gal FLC formulation at 0.25 lb ai/A. Tests must be conducted in representative states in which treatment of field corn is permitted.
- b. Residue data for corn silage harvested from fields treated with a single preemergence broadcast application with the 50% WP or 4 lb/gal FLC at 0.25 lbs ai/A. Tests must be conducted in representative states in which treatment of field corn is permitted.

TABLE A
GENERIC DATA REQUIREMENTS FOR CHEMICAL: METRIBUZIN

§158.125 Residue Chemistry - Continued

27/ The following additional data are required: Data reflecting residues in or on wheat hay harvested at normal maturity after a postemergence broadcast application, after wheat has fully tillered, with the 50% or 75% WP, or the 4 lb/gal FIC formulation at 0.5 or 0.75 lbs ai/A. Both aerial and ground application equipment must be represented. High rate (0.75 lb ai/A) tests must be conducted in OK and low rate (0.5 ai/A) tests must be conducted in ID and UT, east of the Cascades.

28/ A crop group tolerance is not appropriate at this time for the following reasons:
a. Data are required for representative members of the crop group (Bermuda grass, bluegrass, and brumegrass or fescue)
b. A use has not been registered for applications to grass. The currently established tolerances for combined residues of metribuzin in or on grass forage and hay are for residues incurred in mixed stands with alfalfa for which use are registered.

29/ A crop group tolerance is not appropriate at this time for the following reasons:
a. Residue data are required for one additional member of this group (clover). Presently, metribuzin is registered for use on two members of this crop group (alfalfa and sainfoin).
b. Data and a tolerance proposal for residues in or on alfalfa seed are required.

30/ The available data are adequate to support tolerances on alfalfa forage and hay. A tolerance is necessary for residues in or on alfalfa seed. The following data are required: Residue data from mature alfalfa seed harvested 28 days after the record of two applications at 1 lb ai/A using the 4 lb/gal FIC or a W.P. These applications should represent fall and spring dormant applications no more than 5-6 months apart; a smaller treatment to major U.S. alfalfa growing regions. An appropriate tolerance must be proposed.

31/ A tolerance of 0.1 ppm on asparagus must be proposed for the combined residues of metribuzin and its triazinone metabolites.

32/ The following additional data are required. Residues must be determined in or on the sugarcane forage grown at HI at intervals following a spot treatment of the 50%, 70%, or 75% WP or the 4 lb/gal FIC at 5 lb ai/A which was preceded by a postemergence treatment at 3 lb/A; a pregrazing interval and tolerance for residues must be proposed; alternatively, a grazing restriction may be proposed.

33/ The following additional data are required: Residues must be determined in molasses, refined sugar, and bagasse processed from sugarcane bearing measurable weathered residues of metribuzin, DA, DK and DADK. If residues are found to concentrate in refined sugar, an appropriate food additive tolerance must be processed. The established food/feed tolerance must be proposed. The established food/feed additive tolerance for residues in molasses and bagasse will be assessed on receipt of the above-requested data.

34/ The nature of the residue in ruminants (including milk, meat, eggs) is not adequately understood. The adequacy of these tolerances and of the data submitted in support of the established tolerances cannot be assessed at this time. On a receipt of data requested in "Nature of Residue of Animals," the adequacy of the available data and the established tolerance will be assessed.

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.130 Environmental Fate					
DEGRADATION STUDIES-LAB:					
161-1 - Hydrolysis	TGAI or PAIRA	A,B	No		Yes[3A]/ 9 Months
Photodegradation					
161-2 - In Water	TGAI or PAIRA	A,B	No		Yes 9 Months
161-3 - On soil	TGAI or PAIRA	A	Partially	00045259	Yes[3A]/[4]/ 9 Months
161-4 - In Air	TGAI or PAIRA	A	No		No[3A]/
METABOLISM STUDIES-LAB:					
162-1 - Aerobic Soil	TGAI or PAIRA	A,B	No		Yes[3A]/ 27 Months
162-2 - Anaerobic Soil	TGAI or PAIRA	A	No		Yes[3A]/ 27 Months
162-3 - Anaerobic Aquatic	TGAI or PAIRA	___	No		No[6]/
162-4 - Aerobic Aquatic	TGAI or PAIRA	___	No		No[7]/
MOBILITY STUDIES:					
163-1 - Leaching and Adsorption/Desorption	TGAI or PAIRA	A,B	Partially	00025729 00054368 00029887 00045268	Yes[3A,8]/ 12 Month
163-2 - Volatility (Lab)	TEP	A	No		No[9]/
163-3 - Volatility (Field)	TEP	A	No		No[10]/

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.130 Environmental Fate - Continued					
DISSIPATION STUDIES-FIELD:					
164-1 - Soil	TEP	A,B	No		Yes[3A]/ 27 Months
164-2 - Aquatic (Sediment)	TEP		No		No[11]/
164-3 - Forestry	TEP		No		No[12]/
164-4 - Combination and Tank Mixes			No		No[13]/
164-5 - Soil, Long-term	TEP	A	No		No[14]/
ACCUMULATION STUDIES:					
165-1 - Rotational Crops (Confined)	PAIRA	A	No		Yes[15A]/ 39 Months
165-2 - Rotational Crops (Field)	TEP	A	No		Yes[15]/ 50 Months
165-3 - Irrigated Crops	TEP	—	No		No[16]/
165-4 - In Fish	TGAI or PAIRA	A,B	No		Yes 12 Months
165-5 - In Aquatic Nontarget Organisms	TEP	—	No		No[17]/
MONITORING STUDIES:					
Ground water Monitoring Studies			No		Yes[18]/

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

§158.130 Environmental Fate - Continued

1/ Composition: TGAI = Technical grade of the active ingredient; PAIRA = Pure active ingredient, radiolabeled; TEP = Typical end-use product.
2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-food; C = Aquatic, Food Crop; D = Aquatic, Non-food; E = Greenhouse, Food Crop; F = Greenhouse, Non-food; G = Forestry; H = Domestic Outdoor; I = Indoor.
3/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
- 9 Month Due Date is March 31, 1986.
- 12 Month Due Date is June 30, 1986.
- 27 Month Due Date is September 30, 1987.
- 39 Month Due Date is September 30, 1988.
- 50 Month Due Date is February 28, 1989.

3A/ Data in response to the Data Call-In for groundwater including hydrolysis, photodagration in water and on soil, aerobic and anaerobic soil metabolism, mobility, and field dissipation have been received and screened. Any valid studies which meet guidelines will reduce the data gaps.
4/ This study will be acceptable if additional data are provided on the factors affecting the incident sunlight as well as its intensity and duration.
5/ This compound does not require data on photodegradation in air.
6/ Data are not required because metribuzin has no forestry, or aquatic use.
7/ Data are not required because metribuzin has no aquatic use.
8/ Additional data are needed on the leaching or adsorption/desorption of the soil degradation products of metribuzin.
9/ The compound does not require volatility (lab) data.
10/ The compound does not require volatility (field) data.
11/ Data are not required because metribuzin has no aquatic uses.
12/ Data are not required because metribuzin has no forestry uses.
13/ Data requirements for combination products and tank mixes are not addressed in this Standard.
14/ Data are not required since results of the valid terrestrial field dissipation data indicated that greater than 50% of the residues dissipate prior to recommended subsequent application.
15/ For crops rotated on treated areas, any one of the following would apply:
a. A tolerance must be obtained for the rotated crop.
b. The product label must include a restriction against the rotation of crops used for feed or food which are not registered for use with metribuzin.
c. Data must be provided to determine time intervals at which rotated crops planted in treated areas will be free of pesticide residues.

15A/ Conditional on results from confined studies.
16/ No data are required because metribuzin does not have an aquatic food crop or aquatic nonerop use is not used in and around holding ponds used for irrigation purposes, and has no use involving effluents or discharges to water used for crop irrigation.
17/ No data are required because metribuzin has no forestry aquatic noncrop, or aquatic impact use.
18/ Ground water monitoring studies will be required. Notification of types of studies required and sites to be tested (Agency is in process of determining types of studies and test sites), by means of an amendment to the standard 3 months of issuance of the standard. A time limit for submission of data will be set at that time.

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.130 Toxicology					
ACUTE TESTING:					
81-1 - Acute Oral Toxicity - Rat	TGAI	A,B	Yes	00106158	No
81-2 - Acute Dermal Toxicity - Rabbit	TGAI	A,B	Yes	00106149	No
81-3 - Acute Inhalation Toxicity - Rat	TGAI	A,B	No	_____	Yes[4]/ 9 Months
81-7 - Delayed Neurotoxicity - Hen	TGAI	—	No	_____	No[5]/
SUBCHRONIC TESTING:					
82-1 - 90-Day Feeding: - Rodent, and	TGAI	A,B	No	_____	No[6]/
- Non-rodent (Dog)		A,B	No	_____	No[7]/
82-2 - 21-Day Dermal - Rabbit	TGAI	A,B	No	_____	No[8]/
82-3 - 90-Day Dermal - Rabbit	TGAI	A,B	No	_____	No[8]/
82-4 - 90-Day Inhalation: - Rat	TGAI	A,B	No	_____	No[8]/
82-5 - 90-Day Neurotoxicity: - Hen	TGAI	A,B	No	_____	No[8]/
- Mammal		A,B	No	_____	No[8]/

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.130 Toxicology - Continued					
CHRONIC TESTING:					
83-1 - Chronic Toxicity - 2 species:	TGAI				
- Rodent, and		A,B	No	_____	Yes[9]/ 49 Months
- Non-rodent (Dog)		A,B	Yes	00061260	No
83-2 - Oncogenicity - 2 species:	TGAI				
- Rat (preferred), and		A,B	No	_____	Yes[9]/ 50 Months
- Mouse (preferred)		A,B	Yes	00061256 00079527 00087795	No
83-3 - Teratogenicity - 2 species:	TGAI				
- Rat		A,B	No	_____	Yes[10]/ 15 Months
- Rabbit		A,B	Yes	00087796	No
83-4 - Reproduction - Rat 2-generation	TGAI	A,B	No	_____	Yes[11]/ 39 Months
MUTAGENICITY TESTING:					
84-1 - Gene Mutation (Ames Test)	TGAI	A,B	Partially	00086770	Yes[12]/ 9 Months
84-2 - Structural Chromosomal Aberration	TGAI	A,B	Partially	00086766 00086767 00086765 00086768	Yes[12]/ 12 Months

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/	
§158.130 Toxicology - Continued						
84-3 - Other Genotoxic Effects	TGAI	A,B	No	_____	Yes[12]/	12 Months
SPECIAL TESTING:						
85-1 - General Metabolism	PAI or PAIRA	A,B	No	_____	Yes[13]/	24 Months
85-2 - Dermal Penetration	Choice		No	_____	Yes	12 months
86-1 - Domestic Animal Safety	Choice		No	_____	No[8]/	

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TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

§158.130 Toxicology - Continued

1/ Composition: PAI = Pure active ingredient; PAIRA = Pure active ingredient, radiolabeled; Choice = Choice of several test substances determined on a case-by-case basis; TGAI - Technical grade of active ingredient.
2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-food; C = Aquatic, Food Crop; D = Aquatic, Non-food; E = Greenhouse, Food Crop; F = Greenhouse, Non-food; G = Forestry, H = Domestic Outdoor; I = Indoor.
3/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
- 9 Month Due Date is March 31, 1986.
- 12 Month Due Date is June 30, 1986.
- 15 Month Due Date is September 30, 1986.
- 24 Month Due Date is June 30, 1987.
- 39 Month Due Date is September 30, 1988.
- 50 Month Due Date is August 31, 1989.

4/ Additional data are required because the study reviewed was classified as supplementary data.
5/ Since metribuzin is not a cholinesterase inhibitor and does not otherwise indicate neurotoxicity, these data are not required.
6/ An acceptable chronic rat feeding study will fulfill the requirement for a subchronic rat study.
7/ The chronic dog study satisfies the requirement for a subchronic dog study.
8/ The guidelines and uses generally indicate that these data are not required.
9/ The submitted study is classified supplementary data. If additional data can be submitted, this study may be upgraded. If not, a repeat study will be necessary.
10/ A teratogenicity study in rats is required because the study previously submitted was reviewed by the Agency and found to be supplementary.
11/ Additional data are required because the high dose of the study previously submitted did not induce any toxicity, therefore, the study is classified as supplementary data.
12/ The following mutagenicity data are required.
a. Microbial point mutation tests.
b. Mammalian point mutation tests in vitro.
c. In vivo cytogenetics tests in mammals with either heritable translocation or dominant lethal studies.
d. Tests for primary DNA damage such as sister chromatid exchange or unscheduled DNA synthesis assays.
13/ Additional data are needed because previously submitted data were reviewed as supplementary data.

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission
§158.140 Reentry Protection					
132-1 - Foliar Dissipation	TEP	___	No	___	No[3]/
132-1 - Soil Dissipation	TEP	___	No	___	No[3]/
133-3 - Dermal Exposure	TEP	___	No	___	No[3]/
133-4 - Inhalation Exposure	TEP	___	No	___	No[3]/
§158.142 Spray Drift					
201-1 - Droplet Size Spectrum	TEP	___	No	___	No[3]/
201-1 - Drift Field Evaluation	TEP	___	No	___	No[3]/

1/ Composition: TEP = Typical end-use product.
2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-food; C = Aquatic, Food Crop; D = Aquatic, Non-food; E = Greenhouse, Food Crop; F = Greenhouse, Non-Food; G = Forestry; H = Domestic Outdoor; I = Indoor.
3/ Because of its low toxicity category (III), metribuzin does not required reentry data.

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TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.145 Wildlife and Aquatic Organisms					
AVIAN AND MAMMALIAN TESTING:					
71-1 - Acute Avian Oral Toxicity	TGAI	A,B	Yes	GS0181-009	No
	TEP	A,B	Partially	00051482	No [4]/
71-2 - Avian Subacute Dietary Toxicity	TGAI				
- Upland Game Bird, and		A,B	Yes	00065507	No
- Waterfowl		A,B	Partially	00065507	Yes[5]/ 9 Months
71-3 - Wild Mammal Toxicity	TGAI	A,B	No	____	No[6]/
71-4 - Avian Reproduction	TGAI				
- Upland Game Bird, and		A,B	No	____	Reserved[7]/
- Waterfowl		A,B	No	____	Reserved[7]/
71-5 - Simulated Field Testing	TEP				
- Mammals and		A,B	Partially	00035931	No
- Birds		A,B	Partially	00035931	No
- Actual Field Testing	TEP				
- Mammals, and		A,B	Partially	00035931	No
- Birds		A,B	Partially	00035931	No

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.145 Wildlife and Aquatic Organisms - Continued					
AQUATIC ORGANISM TESTING:					
72-1 - Freshwater Fish Toxicity - Coldwater Fish Species, and	TGAI	A,B	Yes	GS0181-008	No
- Warmwater Fish Species		A,B	Yes	GS0181-008	No
72-2 - Acute Toxicity to Freshwater Invertebrates	TGAI	A,B	Yes	00134495	No
72-3 - Acute Toxicity to Estuarine and Marine Organisms - Fish	TGAI	A	No		Yes[8]/ 12 Months
- Mollusk		A	Partially	00106197	Yes[8]/ 12 Months
- Shrimp		A	Yes	00106197	No
72-4 - Fish Early-Life Stage, and	TGAI	A,B	No	____	Reserved[9]/
- Aquatic Invertebrate Life-Cycle		A,B	No	____	Reserved[9]/

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TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[3]/
§158.145 Wildlife and Aquatic Organisms - Continued					
72-5 - Fish - Life-Cycle	TGAI	A,B	No	____	No
72-6 - Aquatic Organism Accumulation	TGAI, PAI or Degradation Product				
- Crustacean		A,B	No	____	Reserved[9]/
- Fish		A,B	No	____	Reserved[9]/
- Insect Nymph		A,B	No	____	Reserved[9]/
- Mollusk		A,B	No	____	Reserved[9]/
72-7 - Simulated Field Testing - Aquatic Organisms	TEP	A,B	No	____	Reserved[9]/
- Actual Field Testing - Aquatic Organisms		A,B	No	____	Reserved[9]/

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

§158.145 Wildlife and Aquatic Organisms - Continued

1/ Composition: TGAI = Technical grade of the active ingredient; PAI = Pure active ingredient, TEP = Typical end-use product.
2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-food Crop; C = Aquatic, Food Crop; D = Aquatic, Non-food; E = Greenhouse, Food Crop; F = Greenhouse, Non-food; G = Forestry, H = Domestic Outdoor; I = Indoor.
3/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
- 9 Month Due Date is March 31, 1986.
- 12 Month Due Date is June 30, 1986.

4/ There are currently no requirements for this type of study.
5/ Additional data are required for upland avian species.
6/ The low avian and mammalian toxicity for metribuzin indicate that these data are not required.
7/ Requirements are reserved pending dietary data on an upland species and appropriate environmental fate information.
8/ Data are needed on an estuarine/marine fish species and an oyster species to support sugarcane and soybean registration.
9/ Appropriate environmental fate information is needed to determine if potentially hazardous concentrations will reach the aquatic environment when products are used as directed.

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TABLE A

GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission
§158.150 Plant Protection					
121-1 - TARGET AREA PHYTOTOXICITY NONTARGET AREA PHYTOTOXICITY	EP		No	—	No[2]/
TIER I					
122-1 - Seed Germination/ Seedling Emergence	TGAI		No	—	No[2]/
122-1 - Vegetative Vigor	TGAI		No	—	No[2]/
122-2 - Aquatic Plant Growth	TGAI		No	—	No[2]/
TIER II					
123-1 - Seed Germination/ Seedling Emergence	TGAI		No	—	No[2]/
123-1 - Vegetative Vigor	TGAI		No	—	No[2]/
123-2 - Aquatic Plant Growth	TGAI		No	—	No[2]/
TIER III					
124-1 - Terrestrial Field	TEP		No	—	No[2]/
124-2 - Aquatic Field	TEP		No	—	No[2]/

1/ Composition: TGAI = Technical grade of the active ingredient; TEP = Typical end-use product. EP = End-use product.

2/ These requirements are generally waived unless it is believed there is a phototoxicity problem.

TABLE A
GENERIC DATA REQUIREMENTS FOR METRIBUZIN

Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission
§158.155 Nontarget Insect					
NONTARGET INSECT TESTING - POLLINATORS:					
141-1 - Honeybee acute contact toxicity	TGAI	A	Yes	00028772	No
141-2 - Honeybee - toxicity of residues on foliage	TEP	A	No		No[4]/
141-4 - Honeybee subacute feeding study	(Reserved)[3]/				
141-5 - Field testing for pollinators	TEP	A	No		No[4]/

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Data Requirements	Composition[1]/	Use[2]/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission
§158.155 Nontarget Insect - Continued					
NONTARGET INSECT TESTING - AQUATIC INSECTS:					
142-1 - Acute toxicity to aquatic insects	(Reserved)[5]/				
142-1 - Aquatic insect life-cycle study	(Reserved)[5]/				
142-3 - Simulated or actual field testing for aquatic insects	(Reserved)[5]/				
143-1 - NONTARGET INSECT TESTING - PREDATORS AND PARASITES thru 143-3	(Reserved)[5]/				

1/ Composition: TGAI = Technical grade of the active ingredient; TEP = Typical end-use product.
2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-food Crop; C = Aquatic, Food Crop; D = Aquatic, Non-food; E = Greenhouse, Food Crop; F = Greenhouse, Non-food, G = Forestry; H = Domestic Outdoor; I = Indoor.
3/ Reserved pending development of test method.
4/ Requirement applied on a case-by-case basis. Data reviewed to date do not indicate the need for a study.
5/ Reserved pending Agency decision as to whether data requirement should be established.

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS CONTAINING METRIBUZIN (94% TECHNICAL)

Guideline Citation and Name of Test	Test Substance	Guidelines Status	Are Data Required Yes	Are Data Required No	Footnote Number	Data Must Be Submitted Within Timeframes Listed Below[1]
§158.120 Product Chemistry						
Product Identity:						
61-1 - Product Identity and Disclosure of Ingredients	MP	R	[ ]	[X]		
61-2 - Description of Beginning Materials and Manufacturing Process	MP	R	[X]	[ ]	2,3	6 Months
61-3 - Discussion of Formation of Impurities	MP	R	[X]	[ ]	4	6 Months
Analysis and Certification of Product Ingredients						
62-1 - Preliminary Analysis	MP	CR	[X]	[ ]	5	12 Months
62-2 - Certification of Limits	MP	R	[X]	[ ]	6,7	12 Months
62-3 - Analytical Methods to Verify Certified Limit	MP	R	[X]	[ ]	8	12 Months
Physical and Chemical Characteristics						
63-2 - Color	MP	R	[ ]	[X]		
63-3 - Physical State	MP	R	[ ]	[X]		
63-4 - Odor	MP	R	[X]	[ ]		6 Months

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS CONTAINING METRIBUZIN (94% TECHNICAL)

Guideline Citation and Name of Test	Test Substance	Guidelines Status	Are Data Required Yes	Are Data Required No	Footnote Number	Data Must Be Submitted Within Timeframes Listed Below1/
§158.120 Product Chemistry						
Physical and Chemical Characteristics (Continued)						
63-7 - Density, Bulk Density, or Specific Gravity	MP	R	[X]	[ ]		6 Months
		CR	[X]	[ ]		6 Months
63-12 - pH	MP					
63-14 - Oxidizing or Reducing Action	MP	CR	[X]	[ ]		6 Months
63-15 - Flammability	MP	CR	[X]	[ ]		6 Months
63-16 - Explodability	MP	R	[X]	[ ]		6 Months
63-17 - Storage Stability	MP	R	[X]	[ ]		15 Months
63-18 - Viscosity	MP	CR	[X]	[ ]		6 Months
63-19 - Miscibility	MP	CR	[X]	[ ]		6 Months
63-20 - Corrosion Characteristics	MP	R	[X]	[ ]		15 Months
Other Requirements:						
64-1 - Submittal of samples	MP	CR	[ ]	[X]		

MP = Manufacturing-use Product; R = Required; CR = Conditionally Required.

1/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.

- 6 Month Due Date is December 31, 1985.
- 12 Month Due Date is June 30, 1986.
- 15 Month Due Date is September 30, 1986.

2/ Details of the manufacturing process including the relative amounts of beginning materials, a description of the equipment used to produce the product, reaction conditions, the duration of each step in the process, purification procedures and quality control measures for the 94% technical must be submitted.

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS CONTAINING METRIBUZIN (94% TECHNICAL)

§158.120 Product Chemistry - Continued

3/ The name and address of the manufacturer, producer, or supplier of each beginning material used to manufacture the 94% technical and a copy of all available technical specifications, data sheets, and other documents by which the manufacturer, producer, or supplier of beginning materials describes its composition and properties.

4/ A discussion of each impurity believed to be present at >0.1% based on knowledge of the beginning maerials, all possible chemical reactions and any contamination.

5/ Five or more representative samples should be analyzed for the amount of active ingredient and each impurity present for which a certified limit is required.

6/ A current Confidential Statement of Formula must be submitted.

7/ The following additional data are required:

a. Upper and lower limits must be provided (and certified) for metribuzin in 94% technical.

b. Upper limits must be provided (and certified) for each impurity present at >0.1% in the 94% technical.

c. All nitrosamines must be identified and quantified in six samples in 94% technical product; two samples of each must be analyzed shortly after production, 3 months after production, and 6 months after production. A method sensitive to 1 ppm of N-Nitroso contaminants must be used. An upper limit must be provided (and certified) for all nitrosamines found to be present.

8/ Quantitative methods to determine all impurities for which a certified limit is required on 94% technical. Each method must be accompanied by the validation studies of precision and accuracy of the method.

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TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACUTRING-USE PRODUCTS CONTAINING METRIBUZIN (94% TECHNICAL)

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/
§158.135 Toxicology				
ACUTE TESTING:				
81-1 - Acute Oral Toxicity - Rat	MP	Yes	00106158	No
81-2 - Acute Dermal Toxicity - Rabbit	MP	Yes	00106149	No
81-3 - Acute Inhalation Toxicity - Rat	MP	No		Yes[3]/ 9 Month
81-4 - Primary Eye Irritation - Rabbit	MP	Yes	GS0181-010	No
81-5 - Primary Dermal Irritation - Rabbit	MP	Yes	GS0181-010	No
81-6 - Dermal Sensitization - Guinea Pig	MP	Yes	00034014	No

1/ Composition: MP = Manufacturing-use product.

2/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
° 9 Month Due Date is March 31, 1986 .

3/ Additional data are needed because the study was classified as supplementary data.

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS CONTAINING METRIBUZIN (50% FI)

Guideline Citation and Name of Test	Test Substance	Guidelines Status	Are Data Required Yes	Are Data Required No	Footnote Number	Data Must Be Submitted Within Timeframes Listed Below1/
§158.120 Product Chemistry						
Product Identity:						
61-1 - Product Identity and Disclosure of Ingredients	MP	R	[X]	[ ]		6 Months
61-2 - Description of Beginning Materials and Manufacturing Process	MP	R	[X]	[ ]	2,3	6 Months
61-3 - Discussion of Formation of Impurities	MP	R	[X]	[ ]	4	6 Months
Analysis and Certification of Product Ingredients						
62-1 - Preliminary Analysis	MP	CR	[X]	[ ]	5	12 Months
62-2 - Certification of Limits	MP	R	[X]	[ ]	6,7	12 Months
62-3 - Analytical Methods to Verify Certified Limit	MP	R	[X]	[ ]	8	12 Months
Physical and Chemical Characteristics						
63-2 - Color	MP	R	[X]	[ ]		6 Months
63-3 - Physical State	MP	R	[X]	[ ]		6 Months
63-4 - Odor	MP	R	[X]	[ ]		6 Months

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS CONTAINING METRIBUZIN (50% FI)

Guideline Citation and Name of Test	Test Substance	Guidelines Status	Are Data Required Yes	Are Data Required No	Footnote Number	Data Must Be Submitted Within Timeframes Listed Below 1/
§158.120 Product Chemistry-(continued)						
Physical and Chemical Characteristics (Continued)						
63-7 - Density, Bulk Density, or Specific Gravity	MP	R	[X]	[ ]		6 Months
63-12 - pH	MP	CR	[X]	[ ]		6 Months
63-14 - Oxidizing or Reducing Action	MP	CR	[X]	[ ]		6 Months
63-15 - Flammability	MP	CR	[X]	[ ]		6 Months
63-16 - Explodability	MP	R	[X]	[ ]		6 Months
63-17 - Storage Stability	MP	R	[X]	[ ]		15 Months
63-18 - Viscosity	MP	CR	[X]	[ ]		6 Months
63-19 - Miscibility	MP	CR	[X]	[ ]		6 Months
63-20 - Corrosion Characteristics	MP	R	[X]	[ ]		15 Months
Other Requirements						
64-1 - Submittal of samples	MP	CR	[ ]	[X]		

MP = Manufacturing-use Product; R = Required; CR = Conditionally Required:

1/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.

- 6 Month Due Date is December 31, 1985.
- 12 Month Due Date is June 30, 1986.
- 15 Month Due Date is September 30, 1986.

2/ Details of the manufacturing process including the relative amounts of beginning materials, a description of the equipment used to produce the product, reaction conditions, the duration of each process, purification procedures and quality control measures for 50% F.I must be submitted.

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS CONTAINING METRIBUZIN (50% FI)

§158.120 Product Chemistry - Continued

3/ The name and address of the manufacturer, producer, or supplier of each beginning material used to manufacture the 50% FI and a copy of all available technical specifications, data sheets, and other documents by which the manufacturer, producer, or supplier of the beginning material describes its composition and properties.

4/ A discussion of each impurity believed to be present at >0.1% based on knowledge of the beginning materials, all possible chemical reactions and any contamination.

5/ Five or more representative samples should be analyzed for the amount of active ingredient and each impurity present for which a certified limit is required.

6/ A current Confidential Statement of Formula must be submitted.

7/ The following data are required:

a. Upper and lower limits must be provided (and certified) for metribuzin and each intentionally added inert in the 50% FI.

b. Upper limits must be provided (and certified) for each impurity present at >0.1% (w/w) in the 50% FI.

c. The purpose of each intentionally-added inert in 50% F.I. must be provided.

d. All nitrosamines must be identified and quantified in six samples in 50% F.I. products; two samples of each must be analyzed shortly after production, 3 months after production, and 6 months after production. A method sensitive to 1 ppm of N-Nitroso contaminants must be used. An upper limit must be provided (and certified) for all nitrosamines found to be present.

8/ Quantitative methods to determine all impurities for which a certified limit is required on 50% F.I. products. Each method must be accompanied by validation studies of the precision and accuracy of the method.

TABLE B

35 PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACUTRING-USE PRODUCTS CONTAINING METRIBUZIN (50% F.I.)

Data Requirements	Composition[1]/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B)? Timeframes For Data Submission[2]/
§158.135 Toxicology				
ACUTE TESTING:				
81-1 - Acute Oral Toxicity - Rat	MP	Yes	00106158	No
81-2 - Acute Dermal Toxicity - Rabbit	MP	Yes	00106149	No
81-3 - Acute Inhalation Toxicity - Rat	MP	No		Yes[3]/ 9 Months
81-4 - Primary Eye Irritation - Rabbit	MP	Yes	GS0181-010	No
81-5 - Primary Dermal Irritation - Rabbit	MP	Yes	GS0181-010	No
81-6 - Dermal Sensitization - Guinea Pig	MP	Yes	00034014	No

1/ Composition: MP = Manufacturing-use product.
2/ Data must be submitted within the indicated time frame, based on the date of the Guidance Document.
° 9 Month Due Date is March 31, 1986.
3/ Additional data are needed because the study was classified as supplementary data.

IV. SUBMISSION OF REVISED LABELING

Note: This section applies to end use products only to the extent described in Section I (Regulatory Position and Rationale). Otherwise, the following information pertains exclusively to manufacturing use products.

FIFRA requires each product to be labeled with accurate, complete and sufficient instructions and precautions, reflecting the results of data concerning the product and its ingredients. Labeling requirements are set out in 40 CFR 162.10 (see Appendix IV-1) and are summarized for products containing this active ingredient as part of this Guidance Document (See Appendix IV-2). Applications submitted in response to this notice must include draft labeling for Agency review.

If you fail to submit revised labeling information complying with this section (supplemented by requirements described in Section I, Regulatory Position and Rationale), EPA may issue a notice of intent to cancel the registration under FIFRA sec. 6(b)(1).

A. Label Contents

40 CFR 162.10 requires that certain specific labeling statements appear at certain locations on the label. This is referred to as format labeling. Specific label items listed below are keyed to Appendix IV-2.

Item 1. PRODUCT NAME - The name, brand or trademark is required to be located on the front panel, preferably centered in the upper part of the panel. The name of a product will not be accepted if it is false or misleading.

Item 2. COMPANY NAME AND ADDRESS - The name and address of the registrant or distributor is required on the label. The name and address should preferably be located at the bottom of the front panel or at the end of the label text.

Item 3. NET CONTENTS - A net contents statement is required on all labels or on the container of the pesticide. The preferred location is the bottom of the front panel immediately above the company name and address, or at the end of the label text. The net contents must be expressed in the largest suitable unit, e.g., "1 pound 10 ounces" rather than "26 ounces." In addition to English units, net contents may be expressed in metric units. See Appendix IV-1. [40 CFR 162.10(d)]

Item 4. EPA REGISTRATION NUMBER - The registration number assigned to the pesticide product must appear on the label, preceded by the phrase "EPA Registration No.," or "EPA Reg. No." The registration number must be set in type of a size and style similar to other print on that part of the label on which it appears and must run parallel to it. The registration number and the required identifying phrase must not appear in such a manner as to suggest or imply recommendation or endorsement of the product by the Agency. See Appendix IV-1. [40 CFR 162.10(e)]

Item 5. EPA ESTABLISHMENT NUMBER - The EPA establishment number, preceded by the phrase "EPA Est." is the final establishment at which the product was produced, and may appear in any suitable location on the label or immediate container. It must also appear on the wrapper or outside container of the package if the EPA establishment number on the immediate container cannot be clearly read through such wrapper or container. See Appendix IV-1. [40 CFR 162.10(f)]

Item 6A. INGREDIENTS STATEMENT - An ingredients statement is required on the front panel. The ingredients statement must contain the name and percentage by weight of each active ingredient and the total percentage by weight of all inert ingredients. The preferred location is immediately below the product name. The ingredients statement must run parallel with, and be clearly distinguished from, other text on the panel. It must not be placed in the body of other text. See Appendix IV-1. [40 CFR 162.10(g)]

Item 6B. POUNDS PER GALLON STATEMENT - For liquid agricultural formulations, the pounds per gallon of active ingredient must be indicated on the label.

Item 7. FRONT LABEL PRECAUTIONARY STATEMENTS - Front panel precautionary statements must be grouped together, preferably within a block outline. The table below shows the minimum type size requirements for various size labels.

Size of Label on Front Panel in Square Inches	Signal Word Minimum Type Size All Capitals	"Keep Out of Reach of Children" Minimum Type Size
5 and under	6 point	6 point
above 5 to 10	10 point	6 point
above 10 to 15	12 point	8 point
above 15 to 30	14 point	10 point
over 30	18 point	12 point

Item 7A. CHILD HAZARD WARNING STATEMENT - The statement "Keep Out of Reach of Children" must be located on the front panel above the signal word except where contact with children during distribution or use is unlikely. See Appendix IV-1. [40 CFR 162.10(h)(1)(ii)]

Item 7B. SIGNAL WORD - The signal word (DANGER, WARNING, or CAUTION) is required on the front panel immediately below the child hazard warning statement. See Appendix IV-1. [40 CFR 162.10 (h)(1)(i)]

Item 7C. SKULL & CROSSBONES AND WORD "POISON" - On products assigned a toxicity Category I on the basis of oral, dermal, or inhalation toxicity, the word "Poison" shall appear on the label in red on a background of distinctly contrasting color and the skull and crossbones shall appear in immediate proximity to the word POISON. See Appendix IV-1. [40 CFR 162.10(h)(1)(i)]

Item 7D. STATEMENT OF PRACTICAL TREATMENT - A statement of practical treatment (first aid or other) shall appear on the label of pesticide products in toxicity Categories I, II, and III. See Appendix IV-1. [40 CFR 162.10(h)(1)(iii)]

Item 7E. REFERRAL STATEMENT - The statement "See Side (or Back) Panel for Additional Precautionary Statements" is required on the front panel for all products, unless all required precautionary statements appear on the front panel. See Appendix IV-1. [40 CFR 162.10(h)(1)(iii)]

Item 8. SIDE/BACK PANEL PRECAUTIONARY LABELING - The precautionary statements listed below must appear together on the label under the heading "PRECAUTIONARY STATEMENTS." The preferred location is at the top of the side or back panel preceding the directions for use, and it is preferred that these statements be surrounded by a block outline. Each of the three hazard warning statements must be headed by the appropriate hazard title. See Appendix IV-1. [40 CFR 162.10 (h)(2)].

Item 8A. HAZARD TO HUMANS AND DOMESTIC ANIMALS - Where a hazard exists to humans or domestic animals, precautionary statements are required indicating the particular hazard, the route(s) of exposure and the precautions to be taken to avoid accident, injury or damage. See Appendix IV-1. [40 CFR 162.10 (h)(2)(i)]

Item 8B. ENVIRONMENTAL HAZARD - Where a hazard exists to non-target organisms excluding humans and domestic animals, precautionary statements are required stating the nature of the hazard and the appropriate precautions to avoid potential accident, injury, or damage. See Appendix IV-1. [40 CFR 162.10(h)(2)(ii)]

Item 8C. PHYSICAL OR CHEMICAL HAZARD

1. Flammability statement. Precautionary statements relating to flammability of a product are required to appear on the label if it meets the criteria in Appendix IV-3. The requirement is based on the results of the flashpoint determinations and flame extension tests required to be submitted for all products. These statements are to be located in the side/back panel precautionary statements section, preceded by the heading "Physical/Chemical Hazards." Note that no signal word is used in conjunction with the flammability statements.

2. Criteria for declaration of non-flammability. The following criteria will be used to determine if a product is non-flammable:

a. A "non-flammable gas" is a gas (or mixture of gases) that will not ignite when a lighted match is placed against the open cylinder valve.

b. A "non-flammable liquid" is one having a flashpoint greater than 350°F (177°C).

c. A "non-flammable aerosol" is one which meets the following criteria:

i. The flame extension is zero inches;

ii. There is no flashback; and

iii. The flashpoint of the non-volatile liquid component is greater than 350°F (177°C).

3. Declaration of non-flammability. Products which meet the criteria for non-flammability specified above may bear the notation "non-flammable" or "non-flammable (gas, liquid, etc.)" on the label. It may appear as a substatement to the ingredients statement, or on a back or side panel, but shall not be highlighted or emphasized (as with an inordinately large type size) in any way that may detract from precaution.

4. Other physical/chemical hazard statements. When chemistry data demonstrate hazards of a physical or chemical nature other than flammability, appropriate statements of hazard will be prescribed. Such statements may address hazards of explosivity, oxidizing or reducing capability, or mixing with other substances to produce toxic fumes.

Item 9A. RESTRICTED USE CLASSIFICATION - FIFRA sec. 3(d) requires that all pesticide formulations/uses be classified for either general or restricted use. Products classified for restricted use may be limited to use by certified applicators or persons under their direct supervision (or may be subject to other restrictions that may be imposed by regulation).

In the Registration Standard, the Agency has (1) indicated certain formulations/uses are to be restricted (Section I indicates why the product has been classified for restricted use); or (2) reserved any classification decision until appropriate data are submitted.

The Regulatory Position and Rationale states whether products containing this active ingredient are classified for restricted use. If they are restricted the draft label(s) submitted to the Agency as part of your application must reflect this determination (see below).

If you do not believe that your product should be classified for restricted use, you must submit any information and rationale with your application for reregistration. During the Agency's review of your application, your proposed classification determination will be evaluated in accordance with the provisions of 40 CFR 162.11(c). You will be notified of the Agency's classification decision.

A. Classification Labeling Requirements

If Section I of this Guidance Document indicates that your product has been classified for restricted use, the following label requirements apply:

1. Front panel statement of restricted use classification.

   a. The statement "Restricted Use Pesticide" must appear at the top of the front panel of the label. The statement must be set in type of the same minimum size as required for human hazard signal word (see table in 40 CFR 162.10(h)(1)(iv).

b. Directly below this statement on the front panel, a summary statement of the terms of restriction must appear (including the reasons for restriction if specified in Section I). If use is restricted to certified applicators, the following statement is required: "For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's Certification."

2. Some but not all uses restricted. If the Regulatory Position and Rationale states that some uses are classified for restricted use, and some are unclassified, several courses of action are available:

a. You may label the product for Restricted use. If you do so, you may include on the label uses that are unrestricted, but you may not distinguish them on the label as being unrestricted.

b. You may delete all restricted uses from your label and submit draft labeling bearing only unrestricted uses.

c. You may "split" your registration, i.e., register two separate products with identical formulations, one bearing only unrestricted uses, and the other bearing restricted uses. To do so, submit two applications for reregistration, each containing all forms and necessary labels. Both applications should be submitted simultaneously. Note that the products will be assigned separate registration numbers.

B. Compliance Schedules

No product with a use classified for restricted use under this Standard may be released for shipment by the registrant or producer after one year from the date of issuance of this Standard, unless such product bears the restricted use classification. All products still in channels of trade after two years from the date of issuance of this Standard must be labeled for restricted use.

Item 9B [There is no Item 9B].

Item 9C. MISUSE STATEMENT - All products must bear the misuse statement, "It is a violation of Federal law to use this product in a manner inconsistent with its labeling." This statement appears at the beginning of the directions for use, directly beneath the heading of that section.

Item 10A. REENTRY STATEMENT - If a reentry interval has been established by the Agency, it must be included on the label. Additional worker protection statements may be required in accordance with PR Notice 83-2, March 29, 1983.

Item 10B [There is no Item 10B].

Item 10C. STORAGE AND DISPOSAL BLOCK - All labels are required to bear storage and disposal statements. These statements are developed for specific containers, sizes, and chemical content. These instructions must be grouped and appear under the heading "Storage and Disposal" in the directions for use. This heading must be set in the same type sizes as required for the child hazard warning. Refer to Appendix IV-4 to determine the disposal instructions appropriate for your products.

Item 10D. DIRECTIONS FOR USE - Directions for use must be stated in terms which can be easily read and understood by the average person likely to use or to supervise the use of the pesticide. When followed, directions must be adequate to protect the public from fraud and from personal injury and to prevent unreasonable adverse effects on the environment. See Appendix IV-1. [40 CFR 162.10]

B. Collateral Labeling

Bulletins, leaflets, circulars, brochures, data sheets, flyers, or other written or graphic printed matter which is referred to on the label or which is to accompany the product are termed collateral labeling. Such labeling may not bear claims or representations that differ in substance from those accepted in connection with registration of the product. It should be made part of the response to this notice and submitted for review.

V. INSTRUCTIONS FOR SUBMISSION

A. For Manufacturing Products (MP) containing (metribuzin) as an active ingredient.

1. Within 90 days from receipt of this document, you must submit to the Product Manager in the Registration Division at the address given at the end of this section the "FIFRA Section 3(c)(2)(B) Summary Sheet" EPA Form 8580-1. Refer to Appendix II-3 with appropriate attachments.

If on the Summary Sheet, you commit to develop the data, request a minor chemical exemption, present arguments that a data requirement is not applicable, or submit protocols or modified protocols for Agency review, you must also submit a copy of the Summary Sheet (and any supporting information) to the Office of Compliance Monitoring, which will be monitoring the data generated in response to this notice. This information should be submitted to the Office of Compliance Monitoring at the address given at the end of this section. (Actual studies are not to be submitted.)

2. Within 6 months from receipt of this document you must submit to the Product Manager on the Registration Division:

a. Confidential Statement of Formula, EPA Form 8570-4.

b. Product Specific Data Report, EPA Form 8580-4 (Appendix III-1).

c. Two copies of any required product-specific data.

d. Two copies of draft labeling, including the label and associated brochures. If current labeling conforms to the requirements of this guidance document and the results of the short-term data, you may submit such labeling. End use product labeling must comply specifically with the instructions in Section I (Regulatory Position and Rationale) of this guidance document. The labeling should be either typewritten text on 8-1/2 x 11 inch paper or a mockup of the labeling suitable for storage in 8-1/2 x 11 inch files. The draft label must indicate the intended colors of the final label, clear indication of the front panel label, and the intended type sizes of the text.

e. Evidence of compliance with data support requirements of FIFRA sec. 3(c)(1)(D). Refer to 40 CFR 152.80-152.99 (enclosed) for latest requirements.

3. Within the times set forth in Table A, you must submit to the Registration Division all generic data, unless you are eligible for the formulator's exemption. If for any reason any test is delayed or aborted so that the agreed schedule cannot be met, notify the Product Manager and the Office of Compliance Monitoring.

B. For Manufacturing Use Products containing (metribuzin) in combination with other active ingredients

1. Within 90 days from receipt of this document, you must submit the "FIFRA Section 3(c)(2)(B) Summary Sheet," EPA Form 8580-1. Refer to Appendix II-3 with appropriate attachments.

If on the Summary Sheet, you commit to develop the data, request a minor chemical exemption, present arguments that a data requirement is not applicable, or submit protocols or modified protocols for Agency review, you must also submit a copy of the Summary Sheet (and any supporting information) to the Office of Compliance Monitoring, which will be monitoring the data generated in response to this notice. This information should be submitted to the Office of Compliance Monitoring at the address given at the end of this section. (Actual studies are not to be submitted.)

2. Within the times set forth in Table A, you must submit to the Registration Division all generic data, unless you are eligible for the formulator's exemption. If for any reason any test is delayed or aborted so that the agreed schedule cannot be met, notify the Product Manager and the Office of Compliance Monitoring.

C. For End Use Products containing (metribuzin))alone or in combination with other active ingredients:

1. Within 90 days from receipt of this document, you must submit the "FIFRA Section 3(c)(2)(B) Summary Sheet," EPA Form 8580-1. Refer to Appendix II-3 with appropriate attachments.

If on the Summary Sheet, you commit to develop the data, request a minor chemical exemption, present arguments that a data requirement is not applicable, or submit protocols or modified protocols for Agency review, you must also submit a copy of the Summary Sheet (and any supporting information) to the Office of Compliance Monitoring, which will be monitoring the data generated in response to this notice. This information should be submitted to the Office of Compliance Monitoring at the address given at the end of this section. (Actual studies are not to be submitted.)

2. Within 6 months from receipt of this document you must submit:

a. Confidential Statement of Formula, EPA Form 8570-4.

b. Product-Specific Data Report, EPA Form 8580-4 (Appendix III-1).

c. Two copies of any required product-specific data. (Refer to Table C).

d. Two copies of draft labeling, including the label and associated brochures. If current labeling conforms to the requirements of this guidance document and the results of the short-term data, you may submit such labeling. End use product labeling must comply specifically with the instructions in Section I (Regulatory Position and Rationale) of this guidance document. Labeling should be either typewritten text on 8 1/2 x 11 inch paper or a mockup of the labeling suitable for storage in 8 1/2 inch files. The draft label must indicate the intended colors of the final label, clear indication of the front panel label, and the intended type sizes of the text.

e. Evidence of compliance with data support requirements of FIFRA sec. 3(c)(1)(D). Refer to 40 CFR 152.80-152.99 (enclosed) for latest requirements.

3. Within the time frames set forth in Table A, submit all generic data, unless you are eligible for the formulator's exemption.

D. For intrastate products containing (Metribuzin) either as the sole active ingredient or in combination with other active ingredients

These products are being called in for full Federal registration. Producers of these products are being sent a letter instructing them how to submit an application for registration.

E. Applications and other required information should be submitted to the following address:

Robert Taylor, Product Manager
Registration Division (TS-767C)
Office of Pesticide Programs
Environmental Protection Agency
401 M St., S.W.
Washington, D.C. 20460
Phone No. (703) 557-1800

The address for submission to the Office of Compliance Monitoring is:

Laboratory Data Integrity Program
Office of Compliance Monitoring (EN-342)
Environmental Protection Agency
401 M St., S.W.
Washington, D.C. 20460

Guide to Use of This Bibliography

1. CONTENT OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Standard. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, will be included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a "study." In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review, and can be described with a conventional bibliographic citation. The Agency has attempted also to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by "Master Record Identifier," or MRID, number. This number is unique to the citation, and should be used at any time specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies; see paragraph 4(d)(4) below for a further explanation. In a few cases, entries added to the bibliography late in the review may be preceded by a nine-character temporary identifier. These entries are listed after all MRID entries. This temporary identifier number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standards of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

a. Author. Whenever the Agency could confidently identify one, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as author. As a last resort, the Agency has shown the first submitter as author.

b. Document Date. When the date appears as four digits with no question marks, the Agency took it directly from the document. When a four-digit date is followed by a question mark, the bibliographer deduced the date from evidence in the document. When the date appears as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing Parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission Date. The date of the earliest known submission appears immediately following the word "received."

(2) Administrative Number. The next element, immediately following the word "under," is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter, following the phrase "submitted by." When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," standing for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume. For example, within accession number 123456, the first study would be 123456-A; the second, 123456-B; the 26th, 123456-Z; and the 27th, 123456-AA.

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00015412 Analytical Biochemistry Laboratories (1976) Recovery of Sencor and Metabolites from Soybeans: Report No. 51072. (Unpublished study received Jan 19, 1977 under 100-583; prepared for Mobay Chemical Corp., submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL: 095747-W)

00015414 Thornton, J.S. (1974) A Modified Gas Chromatographic Method for the Determination of Sencor and Its Deaminated Diketo Metabolite in Soybeans: Report No. 42232. Method dated Dec 4, 1974. (Unpublished study received Jan 19, 1977 under 100-583; prepared by Mobay Chemical Corp., submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL:095748-V)

00015773 Searcy, S.; Herman, D.; Slagowski, J.L. (1978) Metolachlor (Dual (R) 8E); Metribuzin (Sencor 50W); Paraquat (2Cl): AG-A No. 4894 I,II. (Unpublished study including letter dated May 23, 1978 from J.D. Riggleman to Robert A. Kahrs, received Mar 16, 1979 under 100-583; prepared in cooperation with E.I. du Pont de Nemours & Co., Inc. and Chevron Chemical Co., submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL:237821-0)

00015949 Analytical Biochemistry Laboratories (1977) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment: MW-HR-409-75: Report No. 51071. (Unpublished study including report nos. 51065, 51069 and 51070, received Jan 19, 1977 under 100-583; submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL: 095747-AH)

00024503 Monsanto Company (1974) Summary of Residue Data. (Unpublished study received Jan 16, 1978 under 524-285; CDL:232680-B)

00024737 Hilton, H.W.; Nomura, N.S.; Kameda, S.S.; et al. (1976) Some patterns of herbicide and growth regulator intake, persistence, and distribution in sugarcane. Archives of Environmental Contamination and Toxicology 4(4):385-394. (Also in unpublished submission received Jul 19, 1978 under 201-403; submitted by Shell Chemical Co., Washington, D.C.; CDL:234470-AP)

00025729 Obrist, J.J.; Thornton, J.S. (1979) Soil Thin-Layer Mobility of Baycor (TM), (R) Baytan, (R) Drydene and Peropal (TM). (Unpublished study received Dec 21, 1979 under 3125-EX-168; prepared in cooperation with Agricultural Consultants, Inc.; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:099185-M)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00026411 Mobay Chemical Corporation (1977) Residue Data for Sencor, Alachlor in Potatoes. (Unpublished study received Jan 2, 1980 under WA 79/88; prepared in cooperation with Analytical Biochemistry Laboratories, Inc., submitted by State of Washington for Monsanto Co., Washington, D.C.; CDL:241541-A)

00028772 Atkins, E.L.; Greywood, E.A.; Macdonald, R.L. (1973) Toxicity of Pesticides and Other Agricultural Chemicals to Honey Bees: Laboratory Studies. Rev. By Univ. of California--Riverside, Dept. of Entomology. Riverside, Calif.: UC, Agricultural Extension Service. (Also in unpublished submission received Apr 2, 1980 under 464-556; submitted by Dow Chemical U.S.A., Midland, Mich.; CDL:242149-Z)

00029800 Thornton, J.S.; Schumann, S.A.; Boughton, P.J.; et al. (1974) A Gas Chromatographic Method for the Determination of Sencor and Its Deaminated Diketo Metabolite in Soybeans. Rev. Method no. 30387 dated Apr 11, 1972. (Unpublished study received Dec 21, 1974 under 5G1580; prepared by Baychem Corp., submitted by American Cyanamid Co., Princeton, N.J.; CDL:094331-J)

00029887 Thornton, J.S.; Hurley, J.B.; Obrist, J.J. (1976) Soil Thin-Layer Mobility of Twenty Four Pesticides [sic] Chemicals: Report No. 51016. (Unpublished study received Jan. 28, 1980 under 5F1547; submitted by Mobay Chemical Corp., Pittsburgh, Pa.; CDL: 099216-I)

00032428 Stanley, C.W.; Thornton, J.S. (1972) A Gas Chromatographic Method for the Determination of Sencor and Metabolites in Sugarcane and Products: Report No. 35115. Method dated Dec 7, 1972. (Unpublished study received Jul 2, 1975 under 239-2186; submitted by Chevron Chemical Co., Richmond, Calif.; CDL:119807-E)

00032429 Baychem Corporation (1973) Recovery of Sencor from Dry Soybeans: Report No. 35413. (Unpublished study received Jul 2, 1975 under 239-2186; submitted by Chevron Chemical Co., Richmond, Calif.; CDL:119807-F)

00034014 Edwards, D.F. (1978) Primary Skin Irritation and Sensitization Tests on Guinea Pigs: Report No. 443-78. (Unpublished study received Nov 20, 1978 under 352-390; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:236581-I)

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OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00035931 Findlay, G.M.; Baker, S.R. (1972) Assessing the Environmental Hazard of Pesticide Use: Report No. 37553. (Unpublished study received Mar 7, 1975 under 5F1559; prepared by Univ. of Manitoba, Dept. of Entomology, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-O)

00036105 Murphy, J.J.; Jacobs, K.; Lamb, D.W. (1974) The Metabolism of Sencor in a Dairy Cow: Report No. 40708. (Unpublished study received Oct 10, 1974 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:095130-B)

00036106 Bell, R.L.; Murphy, J.J. (1974) The Metabolism of Sencor in Chickens: Report No. 40712. Rev. (Unpublished study received Oct 10, 1974 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:095130-C)

00036107 Shaw, H.R., II; Murphy, J.J. (1974) The Metabolic Fate of 5-14C Sencor in Pigs: Report No. 40768. (Unpublished study received Oct 10, 1974 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:095130-D)

00036110 Thornton, J.S. (1974) Effect of Commercial Processing on Residues of Sencor in Potatoes: Report No. 42341. (Unpublished study received on unknown date under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:095987-B)

00036112 Simmons, C.E.; Gronberg, R.R. (1974) The Fate of Carbon-14-Labeled Sencor in Potatoes Processed by Pan or French Frying: Report No. 42452. (Unpublished study received on unknown date under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:095987-D)

00036216 Stanley, C.W. (1974) Comparison of Hydrolysis Methods for Sencor from Alfalfa: Report No. 40977. (Unpublished study received on unknown date under 4F1432; submitted by Chemagro Corp., Kansas City, Mo.; CDL:095519-A)

00036219 Morgan, J.G. (1972) Preliminary Studies on the Metabolism of Sencor in Tomatoes: Report No. 35013. (Unpublished study received Sep 27, 1973 under 4F1432; submitted by Chemagro Corp., Kansas City, Mo.; CDL:095519-F)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

004262

MRID CITATION

00036220 Morgan, J.G. (1973) Metabolism of Sencor in Tomatoes: Report No. 35969. (Unpublished study received Sep 27, 1973 under 4F1432; submitted by Chemagro Corp., Kansas City, Mo.; CDL: 095519-G)

00036426 Chemagro Corporation (1974) Chemagro Division of Baychem Corporation Residue Experiment 661-4828-73H: Report No. 41349. (Unpublished study including report nos. 41350 and 41351, received May 14, 1975 under 5F1628; prepared in cooperation with Cannon Laboratories, CDL:094425-A)

00036427 Cannon Laboratories (1974) Recovery of Sencor and Dadk from Barley and Wheat Grain: Report No. 41352. (Unpublished study received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094425-B)

00036428 Chemagro Corporation (1974) Chemagro Division of Baychem Corporation Residue Experiment 661-Extra-73D: Report No. 41353. (Unpublished study including report nos. 41354, 41355, 41356..., received May 14, 1975 under 5F1628; prepared in cooperation with Cannon Laboratories; CDL:094425-C)

00036429 Morse Laboratories (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 361-4701-73H: Report No. 41820. (Unpublished study including report nos. 41822, 41823, 41824..., received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094425-D)

00036431 Sandie, F.E.; Gronberg, R.R. (1975) A Gas Chromatographic Method for Determining Residues of Sencor and Metabolites in Animal Tissues, Milk and Eggs: Report No. 42257. Method dated May 5, 1975. (Unpublished study received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094425-F)

00036432 Cannon Laboratories (1974) Recovery of Sencor from Barley and Wheat Straw: Report No. 42292. (Unpublished study received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094425-G)

00036433 Mobay Chemical Corporation (1974) Recovery of Sencor and Metabolites from Barley and Wheat Straw: Report No. 42293. (Unpublished study received May 14, 1975 under 5F1628; CDL:094425-H)

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OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00036434 Mobay Chemical Corporation (1974) Raw Data and Chromatograms for Analysis of Sencor and Dadk on Barley Straw: Report No. 42294. (Unpublished study received May 14, 1975 under 5F1628; CDL: 094425-I)

00036435 Mobay Chemical Corporation (1974) Raw Data and Chromatograms for Analysis of Sencor and Dadk on Wheat Straw: Report No. 42295. (Unpublished study received May 14, 1975 under 5F1628; CDL: 094425-J)

00036436 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-47795-72H: Report No. 42326. (Unpublished study including report no. 42328, received May 14, 1975 under 5F1628; CDL:094425-K)

00036437 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-4779A-72H: Report No. 42327. (Unpublished study including report nos. 42329, 42330 and 42332, received May 14, 1975 under 5F1628; CDL: 094425-L)

00036438 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-4714 Extra--72H: Report No. 42331. (Unpublished study including report no. 42333, received May 14, 1975 under 5F1628; CDL:094425-M)

00036439 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-4832-73H: Report No. 42350. (Unpublished study including report nos. 42351, 42352, 42353..., received May 14, 1975 under 5F1628; prepared in cooperation with Cannon Laboratories; CDL:094425-N)

00036440 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-4822-73H: Report No. 42363. (Unpublished study including report nos. 42364, 42365, 42366..., received May 14, 1975 under 5F1628; prepared in cooperation with Cannon Laboratories; CDL:094425-O)

00036441 Mobay Chemical Corporation (1974) The Effect of Frozen Storage at 0 to -10°F on Sencor and Metabolite Residue in Milk: Report No. 42372. (Unpublished study received May 14, 1975 under 5F1628; CDL:094425-P)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting Registrations Under the Metribuzin Standard

004262

MRID CITATION

00036443 Chemagro Corporation (1974) Chemagro Division of Baychem Corporation Residue Experiment 661-4710-73D: Report No. 40910. (Unpublished study including report nos. 40911, 40912, 40913..., received May 14, 1975 under 5F1628; prepared in cooperation with Morse Laboratories, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094424-C)

00036444 Mobay Chemical Corporation (1974) Raw Data and Chromatograms for the Analysis of Sencor and DADK in Barley Grain: Report No. 41237. Rev. (Unpublished study received May 14, 1975 under 5F1628; CDL:094424-D)

00036445 Cannon Laboratories (1974) Chemagro Division of Baychem Corporation Residue Experiment: 263-4839-73H: Report No. 41339. (Unpublished study including report nos. 41341, 41342, 41343..., received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094424-E)

00036769 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 861-4708A-72D: Report No. 42374. (Unpublished study including report nos. 42466, 42467, 42468..., received May 14, 1975 under 5F1628; CDL: 094426-B)

00036770 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment: 861-4708 G-72H: Report No. 42375. (Unpublished study received May 14, 1975 under 5F1628; CDL:094426-C)

00036772 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment AH-71A-851: Report No. 42449. (Unpublished study received May 14, 1975 under 5F1628; CDL:094426-E)

00036776 Mobay Chemical Corporation (1974) Recovery of Sencor from Sainfoin: Report No. 42470. (Unpublished study received May 14, 1975 under 5F1628; CDL:094426-I)

00036777 Mobay Chemical Corporation (1974) The Effect of Frozen Storage at 0 to -10°F on Sencor Residues in Green Alfalfa: Report No. 42471. (Unpublished study received May 14, 1975 under 5F1628; CDL:094426-J)

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REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

004262

MRID CITATION

00036778 Mobay Chemical Corporation (1974) The Effect of Frozen Storage at 0 to -10°F on Sencor Residues in Poultry Tissues and Eggs: Report No. 42451. (Unpublished study received May 14, 1975 under 5F1628; CDL:094426-K)

00036779 Mobay Chemical Corporation (1975) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 263-4701-72H: Report No. 42484. (Unpublished study including report nos. 42485, 42486, 42487..., received May 14, 1975 under 5F1628; CDL: 094427-A)

00036780 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-4704 Extra-72H: Report No. 42492. (Unpublished study received May 14, 1975 under 5F1628; CDL:094427-B)

00036781 Mobay Chemical Corporation (1974) Chemagro Agricultural Division--Mobay Chemical Corporation Residue Experiment 661-4781-73H: Report No. 42493. (Unpublished study including report nos. 42494, 42495 and 42496, received May 14, 1975 under 5F1628; CDL: 094427-C)

00036782 Morris, R.A. (1975) Interference Study for the Residue Method for Sencor and Its Metabolites in Various Crops: Report No. 42735. (Unpublished study received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094427-D)

00037841 Chemagro Corporation (1974) Chemagro Division of Baychem Corporation Residue Experiment: 861-4723-73H: Report No. 40888. (Unpublished study including report no. 40889, received May 14, 1975 under 5F1628; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094424-A)

00039525 American Cyanamid Company (1975) General Summary: Prowl Herbicide and Its Metabolite and Sencor Residues in or on Potatoes. Summary of studies 095485-Q through 095485-S. (Unpublished study received Feb 9, 1976 under 6G1739; CDL:095485-K)

00039530 Devine, J.M.; Thornton, J.S.; Stanley, C.W. (1975) Sencor (Bay 94337): The Gas Chromatographic Determination of Sencor 4-Amino-6-t-butyl-3-(methylthio)-1,2,4-triazin-5(4H)-one from Fortified Potatoes: Report No. C-767. Includes method, report no. 33005, dated Apr 14, 1972. (Unpublished study received Feb 9, 1976 under 6G1739; prepared in cooperation with Chemagro Corp., submitted by American Cyanamid Co., Princeton, N.J.; CDL: 095485-P)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00039531 Devine, J.M.; Nzewi, G.I.; Boughton, P.J.; et al. (1975) Prowl (R) (CL 92,553): Determination of CL 92,553 N-(1-Ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamide, CL 202,347 4-(1-Ethylpropyl amino)-2-methyl-3,5-dinitro benzyl alcohol and Sencor 4-Amino-6-t-butyl-3-(methylthio)-1,2,4-triazin-5(4H)-one Residues in Potatoes: Report No. C-787. (Unpublished study received Feb 9, 1976 under 6G1739; submitted by American Cyanamid Co., Princeton, N.J.; CDL:095485-Q)

00045255 Chemagro Corporation (1975) Supplement to Synopsis of the Effects of Sencor on the Environment. Summary of studies 094871-C through 094871-F, 094871-I through 094871-O, 094871-Q through 094871-S. (Supplement no. 1; unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-A)

00045256 Stanley, C.W.; Schumann, S.A. (1969) A Gas Chromatographic Method for the Determination of Bay 94337 Residues in Potatoes, Soybeans, and Corn: Report No. 25,838. Method dated Oct 16, 1969. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-B)

00045257 Robinson, R.A.; Gronberg, R.R.; Shaw, H.R., II (1970) Bay 94337 Metabolism in Plants: Report No. 26,175. Rev. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-C)

00045258 Gronberg, R.R.; Flint, D.R.; Shaw, H.R.; et al. (1971) The Metabolism of Sencor (Bay 94337) in Soybean Plants: Report No. 29800. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-D)

00045259 Khasawinah, A.M. (1972) The Metabolism of Sencor (Bay 94337) in Soil: Report No. 31043. Rev. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-E)

00045260 Church, D.D.; Flint, D.R. (1973) The Metabolism of Sencor in Potatoes: Report No. 32047. Rev. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-F)

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OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00045262 Morgan, J.G.; Flint, D.R. (1972) Sencor Residues in Chicken Eggs and Tissue: Report No. 33226. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-H)

00045263 Flint, D.R.; Shaw, H.R., II (1972) Residues in Tissue and Milk from Goats Treated Daily with Sencor-14C in the Diet: Report No. 33255. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-I)

00045268 Houseworth, L.D.; Tweedy, B.G. (1973) Report on Parent Leaching Studies for (R) Sencor: Report No. 37180. (Unpublished study received Mar 7, 1975 under 5F1559; prepared by Univ. of Missouri, Dept. of Plant Pathology, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094871-N)

00045275 Morgan, J.G. (1974) The Metabolism of Sencor in Seedling Potatoes: Report No. 40564. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo., CDL:094870-C)

00045278 Stanley, C.W.; Flint, D.R. (1974) The Metabolism of Sencor in Alfalfa: Report No. 40853. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094870-I)

00045279 Hargroder, T.G.; Rogers, R.L. (1974) Behavior and fate of Metribuzin in soybean and hemp sesbania. Weed Science 22(3):238-245. (Also in unpublished submission received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094870-J)

00045280 Schumacher, R.W. (1974) Metabolism of Metribuzin in Soybeans and Soil: Report No. 40865. Doctoral dissertation, Univ. of Kentucky. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094870-K)

00045282 Sandie, F.E.; Gronberg, R.R. (1974) A Gas Chromatographic Method for Determining Residues of Sencor and Metabolites in Animal Tissues, Milk and Eggs: Report No. 42257. Method dated Dec 5, 1974. (Unpublished study received Mar 7, 1975 under 5F1559; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 094870-M)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00045283 Mobay Chemical Corporation (1974) Sencor Residues in Cattle: Report No. 42373. (Unpublished study received Mar 7, 1975 under 5F1559; CDL:094870-N)

00045284 Mobay Chemical Corporation (1974) Sencor Residues in Poultry: Report No. 42448. (Unpublished study received Mar 7, 1975 under 5F1559; CDL:094870-O)

00045286 Mobay Chemical Corporation (1974) Sencor Residues in Eggs: Report No. 42450. (Unpublished study received Mar 7, 1975 under 5F1559; CDL:094870-Q)

00051482 Shellenberger, T.E. (1969) Letter sent to D.L. Nelson dated Aug 11, 1969: Toxicological evaluations of Bay 94337 with fish and wildlife: GSRI Project No. NC-288; Letter Report No. 5; Report No. 25527. (Unpublished study received Jan 16, 1970 under 3125-EX-114; prepared by Gulf South Research Institute, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:222273-D)

00054354 Thornton, J.S.; Stanley, C.W. (1972) A Gas Chromatographic Method for the Determination of Residues of Sencor and Its Metabolites in Potatoes: Report No. 33005. Method dated Apr 14, 1972. (Unpublished study received Aug 14, 1980 under 3125-314; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:243067-B)

00054355 Thornton, J.S. (1972) Effect of Room Temperature Storage on Residues of Sencor and Metabolites in Mature Potatoes: Report No. 33058. (Unpublished study received Aug 14, 1980 under 3125-314; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 243067-C)

00054356 Mobay Chemical Corporation (1972) Effect of Frozen Storage at 0°F on Sencor and DADK Residues in Soybeans: Report No. 33289. (Unpublished study received Aug 14, 1980 under 3125-314; CDL: 243067-D)

00054358 Mobay Chemical Corporation (1973) The Effect of Frozen Storage at 0 to -10°F on Sencor Residues in Potatoes: Report No. 35845. (Unpublished study received Aug 14, 1980 under 3125-314; CDL: 243067-F)

00054360 Mobay Chemical Corporation (1974) The Effect of Frozen Storage at 0 to -10°F on Sencor Residues in Green Alfalfa: Report No. 42471. (Unpublished study received Aug 14, 1980 under 3125-314; CDL:243067-M)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

004262

MRID CITATION

00054363 Mobay Chemical Corporation (1975) The Effect of Frozen Storage at 0 to -10°F on Sencor (TM) and Metabolite Residues in Green Peas: Report No. 44621. (Unpublished study received Aug 14, 1980 under 3125-314; CDL:243067-P)

00054366 Mobay Chemical Corporation (1974) The Effect of Frozen Storage at 0 to -10°F on (R) Sencor Residues in Tomatoes: Report No. 47371. (Unpublished study received Aug 14, 1980 under 3125-314; CDL:243067-S)

00054368 Savage, K.E. (1976) Adsorption and mobility of Metribuzin in soil. Weed Science 24(5):525-528. (Submitter report no. 51903; also :in unpublished submission received Aug 14, 1980 under 3125-314 submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL: 243067-V)

00054369 Thornton, J.S.; Stanley, O.W. (1977) Gas chromatographic determination of Sencor and metabolites in crops and soil. Journal of Agricultural and Food Chemistry 25(2):380-386. (Submitter report no. 52909; also in unpublished submission received Aug 14, 1980 under 3125-314; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:243067-W)

00056362 Mobay Chemical Corporation (19??) Technical Information: Sencor. (Unpublished study received Jan 23, 1976 under unknown admin. no.; CDL:226026-A)

00061256 Smith, P.S.; Gordon, D.E. (1972) Report to Chemagro, a Division of Baychem Corporation: 18-Month Carcinogenic Study with Sencor (Bay 94337) in Swiss White Mice: IBT No. B9069; Report No. 34481. (Unpublished study including report no. 34481a, received on unknown date under 5F1559; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094258-D)

00061260 Loser, E.; Mirea, D. (1974) Bay 94 337: Chronic Toxicity Studies on Dogs (Two-Year Feeding Experiment): Report No. 4887; Report No. 41814. (Unpublished study received on unknown date under 5F1559; prepared by Bayer, AG, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:094258-J)

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REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00064797 Wilson, G.R.; Baszis, S.R.; Steinmetz, J.R.; et al. (1980) Residues of Acetochlor in Soybean and Corn Grain following Preemergent [illegible]eatment with Acetochlor Alone or in Tank-mix Combinations wi[illegible] Atrazine, Linuron and Metribuzin: Report No. MSL-1242. Final rept. (Unpublished study received Dec 12, 1980 under 524-EX-56; submitted by Monsanto Co., Washington, D.C.; CDL: 099813-A)

00065507 Lamb, D.W.; Burke, M.A. (1977) Dietary Toxicity of (R) Sencor Technical to Bobwhite Quail and Mallard Ducks: Report No. 51593. (Unpublished study received Apr 13, 1977 under 3125-270; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:229312-A)

00067425 Monsanto Company (1980) Residues of Glyphosate and Other Herbicides in Wheat following Chemical Fallow Applications of Roundup (R) Tank Mix Combinations. Includes method dated Jul 1, 1979 and undated methods entitled: 2,4-D in wheat forage, straw and grain; Dicamba in wheat forage, straw and grain; Residues of alachlor in wheat grain, forage and straw; Atrazine in wheat forage, straw and grain; Cyanazine in wheat forage, straw and grain; Metribuzin and metabolites in wheat forage, straw and grain. (Unpublished study, including published data, received Dec 29, 1980 under 524-308; CDL:243990-A; 243991)

00067433 Harrison, S.L.; Boros, E.J. (1980) Chloramben, Trifluralin & Metribuzin (+ DADK) Analyses of Soybeans Treated with Amiben + Treflan + Sencor or Lexone Tank Mix PPI: Project Report 10123/1280A. (Unpublished study received Dec 19, 1980 under 264-138; prepared in cooperation with Southern Illinois Univ., Plant & Soil Science Dept. and others, submitted by Union Carbide Agricultural Products Co., Inc., Ambler, Pa.; CDL:243984-F)

00069067 Thornton, J.S. (1974) A Gas Chromatographic Method for the Determination of Sencor and Metabolites in Various Crops: Report No. 40901. Method dated Dec 11, 1974. (Unpublished study received Sep 13, 1976 under 3125-277; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:226759-H)

00078436 Wilson, G.R.; Dubelman, S. (1981) Residues of Alachlor in Potatoes following Preemergent and Lay-by Treatment with Lasso (R) Alone or in Tank-mix Combinations with Metribuzin: Report No. MSL-1559. Final rept. (Unpublished study received Aug 7, 1981 under 1F2551; submitted by Monsanto Co., Washington, D.C.; CDL: 070279-A)

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OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00078438 Stauffer Chemical Company (1980) Eptam 7-E + Metribuzin Tank Mix on Potatoes: Summary of Crop Residue Data. (Compilation; unpublished study received Jul 27, 1981 under 476-2154; CDL:245620-B)

00078942 Mobay Chemical Corporation (1981) Addition to Synopsis of Sencor Residue Chemistry on Various Crops: Addition No. 6. (Compilation; unpublished study received Jul 13, 1981 under 3125-314; CDL:245572-A)

00078943 Mobay Chemical Corporation (1981) Addition to Synopsis of Sencor Residue Chemistry on Various Crops: Addition No. 5. (Compilation; unpublished study received Jul 13, 1981 under 3125-314; CDL:245573-A)

00079527 Smith, P.S.; Gordon, D.E. (1972) Report to Chemagro, a Division of Baychem Corporation: 18-month Carcinogenic Study with Sencor (Bay 94337) in Swiss White Mice: IBT No. B9069; Report No. 34481. (Unpublished study received Mar 13, 1973 under 3125-EX-120; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:126999-B)

00086681 Mobay Chemical Corporation (1981) Addition to Synopsis of Sencor: Residue Chemistry on Soybeans. Summary of studies 246225-B and 246225-C. (Compilation; unpublished study received Oct 29, 1981 under 3125-277; CDL:246225-A)

00086765 Machemer, L.; Lorke, D. (1974) Evaluation of the Mutagenic Potential of (R) Sencor in an in vivo Cytogenetic Study on Spermatogonia of Chinese Hamster: Report No. 4961; 43067. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-A)

00086766 Machemer, L.; Lorke, D. (1974) Evaluation of (R) Sencor for Mutagenic Effects on the Mouse: Report No. 4942; 43068. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-B)

00086767 Machemer, L.; Lorke, D. (1975) (R) Sencor: Dominant Lethal Study on Male Mice To Test for Mutagenic Effects: Report No. 5523; 45023. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-C)

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Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00086768 Machemer, L.; Lorke, D. (1976) (R) Sencor: Additional Dominant Lethal Study on Male Mice To Test for Mutagenic Effects by an Improved Method: Report No. 6110; 49068. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Bayer AG, West Germany, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-D)

00086770 Inukai, H.; Iyatomi, A. (1977) Bay 94337: Mutagenicity Test on Bacterial Systems: Report No. 67; 54127. (Unpublished study received Nov 3, 1981 under 3125-270; prepared by Nitokuno Agricultural Chemicals Institute, Japan, submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246226-F)

00087795 Hayes, R.H.; Lamb, D.W.; Mallicoat, D.R.; et al. (1981) Metribuzin ((R) Sencor) Oncogenicity Study in Mice: 80050. (Unpublished study received Nov 23, 1981 under 3125-270; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246397-A)

00087796 Unger, T.M.; Shellenberger, T.E. (1981) A Teratological Evaluation of Sencor (R) in Mated Female Rabbits: 80051. Final rept. (Unpublished study received Nov 23, 1981 under 3125-270; submitted by Mobay Chemical Corp., Kansas City, Mo.; CDL:246397-B)

00087925 Mobay Chemical Corporation (1978) (R) Sencor Residue Chemistry on Soybeans: Supplement No. 5. (Compilation; unpublished study received Dec 16, 1981 under 3125-277; CDL:246510-A)

00087926 Mobay Chemical Corporation (1981) (R) Sencor Residue Chemistry on Various Crops: Addition No. 7. (Compilation; unpublished study received Dec 23, 1981 under 3125-277; CDL:246509-A)

00093409 Mobay Chemical Corporation (1978) Nitrosamines in Technical and Formulated Products: Report No. 66197. (Compilation; unpublished study received Jul 5, 1978 under 3125-50; CDL:234223-A)

00101537 Lauer, R.; Dubelman, S. (1982) Residues of Alachlor in Soybeans Following Preemergent Treatment with Lasso ME Alone or in Tankmix Combinations with Roundup, Linuron and Metribuzin: Report No. MSL 2084. (Unpublished study received May 10, 1982 under 524-344; submitted by Monsanto Co., Washington, DC; CDL: 070844-B)

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REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

MRID CITATION

00105212 Frank, R.; Sieck, R.; Shuey, E. (1979) Oryzalin and Metribuzin Residues in White Potatoes When Surface Applied to Control Weeds. (Unpublished study received Jul 1, 1982 under 1471-96; submitted by Elanco Products Co., Div. of Eli Lilly and Co., Indianapolis, IN; CDL:070954-A)

00106149 Crawford, C.; Anderson, R. (1972) The Acute Dermal Toxicity of Sencor Technical and Sencor 50% Wettable Powder to Rats and Rabbits: Report No. 33123. (Unpublished study received May 17, 1972 under 3125-270; submitted by Mobay Chemical Corp., Kansas City, MO; CDL:051077-A)

00106158 Kimmerle, G.; Solecke, B.; Lorke (1969) Bay 94337 Toxicological Studies from Dr. George Kimmerle, M.D. and Dr. Brigitte Solecke, V.M.D.: Report No. 1574; 25942. (Unpublished study received Jul 3, 1971 under 0G0940; prepared by Farbenfabriken Bayer, AG, W. Ger., submitted by Mobay Chemical Corp., Kansas City, MO; CDL: 091606-I)

00106163 Mobay Chemical Corp. (1969) Bay 94337 Metabolic, Analytical, and Residue Information on Potatoes and Soybeans. (Compilation; unpublished study received Jan 16, 1970 under 0G0940; CDL: 091607-A)

00106164 Mobay Chemical Corp. (1972) Sencor (Bay 94337) Metabolic, Analytical, and Residue Information on Soybeans. (Compilation; unpublished study received Oct 5, 1972 under 2F1274; CDL:091806-A; 091807)

00106165 Thornton, J. (1973) Effect of Cooking (Steaming) on the Release of Sencor Residues from Soybeans: Report No. 36826. (Unpublished study received Oct 6, 1972 under 2F1274; submitted by Mobay Chemical Corp., Kansas City, MO; CDL:091809-A)

00106168 Mobay Chemical Corp. (1973) Sencor: Metabolic, Analytical, and Residue Information for Sugarcane (Hawaii). (Compilation; unpublished study received Mar 30, 1973 under 4F1432; CDL: 093822-A; 093820)

00106169 Mobay Chemical Corp. (1972) Sencor (BAY 94337): Metabolic, Analytical, and Residue Information on Tomatoes. (Compilation; unpublished study received Apr 25, 1972 under 4F1432; CDL: 093821-A)

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REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

004262

MRID CITATION

00106173 Mobay Chemical Corp. (1975) Sencor: Analytical, Metabolic, and Residue Information for Various Crops. (Compilation; unpublished study received May 14, 1975 under 5F1628; CDL:094423-A)

00106179 Mobay Chemical Corp. (1975) Sencor ... Residue Chemistry on Lentils and Peas: Document No. AS76-788. (Compilation; unpublished study received Jun 29, 1976 under 3125-277; CDL:095551-A)

00106180 Mobay Chemical Corp. (1976) Addition No. 1 to Brochure Entitled: Sencor: Residue Chemistry on Tomatoes: Document No. AS76-549. (Compilation; unpublished study received May 6, 1976 under 6F1783; CDL:095907-A)

00106182 Mobay Chemical Corp. (1977) Sencor Residue Chemistry on Various Crops: Addition No. 1 to Brochure Entitled: Sencor Analytical, Metabolic, and Residue Information for Various Crops: Document No. AS 77-1557. (Compilation; unpublished study received Sep 21, 1977 under 3125-277; CDL:096367-A)

00106183 Mobay Chemical Corp. (1977) Sencor Residue Chemistry on Soybeans: Supplement No. 4 to Brochure Entitled: Sencor (Formerly Bay 94337) Metabolic, Analytical and Residue Information on Soybeans: Document No. AS 78-153. (Compilation; unpublished study received Feb 13, 1978 under 3125-277; CDL:096820-A)

00106184 Kadoum, A.; Gronberg, R. (1978) Effect of Dry Milling and Gluten Processing on Sencor and DADK Residues in Wheat Grain: Document No. AS78-1271; Report No. 66113. (Unpublished study received Jun 16, 1978 under 3125-277; prepared by Kansas State Univ., Dept. of Entomology, submitted by Mobay Chemical Corp., Kansas City, MO; CDL:097164-A)

00106184 Kadoum, A.; Gronberg, R. (1978) Effect of Dry Milling and Gluten Processing on Sencor and DADK Residues in Wheat Grain: Document No. AS78-1271; Report No. 66113. (Unpublished study received Jun 16, 1978 under 3125-277; prepared by Kansas State Univ., Dept. of Entomology, submitted by Mobay Chemical Corp., Kansas City, MO; CDL:097164-A)

00106185 Mobay Chemical Corp. (1978) Sencor Residue Chemistry on Various Crops: Addition No. 3 to Brochure Entitled: Sencor Analytical, Metabolic and Residue Information for Various Crops: Document No. AS78-1274. (Compilation; unpublished study received Jun 16, 1978 under 3125-277; CDL:097165-A)

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MRID CITATION

00106189 Hilton, H.; Nomura, N.; Yauger, W.; et al. (1973?) Absorption, Translocation, and Metabolism of Metribuzin (BAY-94337) in Sugarcane: 35166. (Unpublished study received Oct 8, 1975 under 4F1432; submitted by Chemagro Corp., Kansas City, MO; CDL: 098168-E)

00106190 Chemagro Corp. (1975) Residues of Sencor in Sugarcane. (Compilation; unpublished study received Oct 8, 1975 under 4F1432; CDL:098168-F)

00106191 Houseworth, L. (1979) Residues of Metolachlor and Metribuzin in Potato Tubers Resulting from the Use of Metolachlor and Metolachlor/Metribuzin Tank Mixes for Weed Control in Potato Culture: Report No.: ABR-79040. (Unpublished study received Apr 25, 1979 under 100-583; submitted by Ciba-Geigy Corp., Greensboro, NC; CDL:098227-A)

00106193 Thornton, J.; Schumann, S. (1971) A Gas Chromatographic Method for the Determination of Sencor and Its Deaminated Diketo Metabolite in Potatoes and Soybeans: Report No. 30387. (Unpublished study received on unknown date under 0G0940; submitted by Chemagro Corp., Kansas City, MO; CDL:093576-A)

00106197 Heitmuller, T. (1975) Acute Toxicity of Sencor to Eastern Oysters (Crassostrea virginica), Pink Shrimp (Penaeus duorarum), and Fiddler Crabs (Uca pugilator): submitter 43851. (Unpublished study received Aug 19, 1975 under 3125-294; prepared by Bionomics--EG & G, Inc., submitted by Mobay Chemical Corp., Kansas City, MO; CDL:165011-A)

00106199 Mobay Chemical Corp. (1973) Sencor (Formerly BAY 94337): Metabolic, Analytical, Residue, and Flavor Evaluation for Potatoes. (Compilation; unpublished study received Mar 8, 1973 under 3125-EX-120; CDL:127000-A; 127001)

00106202 Mobay Chemical Corp. (1976) Sencor: Residue Chemistry on Sugarcane: Addition No. 2 to Brochure Entitled: Sencor: Metabolic, Analytical and Residue Information for Sugarcane (Hawaii): Document No. AS76-1245. (Compilation; unpublished study received Sep 10, 1976 under 3125-277; CDL:226131-A)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metribuzin Standard

004262

MRID CITATION

00106203 Mobay Chemical Corp. (1973) Addition No. 1 to Brochure Entitled: Sencor: Residue Chemistry on Potatoes: Document No. AS77-47. (Compilation; unpublished study received Jan 24, 1977 under 3125-277; CDL:228041-A)

00106205 Mobay Chemical Corp. (1973) Addition No. 2 to Brochure Entitled: Sencor: Residue Chemistry on Potatoes. (Compilation; unpublished study received Nov 30, 1977 under 3125-314; CDL:232357-A)

00106207 E.I. du Pont de Nemours & Co. (1977) Name, Chemical Identity and Composition: Lexone DF Metribuzin Weed Killer. (Compilation; unpublished study received Dec 20, 1977 under 352-EX-97; CDL: 232513-A)

00106211 Mobay Chemical Corp. (1978) Sencor Residue Chemistry on Various Crops: Addition No. 2, Feb 3, 1978, to Brochure Entitled: Sencor Analytical, Metabolic and Residue Information for Various Crops (Dated January 23, 1975): Document No. AS78-1882. (Compilation; unpublished study received Sep 11, 1978 under 3125-314; CDL: 235087-A)

00106212 Mobay Chemical Corp. (1978) Sencor Residue Chemistry on Tomatoes: Addition No. 2, May 3, 1978, to Brochure Entitled: Sencor (Bay 94337) Metabolic, Analytical and Residue Information on Tomatoes (Dated Apr 25, 1972): Document No. AS78-2011. (Compilation; unpublished study received Oct 3, 1978 under 3125-314; CDL: 235319-A)

00106215 BASF Wyandotte Chemical Corp. (1978) Basalin Herbicide Amended Registration: Basalin Tank Mixture and Sequential Application with Metribuzin: Residue Chemistry--Part 03. (Compilation; unpublished study received Nov 8, 1978 under 7969-46; CDL: 235698-B)

00106797 American Cyanamid Co. (1978) Amounts of Residues of Prowl, Its Metabolite (CL 202,347) Metribuzin (Sencor or Lexone) and Eptam in or on Potatoes. (Compilation; unpublished study received Oct 5, 1978 under 241-243; CDL:097433-A; 097434)

00134495 Nelson, D.; Roney, D. (1979) Acute Toxicity of Sencor Technical to Daphnia magna: Report No. 67262. (Unpublished study received Oct 31, 1983 under 3125-277; submitted by Mobay Chemical Corp., Kansas City, MO; CDL:072083-A)

OFFICE OF PESTICIDE PROGRAM
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting Registrations Under the Metribuzin Standard

GS0181-001 Stephenson, G.; McLeod J.; Phatak S. (1976) Differential tolerance of tomato cultivars to metribuzin. Weed Science 24(2)(March): 161-165.

GS0181-002 Interregional Research Project No. 4 (1984) Metribuzin/ Carrots/PR-1431. Unpublished compilation. CDL:072711-A

GS0181-003 Mobay Chemical Corp. (1983) [Sencor in soybeans]: Report Nos. 82828 and 82829. Unpublished amendment to PP #2F2677.

GS0181-004 Makhijani, G. (1975) Letter sent to J. Cummings dated July 18, 1975, in EPA Administrative Record for PP #5F1559. 3p.

GS0181-005 Makhijani, G. (1975) Letter sent to J. Cummings dated September 14, 1975, in EPA Administrative Record for PP #5F1559 and 5F1628. 2p.

GS0181-006 Mayes, J. (1973) Letters sent to B. Puma dated January 16, 1973, in EPA Administrative Record for PP #2F2174. 6p.

GS0181-007 McMahon, B. (1974) Letter sent to W. Cox dated October 31, 1974, in EPA Administrative Record for PP #5F1559. 3p.

GS0181-008 Lamb, D.W.; and Roney, D.J. (1972) Acute Toxicity of Sencor to Fish. Report No. 33124. Prepared by Chemagro Division Research and Development. EPA Accession No. 255025.

GS0181-009 Lamb, D.W.; and Jones, R.F. (1972) Acute Toxicity of Sencor Technical to Bobwhite Quail and Mallard Ducks, Report No. 33172. Prepared by Chemagro Research and Development. EPA Accesion No. 255025.

GS0181-010 Crawford, C.R.; and Anderson, R.H. (1972) The Skin and Eye Irritation Properties of Sencor Technical and 50% Wettable Powder on Rabbits. Report No. 32862. Prepared by Chemagro Division of Baychem Corporation, Kansas City, Missouri EPA Accession No. 112032.

FIFRA SECTION 3(C)(2)(B) SUMMARY SHEET

EPA REGISTRATION NO.

PRODUCT NAME

004262

APPLICANT'S NAME

DATE GUIDANCE DOCUMENT ISSUED

With respect to the requirement to submit "generic" data imposed by the FIFRA section 3(C)(2)(B) notice contained in the referenced Guidance Document, I am responding in the following manner:

☐ 1. I will submit data in a timely manner to satisfy the following requirements. If the test procedures I will use deviate from (or are not specified in) the Registration Guidelines or the Protocols contained in the Reports of Expert Groups to the Chemicals Group, OECD Chemicals Testing Programme, I enclose the protocols that I will use:

☐ 2. I have entered into an agreement with one or more other registrants under FIFRA section 3(C)(2)(B)(ii) to satisfy the following data requirements. The tests, and any required protocols, will be submitted to EPA by:

NAME OF OTHER REGISTRANT

☐ 3. I enclose a completed "Certification of Attempt to Enter Into an Agreement with Other Registrants for Development of Data" with respect to the following data requirements:

☐ 4. I request that you amend my registration by deleting the following uses (this option is not available to applicants for new products):

☐ 5. I request voluntary cancellation of the registration of this product. (This option is not available to applicants for new products.)

REGISTRANT'S AUTHORIZED REPRESENTATIVE	SIGNATURE	DATE
	123	259

EPA Form 8580-1 (10-82)

OMB Approval No. 2000-0468 (Expires: 12-31-83)

CERTIFICATION OF ATTEMPT TO ENTER INTO AN AGREEMENT WITH OTHER REGISTRANTS FOR DEVELOPMENT OF DATA

To qualify, certify ALL four items)

. I am duly authorized to represent the following firm(s) who are subject to the requirements of a Notice under FIFRA Section 3(c)(2)(B) contained in a Guidance Document to submit data concerning the active ingredient:	GUIDANCE DOCUMENT DATE ACTIVE INGREDIENT

NAME OF FIRM	EPA COMPANY NUMBER

This firm or group of firms is referred to below as "my firm".)

. My firm is willing to develop and submit the data as required by that Notice, if necessary. However, my firm would prefer to enter into an agreement with one or more other registrants to develop jointly, or to share in the cost of developing, the following required items or data:

My firm has offered in writing to enter into such an agreement. Copies of the offers are attached. That offer was irrevocable and included an offer to be bound by an arbitration decision under FIFRA Section 3(c)(2)(B)(iii) if final agreement on all terms could not be reached otherwise. This offer was made to the following firm(s) on the following date(s):

NAME OF FIRM	DATE OF OFFER

owever, none of those firm(s) accepted my offer.

My firm requests that EPA not suspend the registration(s) of my firm's product(s), if any of the firms named in paragraph (3) above have agreed to submit the data listed in paragraph (2) above in accordance with the Notice. I understand EPA will promptly inform me whether my firm must submit data to avoid suspension of its registration(s) under FIFRA Section 3(c)(2)(B). (This statement does not apply to applicants for new products.) I give EPA permission to disclose this statement upon request.

'PED NAME	SIGNATURE	DATE
	125	260

PRODUCT SPECIFIC DATA REPORT

EPA Registration No._____ Guidance Document for_____

Date_____

Registration Guideline No.	Name of Test	Test not required for my product listed above (check below)	I am complying with data requirements by		(For EPA Use On Accession Number Assigned
			Citing MRID#	Submitting Data (Attached)	
§158.20 PRODUCT CHEMISTRY					
61-1	Identity of ingredients				
61-2	Statement of composition				
61-3	Discussion of formation of ingredients				
62-1	Preliminary analysis				
62-2	Certification of limits				
62-3	Analytical methods for enforcement limits				
63-2	Color				
63-3	Physical state				
63-4	Odor				
63-5	Melting point				
63-6	Boiling point				
63-7	Density, bulk-density, or specific gravity				
63-8	Solubility				
63-9	Vapor pressure				
63-10	Dissociation constant				
63-11	Octanol/water partition coefficient				
63-12	pH				

Appendix III-1 (continued)

Registration Guideline No.	Name of Test	Test not required for my product listed above (check below)	I am complying with data requirements by		(For EPA Use Only) Accession Numbers Assigned
			Citing MRID#	Submitting Data (Attached)	
63-13	Stability				
63-14	Oxidizing/reducing reaction				
63-15	Flammability				
63-16	Explodability				
63-17	Storage stability				
63-18	Viscosity				
63-19	Miscibility				
63-20	Corrosion characteristics				
63-21	Dielectric breakdown voltage				
§158.135 TOXICOLOGY					
81-1	Acute oral LD-50, rat				
81-2	Acute dermal LD-50				
81-3	Acute inhalation, LC-50 rat				
81-4	Primary eye irritation, rabbit				
81-5	Primary dermal irritation				
81-6	Dermal sensitization				

cant obtained the data from another firm (identify); applicant copied data from a publication; applicant obtained a copy of the data from EPA).

(d) The applicant shall submit with his application a statement that EPA, in its evaluation of the properties, efficacy, and safety of the formulated end-use product, may not consider any data as supporting the application, except the following data:

(1) The data the applicant has submitted to EPA under paragraph (b) of this section;

(2) Other data pertaining to the safety of the product's active ingredients, rather than to the safety of the end-use product; and

(3) Existing tolerances, food additive regulations, exemptions, and other clearances issued under the Federal Food, Drug, and Cosmetic Act.

(e) If the applicant knows that any item of data he submitted under this section was generated by (or at the expense of) another person who originally submitted the data to EPA (or its predecessor, USDA) on or after January 1, 1970, to support an application for registration, experimental use permit, or amendment adding a new use to an existing registration, or for reregistration (unless the applicant and the original data submitter have reached written agreement on the amount and the terms of payment of any compensation that may be payable under FIFRA section 3(c)(1)(D)(ii) with regard to approval of the application), the applicant shall submit to EPA a statement that he has furnished to each such identified original data submitter:

(1) A notification of the applicant's intent to apply for registration, including the proposed product name;

(2) An offer to pay the person compensation, with regard to the approval of the application, to the extent required by FIFRA sections 3(c)(1)(D) and 3(c)(2)(D);

(3) An identification of the item(s) of data to which the offer applies;

(4) An offer to commence negotiations to ascertain the amount and terms of compensation to be paid; and

(5) The applicant's name, address, and telephone number.

(f) If the applicant's product contains any active ingredient other than those that are present solely because of the incorporation into the product, during formulation, of one or more other registered pesticide products purchased from another producer, then the applicant shall also comply with § 162.9-5 as to such active ingredient, and the application shall contain an acknowledgment that for purposes of FIFRA section 3(c)(1)(D) the application relies on (and any resulting registration should be regarded as if it were based on the Administrator's consideration of) the following data:

(1) All data submitted or specifically cited by the applicant in support of the registration; and

(2) Each other item of data in the Agency's files which:

(i) Concerns the properties or effects of any such active ingredient; and

(ii) Is one of the types of data that EPA would require to be submitted for scientific review by EPA if the applicant sought the initial registration under FIFRA Section 3(c)(5) of a product with composition and intended uses identical to those proposed for the applicant's product, under the data requirements in effect on the date EPA approves the applicant's present application.

(Secs. 3, 6, and 25 of FIFRA, as amended, 7 U.S.C. 136 *et seq.*)

[44 FR 27953, May 11, 1979]

§ 162.10 Labeling requirements.

(a) *General*—(1) *Contents of the label.* Every pesticide products shall bear a label containing the information specified by the Act and the regulations in this Part. The contents of a label must show clearly and prominently the following:

(i) The name, brand, or trademark under which the product is sold as prescribed in paragraph (b) of this section;

(ii) The name and address of the producer, registrant, or person for whom produced as prescribed in paragraph (c) of this section;

(iii) The net contents as prescribed in paragraph (d) of this section;

(iv) The product registration number as prescribed in paragraph (e) of this section;

(v) The producing establishment number as prescribed in paragraph (f) of this section;

(vi) An ingredient statement as prescribed in paragraph (g) of this section;

(vii) Warning or precautionary statements as prescribed in paragraph (h) of this section;

(viii) The directions for use as prescribed in paragraph (i) of this section; and

(ix) The use classification(s) as prescribed in paragraph (j) of this section.

(2) *Prominence and legibility.* (i) All words, statements, graphic representations, designs or other information required on the labeling by the Act or the regulations in this part must be clearly legible to a person with normal vision, and must be placed with such conspicuousness (as compared with other words, statements, designs, or graphic matter on the labeling) and expressed in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

(ii) All required label text must:

(A) Be set in 6-point or larger type;

(B) Appear on a clear contrasting background; and

(C) Not be obscured or crowded.

(3) *Language to be used.* All required label or labeling text shall appear in the English language. However, the Agency may require or the applicant may propose additional text in other languages as is considered necessary to protect the public. When additional text in another language is necessary, all labeling requirements will be applied equally to both the English and other-language versions of the labeling.

(4) *Placement of Label*—(i) *General.* The label shall appear on or be securely attached to the immediate container of the pesticide product. For purposes of this Section, and the misbranding provisions of the Act, "securely attached" shall mean that a label can reasonably be expected to remain affixed during the foreseeable conditions and period of use. If the immediate container is enclosed within a wrapper or outside container through which the label cannot be clearly read, the label must also be securely attached to such outside wrapper or container, if it is a part of the package as customarily distributed or sold.

(ii) *Tank cars and other bulk containers*—(A) *Transportation.* While a pesticide product is in transit, the appropriate provisions of 49 CFR Parts 170-189, concerning the transportation of hazardous materials, and specifically those provisions concerning the labeling, marking and placarding of hazardous materials and the vehicles carrying them, define the basic Federal requirements. In addition, when any registered pesticide product is transported in a tank car, tank truck or other mobile or portable bulk container, a copy of the accepted label must be attached to the shipping papers, and left with the consignee at the time of delivery.

(B) *Storage.* When pesticide products are stored in bulk containers, whether mobile or stationary, which remain in the custody of the user, a copy of the label of labeling, including all appropriate directions for use, shall be securely attached to the container in the immediate vicinity of the discharge control valve.

(5) *False or misleading statements.* Pursuant to section 2(q)(1)(A) of the Act, a pesticide or a device declared subject to the Act pursuant to § 162.15, is misbranded if its labeling is false or misleading in any particular including both pesticidal and non-pesticidal claims. Examples of statements or representations in the labeling which constitute misbranding include:

(i) A false or misleading statement concerning the composition of the product;

(ii) A false or misleading statement concerning the effectiveness of the product as a pesticide or device;

(iii) A false or misleading statement about the value of the product for purposes other than as a pesticide or device;

(iv) A false or misleading comparison with other pesticides or devices;

(v) Any statement directly or indirectly implying that the pesticide or device is recommended or endorsed by

any agency of the Federal Government:

(vi) The name of a pesticide which contains two or more principal active ingredients if the name suggests one or more but not all such principal active ingredients even though the names of the other ingredients are stated elsewhere in the labeling;

(vii) A true statement used in such a way as to give a false or misleading impression to the purchaser;

(viii) Label disclaimers which negate or detract from labeling statements required under the Act and these regulations;

(ix) Claims as to the safety of the pesticide or its ingredients, including statements such as "safe," "nonpoisonous," "noninjurious," "harmless" or "nontoxic to humans and pets" with or without such a qualifying phrase as "when used as directed"; and

(x) Non-numerical and/or comparative statements on the safety of the product, including but not limited to:

(A) "Contains all natural ingredients";

(B) "Among the least toxic chemicals known"

(C) "Pollution approved"

(6) *Final printed labeling.* (i) Except as provided in paragraph (a)(6)(ii) of this section, final printed labeling must be submitted and accepted prior to registration. However, final printed labeling need not be submitted until draft label texts have been provisionally accepted by the Agency.

(ii) Clearly legible reproductions or photo reductions will be accepted for unusual labels such as those silk-screened directly onto glass or metal containers or large bag or drum labels. Such reproductions must be of microfilm reproduction quality.

(b) *Name, brand, or trademark.* (1) The name, brand, or trademark under which the pesticide product is sold shall appear on the front panel of the label.

(2) No name, brand, or trademark may appear on the label which:

(i) Is false or misleading, or

(ii) Has not been approved by the Administrator through registration or supplemental registration as an additional name pursuant to § 162.6(b)(4).

(c) Name and address of producer, registrant, or person for whom produced. An unqualified name and address given on the label shall be considered as the name and address of the producer. If the registrant's name appears on the label and the registrant is not the producer, or if the name of the person for whom the pesticide was produced appears on the label, it must be qualified by appropriate wording such as "Packed for • • •," "Distributed by • • •," or "Sold by • • •" to show that the name is not that of the producer.

(d) *Net weight or measure of contents.* (1) The net weight or measure of content shall be exclusive of wrappers or other materials and shall be the average content unless explicitly stated as a minimum quantity.

(2) If the pesticide is a liquid, the net content statement shall be in terms of liquid measure at 68° F (20°C) and shall be expressed in conventional American units of fluid ounces, pints, quarts, and gallons.

(3) If the pesticide is solid or semisolid, viscous or pressurized, or is a mixture of liquid and solid, the net content statement shall be in terms of weight expressed as avoirdupois pounds and ounces.

(4) In all cases, net content shall be stated in terms of the largest suitable units, i.e., "1 pound 10 ounces" rather than "26 ounces."

(5) In addition to the required units specified, net content may be expressed in metric units.

(6) Variation above minimum content or around an average is permissible only to the extent that it represents deviation unavoidable in good manufacturing practice. Variation below a stated minimum is not permitted. In no case shall the average content of the packages in a shipment fall below the stated average content.

(e) *Product registration number.* The registration number assigned to the pesticide product at the time of registration shall appear on the label, preceded by the phrase "EPA Registration No.," or the phrase "EPA Reg. No." The registration number shall be set in type of a size and style similar to other print on that part of the label on which it appears and shall run par-

allel to it. The registration number and the required identifying phrase shall not appear in such a manner as to suggest or imply recommendation or endorsement of the product by the Agency.

(f) *Producing establishments registration number.* The producing establishment registration number preceded by the phrase "EPA Est.", of the final establishment at which the product was produced may appear in any suitable location on the label or immediate container. It must appear on the wrapper or outside container of the package if the EPA establishment registration number on the immediate container cannot be clearly read through such wrapper or container.

(g) *Ingredient statement—(1) General.* The label of each pesticide product must bear a statement which contains the name and percentage by weight of each active ingredient, the total percentage by weight of all inert ingredients; and if the pesticide contains arsenic in any form, a statement of the percentages of total and water-soluble arsenic calculated as elemental arsenic. The active ingredients must be designated by the term "active ingredients" and the inert ingredients by the term "inert ingredients," or the singular forms of these terms when appropriate. Both terms shall be in the same type size, be aligned to the same margin and be equally prominent. The statement "Inert Ingredients, none" is not required for pesticides which contain 100 percent active ingredients. Unless the ingredient statement is a complete analysis of the pesticide, the term "analysis" shall not be used as a heading for the ingredient statement.

(2) *Position of ingredient statement.* (i) The ingredient statement is normally required on the front panel of the label. If there is an outside container or wrapper through which the ingredient statement cannot be clearly read, the ingredient statement must also appear on such outside container or wrapper. If the size or form of the package makes it impracticable to place the ingredient statement on the front panel of the label, permission may be granted for the ingredient statement to appear elsewhere.

(ii) The text of the ingredient statement must run parallel with other text on the panel on which it appears, and must be clearly distinguishable from and must not be placed in the body of other text.

(3) *Names to be used in ingredient statement.* The name used for each ingredient shall be the accepted common name, if there is one, followed by the chemical name. The common name may be used alone only if it is well known. If no common name has been established, the chemical name alone shall be used. In no case will the use of a trademark or proprietary name be permitted unless such name has been accepted as a common name by the Administrator under the authority of Section 25(c)(6).

(4) *Statements of percentages.* The percentages of ingredients shall be stated in terms of weight-to-weight. The sum of percentages of the active and the inert ingredients shall be 100. Percentages shall not be expressed by a range of values such as "22-25%." If the uses of the pesticide product are expressed as weight of active ingredient per unit area, a statement of the weight of active ingredient per unit volume of the pesticide formulation shall also appear in the ingredient statement.

(5) *Accuracy of stated percentages.* The percentages given shall be as precise as possible reflecting good manufacturing practice. If there may be unavoidable variation between manufacturing batches, the value stated for each active ingredient shall be the lowest percentage which may be present.

(6) *Deterioration.* Pesticides which change in chemical composition significantly must meet the following labeling requirements:

(i) In cases where it is determined that a pesticide formulation changes chemical composition significantly, the product must bear the following statement in a prominent position on the label: "Not for sale or use after [date]."

(ii) The product must meet all label claims up to the expiration time indicated on the label.

(7) *Inert ingredients.* The Administrator may require the name of any

inert ingredient(s) to be listed in the ingredient statement if he determines that such ingredient(s) may pose a hazard to man or the environment.

(h) *Warnings and precautionary statements.* Required warnings and precautionary statements concerning the general areas of toxicological hazard including hazard to children, environmental hazard, and physical or chemical hazard fall into two groups; those required on the front panel of the labeling and those which may appear elsewhere. Specific requirements concerning content, placement, type size, and prominence are given below.

(1) *Required front panel statements.* With the exception of the child hazard warning statement, the text required on the front panel of the label is determined by the Toxicity Category of the pesticide. The category is assigned on the basis of the highest hazard shown by any of the indicators in the table below:

Hazard indicators	Toxicity categories			
	I	II	III	IV
Oral LD_{50}	Up to and including 50 mg/kg.	From 50 thru 500 mg/kg.	From 500 thru 5000 mg/kg.	Greater than 5000 mg/kg.
Inhalation LC_{50}	Up to and including .2 mg/liter.	From .2 thru 2 mg/liter.	From 2 thru 20 mg/liter.	Greater than 20 mg/liter.
Dermal LD_{50}	Up to and including 200 mg/kg.	From 200 thru 2000	From 2,000 thru 20,000	Greater than 20,000.
Eye effects	Corrosive; corneal opacity not reversible within 7 days.	Corneal opacity reversible within 7 days; irritation persisting for 7 days.	No corneal opacity; irritation reversible within 7 days.	No irritation.
Skin effects	Corrosive	Severe irritation at 72 hours.	Moderate irritation at 72 hours.	Mild or slight irritation at 72 hours.

(i) *Human hazard signal word*—(A) *Toxicity Category I.* All pesticide products meeting the criteria of Toxicity Category I shall bear on the front panel the signal word "Danger." In addition if the product was assigned to Toxicity Category I on the basis of its oral, inhalation or dermal toxicity (as distinct from skin and eye local effects) the word "Poison" shall appear in red on a background of distinctly contrasting color and the skull and crossbones shall appear in immediate proximity to the word "poison."

(B) *Toxicity Category II.* All pesticide products meeting the criteria of Toxicity Category II shall bear on the front panel the signal word "Warning."

(C) *Toxicity Category III.* All pesticide products meeting the criteria of Toxicity Category III shall bear on the front panel the signal word "Caution."

(D) *Toxicity Category IV.* All pesticide products meeting the criteria of Toxicity Category IV shall bear on the front panel the signal word "Caution."

(E) *Use of signal words.* Use of any signal word(s) associated with a higher Toxicity Category is not permitted except when the Agency determines that such labeling is necessary to prevent unreasonable adverse effects on man or the environment. In no case shall more than one human hazard signal word appear on the front panel of a label.

(ii) *Child hazard warning.* Every pesticide product label shall bear on the front panel the statement "keep out of reach of children." Only in cases where the likelihood of contact with children during distribution, marketing, storage or use is demonstrated by the applicant to be extremely remote, or if the nature of the pesticide is such that it is approved for use on infants or small children, may the Administrator waive this requirement.

(iii) *Statement of practical treatment*—(A) *Toxicity Category I.* A statement of practical treatment (first aid or other) shall appear on the front panel of the label of all pesticides falling into Toxicity Category I on the basis of oral, inhalation or dermal toxicity. The Agency may, however, permit reasonable variations in the

placement of the statement of practical treatment is some reference such as "See statement of practical treatment on back panel" appears on the front panel near the word "Poison" and the skull and crossbones.

(B) *Other toxicity categories.* The statement of practical treatment is not required on the front panel except as described in paragraph (h)(1)(iii)(A) of this section. The applicant may, however, include such a front panel statement at his option. Statements of practical treatment are, however, required elsewhere on the label in accord with paragraph (h)(2) of this section if they do not appear on the front panel.

(iv) *Placement and prominence.* All the require front panel warning statements shall be grouped together on the label, and shall appear with sufficient prominence relative to other front panel text and graphic material to make them unlikely to be overlooked under customary conditions of purchase and use. The following table shows the minimum type size requirements for the front panel warning statements on various sizes of labels:

Size of label front panel in square inches	Points	
	Required signal word, all capitals	"Keep out of reach of Children
5 and under	8	6
Above 5 to 10	10	6
Above 10 to 15	12	8
Above 15 to 30	14	10
Over 30	18	12

(2) *Other required warnings and precautionary statements.* The warnings and precautionary statements as required below shall appear together on the label under the general heading "Precautionary Statements" and under appropriate subheadings of "Hazard to Humans and Domestic Animals," "Environmental Hazard" and "Physical or Chemical Hazard."

(i) *Hazard to humans and domestic animals.* (A) Where a hazard exists to humans or domestic animals, precautionary statements are required indicating the particular hazard, the route(s) of exposure and the precautions to be taken to avoid accident, injury or damage. The precautionary paragraph shall be immediately preceded by the appropriate hazard signal word.

(B) The following table depicts typical precautionary statements. These statements must be modified or expanded to reflect specific hazards.

Toxicity category	Precautionary statements by toxicity category	
	Oral, inhalation, or dermal toxicity	Skin and eye local effects
I	Fatal (poisonous) if swallowed [inhaled or absorbed through skin]. Do not breathe vapor [dust or spray mist]. Do not get in eyes, on skin, or on clothing [Front panel statement of practical treatment required.].	Corrosive, causes eye and skin damage [or skin irritation]. Do not get in eyes, on skin, or on clothing. Wear goggles or face shield and rubber gloves when handling. Harmful or fatal if swallowed. [Appropriate first aid statement required.]
II	May be fatal if swallowed [inhaled or absorbed through the skin]. Do not breathe vapors [dust or spray mist]. Do not get in eyes, on skin, or on clothing. [Appropriate first aid statements required.].	Causes eye [and skin] irritation. Do not get in eyes, on skin, or on clothing. Harmful if swallowed. [Appropriate first aid statement required.]
III	Harmful if swallowed [inhaled or absorbed through the skin]. Avoid breathing vapors [dust or spray mist]. Avoid contact with skin [eyes or clothing]. [Appropriate first aid statement required.].	Avoid contact with skin, eyes or clothing. In case of contact immediately flush eyes or skin with plenty of water. Get medical attention if irritation persists.
IV	[No precautionary statements required.]	[No precautionary statements required.]

(ii) *Environmental hazards.* Where a hazard exists to non target organisms excluding humans and domestic animals, precautionary statements are required stating the nature of the hazard and the appropriate precautions to avoid potential accident, injury or damage. Examples of the hazard statements and the circum-

placement of the statement of practical treatment is some reference such as "See statement of practical treatment on back panel" appears on the front panel near the word "Poison" and the skull and crossbones.

(B) *Other toxicity categories.* The statement of practical treatment is not required on the front panel except as described in paragraph (h)(1)(iii)(A) of this section. The applicant may, however, include such a front panel statement at his option. Statements of practical treatment are, however, required elsewhere on the label in accord with paragraph (h)(2) of this section if they do not appear on the front panel.

(iv) *Placement and prominence.* All the require front panel warning statements shall be grouped together on the label, and shall appear with sufficient prominence relative to other front panel text and graphic material to make them unlikely to be overlooked under customary conditions of purchase and use. The following table shows the minimum type size requirements for the front panel warning statements on various sizes of labels:

Size of label front panel in square inches	Points	
	Required signal word, all capitals	"Keep out of reach of Children
5 and under	8	6
Above 5 to 10	10	8
Above 10 to 15	12	8
Above 15 to 30	14	10
Over 30	18	12

(2) *Other required warnings and precautionary statements.* The warnings and precautionary statements as required below shall appear together on the label under the general heading "Precautionary Statements" and under appropriate subheadings of "Hazard to Humans and Domestic Animals," "Environmental Hazard" and "Physical or Chemical Hazard."

(i) *Hazard to humans and domestic animals.* (A) Where a hazard exists to humans or domestic animals, precautionary statements are required indicating the particular hazard, the route(s) of exposure and the precautions to be taken to avoid accident, injury or damage. The precautionary paragraph shall be immediately preceded by the appropriate hazard signal word.

(B) The following table depicts typical precautionary statements. These statements must be modified or expanded to reflect specific hazards.

Toxicity category	Precautionary statements by toxicity category	
	Oral, inhalation, or dermal toxicity	Skin and eye local effects
I	Fatal (poisonous) if swallowed [inhaled or absorbed through skin]. Do not breathe vapor [dust or spray mist]. Do not get in eyes, on skin, or on clothing [Front panel statement of practical treatment required.].	Corrosive, causes eye and skin damage [or skin irritation]. Do not get in eyes, on skin, or on clothing. Wear goggles or face shield and rubber gloves when handling. Harmful or fatal if swallowed. [Appropriate first aid statement required.]
II	May be fatal if swallowed [inhaled or absorbed through the skin]. Do not breathe vapors [dust or spray mist]. Do not get in eyes, on skin, or on clothing. [Appropriate first aid statements required.].	Causes eye [and skin] irritation. Do not get in eyes, on skin, or on clothing. Harmful if swallowed. [Appropriate first aid statement required.]
III	Harmful if swallowed [inhaled or absorbed through the skin]. Avoid breathing vapors [dust or spray mist]. Avoid contact with skin [eyes or clothing]. [Appropriate first aid statement required.].	Avoid contact with skin, eyes or clothing. In case of contact immediately flush eyes or skin with plenty of water. Get medical attention if irritation persists.
IV	[No precautionary statements required.]	[No precautionary statements required.]

(ii) *Environmental hazards.* Where a hazard exists to non target organisms excluding humans and domestic animals, precautionary statements are required stating the nature of the hazard and the appropriate precautions to avoid potential accident, injury or damage. Examples of the hazard statements and the circum-

stances under which they are required follow:

(A) If a pesticide intended for outdoor use contains an active ingredient with a mammalian acute oral LD_{50} of 100 or less, the statement "This Pesticide is Toxic to Wildlife" is required.

(B) If a pesticide intended for outdoor use contains an active ingredient with a fish acute LC_{50} of 1 ppm or less, the statement "This Pesticide is Toxic to Fish" is required.

(C) If a pesticide intended for outdoor use contains an active ingredient with an avian acute oral LD_{50} of 100 mg/kg or less, or a subacute dietary LC_{50} of 500 ppm or less, the statement "This Pesticide is Toxic to Wildlife" is required.

(D) If either accident history or field studies demonstrate that use of the pesticide may result in fatality to birds, fish or mammals, the statement "This pesticide is extremely toxic to wildlife (fish)" is required.

(E) For uses involving foliar application to agricultural crops, forests, or shade trees, or for mosquito abatement treatments, pesticides toxic to pollinating insects must bear appropriate label cautions.

(F) For all outdoor uses other than aquatic applications the label must bear the caution "Keep out of lakes, ponds or streams. Do not contaminate water by cleaning of equipment or disposal of wastes."

(iii) *Physical or chemical hazards.* Warning statements on the flammability or explosive characteristics of the pesticide are required as follows:

Flash point	Required text
(A) Pressurized Containers	
Flash point at or below 20° F; if there is a flashback at any valve opening.	Extremely flammable. Contents under pressure. Keep away from fire, sparks, and heated surfaces. Do not puncture or incinerate container. Exposure to temperatures above 130° F may cause bursting.
Flash point above 20° F and not over 80° F or if the flame extension is more than 18 in long at a distance of 6 in from the flame.	Flammable. Contents under pressure. Keep away from heat, sparks, and open flame. Do not puncture or incinerate container. Exposure to temperatures above 130° F may cause bursting.
All other pressurized containers	Contents under pressure. Do not use or store near heat or open flame. Do not puncture or incinerate container. Exposure to temperatures above 130° F may cause bursting.
(B) Nonpressurized Containers	
At or below 20° F	Extremely flammable. Keep away from fire, sparks, and heated surfaces.
Above 20° F and not over 80° F	Flammable. Keep away from heat and open flame.
Above 80° F and not over 150° F	Do not use or store near heat or open flame.

(i) *Directions for Use*—(1) *General requirements*—(i) *Adequacy and clarity of directions.* Directions for use must be stated in terms which can be easily read and understood by the average person likely to use or to supervise the use of the pesticide. When followed, directions must be adequate to protect the public from fraud and from personal injury and to prevent unreasonable adverse effects on the environment.

(ii) *Placement of directions for use.* Directions may appear on any portion of the label provided that they are conspicuous enough to be easily read by the user of the pesticide product. Directions for use may appear on printed or graphic matter which accompanies the pesticide provided that:

(A) If required by the Agency, such printed or graphic matter is securely attached to each package of the pesticide, or placed within the outside wrapper or bag;

(B) The label bears a reference to the directions for use in accompanying leaflets or circulars, such as "See directions in the enclosed circular:" and

(C) The Administrator determines that it is not necessary for such directions to appear on the label.

(iii) *Exceptions to requirement for direction for use*—(A) Detailed directions for use may be omitted from labeling of pesticides which are intended

for use only by manufacturers of products other than pesticide products in their regular manufacturing processes, provided that:

(*1*) The label clearly shows that the product is intended for use only in manufacturing processes and specifies the type(s) of products involved.

(*2*) Adequate information such as technical data sheets or bulletins, is available to the trade specifying the type of product involved and its proper use in manufacturing processes;

(*3*) The product will not come into the hands of the general public except after incorporation into finished products; and

(*4*) The Administrator determines that such directions are not necessary to prevent unreasonable adverse effects on man or the environment.

(B) Detailed directions for use may be omitted from the labeling of pesticide products for which sale is limited to physicians, veterinarians, or druggists, provided that:

(*1*) The label clearly states that the product is for use only by physicians or veterinarians;

(*2*) The Administrator determines that such directions are not necessary to prevent unreasonable adverse effects on man or the environment; and

(*3*) The product is also a drug and regulated under the provisions of the Federal Food, Drug and Cosmetic Act.

(C) Detailed directions for use may be omitted from the labeling of pesticide products which are intended for use only by formulators in preparing pesticides for sale to the public, provided that:

(*1*) There is information readily available to the formulators on the composition, toxicity, methods of use, applicable restrictions or limitations, and effectiveness of the product for pesticide purposes;

(*2*) The label clearly states that the product is intended for use only in manufacturing, formulating, mixing, or repacking for use as a pesticide and specifies the type(s) of pesticide products involved;

(*3*) The product as finally manufactured, formulated, mixed, or repackaged is registered; and

(*4*) The Administrator determines that such directions are not necessary to prevent unreasonable adverse effects on man or the environment.

(2) *Contents of Directions for Use.* The directions for use shall include the following, under the headings "Directions for Use":

(i) The statement of use classification as prescribed in 162.10(j) immediately under the heading "Directions for Use."

(ii) Immediately below the statement of use classification, the statement "It is a violation of Federal law to use this product in a manner inconsistent with its labeling."

(iii) The site(s) of application, as for example the crops, animals, areas, or objects to be treated.

(iv) The target pest(s) associated with each site.

(v) The dosage rate associated with each site and pest.

(vi) The method of application, including instructions for dilution, if required, and type(s) of application apparatus or equipment required.

(vii) The frequency and timing of applications necessary to obtain effective results without causing unreasonable adverse effects on the environment.

(viii) Specific limitations on reentry to areas where the pesticide has been applied, meeting the requirements concerning reentry provided by 40 CFR Part 170.

(ix) Specific directions concerning the storage and disposal of the pesticide and its container, meeting the requirements of 40 CFR Part 165. These instructions shall be grouped and appear under the heading "Storage and Disposal." This heading must be set in type of the same minimum sizes as required for the child hazard warning (See Table in § 162.10(h)(1)(iv).)

(x) Any limitations or restrictions on use required to prevent unreasonable adverse effects, such as:

(A) Required intervals between application and harvest of food or feed crops.

(B) Rotational crop restrictions.

(C) Warnings as required against use on certain crops, animals, objects, or in or adjacent to certain areas.

(D) [Reserved]

LABELING REQUIREMENTS OF THE FIFRA, AS AMENDED

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		COMMENTS
			REQUIRED	PREFERRED	
1	Product name	All products	Front panel	Center front panel	
2	Company name and address	All products	None	Bottom front panel or end of label text	If registrant is not the producer, must be qualified by "Packed for . . .," "Distributed by. . .," etc.
3	Net contents	All products	None	Bottom front panel or end of label text	May be in metric units in addition to U.S. units
4	EPA Reg. No.	All products	None	Front panel	Must be in similar type size and run parallel to other type.
5	EPA Est. No.	All products	None	Front panel, immediately before or following Reg. No.	May appear on the container instead of the label.
6A	Ingredients statement	All products	Front panel	Immediately following product name	Text must run parallel with other text on the panel.
6B	Pounds/gallon statement	Liquid products where dosage given as lbs. ai/unit area	Front panel	Directly below the main ingredients statement	
7	Front panel precautionary statements	All products	Front panel		All front panel precautionary statements must be grouped together, preferably blocked.
7A	Keep Out of Reach of Children (Child hazard warning)	All products	Front panel	Above signal word	Note type size requirements.
7B	Signal word	All products	Front panel	Immediately below child hazard warning	Note type size requirements.

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		COMMENTS
			REQUIRED	PREFERRED	
7C	Skull & crossbones and word POISON (in red)	All products which are Category I based on oral, dermal, or inhalation toxicity	Front panel	Both in close proximity to signal word	
7D	Statement of practical treatment	All products in Categories I, II, and III	Category I: Front panel unless referral statement is used. Others: Grouped with side panel precautionary statements.	Front panel for all.	
7E	Referral statement	All products where precautionary labeling appears on other than front panel.	Front panel		
8	Side/back panel precautionary statements	All products	None	Top or side of back panel preceding directions for use	Must be grouped under the headings in 8A, 8B, and 8C; preferably blocked.
8A	Hazards to humans and domestic animals	All products in Categories I, II, and III	None	Same as above	Must be preceded by appropriate signal word.
8B	Environmental hazards	All products	None	Same as above	Environmental hazards include bee caution where applicable.

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ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		COMMENTS
			REQUIRED	PREFERRED	
8C	Physical or chemical hazards	All pressurized products, others with flash points under 150°F	None	Same as above	
9A	Restricted block	All restricted products	Top center of front panel	Preferably blocked	Includes a statement of the terms of restriction. The words "RESTRICTED USE PESTICIDE" must be same type size as signal word.
9C	Misuse statement	All products	Immediately following heading of directions for use		
10A	Reentry statement	All cholinesterase inhibitors	In the directions for use	Immediately after misuse statement	
10C	Storage and disposal block	All products	In the directions for use	Immediately before specific directions for use or at the end of directions for use	Must be set apart and clearly distinguishable from from other directions for use.
10D	Directions for use	All products	None	None	May be in metric as well as U.S. units

PHYSICAL-CHEMICAL HAZARDS

Criteria	Required Label Statement
I. Pressurized Containers	
A. Flashpoint at or below 20°F; or if there is a flashback at any valve opening.	Extremely flammable. Contents under pressure. Keep away from fire, spa and heated surfaces. Do puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
B. Flashpoint above 20°F and not over 80°F; or if the flame extension is more than 18 inches long at a distance of 6 inches from the valve opening.	Flammable. Contents und pressure. Keep away fro heat, sparks, and flame. not puncture or incinera container. Exposure to temperatures above 130°F may cause bursting.
C. ALL OTHER PRESSURIZED CONTAINERS	Contents under pressure Do not use or store nea heat or open flame. Do puncture or incinerate container. Exposure to temperatures above 130° may cause bursting.
II. Non-Pressurized Containers	
A. Flashpoint at or below 20°F.	Extremely flammable. K away from fire, sparks, heated surfaces.
B. Flashpoint above 20°F and not over 80°F.	Flammable. Keep away f heat and open flame.
C. Flashpoint over 80°F and not over 150°F.	Do not use or store nea heat and open flame.
D. Flashpoint above 150°F.	None required.

STORAGE AND DISPOSAL INSTRUCTIONS FOR PESTICIDES

All products are required to bear specific label instructions about storage and disposal. Storage and disposal instructions must be grouped together in the directions for use portion of the label under the heading STORAGE AND DISPOSAL. Products intended solely for domestic use need not include the heading "STORAGE AND DISPOSAL." The STORAGE AND DISPOSAL heading must appear in the minimum type size listed below:

Size of label front panel in square inches	Required type size for the heading STORAGE AND DISPOSAL (all capitals)
10 and under	.6 point
Above 10 to 15	.8 point
Above 15 to 30	10 point
Over 30	12 point

Storage and disposal instructions must be set apart and clearly distinguishable from other directions for use. Blocking storage and disposal statements with a solid line is suggested as a means of increasing their prominence.

A. Storage Instructions:

All product labels are required to have appropriate storage instructions. Specific storage instructions are not prescribed. Each registrant must develop his own storage instructions, considering, when applicable, the following factors:

1. Conditions of storage that might alter the composition or usefulness of the pesticide. Examples could be temperature extremes, excessive moisture or humidity, heat, sunlight, friction, or contaminating substances or media.

2. Physical requirements of storage which might adversely affect the container of the product and its ability to continue to function properly. Requirements might include positioning of the container in storage, storage or damage due to stacking, penetration of moisture, and ability to withstand shock or friction.

3. Specifications for handling the pesticide container, including movement of container within the storage area, proper opening and closing procedures (particularly for opened containers), and measures to minimize exposure while opening or closing container.

"Pesticide wastes are toxic. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency, or the Hazardous Waste representative at the nearest EPA Regional Office for guidance."

Labels for all other products, except those intended for domestic use, must bear the following pesticide disposal statement:

"Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility."

3. Products intended for domestic use only must bear the following disposal statement: "Securely wrap original container im several layers of newspaper and discard in trash."

C. Container Disposal Instructions

The label of each product must bear container disposal instructions appropriate to the type of container.

1. All products intended for domestic use must bear one of the following container disposal statements:

Container Type	Statement
Non-aerosol products (bottles, cans, jars)	Do not reuse container (bottle, can, jar). Rinse thoroughly before discarding in trash
Non-aerosol products (bags)	Do not reuse bag. Discard bag in trash.
Aerosol products	Replace cap and discard containers in trash. Do not incinerate or puncture.

4. Instructions on what to do if the container is damaged in any way, or if the pesticide is leaking or has been spilled, and precautions to minimize exposure if damage occurs.

5. General precautions concerning locked storage, storage in original container only, and separation of pesticides during storage to prevent cross-contamination of other pesticides, fertilizer, food, and feed.

6. General storage instructions for household products should emphasize storage in original container and placement in locked storage areas.

B. Pesticide Disposal Instructions:

The label of all products, except those intended solely for domestic use, must bear explicit instructions about pesticide disposal. The statements listed below contain the exact wording that must appear on the label of these products:

1. The labels of all products, except domestic use, must contain the statement, "Do not contaminate water, food, or feed by storage or disposal."

2. Except those products intended solely for domestic use, the labels of all products that contain active ingredients appearing on the "Acutely Hazardous" Commercial Pesticide Products List (RCRA "E" List) at the end of this appendix or are assigned to Toxicity Category I on the basis of oral or dermal toxicity, skin or eye irritation potential, or Toxicity Category I or II on the basis of acute inhalation toxicity must bear the following pesticide disposal statement:

   "Pesticide wastes are acutely hazardous. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency, or the Hazardous Waste representative at the nearest EPA Regional Office for guidance."

   The labels of all products, except those intended for domestic use, containing active or inert ingredients that appear on the "Toxic" Commercial Pesticide Products List (RCRA "F" List) at the end of this appendix or presently meet any of the criteria in Subpart C, 40 CFR 261 for a hazardous waste must bear the following pesticide disposal statement:

2. The labels for all other products must bear container disposal instructions, based on container type, listed below:

Container Type	Statement
Metal containers (non-aerosol)	Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or by other procedures approved by state and local authorities.
Plastic containers	Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke.
Glass containers	Triple rinse (or equivalent). Then dispose of in a sanitary landfill or by other approved state and local procedures.
Fiber drums with liners	Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into application equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by state and local authorities. If drum is contaminated and cannot be reused[1], dispose of in the same manner.
Paper and plastic bags	Completely empty bag into application equipment. Then dispose of empty bag in a sanitary landfill or by incineration, or, if allowed by State and local authorities, by burning. If burned, stay out of smoke.
Compressed gas cylinders	Return empty cylinder for reuse (or similar wording)

1/ Manufacturer may replace this phrase with one indicating whether and how fiber drum may be reused.

Pesticides that are hazardous wastes under 40 CFR 261.33(e) and (f) when discarded.

"Acutely Hazardous" Commercial Pesticides (RCRA "E" List)
Active Ingredients, (no inerts):

Acrolein
Aldicarb
Aldrin
Allyl alcohol
Aluminum phosphide
4-Aminopyridine
Arsenic acid
Arsenic pentoxide
Arsenic trioxide
Calcium cyanide
Carbon disulfide
p-Chloroaniline
Cyanides (soluble cyanide salts, not specified elsewere)
Cyanogen chloride
2-Cyclohexyl-4,6-dinitrophenol
Dieldrin
0,0-Diethyl S-[2-ethylthio)ethyl] phosphorodithioate
(disulfoton, Di-Syston)
0,0-Diethyl 0-pyrazinyl phosphorothioate (Zinophos)
Dimethoate
0,0-Dimethyl 0-p-nitrophenyl phosphorothioate (methyl parathion)
4,6-Dinitro-o-cresol and salts
4,6-Dinitro-o-cyclohexylphenol
2,4 Dinitrophenol
Dinoseb
Endosulfan
Endothall
Endrin
Famphur
Fluoroacetamide
Heptachlor
Hexanethyl tetraphosphate
Hydrocyanic acid
Hydrogen cyanide
Methomyl
alpha-Naphthylthiourea (ANTU)
Nicotine and salts
Octamethylpyrophosphoramide (OMPA, schradan)
Parathion

"Acutely Hazardous" Commercial Pesticides (RCRA "E" List)
Active Ingredients continued:

Phenylmercuric acetate (PMA)
Phorate
Potassium cyanide
Propargyl alcohol
Sodium azide
Sodium cyanide
Sodium fluoroacetate
Strychnine and salts
0,0,0,0-Tetraethyl dithiopyrophosphate (sulfotepp)
Tetraethyl pyrophosphate
Thallium sulfate
Thiofanox
Toxaphene
Warfarin
Zinc phosphide

"Toxic" Commercial Pesticide Products (RCRA "F" List)
Active Ingredients:

Acetone
Acrylonitrile
Amitrole
Benzene
Bis(2-ethylhexyl)pthalate
Cacodylic acid
Carbon tetrachloride
Chloral (hydrate)
Chlordane (technical)
Chlorobenzene
4-Chloro-m-cresol
Chloroform
o-Chlorophenol
4-Chloro-o-toluidine hydrochloride
Creosote
Cresylic acid
Cyclohexane
Decachlorooctahydro-1,3,4-metheno-2H-cyclobuta[c,d]-pentalen-2-one
(kepone, chlordecone)
1,2-Dibromo-3-chloropropane (DBCP)
Dibutyl phthalate
S-3,3-(Dichloroallyl diisopropylthiocarbamate (diallate, Avadex)
o-Dichlorobenzene
p-Dichlorobenzene
Dichlorodifluoromethane (Freon 12®)
3,5-Dichloro-N-(1,1-dimethyl-2-propynyl) benzamide (pronamide,Kerb)
Dichloro diphenyl dichloroethane (DDD)
Dichloro diphenyl trichloroethane (DDT)
Dichlorethyl ether
2,4-Dichlorophenoxyacetic, esters and salts (2,4-D)
1,2-Dichloropropane
1,3-Dichloropropane (Telone)
Dimethyl phthalate
Ethyl acetate
Ethyl 4,4'-dichlorobenzilate (chlorobenzilate)
Ethylene dibromide (EDB)
Ethylene dichloride
Ethylene oxide
Formaldehyde
Furfural
Hexachlorobenzene
Hexachlorocyclopentadiene
Hexachloroethane
Hydrofluoric acid

"Toxic" Commercial Pesticide Products (RCRA "F" List)
Active Ingredients:

Isobutyl alcohol
Lead acetate
Lindane
Maleic hydrazide
Mercury
Methyl alcohol
Methyl bromide
Methyl chloride
2,2'-Methylenebis (3,4,6-trichlorophenol) (hexachlorophene)
Methylene chloride
Methyl ethyl ketone
4-Methyl-2-pentanone (methyl isobutyl ketone)
Naphthalene
Nitrobenzene
p-Nitrophenol
Pentachloroethane
Pentachloronitrobenzene (PCNB)
Pentaclorophenol
Phenol
Phosphorodithioic acid, 0,0-diethyl, methyl ester
Propylene dichloride
Pyridine
Resorcinol
Safrole
Selenium disulfide
Silvex
1,2,4,5-Tetrachlorobenzene
1,1,2,2-Tetrachloroethane
Tetrachloroethylene
2,3,4,6-Tetrachlorophenol
Thiram
Toluene
1,1,1-Trichloroethane
Trichloroethylene
Trichloromonofluoromethane (Freon 11®)
2,4,5-Trichlorophenol
2,4,6-Trichlorophenol
2,4,5-Trichlorophenoxyacetic acid (2,4,5-T)
Xylene

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"Toxic" Commercial Pesticide Products (RCRA "F" List)
Inert Ingredients:

Acetone
Acetonitrile
Acetophenone
Acrylic acid
Aniline
Benzene
Chlorobenzene
Chloroform
Cyclohexane
Cyclohexanone
Dichlorodifluoromethane (Freon 12®)
Diethyl phthalate
Dimethylamine
Dimethyl phthalate
1,4-Dioxane
Ethylene oxide
Formaldehyde
Formic acid
Isobutyl alcohol
Meleic anhydride
Methyl alcohol (methanol)
Methyl ethyl ketone
Methyl methacrylate
Naphthalene
Saccharin and salts
Thiourea
Toluene
1,1,1-Trichloroethane
1,1,2-Trichloroethane
Trichlorofluoromethane (Freon 11®)
Vinyl chloride
Xylene

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