US EPA ARCHIVE DOCUMENT

DRAFT 2/1/78

ACUTE TOXICOLOGICAL TESTING

Acute Oral Toxicity (Section 162.81-1)

The minimum data requirement for acute oral testing is one test on the laboratory rat.

The acute oral LD_{50} in the laboratory rat is 2780 mg/kg with 95% confidence limits of 2130-3545 mg/kg (Bathe, 1973).

Technical metolachlor in corn oil has been shown to be emetic in Beagle dogs to an extent that precludes the establishment of an oral LD_{50} in dogs (Affiliated Medical Research, 1974). The study did, however, establish the emetic $dose_{50}$ to be 19.0 mg/kg 9.7.

On the basis of acute oral toxicity catagory III labeling is required for technical metolachlor.

The above information is sufficient to satisfy the requirement for acute oral toxicity on technical metolachlor.

Acute Dermal Toxicity (Section 162.81-2)

The minimum data requirement for acute dermal testing is one test preferably on the albino rabbit. This test must be conducted on both intact and abraded skin.

Affiliated Medical Research, Incorporated (1974) established that the LD_{50} to the New Zealand rabbit is greater than 10,000 mg/kg when tested by the unabraded dermal route.

No data is available on the acute dermal toxicity to abraded rabbit skin. This data is required and is discussed further in the portion of the technical metolachlor standard dealing with data gaps (see page).

Based on the available information on acute dermal toxicity, catagory III toxicity labeling is required for technical metolachlor.

The above information is sufficient to meet the rquirement for acute dermal toxicity testing on intact skin for technical metolachlor.

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Acute Inhalation Toxicity (Section 162.81-3)

In preparation

Primary Eye Irritation (Section 162.81-4)

The minimum data requirement for the eye irritation is one test conducted on the albino rabbit.

A study of eye irritation was conducted by Sachsse (1973) on the New Zealand rabbit. In that study 0.1 ml of technical metolachlor was used. The test was evaluated using the system of Draise (1959) and produced the follwing eye irritation indices:

Cornea: 0
Iris: 0
Conjunctivae: 0

This study establishes that technical metolachlor is nonirritating to the rabbit eye and, therefore, that toxicity catagory IV labeling is required with regard to eye irritation.

The above information is sufficient to meet the requirement for primary eye irritation data for technical metolachor.

Primary Dermal Irritation (Section 162.81-5)

The minimum data requirement for primary dermal irritation is one test conducted on a mammal, preferably the albino rabbit.

Sachsse (1973) evaluated the dermal irritation of technical metolachlor on the New Zealand rabbit. In that study, 0.5 ml of technical metolachlor was used. The test was evaluated using the system of Draise (1959) and resulted in a primary irritation index of 0.1.

This information establishes that technical metolachlor is nonirritating to rabbit skin and, therefore, that toxicity catagory IV labeling is required with regard to dermal irritation.

The above information is sufficient to meet the requirement for primary dermal irritation data for technical metolachlor.

DRAFT 2/17/90

Dermal Sensitization (Section 162.81-6

The minimum data requirement for dermal sensitation is an intradermal test on one mammalian species, preferably the male albino guinea pig.

The first evaluation of dermal sensitization was conducted by Affiliated Medical Research, Incorporated (1974). Inappropriate methodology (patch test) and the lack of sensitization in a positive control invalidate this study and preclude its use in the regulatory process.

A second study (Sachsse and Ullman, 1977) used the intradermal injection method: Technical metolachlor dissolved in the vehicle [propylene glycol] or the vehicle alone [negative control] were intradermally injected into the skin of Pilbright guinea pigs. Positive reaction was demonstrated in animals injected with technical metolachlor dissolved in the vehicle; no reaction in animals injected with the vehicle alone.

Based on this study, technical metolachlor is a skin sensitizer in guinea pigs.

This information is sufficient to meet the requirement for dermal sensitization data on technical metolachlor.

Dermal Photosensitization (Section 162.81-7)

This data is not required for technical metolachlor.

Acute Delayed Neurotoxicity Study (Section 162.81-8)

This data is not required for technical metolachlor.

SUBACUTE TOXICOLOGICAL TESTING

Subacute Oral Toxicity (Section 162.82-1)

In Preparation

Subacute Dermal Toxicity (Section 162.82-2)

Status Unknown

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SUBACUTE TOXICOLOGICAL TESTING (Continued)

Subacute Inhalation Toxicity (Section 162.82-3)

Status Unknown

Subacute Delayed Neurotoxicity (Section 162.82-4)

This data is not required for technical metolachlor.

CHRONIC TESTING

Chronic Feeding (Section 162.83-1)

In Preparation

Oncogenicity (Section 162.83-2)

In Preparation

Teratogencity Studies (Section 162.83-3)

The minimum data requirement for teratology is testing in two mammalian species.

A study of the teratogenic effects of technical metolachlor on rats was conducted by Fritz(1976). The study found that doses of either 0, 60, 180 or 360 mg/kg/day during days 6 to 15 of gestation were without effect to the offspring of female Spraque-Dawley rats. No fetotoxic or teratogenic effects of the compound were observed. The only possible effect on the dams was a decrease in food consumption at the highest dose during the first 1/3 of the experiment which may indicate that this was the beginning of toxic maternal doses.

No data is available on a second mammalian series. This data is required and is discussed further in the portion of the technical metolachlor standard dealing with data gaps (see page).

Based on the available teratology data it does not appear that metalochlor presents a teratogenic hazard.

The above study is sufficient to meet the requirement for teratology in one species of mammal.

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Reproduction (Section 162.83-4)

In Preparation

MUTAGENICITY TESTING

Mutagenicity Testing (Section (162.84-1)

The minimum data requirements for mutagenicity is testing in two systems.

The potential of metolachlor to cause genetic changes has been tested for in two test systems--a bacterial system utilizing activation by mammalian microsomes (Arnie and Muller, 1976), and an *in vivo* system to test the effect on developing sperm in the mouse (Fritz, 1976).

The bacterial (*Salmonella*) system tested for base substitutions and point mutations at various ranges (10, 100, 1,000 and 10,000 ug/plate). No increases in background mutation rates were observed. Neither were there any effects noted on fertility rates or zygote or embryo death in the mice after single oral doses of 100 or 300 mg/kg. Malformations of resulting embryos were not reported.

From these two studies, no evidence is presented which suggests that metolachlor has any mutagenic potential.

These studies are sufficient to meet the requirements for mutagenicity testing.

AVIAN AND MAMMALIAN TESTING

Avian Single-Dose Oral LD_{50} (Section 162.71-1)

In Preparation

Avian Dietary LC_{50} (Section 162.71-2)

The minimum data requirement for avian dietary testing is testing on two avian species one species of wild waterfowl (preferably the mallard) and one species of upland game bird (preferably the bobwhite quail or other native quail, or the ring-necked pheasant).

March 20 F+W input on EC

March 17, final chapter

2/24 F+W input on tech study eval

DRAFT

efs topics 2/19/79 statement of F+W data gaps

2/17 - draft of each study's Data Eval/Rec on technical

Reproduction (Section 162.83-4)

In Preparation

MUTAGENICITY TESTING

Mutagenicity Testing (Section (162.84-1)

Reg requ

The minimum data requirements for mutagenicity is testing in two systems.

Summary

The potential of metolachlor to cause genetic changes has been tested for in two test systems--a bacterial system utilizing activation by mammalian microsomes (Arnie and Muller, 1976), and an in vivo system to test the effect on developing sperm in the mouse (Fritz, 1976).

The bacterial (Salmonella) system tested for base substitutions and point mutations at various ranges (10, 100, 1,000 and 10,000 ug/plate). No increases in background mutation rates were observed. Neither were there any effects noted on fertility rates or zygote or embryo death in the mice after single oral doses of 100 or 300 mg/kg. Malformations of resulting embryos were not reported.

any label crefs concl.

From these two studies, no evidence is presented which suggests that metolachlor has any mutagenic potential.

does study meet reg req

These studies are sufficient to meet the requirements for mutagenicity testing.

AVIAN AND MAMMALIAN TESTING

Avian Single-Dose Oral LD_{50} (Section 162.71-1)

In Preparation

Avian Dietary LC_{50} (Section 162.71-2)

The minimum data requirement for avian dietary testing is testing on two avian species one species of wild waterfowl (preferably the mallard) and one species of upland game bird (preferably the bobwhite quail or other native quail), or the ring-necked pheasant.

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Truslow Farms Incorporated has conducted studies on the mallard duck (Anas platyrhynchos) (1974b) and the bobwhite quail (Colinus virginianus) (1974a). The 5 (+3)-day dietary LC_{50} for both species exceeded the highest dosage tested (10,000 ppm).

This data is sufficient to satisfy the requirements for avian dietary LC_{50}.

Mammalian Acute Toxicity (Section 162.71-3)

Status Unknown

Avian Reproduction (Section 162.71-4)

Status Unknown

Simulated and Actual Field Conditioning Testing for Mammals and Birds (Section 162.71-5)

Status Unknown

AQUATIC ORGANISM TESTING

Fish Acute LC_{50} (Section 162.72-1)

The minimum data requirements for acute fish toxicity are tests on one cold water species (preferably rainbow trout), and one warm water species (preferably bluegill).

Data on the acute toxicity of technical metolachlor to fish is limited to the work conducted by Sachsse and Ullman (1974b).

The data presented on a cold water species--rainbow trout (Salmo gairdner) is not considered valid to establish the acute 96 hour LC_{50} due to various deviations from desirable protocols. The most significant flaw is the aeration of holding tanks which could have resulted in the volatilization of the toxicant from the medium.

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Data is presented on four species of warm water fish:

Species	96 Hour LC_{50} (ppm)	95% Confidence Limits
Crucian Carp (Carassius carassius)	4.9	3.6 - 6.8
Channel Catfish (Ictaluris punctatus)	4.9	3.6 - 6.8
Bluegill (Lepomis macrocnirus)	15	*
Guppy (Lebistes reticulatus)	8.6	7.4 -10.5

*The data reported on the bluegill cannot be confirmed by statistical analysis and was not used in the evaluation.

The data on the remaining species is acceptable to establish that metolachlor is moderately toxic to warm water fish. This information meets the requirement for warm water fish acute LC_{50} data.

Since information on cold water fish is required, and the only available data is unacceptable, a data gap exists for this information. This data gap is discussed further in the portion of the technical metolachlor standard dealing with data gaps (see page).

Based on the available information and currently acceptable uses for this data requirement a tentative determination is made that no labeling precaution regarding fish hazard is required.

Acute Toxicity to Aquatic Invertebrates (Section 162.72-2)

The minimum data requirement for acute toxicity testing on aquatic invertebrates is for evaluation of one aquatic invertebrate.

Data is available on the acute toxicity of technical metolachlor to the water flea (Daphnia magna Straus) (Vilkas, 1976). The 48 hour LC_{50} with 95% confidence limits is 25.1 (21.6 - 29.2) ppmg which indicates that metolachlor is slightly toxic to aquatic invertebrates.

No precautionary labeling regarding aquatic invertebrates is required.

This information is sufficient to satisfy the requirement for acute toxicity data on aquatic invertebrates.

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Acute Toxicity to Estuarine and Marine Organisms (Section 162.72-3)

Status Unknown

Embryo-Larvae and Life-cycle Studies of Fish and Aquatic Invertebrates (Section 162.72-4)

Status Unknown

Aquatic Organism Toxicity and Residue Studies (Section (162.72-5)

Status Unknown

Simulated or Actual Field Testing for Aquatic Organisms (Section 162.72-6)

Status Unknown

ENVIRONMENTAL FATE

Physicio-Chemical Degradation (Section 162.62-7)

The minimum data requirements for physico-chemical degradation include (1) hydrolysis, (2) aquatic photodegradation, (3) soil photolysis, and (4) vapor phase photolysis.

(1) Hydrolysis

In Preparation

(2) Aquatic Photolysis

The available information on aquatic photolysis is contained in a study conducted by Aziz and Kahrs (1974) and an addendum to that study (Aziz and Kahrs, (1975). Under natural sunlight approximately 6.6% was photolyzed in 30 days. Under artificial sunlight with a wavelength of less than 280 n.m. 69% was degraded within 15 days. Additional information regarding the degradation products can be found in the Agency evaluation of the individual studies. Since the photolysis was less than 10% of the total chemical, the chemical is considered stable with regard to aqueous photolysis and identification of the photodegradation products is not necessary.

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Aqueous photolysis is not a significant avenue for environmental fate.

This information is sufficient to meet the requirement for aqueous photolysis data on technical metolachlor.

(3) Soil Photolysis

Data on soil photolysis have been developed by Aziz (1974). In that test, metolochlor on soil slides was approximately 50% photolyzed in 8 days under natural sunlight and 52% photolyzed in 8 days under artificial sunlight (wavelength less than 280 n.m.). In neither case was any single degradate in excess of 10% of the total material.

The identified degradate found in the largest quantity was N-propen-1-ol-2-yl-N-chloroacetyl-2-methyl-6-ethylaniline which was located in the chloroform extract. This compound represented 3.9% and 5.6% in the natural and artificial tests respectfully. Additional information on the minor degradates can be found in the Agency evaluation of the individual studies.

Soil photolysis has the potential for being a significant avenue of environmental fate.

This data is sufficient to meet the requirements soil photolysis testing of technical metolachlor.

(4) Vapor Phase Photolysis

Data on vapor phase photolysis is required and no such data has been identified, therefore, a data gap exists. Additional information on the data gap is presented in the portion of the technical metolachlor standard dealing with data gaps (see page).