United States
Environmental Protection
Agency

Office of
Pesticides and Toxic Substances
Special Pesticide Review Division

March 1980
Washington, DC 20460

Pesticide

# Metolachlor
# Pesticide Registration Standard

SAMPLE

# METOLACHLOR

A Sample Pesticide Registration Standard

March, 1980

Special Pesticide Review Division
Office of Pesticides and Toxic Substances

Environmental Protection Agency
401 'M' Street, S.W.
Washington, D.C. 20460

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# PREFACE

This is a Sample Registration Standard, designed to demonstrate the Agency's proposed implementation of Section 3(c)(2)(C) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which calls for a simplified procedure for the registration of pesticides. The new procedure being proposed by the Agency is based on the use of 'Registration Standards', publicly available regulatory position-documents for pesticide active ingredients. The function of a Registration Standard is to determine, through the review of all relevant scientific data, 'standards' of composition, packaging, toxicity, labeling, and data requirements that together ensure the safe use of a pesticide chemical. The 'standards' for a particular active ingredient are the conditions which each product containing that active ingredient must meet if it is to be registered for use in the United States.

There are three ways in which this Sample Registration Standard differs from an actual Registration Standard.

First, though the herbicide 'Metolachlor' is an actual pesticide currently registered with the EPA, this Sample Registration Standard does not have any regulatory status bearing on that registration; it is intended merely as an informational publication. The way in which this Sample Standard's scientific issues are resolved in a 'Regulatory Position' should therefore not be construed as a precedent for regulatory actions involving similar situations with other pesticide chemicals.

Second, the scientific review presented in this Sample Standard does not consider certain recent studies submitted in support of the actual re-registration of Metolachlor. Because the scientific community is constantly testing and re-testing chemicals, the data base used to support any one Registration Standard will be comprised of only those relevant studies which were available as of a certain cut-off date. For an actual Registration Standard, this cut-off date will be within no more than a few months of the publication date, and at least one updating will occur before publication. For Metolachlor, the body of studies now available has grown considerably since the original writing of this Sample Standard, and no updating has been performed. Thus the 'data gaps' identified in the body of this Sample Standard are by no means the actual gaps currently pending for the re-registration of the herbicide 'Metolachlor'. All Registration Standards will be updated periodically through reviews of the latest available scientific data.

Third, because this is an informational publication, a great deal of explanatory text is provided throughout the document. This text, which you will find set in '*Italics*', will be used in actual Registration Standards only when atypical circumstances call for some explanation or qualification. Further, to demonstrate the wide spectrum of information that the Agency considers in the regulation of pesticides, the explanatory text provided in this Sample Standard covers the full range of issues that might potentially be discussed with regard to pesticide safety. In an actual Registration Standard, the Agency will discuss only those issues which are relevant to the safety of the one particular chemical.

Though this Sample Standard is meant to inform the public about the Agency's present intentions, it is also to serve as a tool for modifying and refining these intentions to meet public needs. As was explained in the Federal Register notice (OPP-30032) making this Sample Standard available, your comments, criticisms, and suggestions are encouraged. Please direct your

comments to the general regulatory concepts illustrated by the discussions and to the format and principles of the presentation, and not to the specific scientific issues that have been portrayed for the herbicide 'Metolachlor'.

We suggest that you read this sample document through from front to back, as there is a logical development to the discussions, which lead through a consideration of available information, to an assessment of potential hazard, to a consideration of regulatory means of delimiting those hazards, and finally to a regulatory position. We also suggest, for persons interested in data requirements for registration, that you have at hand the 'Proposed Guidelines' for hazard evalution testing (40 CFR Part 163: Federal Register notices of July 10, 1978 and August 22, 1978), so that you can read in more detail about the nature of the Agency's minimum data requirements and when they apply to particular types of pesticide products or uses.

The consideration of available information and the assessment of potential hazard are accomplished in five separate 'disciplinary chapters', each specializing in some aspect of hazard evaluation, and each building on the conclusions of the previous chapters.

First, in the Product Chemistry chapter, the scope of the Standard is determined in a review of the composition and chemical nature of the pesticide and the products which contain it. The physical/chemical properties that are discussed in this chapter sometimes indicate hazards for those who handle the products.

The Environmental Fate chapter then examines the chemical's tranformation, degradation, movement, and potential accumulation after it is applied according to label directions. The Exposure Profile in the Environmental Fate chapter extrapolates from the fate information to estimate who or what non-target organisms may be exposed to the chemical as a result of its manufacture, handling, and application. For those organisms which are expected to bear significant exposures, an attempt is made to quantify the level of these exposures.

In the Toxicology chapter, an evaluation is made of the effects that could potentially occur in humans or domestic animals as a result of certain levels of exposure. With these potential effects and the Exposure Profile in mind, a 'Toxicology Hazard Assessment' is performed to point out potential problems for handlers of pesticide products, for applicators, and for workers or domesticated animals in the vicinity of the application.

Next, in the Residue Chemistry chapter, the level of residues and the nature of the metabolites to be expected in food or feed is determined, and the currently allowable levels of residues are compared to the potentially harmful dosage levels identified in the Toxicology Chapter.

In the last disciplinary chapter, the Ecological Effects chapter, an evaluation is made of the potential effects which may occur to microorganisms, non-target plants, and wildlife species as a result of certain levels of exposure, and the potential damage that these effects might have on vital ecological balances. As in the Toxicology Chapter, an 'Ecological Effects Hazard Assessment' is performed using the estimations in the Exposure Profile, and potential hazards to the specific species or to the general ecology are identified.

Then, in the Regulatory Rationale, means of preventing or mitigating the potential hazards identified in the 'Toxicology Hazard Assessment' and the 'Ecological Effects Hazard Assessment' are discussed. Finally, the regulatory actions recommended by the Rationale are brought into effect in the Regulatory Position, and a sample label is constructed for each type of product, bearing all the required restrictions and precautions.

Until the Agency begins to routinely inform registrants, in advance of initiating the building of a Standard, that certain data required under the authority of the 'Proposed Guidelines' have not been supplied, most early Standards will be 'Conditional Standards', with their regulatory positions conditional upon the generation of the missing data. When these data are later supplied by registrants seeking registration or re-registration, the hazards will be re-assessed and the regulatory position will be changed to reflect the new information.

To aid present and potential registrants in using the Standard to register or re-register their products, a section will be provided at the end of each Standard called 'Registration Under this Standard'. This section will list the data requirements which must be filled to turn the Conditional Standard into a Final Standard, the tests needed to demonstrate that the composition of the proposed product falls within the scope of the Standard, the procedure used to petition the Agency to amend the Standard to include product compositions or uses not presently covered, and the routine procedure to be used for registration and re-registration.

The disciplinary chapters and the Regulatory Rationale, by making explicit the thinking behind the Agency's decision-making, should be of help to public interest groups and environmental interest groups in evaluating the efficiency and thoroughness of the Agency's protection of the public health and the natural environment. Though representatives of the pesticide chemical industry will be most interested in what is required of them in order to accomplish registration or re-registration, they too will have the opportunity to see how those requirements and any accompanying regulatory restrictions were derived in a clear and logical manner from the available information on the potential hazards of the pesticide.

In addition to providing a simplified means of pesticide registration, the goal of the Registration Standards process is to give the Agency's decisions a broader scientific base and to open the Agency's decision-making to public scrutiny. Together this will ensure that the Agency's regulatory decisions on pesticides afford an effective protection of man and the environment as well as a fair and equitable treatment of pesticide producers and users.

# PRODUCT CHEMISTRY

*INTRODUCTION*

*The Product Chemistry chapter begins our review of the information about the chemical and its pesticide products by discussing the chemical's identity, how it is manufactured, and how it may be detected or measured, and by summarizing data which reports characteristic physical/chemical properties.*

TOPICAL DISCUSSIONS

Corresponding to each of the Topical Discussions listed below is the number of the section in the 'Proposed Guidelines for Registering Pesticides' of July 10, 1978 (40 CFR Part 163), which explains the minimum data that the Agency usually requires in order to adequately assess a pesticide's Product Chemistry.

| | Guidelines Section |
|---|---|
| Chemical Identity | 163.61-3 |
| Manufacturing Process | 163.61-4 |
| Percentages of Components in Pesticide Products | 163.61-6 |
| Product Analytical Methods and Data | 163.61-7 |
| Physical/Chemical Properties | 163.61-8 |

## Chemical Identity

*A definition of Metolachlor's chemical identity is necessary as the starting point in the Standard for three reasons: to locate relevant scientific sources, to make clear which pesticide products come under the regulatory authority of the Standard, and to identify the essential compounds to be studied in the evaluation of pesticide hazards.*

*In general, a chemical's identity is defined by names, numbers, and symbols. This can include common names, chemical names, representative trade names, names of manufacturers, molecular formulas and structures, CAS numbers, Shaughnessy numbers, or other alpha/numeric codes.*

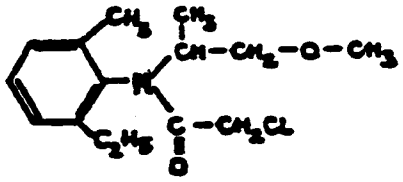
*Beyond a list of synonyms, the identity of the generic chemical may need qualification in two additional ways. First, the Standard may discuss as one, several stereoisomers of a single molecule, several distinct molecules which occur simultaneously, or various complex molecules of indeterminate structure. Secondly, a single Standard may encompass several distinct derivatives of an active ingredient which are assumed to have similar behavior and effects, as may often be the case with various salts and esters of an acid.*

'Metolachlor' is the acceptable common name for 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide as determined by the American National Standards Institute (1975). Ciba-Geigy Corporation, presently the sole manufacturer of Metolachlor in the United States, has assigned Metolachlor the experimental number 'CGA-24705' (for the active ingredient), and the trade name 'Dual'. The name 'Metolachlor' will be used in the Standard in place of the more complex chemical name or trade name.

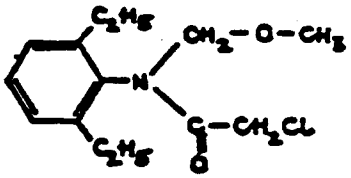
Metolachlor is both a 2-chloroacetamide and a 2-chloroacetanilide. Figure 1.1 shows the relationship between Metolachlor and other pesticide active ingredients similar in chemical structure. See the 'Chemical Data Sheet' for 'COM-001' in Appendix A for a complete chemical characterization of Metolachlor.

METOLACHLOR AND RELATED

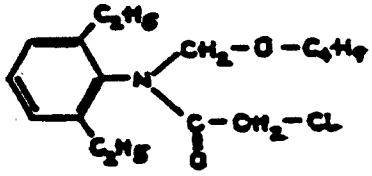
HERBICIDES



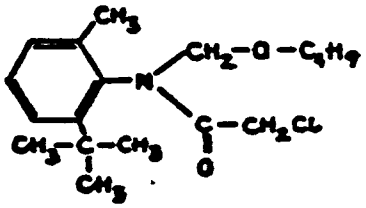
Metolachlor



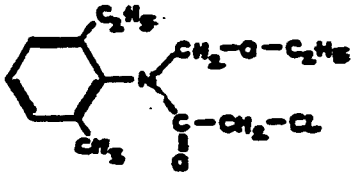
Alachlor



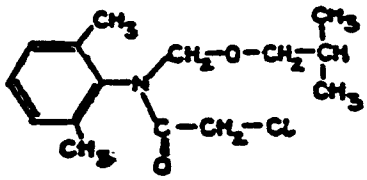
Butachlor



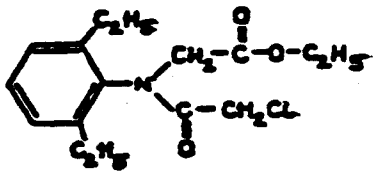
Terbuchlor



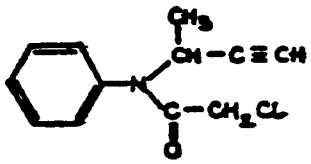
Acetochlor



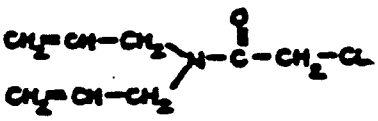
Delachlor



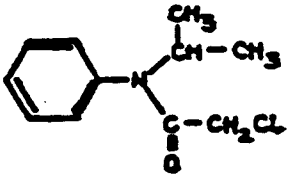
Diethathyl-ethyl



Prynachlor



Allidochlor



Propachlor

FIGURE 1.1

## Manufacturing Process

*The chemical reactions employed in the synthesis and/or purification of the active ingredient may suggest the presence of potentially harmful impurities and can serve as a verification of product composition. Because it is considered 'Confidential Business Information', a discussion of the specific procedures, equipment, and conditions required for commercial manufacture will not be published in the body of a Registration Standard.*

Though specific manufacturing information is withheld, the publicly-available U.S. Patent for the synthesis of Metolachlor shows that it may be produced by reacting the N-substituted aniline below with a chloroacetylating agent, preferably an anhydride or halide of chloroacetic acid. The general process is shown in Figure 1.2 below, which is taken from Vogel and Aebi, U.S. Patent 3,937,730 (1975) and German Patent 2,328,340 (1973).

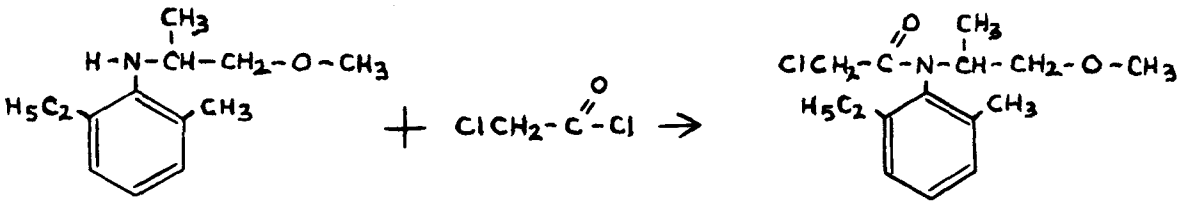



Figure 1.2

## Percentages of Components in Pesticide Products

*The Registration Standard will describe the composition of the technicals, manufacturing-use, and/or end-use formulations which contain the active ingredient. This information is needed to define the acceptable ranges of concentration allowable in registered products, to prescribe appropriate test material concentrations in hazard evaluation testing, and later, to estimate likely exposures to each component resulting from the handling or use of the products which contain it. Information on the identity and quantity of components which is claimed to be Confidential Business Information is normally to be withheld from publication.*

For all pesticide products, the Agency requires a listing of the upper and lower limit established (by the producer or formulator) for each active ingredient, and the upper limit for each impurity, reaction product, and degradation product which is known to be present or which might reasonably be identified.

Though the Agency has been supplied with all this information for Technical Metolachlor, the manufacturer has claimed that the identity of impurities can indirectly disclose details about the manufacturing process, and that the identity of Metolachlor impurities is therefore Confidential Business Information. The identity of impurities is thus not reported in this discussion, but is instead recorded in a 'Confidential Discussion Appendix' to be retained by the Agency for internal reference. (Accordingly, in Appendix A, the Chemical Data Sheets for components COM-002 through COM-011 are also withheld from publication and are included instead in the Agency's internally used 'Confidential Discussion Appendix'.)

Only the percentage of active ingredient has been supplied for the presently registered formulated end-use products containing Metolachlor.

Technical Metolachlor (manufacturing-use preparations)
1 presently registered: Technical Metolachlor is comprised of 95 to 100% the active ingredient 'Metolachlor', i.e., 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide.

Thus, one condition that manufacturing-use Metolachor preparations must meet in order to be registered under this Standard is that they must contain at least 95% the active ingredient 'Metolachlor' as defined in the Topical Discussion on 'Chemical Identity'.

Emulsifiable Concentrate Metolachlor (end-use pesticide)
2 presently registered: (a) Emulsifiable Concentrate with six pounds of active ingredient per gallon is comprised of 68.5% the active ingredient 'Metolachlor' and 31.5 % inerts.
(b) Emulsifiable Concentrate with eight pounds of active ingredient per gallon is comprised of 86.4% the active ingredient 'Metolachlor' and 13.6 % inerts.

Thus, one condition that formulated end-use products containing Metolachlor must meet in order to be registered under this Standard is that they must be emulsifiable concentrates containing 86.4% or less of the active ingredient 'Metolachlor' as defined in the Topical Discussion on 'Chemical Identity'.

## Product Analytical Methods and Data

*First, in order to ensure that products contain only those percentages of active ingredient which they properly claim to contain, it is necessary to have available analytical methods which may be used to determine the concentration of active ingredient in each formulation.*

*Second, the commercial production of pesticide chemicals, reactions between pesticide ingredients, reactions with packaging materials, as well as degredation during the long period over which some products may be stored before use, can result in the formation of chemical impurities. Because of the potential toxicity of impurities, analytical methods must be provided for their detection, both to improve the reliability of the Agency's hazard assessment and to ensure that marketed products conform to the standards of purity agreed upon by the pesticide producer.*

Methods for detecting and measuring the Metolachlor compound in its registered formulations have been submitted (Helseth and Cole, 1973). Though all the non-Metolachlor components of the Technical product have been identified by its manufacturer (Ciba-Geigy Corporation, 1974), methods have not been reported for determining or measuring any of the impurities in Metolachlor products. The lack of analytical methods for impurities constitutes a data gap in the information needed to support this Standard.

## Physical/Chemical Properties

*Physical/chemical properties can serve as a means of chemical identification: for instance, as an emergency means of identifying displaced or unlabeled pesticides, or as a confirmation of the reliability of other composition data. Physical/chemical properties can also disclose a direct hazard potential in the storage, mixing, dilution, or use of pesticide chemicals, and can indirectly indicate the chemical's environmental fate, or determine the compatibility of the components of a proposed formulation or tank mix. Because these properties vary with chemical composition, each technical and formulation type will have its own unique characteristics.*

Color: *the color of a pesticide chemical may be helpful to medical personnel in identifying the causative agent in accidental poisonings, and can be used in identifying particular formulation types of an active ingredient.*

Technical Metolachlor is white to tan. The color of each Emulsifiable Concentrate was not reported.

Odor: *a pesticide's characteristic odor may also give clue to the identity of the ingredients in emergency situations or under re-entry conditions, and may give an indication of the palatability of residues in the diet.*

Technical Metolachlor is odorless. The odor of each Emulsifiable Concentrate was not reported.

Solubility: *the solubility of technical products in various solvents factors in an estimation of the mobility of the pesticide chemical from the site of application, and provides one basis for considering the suitability of various solvents for formulation.*

The solubility of Technical Metolachlor was reported as follows:

In water - 530 ppm at 20°C

In organic solvents -

- Insoluble in 1,2-ethanediol (ethylene glycol)
- Insoluble in 1,2-propanediol (propylene glycol)
- Miscible with dimethylbenzene (xylene)
- Miscible with methylbenzene (toluene)
- Miscible with N,N-dimethylformamide
- Miscible with 2-methoxyethanol (methyl cellosolve)
- Miscible with 2-butoxyethanol (butyl cellosolve)
- Miscible with 1,2-dichloroethane (ethylene dichloride)
- Miscible with cyclohexanone

Stability: *the stability of the technical products suggests the rate of decomposition of the pesticide chemical so that environmental chemists can estimate the accompanying change in hazard potential.*

For Technical Metolachlor, the half-life of a 0.25% aqueous solution at 100°C is 30 hours at pH 3, 18 hours at pH 7, and 1.5 hours at pH 10.

Octanol/Water Partition Coefficient: *this coefficient, derived from tests on technical products, is a theoretical indicator of the relative potential of a pesticide chemical to accumulate in fatty tissue.*

No coefficient has been reported for Technical Metolachlor.

Physical State: *the physical state of a technical, manufacturing-use product, or formulated product is correlated to the types of studies which will be required to evaluate its potential hazards.*

Both Technical and Emulsifiable Concentrate Metolachlor products are in liquid form at room temperature.

Specific Gravity: *the density of pesticide products helps confirm their chemical compositions, and may be a factor in the Agency's assessments of the hazard involved with such application methods as aerial spraying.*

The specific gravity of Technical Metolachlor is 1.085 (+/- 0.005) at 20°C. The specific gravity of the six pound active ingredient per gallon Emulsifiable Concentrate is 1.04 (+/- 0.005) at 20°C, and the specific gravity of the eight pound per gallon Emulsifiable Concentrate is 1.11 (+/- 0.005) at 20°C.

Boiling Point: *the boiling points of liquid-form pesticide products helps to confirm their identity. Deviations from a standard boiling point may suggest the presence of impurities.*

At 0.001 mm Hg, the boiling point of Technical Metolachlor is 100°C. For six pound per gallon Emulsifiable Concentrate, it is 118°C, and for eight pound per gallon, it is 140 to 160°C.

Vapor Pressure: *the vapor pressures of pesticide products are indicative of inhalation hazards that may be encountered in their packaging, handling, and application, and is an important factor in the assessment of volatility.*

For the Technical, the vapor pressure is about $10^{-5}$ mm Hg at 20°C. For the six pound per gallon EC, the vapor pressure was reported to be $0.05 \times 10^{-1}$ mm Hg at 20°C, and for the eight pound per gallon EC, it was $0.5 \times 10^{-1}$ mm Hg at 20°C.

pH: *the pH's of those pesticides which can be diluted or dispersed with water, directly indicate hazards resulting from high corrosiveness and from the mixing of pH-incompatible products.*

The pH of a 10% solution of six pound active ingredient per gallon Emulsifiable Concentrate is between 7 and 8, and that of an eight pound per gallon EC is between 6 and 8.

Storage Stability: *the stability of the manufacturing-use or end-use formulations of a pesticide, when stored under typical conditions, is the basis for assessing reasonable efficacy-related expiration dates, and for assessing changes over time of such physical/chemical properties as pH, viscosity, color, odor, and density, as well as of the 'effective' concentration of the active ingredient.*

Results of ongoing studies show that Technical Metolachlor is stable for a minimum of one year at room temperature. The shelf life of both concentrations of the Emulsifiable Concentrate is estimated to be a minimum of 5 years.

Flammability: *this determines whether labels of pesticide products should bear an appropriate 'flammability' warning.*

No data were available on the combustability of the Technical. The flash point of the six pound per gallon Emulsifiable Concentrate was found to be 118°F (Setaflash C.C.T.), and that of the eight pound per gallon was found to be 185 (+/- 5)°F (TCC).

Oxidizing or Reducing Action: *the oxidation/reduction reactivity of each pesticide product must be determined to prohibit the hazardous mixing of incompatible product types.*

No data were available for the Technical, but the Emulsifable Concentrates were reported to be clearly non-reactive.

Explosiveness: *the safe packaging, transport, storage, and application of pesticide products is clearly dependent upon an understanding of their impact explosion characteristics.*

Again no data were available about the Technical. A study on the explosiveness of the six pound per gallon Emulsifiable Concentrate has shown that the material is thermally stable at 200°C, can be processed or handled at temperatures up to 150°C, (under normal use and application practices) does not form (nor does its vapor form) explosive mixtures, and is not shock sensitive. The study on the eight pound per gallon EC is currently in progress.

Miscibility: *some end-use pesticide products may separate out from their solvents when diluted in accordance with label directions, and this may decrease the product's efficacy and may make the distribution of the active ingredient on the application site dangerously uneven. The suitability of various solvents may hereby be brought into question.*

Both Emulsifiable Concentrate formulations form a stable emulsion with water.

Viscosity: *special concerns in mixing and diluting either the manufacturing-use or the end-use formulations, and in applying the end-use formulations of a pesticide, may be suggested by an examination of the viscosity of the solutions.*

No data were available on the viscosity of the Technical. The six pound per gallon Emulsifiable Concentrate has a viscosity of 15.6 (+/- 0.3) CS at 25°C. The eight pound per gallon, a viscosity of 120 (+/- 5) CD at 25°C.

Corrosion Characteristics: *to prevent the accidental leakage of those pesticide chemicals which are packaged in or applied from metal containers, an assessment must be made of each chemical's corrosion potential.*

Again no data were available on the Technical. For the Emulsifiable Concentrates, however, it was discovered that the six pound per gallon formulation was not corrosive to steel or tin, while the eight pound per gallon did show a slight corrosiveness. Lined containers are therefore a must for the eight pound per gallon EC.

Dielectric Breakdown Voltage: *if a chemical is applied around electrical equipment, such as telephone poles or tranformer stations, then it is necessary to determine the dielectric breakdown voltage so that risks of electrical shock to applicators can be appropriately assessed.*

Metolachlor is not registered for industrial weed control and so will not be used around high power electrical machinery.

DISCIPLINARY REVIEW

Chemistry Profile
Generic Data Gaps
Suggested Labeling

## Chemistry Profile

The technical material for a pesticide is the toxicant in pure form (usually 95 to 100% active ingredient) as it is manufactured by a chemical company prior to being formulated into an end-use pesticide product. Technical Metolachlor, which is 95 to 100% active ingredient, is an off-white, odorless liquid, soluble in water, and miscible with several organic solvents. Because it is intended only for re-formulation into the end-use pesticide, Technical Metolachlor is a 'manufacturing-use product'. The physical/chemical properties which have so far been determined for the Technical do not suggest any imminent hazards to packagers, shippers, or formulators - the only intended users of the Technical product. In order to be registerable under this Standard, a Technical Metolachlor product must have between 95 and 100% the Metolachlor active ingredient, identifiable non-Metolachlor components, and physical/chemical properties equivalent to or less hazardous than those reported above.

An emulsifiable concentrate is an end-use pesticide product, consisting of a toxicant suspended or dissolved in a water-insoluble organic solvent, stabilized by an emulsifying agent. The strength of an emulsifiable concentrate is usually stated in pounds toxicant per gallon concentrate. The only formulated end-use products containing Metolachlor which are considered registerable under this Standard are emulsifiable concentrates of eight pounds or less Metolachlor active ingredient per gallon (86.4% Metolachlor or less), with identifiable non-Metolachlor components, and with physical/chemical properties equivalent to or less hazardous than those reported above.

Two strengths of Emulsifiable Concentrate Metolachlor are currently registered: six pounds active ingredient per gallon and eight pounds per gallon. These are somewhat viscous liquids, miscible with water, and having a slightly greater density than water. The physical/chemical properties which have so far been determined for these emulsifiable concentrates indicate a few notable characteristics, due primarily to the presence of the organic solvents: a significant vapor pressure, a relatively low flash point temperature, and a slight corrosiveness to metal containers for the eight pound per gallon. These properties suggest the need for two warnings on the labels of emulsifiable concentrates: due to the vapor pressure and high flammability of the solvent in the six pound per gallon formulation, the user should keep any six pounds or less per gallon formulation away from open flame or high heat; to prevent potential leaks of the eight pound per gallon formulation due to its slight corrosiveness, it should be placed only in application equipment tanks that are protectively lined.

## Generic Data Gaps

The following tests or determinations are gaps in the Product Chemistry data base needed to adequately support a Registration Standard for Metolachlor. After each gap is listed the section in the Proposed Guidelines (July 10, 1978 40 CFR Part 163) which describe that type of data and when it is required.

For Technical Metolachlor:

| | | |
|---|---|---|
| 1) | Octanol/Water Partition Coefficient | 163.61-8(c)6 |
| 2) | Flammability | 163.61-8(c)13 |
| 3) | Oxidizing or Reducing Action | 163.61-8(c)14 |
| 4) | Explosiveness | 163.61-8(c)15 |
| 5) | Viscosity | 163.61-8(c)17 |
| 6) | Corrosion Characteristics | 163.61-8(c)18 |
| 7) | An analytical method (or reference to a method) for detecting and measuring each identifiable impurity (associated with the manufacturing of the technical grade of the active ingredient) in the formulated products of Metolachlor. | 163.61-7 |

For Emulsifiable Concentrate (6 lbs./gallon):

| | | |
|---|---|---|
| 1) | Color | 163.61-8(c)1 |
| 2) | Odor | 163.61-8(c)2 |

For Emulsifiable Concentrate (8 lbs./gallon):

| | | |
|---|---|---|
| 1) | Color | 163.61-8(c)1 |
| 2) | Odor | 163.61-8(c)2 |
| 3) | Explosiveness | 163.61-8(c)15 |

## Suggested Labeling

Ingredient Statement : The ingredient statement for manufacturing-use Metolachlor will list the active ingredient 'Metolachlor' as:

"Metolachlor: 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide"

Physical Hazard Precautionary Labeling : The labels of the Emulsifiable Concentrates should bear the following:

For 6 lbs.(or less)/gallon EC:

"Do not use or store near heat or open flame."

For the 8 lbs./gallon EC only:

"Do not place in unlined metal containers or tanks."

## BIBLIOGRAPHY
(Reserved)

*In order for the provisions of FIFRA concerning data compensation (Section 3(c)(1)(d)) to be effective under Registration Standards, data used in direct support of the Standard for each type of product must be accurately listed, enabling applicants and their arbitrators to determine what data do and do not support the registrations of individual pesticide products. Thus, for each disciplinary chapter, studies used to evaluate hazard and establish Standards for the manufacturing-use chemical and for each type of end-use formulation will be listed separately.*

To protect present and potential applicants for the registration or re-registration of products containing Metolachlor, the citations appropriate to each disciplinary chapter will not be published in this Sample Standard, though a complete Bibliography is provided at the end of the document.

## ENVIRONMENTAL FATE

*INTRODUCTION*

*'Environmental fate' studies are used to predict and estimate the presence of potentially harmful pesticide residues in the man-made and natural environment. A pesticide chemical released into the environment may be transformed by chemical or photochemical reaction, be metabolized by living organisms, or persist unaltered. Some degradation and transformation products can be hazardous in their own right. The goal of an environmental fate review is to identify the dominant pathways by which a pesticide chemical degrades, dissipates, and accumulates, and then to relate this behavior to various chemical, physical, and biological conditions.*

*When the pesticide, its degradation products, or its metabolites reaches a non-target organism, an 'exposure' has occurred, with the potential of causing adverse effects. Our undertanding of a pesticide's likely fate in the environment can be used to infer what organisms (including man) may be inadvertently exposed to the chemicals, by what route, how often, and in what concentrations.*

TOPICAL DISCUSSIONS

Corresponding to each of the Topical Discussions listed below is the number of the section(s) in the 'Proposed Guidelines for Registering Pesticides' of July 10, 1978 (40 CFR Part 163) which explain(s) the minimum data that the Agency usually requires in order to adequately assess a pesticide's Environmental Fate. Where no section number is listed, a minimum requirement has not been set for such information.

| | Guidelines Section |
|---|---|
| Use Patterns and Restrictions | |
| Physico-Chemical Transformation | 163.62-7 |
| Soil Metabolism | 163.62-8 |
| Aquatic Metabolism | 163.62-8 |
| Microbial Metabolism | 163.62-8 |
| Mobility | 163.62-9 |
| Spray Drift | 163.126-2, -3, and/or -4 |
| Field Dissipation | 163.62-10 |
| Bioaccumulation | 163.62-11 |
| Contamination and Control | |
| Alternative Pest Management Practices | |

### Use Patterns and Restrictions

*The environmental fate of a pesticide depends upon the formulation type, initial concentrations, and method of application, as well as the environmental conditions of the application site. Environmental conditions are those relating to the climate and geology of representative application locations. Initial concentrations depend upon dosage rates and dilutions, label and packaging information, methods of mixing and loading, application techniques, application schedules, the amount of area treated, common safety practices, and pounds used in a typical application.*

*Distinctly different use patterns may result in significantly different patterns of chemical behavior. It may sometimes be necessary to discuss separately the environmental fate resulting from each significantly different type of application or use pattern.*

The currently available end-use formulations of Metolachlor are two Emulsifiable Concentrates, one at six pounds active ingredient per gallon, the other at eight pounds per gallon. Metolachlor is a selective herbicide, used either as a pre-plant incorporated or pre-emergence surface-applied treatment for the control of most annual grasses and certain broadleaf weeds in corn (grown for grain only [excluding popcorn]) and soybean fields:

pre-plant incorporated - 1.5 to 3.0 pounds active ingredient per acre (depending upon soil type), used when field has furrow irrigation, or when a period of dry weather is expected. Fourteen days before planting, (but after bed formation if the corn or soybeans are to be planted on beds), the chemical is diluted appropriately with water or fluid fertilizer, applied to the soil with conventional ground sprayers (or center pivot irrigation system) and incorporated into the top 2 inches of soil. A finishing disc, harrow, rolling cultivator, or similar implement is used to provide a uniform 2 inch incorporation.

pre-emergence surface-applied - 1.5 to 3.0 pounds active ingredient per acre (depending upon soil type), applied with conventional ground sprayer (or center pivot irrigation system) during planting (behind the planter), or after planting but before weeds or crop emerge.

Present use restrictions include: for rotational crops on a treated corn or soybean field, rotational crops other than corn or soybeans may not be planted earlier than 18 months after application; should not be used on sweet or popcorn; should not graze or feed corn forage and fodder to livestock or use for silage; should not graze or feed soybean hay or forage treated with Metolachlor alone or with tank mixes containing Metolachlor.

The restrictions against: (1) the grazing or feeding of corn forage, corn fodder, (2) the use for silage, (3) the grazing or feeding of soybean hay or forage, were needed because their feed uses were classified as Section 180.6(a)(2), CFR 40. Feeding restrictions for soybeans were required because no permanent tolerances have been set for soybean forage or for its hay (including the fodder or straw left after harvesting the beans).

The U.S. Department of Agriculture Crop Reporting Board in June 1975 listed 77,527,000 acres of corn planted in 1975 (Ciba-Geigy Corp., 100-EUP-38,1975). Seven mid-western states (South Dakota, Nebraska, Minnesota, Iowa, Illinois, Indiana, and Ohio) produce four fifths of the corn crop. Within this region, the usual planting dates are between April 20 and May 9.

## Physico-Chemical Transformation

*Chemicals introduced into the environment can react with any number of other chemicals already present in the air, water, or soil. These reactions can be dependent upon such factors as pH, concentration, the nature of the substances present, or temperature. Reactions with water itself, in bodies of water and in soil, are of particular importance with pesticides released into the natural environment. The importance of hydrolysis as a dominant pathway for pesticide degradation can be determined quantitatively from data on the rate of hydrolysis, and the identity, quantity, and persistence of hydrolysis products.*

*In addition to reacting with other chemicals, a pesticide in the air, adsorbed on soil surfaces, or in the water, may undergo transformation by direct photolysis in sunlight. Photolysis reactions vary with the intensity and wavelength of radiation, the physical or chemical state of the pesticide, the matrix (air, soil, or water) in which the pesticide resides, and the presence of other reactants. The importance of photolysis by sunlight as a transformation pathway of a pesticide chemical can be established through a study of the rate of photolysis, and the identity, quantity, and persistence of photolysis products.*

Hydrolysis

Metolachlor in buffer pH 5, 7, and 9 at 30°, was respectively 97, 100, and 96% stable for 28 days (Burkhard 1974). From rate constants, Arrhenius parameters for each pH value were calculated. Using the Arrhenius parameters, half-lives for Metolachlor at 20°C were calculated to be greater than 200 days in 0.1N HCl (pH 1) and in buffer pH 5, 7, and 9. In 0.1N NaOH (pH 13), the calculated half-life was 97 days. Hydrolysis of Metolachlor in 0.1N NaOH at 30°C yields N-(2' methoxy-1-methyl-ethyl)-2-ethyl-6-methyl hydroxyacetanilide. In 0.1N HCl at 70°C, Metolachlor hydrolyzed to 4-(2-methyl-6-ethyl-phenyl)-3-methyl-morpholinone-5.

These data were sufficient to show that hydrolysis products are not of environmental concern because Metolachlor is considered to be stable. The extreme basic and acidic conditions which caused the hydrolysis of Metolachlor are not likely to occur in the natural environment.

Photolysis

Because Metolachlor is used on outdoor crops, studies on photolysis in both soil and water are needed. Because an assessment of re-entry hazard is not required for any of the proposed uses of products containing Metolachlor, a study on photolysis in the vapor phase is not necessary.

Photolysis in Aqueous Solution

Metolachlor was found to be relatively stable in aqueous solution under natural sunlight (Aziz and Kahrs 1975). Approximately 6.6% was photolyzed in 30 days, which was less than 10% of the exposed activity. Five photoproducts, accounting for about 4.7% of the activity, were found in the chloroform soluble fraction. One photoproduct was identified as 4-(2-methyl-6-ethylphenyl)-5-methylmorpholine. Four of the photoproducts were not identified. One unknown was found in the aqueous fraction and amounted to about 1.9% of total activity. These photoproducts do not need to be identified because they represent less than 10% of the exposed activity.

Under high intensity artificial sunlight conditions, Metolachlor in aqueous solution was approximately 69% degraded in 15 days (Aziz and Kahrs 1974). Five photoproducts comprising about 13% of total radioactivity were found in the chloroform soluble fraction. Three of the products were identified as 4-(2-methyl-6-ethylphenyl)-5-methylmorpholine (MET-009), N-(2-hydroxyacetyl-N-methoxyprop-2-yl) 2-ethyl-6-methylaniline (MET-001), and N-chloroacetyl-2-ethyl-6-methylaniline (MET-010). (See Appendix A for identities of chemicals referred to by MET numbers.) Photolysis products in the aqueous phase amounted to 23% of the activity. Chloroform soluble products which stayed at the origin on thin layer chromatography (TLC),

amounted to 17.2% of the activity. Mass spectroscopy and TLC analyses of this activity indicated that at least five major products were present. Further efforts were taken to separate and identify these products using TLC with a developer of chloroform and methanol (9:1) and chromotropic acid, methanolic sodium hydroxide, and diazonium fluoroborate as specific spray reagents. With this TLC system, at least seven photolysis products were separated. None represented more than 4% of the original $^{14}C$ activity. These polar products did not contain hydroxyl, aldehyde, or N-hydroxymethyl groups as judged from tests with the specific chromatographic agents.

Based upon the data discussed in this section, Metolachlor is considered to be stable in aqueous solution under natural sunlight.

Photolysis in Soil

Studies on soil slides were performed by Aziz (1974). Under natural sunlight conditions, Metolachlor on soil slides was approximately 50% photolyzed in 8 days. Activity in chloroform extract amounted to 44.9% of the applied radioactivity, of which 32.7% was determined to be parent, 3.9% was identified as N-propen-1-ol-2-yl-N-chloroacetyl-2-methyl-6-ethylaniline, and three unknowns accounted for 7.7%. Each unknown was less than 10% of the applied activity. Non-extractable $^{14}C$-activity in soil amounted to 39% of the applied activity. Volatiles accounted for 10.5% of the applied activity, of which 5.2% was determined to be parent.

Under artificial sunlight conditions, Metolachlor on soil slides was approximately 52% degraded in 7 days. Activity in the chloroform extract amount to 47.1% of the applied activity, of which 24.1% was determined to be parent, 5.6% was identified as N-propen-1-ol-2-yl-N-chloroacetyl-2-methyl-6-ethylaniline, and 16.4% was comprised of 3 unknowns. (Each unknown was less than 10% of the applied activity.) Nonextractable $^{14}C$-residue in soil amounted to 39%. Volatiles accounted for 6.8% of applied activity, of which 4.12% was determined to be parent.

Though either study would have been adequate alone, these studies, the one conducted under natural sunlight and the other under simulated sunlight, provide sufficient information about the photodegradation of Metolachlor in soil.

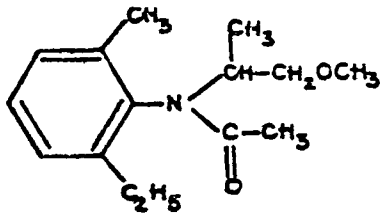
## Soil Metabolism

*A chemical in the environment can also be transformed by the metabolic activity of biological systems, including microbes, plants, and animals. Biodegradation is an important degradative pathway for organic compounds in nature, in terms of mass of material transformed and extent of breakdown. Microbes, because they need not absorb what they metabolize, and because of their widespread occurrence in soil, are the primary organisms responsible for biodegradation on land.*

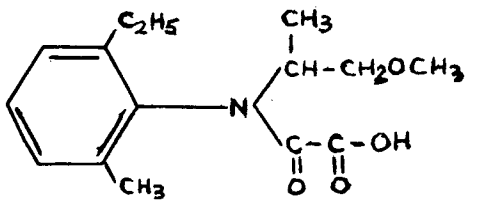
*The rate, pathway, and degree of pesticide degradation by soil microbes varies most significantly with moisture, temperature, soil chemistry, soil composition, and soil aeration. Because microbes that require oxygen may have different metabolic paths from those that function without it, metabolism studies should be performed under both aerobic and anaerobic conditions. One may also observe different effects in specifically cultured soil mediums.*

Elleghausen (1976a and b) studied the degradation of Metolachlor in soil under sterile aerobic, nonsterile aerobic, and nonsterile aerobic followed by nonsterile anaerobic conditions. Under sterile aerobic conditions, at the end of 12 weeks, 30% of the reductively dechlorinated analog of Metolachlor (MET-005) was found. No other metabolite could be detected. The remaining radioactivity existed as undegraded Metolachlor.

Also at a time interval of 12 weeks, both the aerobic nonsterile and aged aerobic/anaerobic nonsterile tests resulted in a degradation pattern wherein about 18% of the radioactivity was identified as MET-025. Another 10%



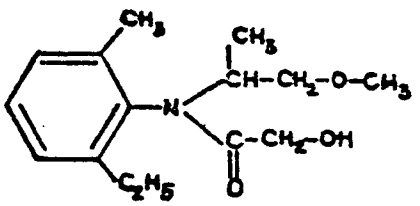
MET-005



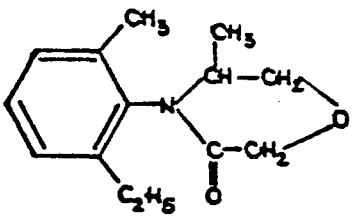
MET-025

of the initially applied radioactivity was found as polar, water soluble products. They were inseparable by TLC, but could be methylated with diazomethane to form three distinct components, separable by gas liquid chromatography (GLC). The investigator considers these to be ring hydroxylated analogs of MET-025. A $CHCl_2$-soluble nonpolar metabolite, representing about 5% of initial radioactivity was compared, by TLC and GLC co-chromatography, to 26 model Metolachlor metabolites with no identity fit. Small amounts of MET-005 as well as unidentifiable polar and nonpolar extractables were also found.

Sumner, Szolics, and Cassidy (1976) studied the products of degradation of ring labeled $^{14}C$ Metolachlor in silt loam treated at an exaggerated rate (100 ppm) and incubated out-of-doors in open bottomed containers. Besides



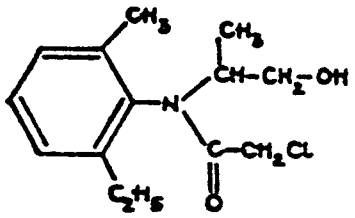
MET-001



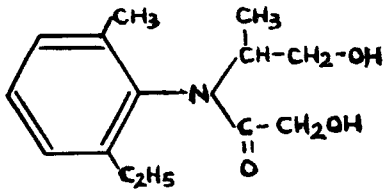
MET-008

41.7% of total initial radioactivity found as Metolachlor, 0.9% of MET-001 and 0.1% MET-008 were found. Additionally, an oxalic acid derivative was tentatively identified as MET-025. Chemicals contained in the leachate from this study were qualitatively similar, as determined by comparative radioassay of various TLC $R_f$ zones.

Concurrently, Sumner, Szolics, and Cassidy (1976) conducted a field plot study of silt loam soil treated at 2 lbs ai/A and aged 12 months. This study yielded in addition to MET-001, MET-008, and MET-025, the additional compounds MET-003 and MET-026.



MET-003



MET-026

All metabolites in both substudies were less than 1% of total radioactivity, except MET-001 in the leachate, which represented 2.5% of total radioactivity. Two TLC spots, representing metabolites less polar than MET-003 were also noted, both at the 1% level, in the extracts from the field experiment; the two spots as well as a spot near the TLC plate origin represented 6.4% of the total radioactivity.

Sumner and Cassidy (1975a) showed that under field conditions, over a one year period, the relative percentage of unextractable residues reached a steady state (ca. 80% of total). During the latter stages of the test, the relative amount of extractable residue in the organic fulvic and humic acid fractions decreased with a concomitant increase in the amount remaining in $H_2O$ soluble and mineral fractions. The fractionation procedure used was described by Sumner (1974).

Dupre (1974a) conducted an anaerobic soil metabolism study as described in the Agency's Proposed Guidelines for testing and found that the gross character (extractable polar, extractable nonpolar, or nonextractable) of soil metabolites did not change over a 60-day anaerobic period following a 30-day pre-conditioning aerobic period, as compared to the character of degradates during a similar period of continued aerobic metabolism.

Evidence is provided by Sumner and Cassidy (1975a) that nonextractable bound residues of Metolachlor and its metabolites are in dynamic equilibrium with soluble forms and that the nonextractable portion may therefore serve as a long term reservoir for extractable residues.

When viewed as a composite, these tests are sufficient to meet the needs of the Agency's interests in soil metabolism for Metolachlor. (The following additional studies contain information related to metabolic transformation in soil but did not by themselves supply adequate information about soil metabolism: Kaiser 1974, Sumner and Cassidy 1974g, k, l, m, f, and e).

## Aquatic Metabolism

*The rate, pathway, and degree of pesticide biodegradation in the aquatic environment may vary with the pH and other chemical properties of water, oxygen content, organic content, and the type of sediment present. As with terrestrial biotransformation studies, one should observe the different effects under anaerobic or aerobic conditions, and may attempt to observe the effects of specifically cultured water mediums. Pesticide degradation and transformation must be studied to determine the dominant pathways of breakdown, so that a pesticide's fate can be related to the environmental conditions at its site of application. Also, pesticide transformation products, whether caused by aquatic metabolism, terrestrial metabolism, or physico-chemical reaction, may themselves be as hazardous, or even more hazardous, than the parent compounds.*

Neither aerobic nor anaerobic aquatic metabolism studies are ordinarily needed to assess the environmental fate of pesticides intended solely for terrestrial uses, and no products formulated with Metolachlor have yet been proposed for any uses other than the protection of corn and soybean fields.

## Microbial Metabolism

*In order to refine our understanding of how a pesticide may actually be tranformed by specific kinds of microorganisms, or by the microorganisms that populate a specific type of soil or aquatic habitat, it may be useful to measure the direct impact of microbes on pesticide transformation. This may be done by a comparison of metabolic effects under sterile and non-sterile conditions, or by the use of specifically pure cultures.*

Three studies of this sort were submitted. One was conducted according to the alternative pure or mixed culture technique and two were conducted by the sterile and non-sterile soil approach.

In the pure and mixed culture study (McGahen and Tiedje), American Type Culture Collection number 34507, identified as Chaetomium globosum, a soil fungus, was used in resting cell experimentation at 0.035 mM concentrations of Metolachlor including control flasks without Metolachlor and without C. globosum. Control flasks did not exhibit any degradation for 144 hours. Flasks with C. globosum and Metolachlor exhibited substantial degradation with only 55% of Metolachlor remaining after 5-7 days. An adaptive lag period of approximately 20 hours was observed. A total of at least eight extractable products were identified or tentatively identified. MET-009, MET-003, MET-018 and MET-019 were firmly identified. Identifications of MET-020, MET-021, MET-022, MET-023, and MET-024 were tentative. The formation of the oxoquinoline is unique to pesticide metabolism, with the three quinolines of Metolachlor unique to Metolachlor itself. It is apparent that the fungus did not remove any group from the ring, although it dehydrogenated the ethyl moiety to form a vinyl on the ring.

Kaiser, using labeled Metolachlor (position of label unspecified) added Metolachlor to both sterilized and unsterilized sandy loam soil at a concentration of 10 mg/250 gm of soil (40 ppm) (Kaiser, 1974). Essentially no loss of total activity was noted in either sterile or non-sterile soil (5-15% of the residual activity was found to be degradation products of Metolachlor). This study is not considered acceptable for the purpose of describing the effects.

In another sterile and non-sterile soil study (Ellgehausen, 1976b,c), a clay loam (Stein, Switzerland) which was treated with ring-labeled Metolachlor at a concentration of 1 mg/232 gm of soil (ca. 4 ppm) and a control sample (autoclaved soil) were monitored for degradation. After a short lag phase, a slow but steady evolution of $^{14}CO_2$ was evolved in the non-sterile soil reaching 4.8% of the applied dose after 12 weeks. Analysis of the soils after 12 weeks indicated that 10% of the residual activity in the non-sterile soil was parent compound versus 65% Metolachlor in the sterile soil.

On the basis of these studies, a general microbial transformation scheme can be postulated which involves dehalogenation, dehydrogenation, dealkylation, ring formation, and oxidation of the acetyl group and/or ring oxidation. Ring oxidation apparently results after extended incubation of the compound in the presence of microbes, but it is not a significant route of degradation.

The studies by McGahen and Tiedje and by Ellgehausen followed acceptable protocols, and are sufficient to support this facet of the fate assessment for the present uses of Metolachlor.

## Mobility

*The movement of a pesticide chemical away from its site of application may transfer its hazardous effects to non-target organisms, may contaminate the air, water, and soil phases of the environment, causing loss of usable land and water resources to man and loss of habitat to wildlife, may infiltrate food webs including non-target crops, and may result in a loss of effectiveness against the target pest. Where a chemical goes in the environment is directly dependent upon how it moves.*

*Different types of pesticide products and applications will bring into play different mechanisms of movement. For example, pesticides applied by plane will be subject to aerial drift, systemic pesticides will be removed from the the soil by plant uptake, and surface applications will runoff more easily than soil incorporations. However, the most common pathways for pesticide mobility in the environment are:*

1) *Leaching, which is the movement of a pesticide through soil, usually by a mass transport process, which varies with the soil's adsorption potential, rainfall, flow rate, diffusion and dispersion, and pesticide solubility, and which possibly results in a contamination of groundwater or drainage effluent; and Surface Runoff, which is the washing of a pesticide over the surface of the soil by rain;*
2) *Volatility, which determines the availability of residues to the atmosphere, which is affected by surface type, soil particle size, interaction with environmental substrates or product ingredients, vapor pressure, soil moisture, and climate, and the rate of which depends upon the moisture conditions at the soil surface, because a surface layer of dry soil can act as a barrier to volatilization;*
3) *Adsorption to and desorption from various types of soil, sediments, and particulate matter, which helps determine the availability of residues to the aqueous phase of the environment, and varies with soil composition, particle size, moisture content, water solubility, and the length of time that the pesticide has remained in contact with soil;*
4) *Water Dispersal, which is determined by measuring residue concentrations in water at selected distances from a point of release, and which is of particular interest with pesticides discharged directly into bodies of water.*

*The importance of each of these mechanisms as a dominant pathway for pesticide movement should be established quantitatively. Predictions may then be made about how much, where, and at what rate a pesticide may move under particular environmental conditions.*

### Leaching

Data on leaching have been developed by Dupre (1974c) and Houseworth (1973b). Parent Metolachlor leaches readily in sandy loam and sandy soils low in organic matter. Twenty to 33% of the applied Metolachlor leaches more than 12 inches in the above soils when an equivalent of 20 inches of rainfall are applied to a soil column overlayered with Metolachlor. Conversely, insignificant leaching is expected in muck soils high in organic matter. Field studies (Ballantine, 1975) showed substantial leaching into the 6"-12" soil horizon in 5 different states with various soil types. Metolachlor residues, aerobically aged for 30 days in soil, will also leach in soils low in organic matter. These data are sufficient to assess leaching potential for Metolachlor.

Volatility

A volatility study, which is conducted on the end-use formulations of a pesticide, is not currently available for the Emulsifiable Concentrates of Metolachlor.

Adsorption

An adsorption/desorption study using four concentrations of radiolabeled active ingredient in a soil sediment representative of the proposed use area is not presently available for Metolachlor.

## Spray Drift

*Spray drift may result in a significant exposure to non-target organisms when pesticides are applied by aircraft, air carriers (mistblowers), or ground application equipment such as overhead sprinklers, and sprayers for rights-of-way. Damage from drift has been demonstrated at distances up to several miles from the site of application. Studies conducted under actual field conditions or under simulated conditions in wind tunnels can determine the probable drift potential, (i.e. the greatest volume of droplets less than 100 um in diameter), under various conditions. The parameters that may significantly alter droplet volume spectra include nozzle types and cores, pressure settings, discharge orientations, wind speeds, temperature, and relative humidity. The physical properties of different formulations, such as surface tension, viscosity, density, and vapor pressure and the use of diluents, adjuvants, and tank mixes may also alter the hazard associated with swath displacement.*

Information on the likelihood or extent of spray drift for Emulsifiable Concentrate Metolachlor when conventional ground sprayers are used is not presently available, except for what is generally understood about the spray drift behavior of similar agricultural chemical preparations.

## Field Dissipation

*By delimiting the variables of a chemical's behavior, laboratory studies on transformation and mobility can determine the dominant pathways by which pesticides may dissipate in the environment. But field studies introduce important new variables, such as the presence of a crop, and allow all variables to operate simultaneously, thus verifying laboratory predictions of primary mechanisms. Residue decline curves obtained under field conditions are directly used to estimate the duration of residues in the environment. This allows the direct estimation of potential exposures, including those which might be suffered by agricultural workers re-entering a treated area, by the general public ingesting rotated crops, by wildlife consuming residues through the food web, or by any organisms making use of treated or contaminated land or water resources.*

Field dissipation studies were conducted by Ballantine (1975) on five different soil types representing five geographical locations. The following conclusions were drawn from the studies: 1) Approximately 10% of applied Metolachlor was found in the upper 12 inches of Mississippi loam after 60 days for both 2 and 4 lbs. ai/A application rates. 2) In Nebraska silt loam, approximately 10% of applied Metolachlor was found in the upper 12 inches after 162 days for both 2 and 4 lbs. ai/A application rates. 3) In New York,

California, and Illinois, soils that were not analytically characterized, Metolachlor dissipated to about 10% of the applied in 60 to 150 days for both 2 and 4 lbs. ai/A application rates.

These field dissipation studies under actual use conditions are sufficient to show that Metolachlor, applied alone, dissipates to approximately 10% of the applied amount in 60 to 160 days in each soil type tested, and that it leaches to approximately 12 inches in loam and silky loam soils. If uses were proposed at greater than 4.0 pounds ai/A pre-emergent, then additional field dissipation tests, at the proposed rates, would be needed.

Combination and Tank Mix Dissipation

Because Metolachlor may be applied in combination or tank mixes with other pesticides or with fertilizers, a study is also needed that compares the dissipation characteristics of each active ingredient of the mixture when applied to the soil as a mixture, with the separate dissipation characteristics of each active ingredient in soil when applied individually. Ballantine (1976a) conducted field studies to determine the comparative persistence of Metolachlor and Atrazine in silty clay loam (Illinois) and sand soil (Florida). Rates were the maximum specified in the presently proposed labeling. Samples were collected from the 0-6 inch soil depth at 0.2, 4, 8, and 12 months.

The study was sufficient to conclude that there are no significant differences in the dissipation rates of the chemicals when applied individually. Metolachlor dissipated to less than 0.05 ppm in eight months in Illinois and one year in Florida. But the study was not sufficient to evaluate the dissipation characteristics of each active ingredient of the mixture when applied as a mixture.

## Bioaccumulation

*Dissipation is the study of the disappearance of a chemical in the environment. Bioaccumulation is concerned with the concentration of a pesticide or its transformation products in living organisms. There are four stages through which bioaccumulation may proceed:*

*1) Some pesticide chemicals may be very slow to break down, and so could be absorbed or adsorbed by living organisms.*

*2) Organisms can attempt to metabolize the chemical. The chemical may be completely metabolized to simple, naturally-occurring compounds, or partly metabolized to potentially toxic compounds.*

*3) If the compound or its metabolites are fat-soluble and are stored in fatty tissue they may be released very slowly, as fat is burned off. If the compounds or its metabolites are water soluble, they may sometimes be stored as carbohydrates.*

*4) These plants and animals may in turn be eaten by other animals, including man. Where a pesticide compound is stored by populations of organisms, each successively higher member in their food chain may accumulate greater amounts of residues.*

*Bioaccumulation studies can examine the rate and degree of each of these stages. First, residue levels in rotational crops can suggest safe rotation intervals and crop selection for human food sources, and can also suggest the extent of plant uptake from the soil. Second, studies on irrigated crops do the same for uptake from water sources. Third, the accumulation of residues in non-target organisms, and particularly in aquatic organisms such as fish, can provide a useful indication of general food web contamination.*

Rotational Crops

Oats in the greenhouse, and carrots and soybeans in the field, were grown as rotational crops to corn 9 months after soil treatment at 2 lbs/acre using $^{14}C$-ring labeled Metolachlor. Low levels of residues ranging from .02 to .27 ppm, expressed as Metolachlor, were found in different portions of the various crops (Sumner and Cassidy 1974e; Sumner and Cassidy 1974f; Sumner and Cassidy 1974g). The preponderance of extractable residues were polar in nature (partition into $H_2O$/MeOH vs. $CHCl_3$) and the two major fractions constituting these polar residues were neutral and acidic in nature, as determined by ion exchange chromatography. A typical analysis of such plant residues is provided by the following example for oat straw derived from oats grown as a rotational crop to corn where Metolachlor was applied at a rate of 2 lbs/acre (Sumner and Cassidy 1974f).

| | | | Calculated ppm as Metolachlor |
|---|---|---|---|
| 1) | Total $^{14}C$ activity | = 0.27 ppm | |
| 2) | $H_2O$/MeOH extractable, % of total activity | = 67% | .18 |
| | - Neutral Fraction, % of total activity | = 19% | .05 |
| | - Acidic Fraction, % of total activity | = 45% | .12 |
| 3) | $CHCl_3$ extractable, % of total activity | = 7.0% | .02 |

The text of the review by Marco (1974) of metabolism studies with Metolachlor in corn implies that only highly polar acid metabolites, such as conjugates involving the N-acetyl group of Metolachlor are present. However, the data presented in Table IV of Marco (1974) show that the relative amounts of polar neutral and polar acidic constituents in extracts of mature stalks differ by about 4 to 1. These data support the contention that TLC characterization of the polar neutral constituents should be possible. Sumner and Cassidy (1974d) did not adequately characterize the polar neutral constituents, though the very low levels of radioactive content in these fractions made further characterization difficult by means of present-day technology.

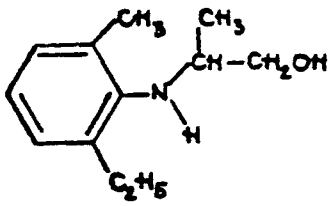
(Adapted From Table IV, Marco-1974)
Ionic Characterization of Radioactive Metabolites in Polar Fraction of Corn Treated with 2 lb. ai/A $^{14}C$ Metolachlor

| Location | Ionic Charge | Percent of Total $^{14}C$ in Plant | | | |
|---|---|---|---|---|---|
| weeks after treatment | | 8 | 12 | 16 | (mature forage) |
| Greenhouse | Neutral | 7.0 | 7.9 | a | (a = sample |
| | Acid | 73.1 | 53.6 | a | decomposed |
| | Base | 0.6 | 0.9 | a | in shipment) |
| | Zwitterion | 6.2 | 21.4 | a | |
| Field | Neutral | 7.4 | 10.8 | 7.3 | |
| | Acid | 68.2 | 70.4 | 26.3 | |
| | Base | 1.7 | 1.2 | 1.0 | |
| | Zwitterion | 2.7 | 8.4 | 15.3 | |

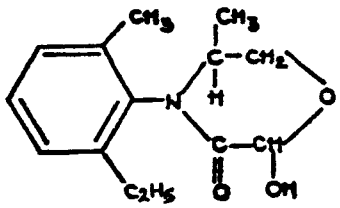
Marco (1975), and Sumner and Cassidy (1975), argue that the metabolic pathways in rotational carrots and soybeans are qualitatively similar based on comparison of the ionic and TLC comparative characteristics of acidic constitutents. While it is conceded the conjugated metabolites of

Metolachlor in corn grain may be the only ones worthy of consideration, the same is not necessarily true with rotational crop uptake. Compounds unable to readily form sugar and/or S-glutathione conjugates may be taken up by rotational crops and exist as discrete residues. These may therefore be worthy of individual consideration by the toxicologists.

Also, it should be noted that the official regulatory method for Metolachlor and its metabolites in corn is based on an acid hydrolysis which forms HP-001 and HP-002. (Aziz and Ross 1975).



HP-001



HP-002

This method will not detect MET 002, 004, 008, 009, or 010, all of which are postulated degradation products of Metolachlor (Marco 1974), and none of which can readily form the conjugates, but only oxo-neutral conjugates. Again, using the oat (straw) example, cited above, one can conclude that the entire neutral fraction of the $H_2O$/MeOH extractables equaling 0.05 ppm could be a mixture of MET 002, 004, 008, 009, and 010 (or other degradates of a similar nature) and would not be detectable by the method of Balasubramanian, Aziz, and Ross (1975). Such compounds should be readily amendable to GLC and TLC separation $R_f$ zone and retention time comparisons with model compounds.

Based on information submitted by Ballantine,(1975) the roots of root crops, grain of small grains and oil from oil seed crops can reasonably be expected to contain little, if any, residue of Metolachlor per se or its metabolites hydrolyzable to HP-001 or HP-002 using the method of Balasubramanian, Aziz and Ross (1975). All residue analyses for MET-007 were .03 ppm or less and were 0.10 ppm or less for MET-015. The question as to whether this regulatory method for corn-related products is applicable to rotational crops is moot and must await further elucidation of the nature of the neutral polar metabolites in rotational crops.

The studies cited above show that levels of Metolachlor-derived residues in other plant portions of these crops (carrot tops, soybean stalks, sugar beet tops and wheat straw) may at times be expected to exceed this analytical "baseline" level when grown as rotational crops to corn and analyzed by the procedure of Balasubramanian, Aziz, and Ross, 1975.

The data on rotational crop residues are deficient in two respects: first, data are not available on residues in leafy vegetable, rotational crops; second, though it is agreed that present analytical technology is not easily adapted to the task, the extractable nonpolar metabolites in rotational crops were not sufficiently characterized to dispel concern over their potential toxicity. Until these problems are resolved, any product formulated with Metolachlor and intended for use on food crops should carry: a label restriction that calls for an 18-month interval between application time and the planting of rotational crops, to allow for a complete degradation of residues; and also a warning against using corn forage or fodder for silage or to graze or feed livestock, to prevent uncharacterized residues from being passed on to human consumers.

Irrigated Crops

*An irrigated crop residue study under actual field use conditions is needed only when a pesticide is used in holding ponds or effluent and other discharged sources used to irrigate crops.*

No such aquatic uses have been proposed for Metolachlor.

Fish Accumulation

Elleghausen (1977) tested the uptake, transfer and degradation of Metolachlor by algae, daphnia, and catfish. After 90 minutes exposure to 0.1 ppm Metolachlor, algae accumulated 10.4 ppm. However, following 2 hours depuration, less than 2 ppm remained in the cells. Daphnia, exposed for 24 hours to 0.1 ppm, accumulated 0.60 ppm. Eight hours depuration was needed to achieve a 50% loss. Daphnids accumulated only 20% more when exposed to both algae with 10.4 ppm Metolachlor and water containing 0.1 ppm Metolachlor as compared to fortified water in the absence of algae. Catfish, exposed to 0.1 ppm $^{14}C$ Metolachlor incorporated 1.20 ppm Metolachlor in their tissues after 96 hours. However, a plateau was not reached.

Metabolites of Metolachlor were noted but not identified in the algae, daphnids, and catfish. At the end of the 96-hour catfish study, only 1/2 of the $^{14}C$-activity remaining in the water was Metolachlor. The remainder was present as 3 unidentified degradation products. The theoretical basis for the model system used was discussed in another paper (Elleghausen 1976b). Smith (1977) conducted a 30-day catfish exposure study in a soil/water/fish ecosystem. At an average concentration of 0.08 ppm in the water, bioaccumulation factors were 6.5 - 9.0 for edible portions of the fish and 55.0 - 92.4 in the viscera. After 14 day withdrawals, these values dropped to 0.03 and 0.18 ppm, respectively, corresponding to a bioaccumulation factor of less than 1. The accumulated residues in the edible portions remained relatively constant in terms of extractable vs. nonextractable (about 8:1). On days 1 and 30 there was 16 times more organically soluble activity than aqueous soluble (ethyl acetate-water system). A cysteine conjugate of Metolachlor was identified as a metabolite and reached a high of 12.8% of total $^{14}C$ activity in the edible tissue on day 14. Smaller amounts of other metabolites were found in edible and/or visceral tissues but were not identified.

N-(2'hydroxy-1'-methylethyl)-2-ethyl-6-methyl chloroacetanilide (MET-003), N-2(2-hydroxy acetyl)-N-(1-methyl propane-2-yl)-2-ethyl-6-methyl aniline, and a cysteine metabolite of Metolachlor were all found in water along with three other unidentified degradation products.

Barrows (1974) reported on a bluegill sunfish flow-through study at $^{14}C$ Metolachlor exposure levels of 10 and 1000 ug/liter. Bioaccumulation levels at the 1000 ug/liter exposure level reached 28 ppm in edible tissues and 702 ppm in the nonedible tissues. Existence of a plateau could not be established. After 28 days depuration, residues in edible portions of fish decreased to 0.08 ppm for the 10 ug/liter $^{14}C$ Metolachlor exposure and to 11.7 ppm for the 1000 ug/liter exposure. The chemical nature of the fish residues was not defined. When the above studies are considered as a composite, they are sufficient to adequately characterize the fish accumulation characteristics of Metolachlor.

## Contamination and Control

*The prevailing fate of a pesticide chemical, and any resulting exposure to non-target populations, can be significantly affected by certain safety-related practices. First, pesticide chemicals may be unintentionally released into the environment by means other than intended applications, such as improper disposal or storage, accidental spillage, container leakage, fire, explosion, factory mishap, leaching from landfill sites, or misuse. Second, the fate of pesticide chemicals having already entered the environment can be significantly controlled by various intentional practices and precautions, such as by land management techniques to reduce runoff, environmental decontamination techniques, and various monitoring systems. Third, particular ecological habitats and populations can be protected from exposure to stray pesticide chemicals by certain equipment and techniques for applicators, re-entry intervals, water quality standards, and various forms of safety packaging.*

*Information about the prevalence, effects, or importance of any such practices which either precipitate or mitigate pesticide chemical displacement, would naturally be of direct importance in an assessment of the overall fate of pesticide chemicals.*

Because such information is not yet available for Metolachlor, the Agency can only offer some common precautions with regard to the prevention and mitigation of unintentional environmental contamination: For disposal purposes, open dumping should be prohibited, and pesticide, spray mixture, or rinsate that cannot be used or chemically reprocessed should be disposed of in a landfill approved for pesticides or buried in a safe place away from water supplies.

## Alternative Pest Management Practices

*Studies which examine the use of a pesticide in integrated pest management schemes may suggest ways of reducing exposure to toxic chemicals, without reducing the degree of pest control achieved. IPM schemes may rely on the use of a chemical in conjunction with some of the following biological and cultural methods of control: the development of resistant varieties of host plants and animals, the introduction of natural enemies, adjustments in crop rotations, cropping systems and planting time, water management and tillage practices and the identification of pest population levels at which chemical control is called for.*

Information about the use of Metolachlor in IPM or diagnostic weed control programs is not presently available, though information is expected to become available as more IPM schemes are developed that require the use of herbicides in combination with alternative weed control methods.

DISCIPLINARY REVIEW

Environmental Fate Profile
Exposure Profile
Generic Data Gaps
Suggested Labeling

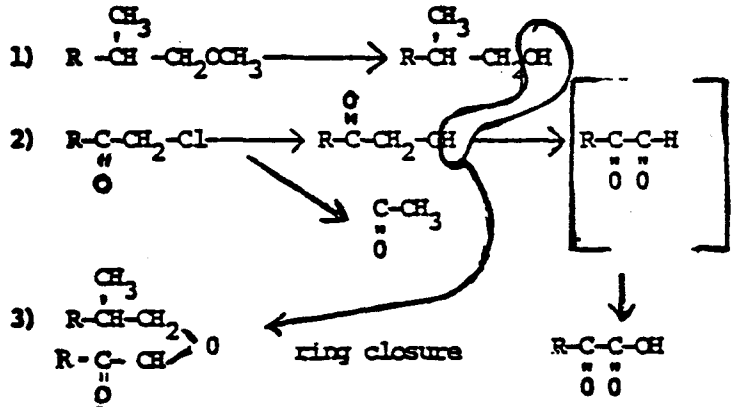
## Environmental Fate Profile

Metolachlor is applied at a rate of 1.5 to 3.0 pounds active ingredient per acre to soil where corn and soybeans are to be grown. Normally, the chemical is sprayed on the soil during or soon after planting, before sprouts emerge. However, when dry weather is expected, or if furrow irrigation is being used, the chemical is sprayed on the soil before planting, and incorporated into the top 2 inches of soil.

Metolachlor is quite stable to hydrolysis over the environmental pH range of 5 to 9 (the half-life is 200 days over this entire pH range). Photolysis appears to be a more significant degradation pathway, as approximately 50% was found to have degraded in sunlit soil over a period of eight days. Soil metabolism, by both aerobic and anaerobic microorganisms, would also play an important role in the degradation of Metolachlor in the soil (McGahen and Tiedge, 1978).

About 30% of the photoproducts were represented by MET-009 and MET-001. (See the Chemical Fact Sheets in the Appendix for characterizations of these and other metabolites.) Another 30% was represented by $CHCl_3$ and water-soluble polar metabolites. Indirect evidence obtained from analysis of aqueous photoproducts produced by artificial light of <280 mm suggests that the polar products, both aqueous soluble and $CHCl_3$ soluble, are not aldehydes or phenolic in nature (Aziz and Kahrs, 1975). Exposure of $^{14}C$ Metolachlor treated soil thin layers to natural sunlight (Aziz, 1974) resulted in gradual photolysis to MET-003 and three unidentified products. Two unidentified products have moderate polarity and one was relatively high in polarity. After 8 days exposure about 1/2 of the initially applied dose had decomposed.

Soil metabolism of Metolachlor appears to proceed initially by hydrolytic cleavage of the N-alkyl terminal constituents followed by oxidation and/or ring closure. The following reactions were found to occur on the N-alky groups:




(Elleghausen 1976a and 1976b; Sumner, Szolics, and Cassidy 1976; Sumner and Cassidy 1974 and 1975)

Attack of the benzenoid portion of the molecule to form phenolic metabolites was speculated but not proven (Elleghausen 1976b). The likelihood of such ring attack is contraindicated by the following observations: (1) Evidence is

provided by Sumner and Cassidy (1974) that non-extractable bound residue: Metolachlor are in dynamic equilibrium with soluble forms, (2) unextractable residues represented by fulvic and humic acid fractions decrease with increased aging. Incorporation of polyphenolic metabolites into the soil organic matrix would mitigate against both of the above findings.

Studies were also available on Metolachlor's environmental mobility. Houseworth (1973b), in a laboratory column leaching study, using a wide range of soil types, showed that Metolachlor per se is subject to extensive leaching when applied to soils having low organic content. Extensive leaching can thus be expected in soils such as agricultural sands and sandy loams having organic contents of 2% or less. Residues of aged $^{14}C$-Metolachlor were also found to leach extensively in sandy loam soil (Dupre 1974). Based on incremental $^{14}C$ activity at different soil depths, several discrete chemicals of different mobilities were probably involved. A runoff study by Dupre (1974c) showed that Metolachlor can be expected to move from agricultural sites of application both by sheet erosion and leaching.

With the stability to hydrolysis and the likelihood of leaching, we should consider in more detail the potential for Metolachlor residues in the aquatic environment. Metolachlor residues will be contained in runoff (soil and water) from adjacent corn fields. During the midspring and early summer months when corn fields contain little or no vegetation to reduce runoff, more than 30% of the erosive rainfall occurs. The average monthly rainfall during April, May and June is approximately 3 inches (USDA YearBook, 1941). This results in greater than 40% of the annual runoff and causes a range from 1 inch to 3 inches of water in most of the cornbelt; parts of Southern Illinois, however, lose up to 7 inches of runoff water (EPA-600/2-75-026 a, 1975). A runoff study by Dupre (1974) demonstrated that three simulated rainfalls (totaling 1.5 inches) removed 3.2% of the applied Metolachlor in runoff water and 1.4% in soil, from an experimental plot with an $8^{o}$ slope. This study suggests that individual rainfall events of 0.5-3.0 inches may move 1.5% to 2.5% of soil-incorporated Metolachlor from a treated field (Personal communication with Environmental Fate Branch, 1978). If Metolachlor is sprayed on the soil surface and not incorporated, the percentage of residues in runoff is expected to be greater than 2.5% for 2.5-3.0 inches of rain. This range of values appears to be reasonable in light of levels observed in field studies for various pesticides (Bailey, Leonard, and Swank, 1976). Both the 6E and 8E formulations of Metolachlor are registered for ground application at a maximum rate of 3 lb. ai./acre. Assuming field application and climatic conditions result in a loss of 2.5% of the applied Metolachlor, then each acre of treated field would contribute 0.075 lbs. to an adjacent aquatic site. This amount of active ingredient in an acre foot of water would yield Metalochlor residues of .055 ppm in 6 inches of water and .0176 ppm in 12 inches of water.

Field dissipations studies confirmed Metolachlor's potential for significant movement in the soil, but left open the question of whether Metolachlor may sometimes persist undegraded. Skipper, Gossett, and Smith (1976), in field dissipation tests, concluded that extensive leaching was the major cause of dissipation from the upper 3-inch soil horizon in two different plots containing sandy loam soils. Field dissipation studies of Metolachlor applied at up to 4 lbs. ai/acre (pre-emergent) showed residues generally less than 10% of the amount originally applied over time spans ranging between 107 and 162 days. A total of 5 states representing continental USA climate extremes were involved. But absolute losses of Metolachlor between the day of application and final sampling were not always so great. For example, in a Nebraska study, residues declined only 44% over a 107-day time span. In some cases, substantial residues were found in the 6" to 12" soil horizon suggesting

extensive leaching. This high soil mobility, in combination with a potential for long-term environmental stability, may prove to be of significant concern in projecting potential exposures to Metolachlor residues.

Additional studies were performed to estimate the possibility of Metolachlor bioaccumulation. Bluegill sunfish exposed for 70 days to a mean level of 1.2 ppm $^{14}C$ Metolachlor accumulated 18 ppm of $^{14}C$ activity (expressed as Metolachlor) in their edible tissues and 486 in non-edible tissues. After a 28-day depuration, the respective residue levels decreased to 12 and 13 ppm respectively. The chemical nature of the residues was not investigated (Barrows, 1974). A catfish study (Smith, 1977) involving aged Metolachlor on sandy loam soil sediments resulted in an accumulation of 0.53 ppm in edible catfish tissue at the end of 30-day exposure. After 14 days of depuration, the level decreased to 0.03 ppm. Respective values for viscera at the end of the 30 day exposure and after 14 days depuration were 4.4 and .18 ppm, respectively. The major identified metabolite found in the edible tissues was CGA-46576.

Though the available data do not indicate significant long-term accumulation in fish, there is a possibility that residues may result in rotated crops grown on Metolachlor-treated soil. Roots of root crops, grain of small grains, and oil from oil seed crops, grown as rotational crops to corn in a Metolachlor-treated field, were shown to have little, if any, residues of metabolites, as analyzed by the officially accepted regulatory method for corn grain, forage, and fodder (Balasubramanian, Aziz, and Ross 1975; Ballantine 1975. This method will detect Metolachlor per se and a series of sugar and glutathione conjugates which can form after hydrolysis of the N-alkyl groups of Metolachlor to terminal OH groups.) $^{14}C$ studies on rotational crops to corn, however, gave evidence of other possible metabolites which, if present in a rotational crop, would not be detected by the official regulatory method for corn products. Also, the following types of rotational crop products were found to contain finite residues in one or more samples collected for analysis by the method of Balasubramanian, Aziz, and Ross (1975): carrot tops, soybean stalks, sugar beet tops, and wheat straw.

## Exposure Profile

Technical Metolachlor: For persons involved in the manufacture, handling, storage, or shipment of Technical Metolachlor, there is little likelihood of oral exposure, and because of the low vapor pressure of the viscous liquid, there is also little chance of inhalation exposure. The most likely human exposure is a repeated dermal exposure, and occasionally, by accident, an occular exposure.

For wildlife in the proximity of Technical Metolachlor manufacture, storage, shipping, or disposal, because of the relative stability of Metolachlor to hydrolysis, its high mobility in the terrestrial environment, and its potential resistance to metabolic degradation, there is a significant potential for exposure to occur to various species, but particularly aquatic species. Should significant amounts of the chemical be spilled, drained, discharged, or disposed of in the natural environment, aquatic life in drainage waters, or in bodies of water adjacent to contaminated soil, would be likely to receive a long-term exposure, though the chemical would not be expected to bioaccumulate in aquatic or terrestrial food chains. Considering Metolachlor's potential for rotational uptake, however, plants growing on contaminated soil could well pass on residues to herbivores in that habitat.

Emulsifiable Concentrate Metolachlor: Though all chemical products present some possibility of accidental ingestion, for persons involved in the dilution, mixing, and application of Metolachlor formulations, there is little chance of oral exposure. But there is a significant possibility of dermal and eye exposure from the splashing that may occur in diluting and tank mixing, and in the loading of spray equipment. While the vapors from the Emulsifiable Concentrates are limited by the vapor pressure and the viscosity of the solutions, the spray droplets generated by the application of end-use Metolachlor may result in an inhalation exposure for applicators, and for agricultural workers or livestock who may be in the proximity of the spraying.

Though 'spray drift' has not been studied for Metolachlor, we should assume that terrestrial non-target plants and animals may occasionally be subjected to a single direct exposure from a nearby spraying. But more importantly, the relative stability of Metolachlor to hydrolysis, its high mobility in the terrestrial environment, and its potential resistance to metabolic degradation, together suggests that more significant, and longer-term exposures may be expected for fresh-water aquatic plants and animals in low-lying streams or ponds near the fields where Metolachlor is applied. The Environmental Fate Profile estimates this potential aquatic exposure to be near .055 ppm in 6 inches of water or .0176 ppm in 12 inches of water. As with the Technical, Metolachlor's potential for rotational uptake suggests that plants growing on contaminated soil could pass on residues to herbivores in that habitat.

Because Metolachlor is applied primarily in seven midwestern states, once annually, usually between the dates of April 20 and May 9, nontarget terrestrial and aquatic organisms in those regions that may encounter residues from a pre-planting or a pre-emergent application of Metolachlor will suffer the highest exposure between April and June (USDA #283, 1972).

The possibility for Metolachlor residues to occur in food or feed, which may result in dietary exposures to the general public, is discussed in the 'Residue Chemistry' chapter.

## Generic Data Gaps

The following is a gap in the Environmental Fate data base needed to adequately support a Registration Standard for Metolachlor. Opposite the gap is given the section in the Proposed Guidelines of July 10, 1978 (40 CFR Part 163) which describes that type of data and when it is required.

For Technical Metolachlor:

| | |
|---|---|
| 1) Adsorption/desorption studies | 163.62-9 |

For Emulsifiable Concentrate Metolachlor: none

## Suggested Labeling

There are no environmental fate labeling requirements for manufacturing-use Metolachlor labels.

Emulsifiable Concentrate Metolachlor should carry the following statements on its label: the requirement of an 18-month interval before planting rotational crops, and a warning against the using of corn forage or fodder for silage or to graze or feed livestock.

## BIBLIOGRAPHY
(Reserved)

*In order for the provisions of FIFRA concerning data compensation (Section 3(c)(1)(d)) to be effective under Registration Standards, data used in direct support of the Standard for each type of product must be accurately listed, enabling applicants and their arbitrators to determine what data do and do not support the registrations of individual pesticide products. Thus, for each disciplinary chapter, studies used to evaluate hazard and establish Standards for the manufacturing-use chemical and for each type of end-use formulation will be listed separately.*

To protect present and potential applicants for the registration or re-registration of products containing Metolachlor, the citations appropriate to each disciplinary chapter will not be published in this Sample Standard, though a complete Bibliography is provided at the end of the document.

# TOXICOLOGY

*INTRODUCTION*

*The chapter on Environmental Fate has explored the routes and mechanisms by which Metolachlor may be transformed and displaced from the point of its release into the environment, and the possibility of exposure for organisms other than the target pests.*

*Because man applies pesticides where he lives and works, and to the crops and livestock that he uses for food, he and his domesticated animals are particularly susceptible to unintentional exposure. This exposure may come as food, feed, or water residues, surface or airborne traces, poisonings or misapplications, or occupational exposures for pesticide applicators and agricultural workers.*

*Studies of the toxic effects that may result from such exposures usually fall into five categories: metabolism and pharmacodynamics studies, which detail the fate of a pesticide within a mammalian body; dose-response studies, which disclose the observable effects that can be tied to particular ranges and conditions of exposure; studies that investigate the biological variables influencing specific toxicological effects; reproduction studies, which examine effects upon multi-generation reproductive viability for both cells and organisms; and clinical reports, which discuss experiences with actual human or domestic animal exposures.*

TOPICAL DISCUSSIONS

Corresponding to each of the Topical Discussions listed below is the number of the section(s) in the 'Proposed Guidelines' of August 22, 1978 (40 CFR Part 163) which explain(s) the minimum data that the Agency usually requires in order to adequately assess a pesticide's Toxicology. Where no section number is listed, a minimum requirement has not been set for such information.

| | Guidelines Section(s) |
|---|---|
| Metabolism and Pharmacodynamics | 163.85-1 |
| Acute Effects and Neurotoxicity | 163.81-1, -2, -3, and -7 |
| Local Irritation | 163.81-4 and 163.81-5 |
| Subchronic Effects and Neurotoxicity | 163.82-1, -2, -4, -5, and -6 |
| Sensitization | 163.81-6 |
| Chronic Effects | 163.83-1 |
| Biological Parameters of Specific Effects | |
| Oncogenicity | 163.83-2 |
| Genetic Effects | 163.84-2, -3, and -4 |
| Teratology | 163.83-3 |
| Reproductive Effects | 163.83-4 |
| Clinical Experience | |
| Prevention and Treatment of Intoxication | |

## Metabolism and Pharmacodynamics

*Just as environmental chemists investigate the fate of a pesticide chemical in the environment to estimate the potential for non-target exposures, so may toxicologists investigate the fate of the chemical in the body, to see what form it may take, how long it may stay, and what organs, tissues, or functions may be affected by it. The term 'metabolism' refers to the effect of an organism on the chemical structure of a foreign compound; 'pharmacodynamics' is here used to encompass the other aspects of a chemical's fate in the body - its adsorption, distribution, storage, and excretion. The degree to which a pesticide chemical can penetrate the body by gastrointestinal, respiratory, or dermal absorption can be measured by comparisons with intravenous injection, by remainder analysis, or by direct detection in blood, lymph, tissue, or waste. Once a compound is absorbed, biochemical mechanisms of transport in the blood, such as binding to plasma proteins, will enable its distribution to other tissues. Initial distribution is directed mainly by the rate of blood flow to a particular tissue; final distribution is dependent upon the inherent affinity of various tissues for the compound.*

*As a chemical is distributed, it can also undergo metabolic transformation, which generally occurs in at least one of three phases: the first involves oxidations, reductions, and hydrolyses; the second involves synthesis or conjugation of the foreign compound with a normal metabolite of the body to form a more water-soluble, and therefore more readily excreted, product; further chemical changes have been traced to microsomal enzymes, especially in the liver. Though metabolic transformation often results in an expedited excretion, at least some storage of the chemical is likely to occur. The storage of pesticides or their metabolites is effectively just that portion of the dosage which has not been eliminated, and so it can be measured and simply expressed as a concentration in particular tissues. But the dynamics of storage can constitute a complex mathematical study, involving time, steady states, and half-lives, as determined by the biology of tissue binding, detoxification, and excretion. In any chronic exposure, if the rate of administration exceeds the rate of elimination from the body, the toxic substance will accumulate in the body until a steady state is reached, at which point the rate of elimination will become equal to the rate of administration. The elimination of absorbed compounds may occur by way of expired air, urine, feces, milk, and dermal secretions, and can often be impeded by toxicological damage to the excretory organs themselves.*

*The sum of all these functions should account for all the chemical absorbed. A 'balance study' is sometimes attempted to describe the long-term equilibrium of a pesticide's metabolic fate.*

Metabolism studies on Metolachlor (Hambock 1974 a,b) demonstrated that:

(a) Most orally administered Metolachlor is rapidly absorbed, metabolized, and excreted.

(b) The urine and feces of treated animals contained a complex pattern of metabolites; each metabolite accounted for less than 5% of the administered dose. No unchanged chemical was detected in urine or feces samples.

(c) Approximately half the urinary and fecal radioactivity was extractable with organic solvents.

(d) No glucuronide or sulfate conjugates were found in the excreta.

(e) Several excreted metabolites were tentatively identified and appear to result from dechlorination, O-methylation, N-dealkylation, and side chain oxidation in the rat.

In additional studies (Hambock, 1974c), male rats were treated with $^{14}C$ Metolachlor (approximately 31 mg/kg, p.o.), and urine and feces were collected for 48 hours. The urine and feces contained 21.5% and 51.4% of the administered dose, respectively, and the halflife was determined to be approximately 28 hours. TLC, GLC, HVE (high voltage electrophoresis), column chromatography, gel permeation chromatography, and enzymatic hydrolysis were adequately utilized to identify radioactive metabolites, which were identified as 2-ethyl-6-methylhydroxyacetanilide (MET-002) and N-(2-ethyl-6-methylphenyl)-N-(hydroxyacetyl)-DL-alanine (MET-004) in the urine and 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)acetamide (MET-003) and MET-004 in the feces. The 48 hour excreta contained 1, 15, and 22% of the administered dose as MET-002, MET-004, and MET-003 respectively. (See Appendix A for Chemical Data Sheets on MET-002, MET-003, and MET-004.)

These studies demonstrate the relatively rapid metabolism and excretion of Metolachlor, and are sufficient to fulfill the requirement for this type of information.

## Acute Effects and Neurotoxicity

*The acuteness or chronicity of a toxicological effect is indicated by the degree of its reversibility, and the occurrence of certain damages, especially scarring and atrophy. By 'acute' effects we will here mean not only those which are reversible, but also those effects, including death, which can occur by means of a single exposure.*

*The 'single-dose ED-50', the dosage (milligram toxin per kilogram animal) at which fifty percent of the subjects experience a toxic effect, is the primary way of expressing the acute effects of one-exposure contaminations. An LD-50 is a special case of the ED-50, in which the effect measured is death. The ED-50 or LD-50 values permit useful comparisons between the acute effects of different compounds or of the same compound by different routes.*

*The dosage-response relationship is the most fundamental principle in toxicology. It can extend to all kinds of injurious effects, but in the case of this topic, applies to acute systemic or whole-body effects such as changes in behavior, histopathology, immunology, body weight, and mortality, as well as delayed systemic effects resulting from a single exposure, such as acute delayed neurotoxicity. It can also extend to all routes of exposure, but for pesticides we emphasize the oral, dermal, and inhalation routes.*

*The hazard evaluation of pesticides has three direct uses for acute toxicity data. First, the dosage-response relationship implies the existence of a threshold dosage for each compound, below which, under defined conditions, no harmful effect is observed. Such a 'no observable effect' level is often used as a basis for estimating a value considered safe under more varied conditions, including exposure of another species, especially man. Second, acute effects levels can be used as an indication of suitable dosages for long-term or chronic studies. Third, acute oral, dermal, and inhalation toxicity data are used directly for a number of regulatory purposes, including pesticide classification, labeling, and packaging specifications.*

Acute Oral Toxicity

The minimum testing needed on acute oral toxicity is one test on the laboratory rat for each registered product.

For Technical Metolachlor, the acute oral LD-50 in the laboratory rat is 2,780 mg/kg with 95% confidence limits of 2,180-3,545 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, Incorporated, 1974e). The study did, however, establish the 'emetic dose 50' to be 19.0 (+/- 9.7) mg/kg. The Technical therefore falls into Category III with regard to acute oral toxicity.

Tests were also done on the two Emulsifiable Concentrate formulations. In a test involving a 6-pound per gallon E.C. formulation, the acute oral LD-50 was found to be more than 2,000 mg/kg but less than 5,000 mg/kg in the rat (Affiliated Medical Research, Incorporated, 1974d). In a test involving an 8-pound per gallon EC formulation, the acute oral LD-50 in the laboratory rat was 2,530 mg/kg with 95% confidence limits of 1,890-3,400 mg/kg (Nham and Harrison, 1977a). A related study (Affiliated Medical Research, Incorporated, 1974f) established that the 'emetic dose 50' in dogs to a 6-pound per gallon E.C. was 24.5 (+/- 9.2) mg/kg. Based on the above data, it is anticipated that E.C. formulations of Metolachlor as high as 8-pounds per gallon can be expected to produce an oral LD-50 of not less than approximately 1,890 mg/kg in the rat. The available data, then, place existing E.C. formulations of 8 lbs. per gallon or less in Category III with regard to acute oral toxicity.

Acute Dermal Toxicity

The minimum testing needed on acute dermal toxicity is one test, preferably on the albino rabbit, for each registered product. This test should be conducted on both intact and abraded skin.

Affiliated Medical Research, Incorporated (1974a) established that the LD-50 of the Technical to the New Zealand rabbit is greater than 10,000 mg/kg when tested by the unabraded dermal route. Though the above information is sufficient to meet the requirement for acute dermal toxicity data on intact skin, data are not available on the acute dermal toxicity to abraded rabbit skin. The unabraded dermal test results place the Technical in Category III with respect to acute dermal toxicity.

In a test involving a 6-pound per gallon E.C. formulation, the acute dermal LD-50 to the New Zealand rabbit was found to be greater than 10,000 mg/kg by the intact dermal route (Affiliated Medical Research Incorporated, 1974b). For an 8-pound per gallon E.C. formulation, it was established that the acute dermal LD-50 to the New Zealand rabbit is greater than 3,038 mg/kg via the intact dermal route (Nham and Harrison 1977b). A related study (Tryzna and Paa, 1976) determined that the acute dermal LD-50 of a 1 to 10 dilution of a 6-pound per gallon E.C. formulation was greater than 16,000 mg/kg via the intact dermal route.

Based on the above data, it is anticipated that E.C. formulations of Metolachlor as high as 8-pounds per gallon can be expected to produce an intact dermal LD-50 of not less than 3,038 mg/kg in the New Zealand rabbit. The available data, then, place existing E.C. formulations of 8 lbs. per gallon or less in Category III with respect to acute dermal toxicity.

Acute Inhalation Toxicity

The minimum data needed on acute inhalation toxicity is one inhalation LC-50 test, using one mammalian species, preferably the albino rat.

Acute inhalation toxicity was tested by Sachsse and Ullman (1974a). In that test there were no deaths in albino rats at the maximum achievable level of exposure (1.752 mg/l with four hours of exposure). This study is adequate to establish a Category IV toxicity with regard to inhalation exposure for Technical Metolachlor.

In a test involving a 6 pound per gallon E.C. formulation, the acute inhalation LC-50 was found to be greater than 247 mg/l of air (with four hours of exposure) in the albino rat (Affiliated Medical Research, Incorporated 1974c). The acute inhalation LC-50 for an 8 pound per gallon E.C. formulation was determined to be greater than .94 mg/l of air (with four hours of exposure) in the albino rat (Dreier 1977).

Based on these tests, it is anticipated that EC formulations of Metolachlor as high as 8 pounds per gallon can be expected to produce an inhalation LC-50 of not less than .94 mg/l of air, in the albino rat. The available data, then, place existing E.C. formulations of 8 lbs. per gallon or less in Category II (for 8 lbs.) or Category IV (for 6 lbs.) with regard to acute inhalation toxicity.

Acute Delayed Neurotoxicity

This type of data is needed only if the active ingredient or any of its metabolites, degradation products, or impurities cause esterase depression or are structurally related to a substance that induces the specific neuropathy, delayed neurotoxicity. Metolachlor is a chloroacetanilide herbicide and is not expected to cause esterase depression or delayed neurotoxicity. Therefore, this type of data is not required for Metolachlor.

Local Irritation

*Systemic effects like those observed in tests of acute toxicity can only occur where there has been a significant absorption of the pesticide chemical into the body. But whether an exposure is absorbed or not, harm may be done to that part of the body which suffered the initial contact, resulting in a localized, though sometimes debilitating irritation. The eyes, skin, and lungs are particularly susceptible to damage on contact with many compounds and their solvents.*

*Frequently, toxicity manifested at the site of exposure is the result of the caustic or corrosive nature of the chemical or its solvents. Such agents are commonly referred to as 'primary irritants' because their action is non-specific and can occur on all cells regardless of type. Damage done by these compounds is usually directly related to the exposure concentration. Some other agents, such as gases which are converted to acids on contact with water, may have a more specific action on certain tissues, and may be especially harmful to mucous membranes.*

*The dosage-response relationship that governs localized irritation can be quantified through the use of irritation scores, and qualified by observations of the reversibility of the effects.*

Primary Eye Irritation

The minimum testing needed to evaluate eye irritation potential is one test for each pesticide product, conducted on the albino rabbit.

A study of eye irritation for the Technical was conducted by Sachsse (1973a) on the New Zealand rabbit. In that study 0.1 ml of Technical Metolachlor was used. The test was evaluated using the system of Draize (1959) and produced the following eye irritation and indices at 24 hours and 7 days:

| | |
|---|---|
| Cornea: | 0 |
| Iris: | 0 |
| Conjunctivae: | 0 |

This study establishes that Technical Metolachlor is non-irritating to the rabbit eye.

In a test involving a 6-pound per gallon E.C. formulation, the data indicates that this formulation is a severe irritant which can cause irreversible corneal opacity in the unrinsed albino rabbit eye (Affiliated Medical Research, Incorporated, 1974i). In a study involving an 8-pound per gallon E.C. formulation (Scribor and Mastri, 1977a): the results from tests conducted with unrinsed eyes showed moderate corneal opacity (reversed in 7 days) and conjunctival effects (partially reversed in 7 days); the results from tests on rinsed eyes showed slight iris and moderate conjunctival effects (reversed in 3 days).

Based on the above data, it is anticipated that E.C. formulations of Metolachlor as high as 8-pounds per gallon can be expected to produce a reversible primary eye irritation, no more than a moderate corneal opacity, and at least partially reversible conjunctival effects in unrinsed eyes. Primary eye irritation, involving slight iris and moderate conjunctival effects (reversed in 3 days) in rinsed eyes can be expected to occur from E.C. formulations of 8 pounds per gallon. The available data, then, place existing E.C. formulations of 8 lbs. per gallon or less in Category I (for 6 lbs.) or Category II (for 8 lbs.) with regard to primary eye irritation. Considering the lack of irritation effects due to the active ingredient alone (in the Technical), and the difference in eye irritation effects between the two formulations, the degree of eye irritation produced by Metolachlor formulations appears to be directly dependent upon the type and amount of inert formulants used.

Primary Dermal Irritation

The minimum testing needed to determine a pesticide's potential for primary dermal irritation is one test conducted on a mammal, preferably the albino rabbit. Sachsse (1973b) evaluated the dermal irritation of Technical Metolachlor on the New Zealand rabbit. The test was evaluated using the system of Draize (1959) and resulted in a primary irritation index of 0.1. This information is sufficient, and it establishes that Technical Metolachlor is non-irritating to rabbit skin.

In a test involving a 6-pound per gallon E.C. formulation, the primary irritation index was determined to be 1.62 (Affiliated Medical Research Incorporated, 1974h). In a test involving an 8-pound per gallon E.C. formulation, the dermal irritation was described as: moderate erythma, edema, and second degree burns at 72 hours (Scribor, 1971). Based on the above data, it is anticipated that E.C. formulations of Metolachlor as high as 8 pounds per gallon can be expected to produce not less than a primary irritation index value of 1.62 (mild irritation) in the albino rabbit. The available data, then, place existing E.C. formulations of 8 lbs. per gallon or less in Category II (for 8 lbs.) or Category IV (for 6 lbs.)

with regard to primary dermal irritation. As with eye irritation, the degree of dermal irritation appears to be dependent upon the type of inert components used in the formulations rather than on the concentration of the active ingredient, Metolachlor.

## Subchronic Effects and Neurotoxicity

*Single-dose toxicity studies are sometimes only fact-finding experiments whereby an evaluation of biological effect is made that can be applied to more prolonged repeated-dose studies on the compound. A study of subchronic effects is a multiple-dose schedule carried out for a period equivalent to about ten percent of the life-span of the animal. Because of the duration of the exposures, dosages to be used are more critical, and can be based upon what has been learned from the single-dose studies. In prolonged toxicology tests, experimenters usually use the route of administration (oral, dermal, or inhalation) corresponding to the route of exposure that is most likely to result from the actual use of the pesticide.*

*An evaluation of subchronic toxicity in turn helps to set the dosage levels and suggests target organs of interest for long-term, chronic studies yet to be done. Or it can serve as the definitive test for agents that are not to be subjected to chronic tests because their pattern of use is such as to preclude the possibility of life-span exposures. The shorter-term subchronic studies have a number of advantages over the longer-term chronic studies, apart from decreased time and expense. Often, the pathological damages due to subchronic exposure are more clear-cut because they are occurring more quickly with larger doses, because they are not obscured by natural chronic changes such as aging, and because some toxic effects are overcome by long-term physiological adaptations.*

### Subchronic Oral Dosing

Testing should be performed in at least 2 mammalian species. One species should be a generally recognized strain of laboratory rat while the second species should be a non-rodent.

Three-month feeding studies were performed with Sprague-Dawley rats (Coquet, Galland, Guyot, Fouillet, and Rouaud 1974d) and with beagle dogs (Coquet, Galland, Guyot, Fouillet, and Rouaud 1974c). It has been determined that the histopathology evaluations for both the rat and the dog study were not performed by a pathologist. These studies cannot serve in support of this Standard, until the histopathology evaluations are properly made and submitted. Therefore, data on subchronic oral dosing in two mammalian species is currently a data gap.

### Subchronic 21-Day Dermal

The minimum testing needed is one study in one mammalian species. Although no data is presently available on Technical Metolachlor, a 21-day dermal study was performed using Metolachlor 6E (68.5% active ingredient) and is considered to provide sufficient information (Affiliated Medical Research Inc., 1974f). The study reported no significant evidence of systemic effects at a dose level of 540 mg Metolachlor per kilogram, per day. At 1080 mg Metolachlor per kilogram, per day, the only indication of systemic effects was decreased body weight gain.

Subchronic 90-Day Dermal

This study is not needed because the existing acceptable end-uses should not result in repeated human skin contact for this long a period.

Subchronic Inhalation

The existing acceptable end uses should also not result in repeated inhalation exposure at a concentration which is likely to be toxic as determined by an acute inhalation test. Therefore, this study is not needed.

Subchronic Neurotoxicity

Metolachlor is a chloroacetanilide and is related in structure to registered chemicals that have not induced neuropathy nor delayed neurotoxicity, as evidenced by the results of an acute test. This type of data is therefore not needed.

## Sensitization

*In addition to subchronic effects on histology, blood chemistry, neurological functions (such as cholinesterase inhibition), excretion functions, normal tissue growth, body weight, and enzyme functions, short-term multiple-dose exposure can lead to sensitization of the immune system. The sensitization response is a multiple-dose reaction because it is caused by the gradual incitement of the body to produce antibodies specific to the compound tested. It can be observed as a dermal irritation resulting from repeated local exposure.*

The minimum data needed to assess dermal sensitization can be provided by 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 (1974g). Inappropriate methodology (the 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, 1977) used the intradermal injection method: Technical Metolachlor dissolved in the vehicle (propylene glycol) and 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; there was no reaction in animals injected with the vehicle alone. Based on this second study, which is sufficient, it is established that Technical Metolachlor is a skin sensitizer in guinea pigs. Though there are no studies available in which the E.C. formulations were directly tested, it is anticipated that E.C. formulations of 8 lbs. per gallon or less will also cause skin sensitization in guinea pigs.

## Chronic Effects

*The basis for the chronic study is the contention that nothing less than a life-span observation is adequate to assess the hazard of potentially life-long exposures to a toxic agent. With pesticides, only those chemicals which may be expected to leave residues in food, feed, or potable water, or those which may result in occupational exposure, will be likely to present the possibility of lifetime exposure for man or domestic mammals. This is why the chronic study is usually performed as a chronic 'feeding' study.*

*On the basis of acute effects and subchronic studies, dosage levels are commonly selected to include a 'no observable effect' level, another that is clearly toxic, and at least one dosage that falls between these two reference points. Mortality, life-span, growth rate, food consumption, and the gross appearance and behavior of the animal are routine observations in chronic studies. Other measures of toxicity, such as pharmacology, histopathology, hematology, blood chemistry, neurotoxicology, residue analysis, body-weight changes, neoplasm and lesion counts, are also commonly recorded. It is frequently useful to obtain evidence regarding the reversible nature of chronically induced toxicities by discontinuing administration for select dosage groups, and observing final differences. All animals in chronic toxicity studies are eventually subjected to complete pathological evaluation.*

Chronic testing should be available on at least one mammalian species. The species should normally be a generally recognized strain of the laboratory rat. No chronic study is currently available for Metolachlor, and this constitutes a data gap.

## Biological Parameters of Specific Effects

*The tests on dose-response relationships may reveal the need for further studies to investigate specific effects of particular concern. These studies may be suggested by the analyses of histopathology, hematology, body weight changes, and lesions, routinely conducted in the investigations of dose-response relationships. Studies on specific effects either investigate the chemical or biological conditions that influence the effect, or else attempt to isolate and characterize the effect by experimental modeling.*

*There are a wide range of potential effects which may be investigated in this manner, and different types of effects will be subjected to different sorts of investigations.*

*Some toxicological injuries affect all cells equally, but are highly specific in their mode of action. An example of this is the universal inhibition of mitochondrial respiration by the cyanide ion. In vitro studies of such universal cellular effects are often useful indicators of in vivo toxicity. With universal cellular effects, isolated cells and intact organisms will be affected in a parallel way.*

*Other effects on cells may be more specific to a particular type of cell, (i.e. a tissue), or may involve interference with the biochemical interactions between types of cells, as with the inhibition of acetylcholinesterase. Toxic compounds that significantly interfere with the 'integration' of cellular activity into essential bodily functions are said to be toxic at the 'systemic' level.*

*Systemic effects may be further divided into 'biochemical' ones and 'physiological' ones. Examples of 'biochemical' lesions include: the inhibition of critical enzymes, such as SH-enzymes, acetylcholinesterase, and cytochrome oxidase; the inactivation of critical transfer molecules, such as hemoglobin; and bindings to membranes which might affect membrane permeabilities, such as the sodium and potassium gates of the nerve axon. Specific 'physiological' effects on tissues and organs might include: alterations in the function of the blood and lymph vessels, including abnormal constriction and sensitivities to temperature; mild lesions in the hypothalamus, such as to cause changes in body weight or appetite; fibrosis of the lungs; maladies of muscles and supportive tissues such as the pericardium; necrosis in the liver and kidney, which because of their importance in*

*biotransformation and excretion often suffer high concentrations of toxins or their metabolities; injuries to the central and peripheral nervous system; inducements of cataracts and retinal damage in the eye; histological alterations in the endocrine glands, such as to cause diabetes by damage to the pancreas; and epithelial injuries, as in the digestive or respiratory tracts.*

*Studies on the chemical and biological pre-conditions and co-conditions that influence the rate, severity, and nature of specific cellular, systemic biochemical, or systemic physiological toxic effects, can be instructive about both the toxicology of the chemical and the facet of human physiology which it alters or impacts.*

The currently available dose-response studies on Metolachlor do not suggest any specific toxicological effects which necessarily require further investigation, nor are any such studies currently available for Metolachlor.

Oncogenicity

*Certain chemical substances appear to have the effect of causing cells to reproduce uncontrollably, which in turn may produce lesions, tumors, or other neoplasms, or physiological chaos in the blood, lymph, or immune systems. The chemical-induced formation of neoplasms - 'oncogenesis', and the continued uncontrolled multiplication of cells - 'carcinogenesis', differ from other toxicological effects in three ways: the action is usually residual and irreversible; single doses that have no detectable effect may nevertheless act in an additive manner to initiate a serious pathology; and synergistic effects with other environmental factors are of vital importance in determining whether an effect occurs at all. The essential relationship between oncogenicity and carcinogenicity is that oncological neoplasms, though they may appear to have limits in growth, have a greater likelihood of becoming cancerous than most naturally occurring tissues.*

*Some carcinogens appear to have their primary effect at the point of application to animals. These 'direct-acting' agents do not commonly require metabolic activation but appear to be subject to detoxification and excretion. Other carcinogens seem to have their primary effect on specific tissues regardless of the route of application. These 'procarcinogens' must undergo some type of metabolic activation, but also may be subject to detoxification. A third type of cancer-causing agent is the 'cocarcinogen', which is not significantly carcinogenic alone, but dramatically potentiates the effect of other carcinogens.*

For the adequate assessment of oncogenicity, studies are needed in two mammalian species: normally, the laboratory rat and the mouse. A mouse study was conducted with Charles River CD-1 albino mice (50 of each sex) at levels of 0, 30, 1,000, and 3,000 ppm fed in the diet. The duration of the study was 18 months for males and 20 months for females. It was conducted by Industrial Bio-Test Laboratories and validated by Ciba-Geigy Corporation (Gesme, Albanese, Marias, and Arceo, 1977). The Agency is currently evaluating the significance of some flaws in the experimental procedures and seeking additional information from Ciba-Geigy Corporation. Although the available data show no oncogenic potential associated with Metolachlor, the use of this

study in the regulatory process depends upon the resolution of the unsettled technical issues. Along with testing on another mammal, preferably the laboratory rat, this present lack of two oncogenicity studies constitutes a data gap.

## Genetic Effects

*In addition to aberrations in the rate of cell reproduction, other cellular reproductive effects, such as spindle poisoning or mutations, may also result from exposure to pesticide chemicals. Mutations are aberrations in the genetic material transmitted from parent cell to offspring, and when the cell is a gamete, from parent animal to offspring.*

*Genetic effects at the cellular level are of interest for two reasons. First, because a cell's genetic material is partially responsible for the control of cell reproduction, mutagenic agents may also have a carcinogenic effect. Second, alterations specifically in the inheritable genetic material of the paternal or maternal gametocyte may result in birth defects. Two major kinds of genetic change in the gametes are recognized: a 'point mutation', which involves a single gene (a change in as many as three DNA base pairs), and which, because it does not interfere otherwise with the integrity of the chromosome of which the gene is a part, may be reversible; and a 'chromosome aberration', which includes chromosome loss or non-separation in cell division, segment changes, inversions, or translocations. It is not clear whether an increased rate in genetic change is caused by direct action on genetic material, or is the indirect effect of injury to normal repair mechanisms.*

*Point mutations, chromosome aberrations, and specific functional effects such as on DNA repair and synthesis, can be tested for separately by a variety of means in various experimental systems.*

The minimum testing needed to assess mutagenicity is testing in two experimental systems. The potential of Metolachlor to cause genetic changes has been tested for in a bacterial system utilizing activation by mammalian microsomes (Arni and Muller, 1976), and in an in vivo system to test the effect on developing sperm in the mouse (Ciba-Geigy Limited, 1976a).

The bacterial (Salmonella) system was tested for base substitutions and point mutations at various ranges (10, 100, 1,000 and 10,000 ug/plate). No increase in background mutation rates was observed. Nor were there any effects noted, in the mouse study, on fertility rates, or on zygote or embryo survivals, after single oral doses of 100 and 300 mg/kg. Also, no malformations of resulting embryos were reported. From these two studies, which are sufficient for mutagenicity testing, no evidence is presented which suggests that Metolachlor has any mutagenic potential.

## Teratology

*While a fetus may be misdirected in its development by chemically induced damages to its genetic foundation, its health, growth, and maturation may also be directly affected by the presence of certain chemicals in the body of its mother.*

*'Fetotoxicity' refers to any detrimental effect upon the health of a fetus. For chemical doses which produce sublethal effects in the pregnant mother, it is often not possible to distinguish between direct effects of the*

*chemical upon the fetus, and effects on the fetus due to the impaired health of the mother. Thus maternal toxicity should always be noted in observations of fetotoxic effects. 'Fetotoxic' effects include degenerative changes in any anatomic, physiologic, or biochemical system that has already been formed, even though the formation may not yet be complete.*

*'Teratogenicity' refers more specifically to aberrations in the growth and development of the fetus. Most teratogenic malformations which begin during early embryonic development are made clearly visible by the subsequent growth of the organ or tissue affected.*

*Though either fetotoxic or teratogenic effects may sometimes be termed 'congenital' because they were discovered at birth, an examination of when certain exposures occurred, and how the observed effects may have developed, can help distinguish genetically determined maladies from those induced during fetal development. Experimental tests for teratogenicity do not usually schedule dosages for the female animal until after confirmed conception.*

*The major factors influencing chemical fetotoxicity and teratogenicity include dosage, genetic background of the mother, genotype of the embryo, and the embryo's stage of development. The effective dosage of teratogens is far less in the first third of gestation because malformations of the early embryo are more pervading and irreparable. The effective dosage for general fetotoxins, notably anticholinesterases, is less during the latter two-thirds of gestation, because the critical injury is not to individual cells or tissues, but to their functional integration. A significant factor for any chemically induced fetal effect is the function of placental metabolism and transfer, which matures with the embryo and fetus.*

The minimum testing needed to evaluate the potential fetotoxic or teratogenic effects of a pesticide are tests 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 6 to 15 days of gestation did not affect the offspring of female Sprague-Dawley rats. No fetotoxic effects of the compound were observed. The only possible effect on the rats 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. This study is sufficient for the assessment of teratology in one species of mammal, and does not show any evidence of a teratogenic hazard for Metolachlor. Data is still needed on a second mammalian species.

## Reproductive Effects

*The health and development of the fetus is just one phase in a complex series of interrelated functions necessary to successful mammalian reproduction. These include the general health of the adults, including the health of the mother during pregnancy, the fertility of the male and female, gametogenesis, implantation, nutritional supplies to the developing fetus, parturition, lactation, and the health, growth, development, and sexual maturation of the young.*

*Of special interest amongst potential multigeneration effects is the degree to which the young have an enhanced susceptibility to pesticide toxicity. Pesticide metabolism, distribution, storage, and excretion may be significantly different in younger bodies, and tissues which are changing and developing may have special sensitivities to the presence of toxic chemicals.*

*Infants and children may be affected in health, growth, and development by exposure to, and early storage of, pesticide residues in mother's milk and commercial foods, on disinfected surfaces, and ingested accidentally.*

The minimum data needed for measuring reproductive effects can be provided by one study with rats lasting two generations. Diets containing up to 1,000 ppm Metolachlor did not affect reproduction during a three-generation, 2 litters per generation, reproductive study in the rat (Smith and Adler 1978). These data are sufficient to satisfy the minimum needed for Metolachlor.

## Clinical Experience

*Of all the factors that quantitatively and qualitatively determine toxic response, 'species tested' is second only to 'dosage' in importance. Thus the best subject for the study of toxic effects to man, is man himself, and for the study of effects to domestic animals, is the species of concern. Information about the effects of a pesticide chemical to man can be obtained in three situations: cases of poisoning; the use of the compound as a drug; and actual-use experience, especially that involving occupational exposure.*

*Cases of poisoning constitute our only source of information on symptomology and the approximate dosages of pesticides required to produce illness in humans. Dosage range is more established in studies of the medical uses of certain pesticide compounds, some of which are applied directly to the body for the control of internal and external parasites, others of which simply have medically useful effects in humans, such as antibiotic or anaesthetic effects. 'Actual-use experience' studies would include any retrospective clinical measures of residues in a particular environment, and the comparison of those findings with symptoms, deaths, or residues in tissues or excreta. Most such information centers around studies with workers and the workplace, because of the greater knowledge the investigator can have about dosage, schedules and length of exposure, residue samples, and the dynamics of the occupational environment.*

Though information from clinical studies may be useful to the assessment of a pesticide's toxicology, the Agency does not routinely require such data. A review of Agency pesticide accident records and a survey of poison control centers failed to turn up any data on accidents involving Metolachlor. Neither have any data from occupational exposures, epidemiological studies, or clinical trials been reported for Metolachlor.

## Prevention and Treatment of Intoxication

*Responsibility for the possible adverse effects of pesticide use must accompany the introduction of these chemicals into the home, factory, hospital, or field. As has been stressed so far in this Standard, measures for preventing and alleviating injury by pesticides must be based on a firm knowledge of their physical, chemical, and biological properties.*

*Should accidental poisoning occur, we must also be prepared to correctly diagnose and treat the victim before the onset of serious effects. Of interest to clinicians in this regard would include: studies about diagnostic techniques, such as epidemiological analyses of cause and effect, patient histories, case studies, laboratory tests for residues or secondary pharmacological effects, and symptomologies; and studies about treatment,*

*including the removal of poison by emesis, gastric aspiration, lavage, and washing, the temporary support of the victim by artificial respiration and the maintenance of the airway, and curative therapy, including oxygen therapy, infusions and transfusions, sedatives, stimulants, antiemetics, steroids, antibiotics, and antidotes.*

Though the Agency does not routinely require studies to be performed on the prevention and treatment of intoxication, it is critical to the registerability of a pesticide that an effective first aid treatment be available for the treatment of accidental exposures [see 40 CFR 162.11 (a)(3)(iii)].

In first aid treatments for accidental ingestion, vomiting should be induced only for chemical preparations which do not contain petroleum distillates, or if they do, also have a very high acute oral toxicity. Technical Metolachlor does not contain petroleum distillates, and so the inducement of vomiting is an appropriate first aid for accidental ingestion of the Technical. The presently registered Emulsifible Concentrates, however, do contain petroleum distillates, but do not have a high enough acute oral toxicity (Category III) to risk the lung damage that may result if some of the chemical is breathed in when vomiting.

The first aid treatment recommended for Technical Metolachlor, or any formulation of Metolachlor which does not contain petroleum distillates, is as follows: 'If inhalation exposure occurs, the victim should be moved into fresh air, and medical attention should be immediately sought. If Metolachlor is swallowed, vomiting should be induced. If contact is made with eyes and/or skin, the exposed area should be flushed with water.'

The first aid treatment for formulations of Metolachlor which do contain petroleum distillates is as follows: 'If inhalation occurs, the victim should be moved into fresh air, and medical attention should be immediately sought. If contact is made with eyes or skin, the exposed area should be flushed with water, and medical attention should be sought. If swallowed, promptly drink egg white or gelatin solutions; or if these are not available, water. Call a physician immediately. [Note to Physician: If swallowed, there is no specific antidote. Do not induce emesis as a chemical pneumonitis may occur if aspirated. Lavage stomach. Deposit 50 grams of activated charcoal in a water slurry in the stomach. Give a saline laxative and supportive therapy as needed.]'

A more complete account of an effective medical treatment for intoxication with pesticide products containing Metolachlor is currently in preparation.

DISCIPLINARY REVIEW

Toxicology Profile
Toxicology Hazard Assessment
Generic Data Gaps
Registration Requirements
Suggested Labeling

## Toxicology Profile

Technical Metolachlor: Sufficient data were available to support an assessment of the Technical's acute toxicity. The relatively high acute oral LD-50 in rats (2780 mg/kg) and the emetic effects in dogs indicate a low acute oral toxicity to humans. Dermally, at least in the rabbit, Metolachlor does not appreciably penetrate intact skin. Doses of up to 10,000 mg/kg caused no signs of toxicity and little irritation. Pending receipt of data on abraded skin, it would appear that Metolachlor would not be readily absorbed through human skin. The lack of toxic signs or irritation from high acute dermal exposure in test animals indicates that manufacturing-use Metolachlor has a low dermal toxicity to humans. Testing of acute inhalation toxicity in rats failed to elicit any deaths at the maximum achievable concentration (1.752 mg/l for 4 hours exposure), and so a very low inhalation toxicity to humans for manufacturing-use Metolachlor may be expected.

Information was also available on the irritation and sensitization potential of Technical Metolachlor. In a primary eye irritation study conducted on albino rabbits, no signs of irritation were observed. Based on the rabbit as an indicator species, Metolachlor is not expected to be irritating to human eyes. A dermal sensitization study in guinea pigs indicated that Metolachlor was a skin sensitizer to that species. Metolachlor should therefore be considered a potential skin sensitizer in humans.

Adequate chronic toxicity data were not available for Metolachlor. No study on chronic feeding has yet been submitted; oncogenicity data are not currently usable. Though data on a second species will be needed, there was one study of teratogenic effects in rats, and it reported no observations of teratogenic or fetotoxic effects due to Metolachlor. The one available test of reproductive effects in the rat showed no effects on reproduction through three generations. Metolachlor has been tested in two systems for mutagenicity: a bacterial system, and an *in vivo* system in the mouse. No evidence is presented in either study to suggest that Metolachlor has any mutagenic potential.

Emulsifiable Concentrate: For E.C. formulations of less than or equal to 8 lbs. per gallon, the reported values of 1,890 mg/kg or higher indicate a relatively high acute oral LD-50 in rats. This relatively high value implies a low acute oral toxicity to humans for E.C. formulations of 8 lbs. per gallon or less. Dermally, at least in the rabbit, existing E.C. formulations of Metolachlor of 8 lbs. per gallon or less do not appreciably penetrate intact skin, and doses of up to 3,038 mg/kg produced no signs of toxicity in the New Zealand rabbit. Pending receipt of data on abraded skin, it would appear that E.C. formulations of 8 lbs. per gallon or less would not be readily absorbed through human skin. From existing data, it can thus be assumed that E.C. formulations

of 8 lbs. per gallon or less present a low overall acute toxicity to humans via the intact dermal route. While the oral and dermal routes presented a relatively low toxicity, the inhalation route resulted in a more significant effect. Testing of acute inhalation toxicity in rats elicited LC-50 values of not less than .94 mg/l of air for existing E.C. formulations of less than or equal to 8 lbs. per gallon. This constitutes a high toxicity from inhalation exposure.

The potential for local irritation and sensitization also appears to be significant. Based on the albino rabbit as an indicator species, existing E.C. formulations of 8 lbs. per gallon or less will produce moderate erythma, edema, and second degree burns (severe irritation). A dermal sensitization study in guinea pigs indicated that E.C. formulations are also potential skin sensitizers in humans. In a primary eye irritation study conducted on the albino rabbit, E.C. formulations of Metolachlor of 8 lbs. per gallon or less were found to cause irreversible corneal opacity and severe irritation in unrinsed eyes. The potential effects on the human eye are expected to be as serious.

## Toxicology Hazard Assessment

Technical Metolachlor: Considering first the potential for human (or domestic animal) exposure to manufacturing-use Metolachlor, it was stated in the Exposure Profile that there is little likelihood of oral exposure, and that because of the low vapor pressure of the viscous liquid, there is also little chance of inhalation exposure. The most likely type of exposure for persons involved in the manufacturing, handling, storage, or shipment of Technical Metolachlor is a repeated dermal exposure, and occasionally, by accident, a single occular exposure.

Because of Technical Metolachlor's low acute oral toxicity, and very low inhalation toxicity, we may dismiss these unlikely exposure routes as significant sources of hazard. The occasional occular exposure is also not of serious concern, as no eye irritation effects would be expected. But with respect to dermal exposures, though it has been shown (pending receipt of data on abraded skin) that Metolachlor is not readily absorbed by the skin, the likelihood of repeated dermal exposures raises two significant concerns: first, Metolachlor has been observed to elicit a dermal sensitization reaction; second, though no evidence of teratogenic, fetotoxic, reproductive, or mutagenic effects have so far been presented, the available information is presently insufficient to be certain of the absence of chronic effects. Thus the risks to humans caused by repeated dermal exposures to a Technical Metolachlor solution cannot be concluded, and the only presently known hazard of manufacturing-use Metolachlor is the potential dermal sensitization problem for factory, transport, or re-formulation workers.

Emulsifiable Concentrate: *The hazards to humans and domestic animals that may arise from the end-use of an agricultural pesticide are of three kinds: those hazards to humans which arise in the tank mixing, dilution, application, storage, or disposal of the end-use chemical; those hazards to humans and domestic animals which arise as a result of ambient residues from pesticide application, storage, or disposal, including residues in air, water, and edible wildlife; and, finally, those hazards to humans or domestic animals which may arise as a result of anticipated*

*residues in harvested food or feed. The first two kinds are considered here in the Toxicology chapter. The last kind will be considered in the 'Tolerance Reassessment' section of the Residue Chemistry chapter.*

As was stated in the Exposure Profile, there is little chance for oral exposure to E.C. Metolachlor, except by accidental ingestion. But there is a significant chance for dermal and eye exposure for chemical applicators who are tank mixing, diluting, or loading. There is also a significant chance of inhalation exposure for applicators, agricultural workers, and livestock in the proximity of the spraying. Though spray drift properties of Metolachlor applications have not been established, ambient air residue exposures may conceivably occur to persons or livestock outside the spray area. Due to leaching and a stability to hydrolysis, residues may also be found in nearby freshwater streams or ponds, thus posing the threat of repeated exposures to livestock drinking the water or grazing on nearby plants, or to persons ingesting contaminated fish.

Accidental oral exposures, because of the E.C.'s relatively low acute toxicity, do not present an unusually serious accidental poisoning hazard. However, the routine use of E.C. Metolachlor directly results in a number of significant hazards. Eye exposures can be seriously damaging, and the applicator whose eyes are unprotected during mixing, loading, or diluting, runs a significant risk of irreversible corneal opacity and severe irritation. Similarly, the applicator with unprotected hands or face runs an acute risk of erythma, edema, and second degree burns, and if the exposures are repeated, a risk of a sensitization reaction. Thirdly, a significant acute toxicity risk is borne by applicators whose respiration is unprotected during spraying. Agricultural workers or domestic animals in the immediate proximity of this spraying are similarly endangered. Finally, though Metolachlor is not readily absorbed through the skin, chronic effects from a repeated dermal exposure or inhalation exposure to E.C. Metolachlor cannot presently be ruled out.

Ambient residues from the application of E.C. Metolachlor will present parallel, though lesser, hazards to persons or livestock outside the spray area. The most significant acute hazard from ambient residues would be an inhalation hazard. Of potential concern are the long-term, repeated exposures for livestock and humans feeding on nearby aquatic and plant life, possibly resulting in undetermined chronic effects.

## Generic Data Gaps

The following are gaps in the Toxicology data base needed to adequately support a Registration Standard for Metolachlor. After each gap is listed the section in the Proposed Guidelines of August 22, 1978 (40 CFR Part 163) which describe that type of test and when it is required.

For Technical Metolachlor:

| | | |
|---|---|---|
| 1) | Subchronic Oral Dosing - Acceptable pathology evaluation is required for both the rat and dog studies. | 163.82-1 |
| 2) | Oncogenicity - Completion of the mouse study and testing on a mammal other than the mouse (the laboratory rat is preferred) is required. | 163.83-2 |

3) Chronic Feeding - A chronic feeding study using the laboratory rat is required. 163.83-1

4) Teratology - A teratology study in a mammalian species other than the rat is required. 163.83-3

For Emulsifiable Concentrate Metolachlor: none

Registration Requirements

In order to ensure that their products fall under the regulatory authority of this Registration Standard, and in order to ensure that the parameters of potential hazard presented in this Standard are not exceeded, certain data submissions pertaining to Toxicology are required of each individual applicant for the registration of the manufacturing and end-use formulations of Metolachlor. General Toxicology requirements for registration are outined and discussed in the Proposed Guidelines for Registration of August 22, 1978 (40 CFR Part 163). Special Toxicology requirements for pesticide products containing Metolachlor are listed below.

For both Technical and Emulsifiable Concentrate Metolachlor:

Dermal Sensitization (Guidelines Section 163.81-6) - Applicants for registration of Technical or Emulsifiable Concentrate Metolachlor will be required to document the lack of dermal exposure in manufacturing facilities or to monitor and submit skin sensitization data from such exposure.

For Emulsifiable Concentrate Metolachlor (8 lbs./gallon or less):

So as to establish the chemical equivalency (the same active and inert constituents in equivalent percentages) of a proposed product to the composition of the pesticide formulations on which this Standard is based, each applicant must submit or cite data that demonstrate that the proposed product is within the established range for each of the following properties. In the event that the result of any of the required tests is outside the established range, the applicant must successfully petition the Agency to amend the Standard to include the wider range prior to seeking registration. (See Section 162.10 of the CFR 40 for an explanation of Toxicity Categories I through IV.)

1. Acute Oral Toxicity
   Any E.C. Metolachlor of 8 pounds per gallon or less which falls into Category III or Category IV will be considered within the scope of this Standard with regard to acute oral toxicity.
2. Acute Dermal Toxicity
   Any E.C. Metolachlor of 8 pounds per gallon or less which falls into Category III or Category IV will be considered within the scope of this Standard with regard to acute dermal toxicity.
3. Acute Inhalation Toxicity
   Any E.C. formulation Metolachlor of 8 pounds per gallon or less which falls into Category II or a numerically higher category will be considered within the scope of this Standard with regard to acute inhalation toxicity.

4. Primary Eye Irritation
   Any E.C. Metolachlor of 8 pounds per gallon or less which falls into Category I or a numerically higher category will be considered within the scope of this Standard with regard to primary eye irritation.
5. Primary Dermal Irritation
   Any E.C. formulation Metolachlor of 8 pounds per gallon or less which falls into Category II or a numerically higher category will be considered within the scope of this Standard with regard to primary dermal irritation.

Suggested Labeling

*See Section 162.10 of the CFR 40 for an explanation of the Agency's established toxicity labeling requirements.*

For Technical Metolachlor:

The required signal word is "CAUTION" followed by "Keep out of reach of children."

To reduce the risk from oral exposure, the Category III statement, "Harmful if swallowed," is required. Technical Metolachlor is in Category IV with regard to inhalation exposure, therefore, no inhalation hazard precautionary labeling is required. Except for the risk of skin sensitization, the Technical is in Category IV with regard to dermal exposure; therefore, no dermal hazard precautionary labeling is required other than the following dermal sensitization warning: "May cause skin sensitization. Wear protective clothing while handling or using this product." Technical Metolachlor is in Category IV with regard to eye irritation, therefore, no eye hazard precautionary labeling is required.

The required first aid statement for manufacturing-use Metolachlor is: "If swallowed, induce vomiting. Flush exposed eyes and skin with water."

For Emulsifiable Concentrate Metolachlor (8 lbs./gallon or less):

The required signal word for E.C. formulations varies as a function of the numerically lowest toxicity category assigned as a result of the five 'Registration Requirements' tests performed on the particular formulation: If the lowest toxicity category assigned is Category I, then the Category I signal word "Danger" followed by "Keep out of reach of children" shall be employed. In addition if the Category I requirements have been satisfied for oral, inhalation, or dermal toxicity, the word "Poison" shall appear in proximity to a skull and cross bones. If the lowest toxicity category assigned is Category II, then the Category II signal word "Warning" followed by "Keep out of reach of children" shall be employed. If the lowest toxicity category assigned is Category III or IV, then the Category III/IV signal word "Caution" followed by "Keep out of reach of children" shall be employed.

Products with a demonstrated oral LD-50 in rats of 500-5,000 mg/kg must bear the Category III labeling precaution "Harmful if swallowed", to reduce the risk of hazard from oral exposure.

Products with a demonstrated oral LD-50 in rats of greater than 5,000 (Category IV) are not required to bear precautionary labeling with regard to oral exposure.

Products with a demonstrated intact dermal LD-50 in New Zealand rabbits of 2,000-20,000 mg/kg must bear the Category III labeling precaution "Avoid contact with skin", to reduce the risk of hazard from dermal exposure. Products with a demonstrated intact dermal LD-50 in New Zealand rabbits of greater than 20,000 mg/kg (Category IV) are not required to bear precautionary labeling with regard to dermal exposure.

Products with a demonstrated inhalation LC-50 in albino rats of .2-2 mg/l of air must bear the Category II labeling precaution "Do not breathe vapors", to reduce the risk of hazard from inhalation exposure. Products with a demonstrated inhalation LC-50 in albino rats of 2-20 mg/l of air (Category III) must bear Category III labeling precaution "Avoid breathing vapors", to reduce the risk of hazard from inhalation exposure. Products with a demonstrated inhalation LC-50 in albino rats of greater than 20 mg/l (Category IV) are not required to bear precautionary labeling with regard to inhalation exposure.

Products with a demonstrated primary eye irritation effect of severe irritation in unrinsed eyes or irreversible corneal opacity must bear the Category I label precaution "Corrosive, causes eye damage. Wear goggles or face shield when handling" to reduce the risk of hazard from eye exposure. Products with a demonstrated primary eye irritation effect of reversible corneal opacity (7 days) and conjunctival effects (partly reversible in 7 days) in unrinsed eyes, and slight iris and moderate conjunctival effects (reversed in 3 days) in rinsed eyes must bear the Category II label precaution "Causes eye irritation" to reduce the risk of hazard from eye exposure. Products with a demonstrated primary eye irritation effect of reversible irritation (7 days) must bear the Category III label precaution "Avoid contact with eyes" to reduce the risk of hazard. Products with no demonstrated primary eye irritation problems are not required to bear precautionary labeling with regard to primary eye irritation.

Products with a demonstrated primary dermal irritation effect described as severe irritation or as moderate erythma, edema, and 2nd degree burns at 72 hours must bear the Category II label precaution "Causes skin irritation" to reduce the risk of hazard from dermal exposures. Products with a demonstrated primary dermal irritation effect described as moderate irritation at 72 hours must bear the Category III label precaution "Avoid contact with skin" to reduce the risk of hazard from dermal exposures. Products with a primary dermal irritation effect described as mild or slight at 72 hours, or as possessing a primary irritation index of 1.62, are not required to bear precautionary labeling with regard to dermal exposure.

Products with a demonstrated ability to cause dermal sensitization must bear the label precaution "May cause skin sensitization. Wear protective clothing while handling this product" to reduce the hazard.

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The required first aid statement for E.C. formulations (containing petroleum distillates) is: "If inhalation occurs, the victim should be moved into fresh air, and medical attention should be immediately sought. If contact is made with eyes or skin, the exposed area should be flushed with water, and medical attention should be sought. If swallowed, promptly drink egg white or gelatin solutions; or if these are not available, water. Call a physician immediately. [Note to Physician: If swallowed, there is no specific antidote. Do not induce emesis as a chemical pneumonitis may occur if aspirated. Lavage stomach. Deposit 50 grams of activated charcoal in a water slurry in the stomach. Give a saline laxative and supportive therapy as needed.]"

## BIBLIOGRAPHY
(Reserved)

*In order for the provisions of FIFRA concerning data compensation (Section 3(c)(1)(d)) to be effective under Registration Standards, data used in direct support of the Standard for each type of product must be accurately listed, enabling applicants and their arbitrators to determine what data do and do not support the registrations of individual pesticide products. Thus, for each disciplinary chapter, studies used to evaluate hazard and establish Standards for the manufacturing-use chemical and for each type of end-use formulation will be listed separately.*

To protect present and potential applicants for the registration or re-registration of products containing Metolachlor, the citations appropriate to each disciplinary chapter will not be published in this Sample Standard, though a complete Bibliography is provided at the end of the document.

## RESIDUE CHEMISTRY

*INTRODUCTION*

*For any pesticide which has uses that may directly result in residues on food or feed, the Agency sets an allowable residue level for each commodity on which it may occur. An allowable residue level for a particular chemical on a particular commodity is a function of the chemical's toxicity, the percentage of an average daily diet comprised by the commodity, and the amount of residue that can be expected to occur on that commodity at the maximum directed rate of application. The total amount of chemical to which a person may be exposed from all sources should always be less than the toxicological estimate of a safe 'Allowable Daily Intake.'*

TOPICAL DISCUSSIONS

Metabolism in Plants
Metabolism in Animals
Analytical Methods
Residue Data
Present Tolerances
Regulatory Incidents

Metabolism in Plants: (Corn and Soybeans)

*In addition to what may remain of an original application of the chemical, residues may also consist of the chemical's metabolites, as formed by the plant crop which it was applied to protect. The major and minor pathways of the chemical's absorption, transformation, and distribution can be deduced experimentally from the analysis of radiolabeled applications. Applications by various routes, for example to the roots or leaves, will show differences in absorption rates. The distribution of the chemical and its metabolites can be examined by measuring the radioactivity present in various plant fractions. Isolated metabolites can then be characterized by chromatography, partitioning, or electrophoresis. Metabolic transformations often result in the polarization of the foreign chemical to facilitate elimination. Metabolites characterized as highly polar may have undergone conjugation with naturally occurring amino acids, sugars, or sugar acids. Further chemical analysis can help identify the exact nature of the conjugations. Other possible major transformations can occur by hydrolysis, oxidation/reductions, or the breaking of unstable bonds. The absorption, distribution, and metabolic fate of the chemical determine the potential quantity and identity of pesticide residues in plants used for food or feed.*

The absorption, distribution, and metabolic fate of Metolachlor were investigated in corn plants grown under field and greenhouse conditions (Sumner and Cassidy, 1974c,d) and in soybeans grown under greenhouse conditions only (Sumner and Cassidy, 1975).

Ring-labeled Metolachlor was applied as a pre-emergence treatment at 2 lbs. ai/acre. For corn, it was mixed with soil to result in a concentration of approximately 2 ppm and applied to field and greenhouse soils. For soybeans, it was added to soil and plantings were incubated in the greenhouse. The maximum levels of residues found in the various plant parts, based on total radioactivity, were as follows: corn grain, greenhouse and field, 0.05 ppm and 0.02 ppm, respectively; corn forage, greenhouse and field, 0.72 and 0.17 ppm, respectively; soybeans 0.17 ppm, soybean hay 2.66 ppm, soybean oil 0.01 ppm and soybean meal 0.14 ppm. These data show that the total residues in soybeans are higher than those in corn.

The metabolism of Metolachlor by corn plants consists of a major and a minor pathway. The Figure in the Residue Chemistry Disciplinary Review depicts these pathways for both corn and soybean plants (Marco 1975).

When corn plants were grown in soil treated with Ø-$^{14}$C-Metolachlor at 2 lbs. ai/acre (Sumner and Cassidy 1974d), extracts of 4-week old corn plants contained less than 10% of the extractable radioactivity present in the organic fraction. Very little, if any, of the activity was present as parent Metolachlor. More than 80% of the remaining activity was found in the polar fraction. TLC characterization indicated the presence of at least 10 metabolites. The highly polar nature of these metabolites indicated conjugation of the parent and/or its metabolites had occurred with natural products such as amino acids, sugars, or sugar acids (Sumner and Cassidy, 1974c).

One metabolic pathway in the corn plants involves conjugation of Metolachlor with glutathione (Sumner and Cassidy, 1974b). Fourteen percent of the radioactive Metolachlor recovered from corn leaves was found conjugated with glutathione. It appears that degradation occurs through a thio-ether bond forming a glutathione conjugate via the reactive chloroacetyl moiety of Metolachlor.

Metabolites, which upon hydrolysis, produce 2-[(2-ethyl-6-methylphenyl) amino]-1-propanol (HP-001) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (HP-002) were found to be common in plants and in animals, from high level feedings of Metolachlor (Hambock, 1974a,b,c; Mattson, 1975). When partly purified plant conjugates were cleaved by a reduction reaction with Raney nickel, which breaks thio-ether bonds (Gross, 1974a and Gross, 1974b), two compounds, N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide (MET-005), and N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)acetamide (MET-006) were produced, indicating that these compounds were moieties of sulfur-bonded conjugates. These two compounds represent 80% of the radioactivity extracted from the corn leaves. They were positively identified by GLC and mass spectrometry.

Further residue characterization, involving rigorous HCl hydrolysis (Sumner, Thomas, and Cassidy, 1975), showed the presence of either 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (HP-001) or 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (HP-002). These data suggest that the compounds present before hydrolysis are predominantly alpha-thioglycoside metabolites and the alpha-oxygen glycoside analogues. The relative amounts of the compounds indicate that the major pathway of metabolism involves conjugation with glutathione, breakage of the thio- bond to form the mercaptan, conjugation of mercaptan with glucuronic acid, hydrolysis of methyl ether, and conjugation of the alcohol with a neutral sugar. A minor pathway

involves chloro replacement by hydroxyl and/or direct conjugation with glucuronic acid, followed by demethylation and conjugation of the hydroxyl with a neutral sugar, all forming oxo-conjugates.

When radiolabeled Ø-$^{14}$C-Metolachlor was applied to growing soybeans (Sumner and Cassidy 1975b), characterization of the extracted residues indicated that the metabolic pathways in soybeans are similar to those observed in corn. Thin-layer chromatography and partitioning data indicated that higher concentrations of less polar metabolites will occur in soybeans when compared to corn grain.

Toxicology reviewers expressed concern about the possible presence of monochloroacetic acid as a component of the residues of Metolachlor, resulting from metabolism or degradation of the parent compound. Toxicology postulated that the chloroacetyl group could split off as monochloroacetic acid and occur as part of the terminal residue. However, Residue Chemistry reviewers can find no reason to expect monochloroacetic acid to occur as a residue following use of Metolachlor. While there is no definitive data on the matter, the conclusion is based upon the unique chemical and biological stability of the amide bond and the relatively unstable carbon-chlorine bond in Metolachlor. Thus, it is postulated that any hydrolysis of the amide would be preceded by displacement of the chlorine. Consequently, the presence of monochloroacetic acid as a product of metabolism is not likely to occur.

The above studies adequately define the fate of Metolachlor in soybeans and corn for the purposes of establishing tolerances.

## Metabolism in Animals

*The identity of residues in animal products used for food may, as with plants, be largely determined by the metabolic fate of the chemical in the living organism. Of livestock that may ingest chemicals through treated feed or forage, or that are treated directly with dips or sprays, ruminants or cud-chewing animals (such as cattle and goats) may produce a different metabolic effect than non-ruminants, and poultry may produce a third type of effect. Gastrointestinal absorption, biotransformation, and body distribution are usually studied by the feeding of animals with the unlabeled or radiolabeled chemical. The degree to which the parent compound and its plant metabolities are absorbed or excreted can often vary with the forage or fodder crop on which the chemical was administered, and so actual feeding practices are usually approximated. Residues in excreta, blood, milk, eggs, or tissue are then measured and characterized. Where the chemical identity of the metabolites is inaccessible to simple analysis, the subjection of these residues to further controlled reactions, such as acid hydrolysis, may itself yield identifiable products. These products can then serve as a reference for the original residue, so that other residue analyses can be performed to test for its presence.*

Metolachlor is rapidly metabolized and almost totally eliminated in the urine and feces of ruminants (goats), non-ruminants (rats), and poultry (Roger and Cassidy, 1974a; Hambock, 1974a; Guth, 1974). These findings were made in studies using both unlabeled and $^{14}$C-ring-labeled Metolachlor. Metolachlor per se was not detected in any of the excreta or tissues.

Additional studies with goats (Counselman and Roger, 1973; Roger and Cassidy, 1974a,b) confirmed the finding that the urine and feces contain almost all the metabolized products.

In animals, trace amounts of metabolized Metolachlor were found in kidneys, liver, blood, and milk (Biometric Testing Incorporated, 1973; Hambock, 1974a, b,c; Schenker, 1975a).

No residues were found in eggs, meat, or fat samples of laying chickens. The only metabolite found, in the liver (at 0.02 - 0.03 ppm), was the one which upon hydrolysis yields HP-001 (Mattson, 1974, 1975). No precursor of the hydrolysis product HP-002 was found in the liver (Guth, 1974).

When $^{14}C$-labeled metabolites of Metolachlor, bio-synthesized in corn, were fed to goats, no parent Metolachlor nor any metabolites were found in the animals' tissues or milk (Ciba-Geigy Limited, 1973; Schenker, 1974, 1975b).

It is concluded that the metabolism of Metolachlor in animals appears to be similar to and as complex as that in plants. Whereas plants retain their metabolic products, animals eliminate their Metolachlor metabolic products almost entirely. Various studies with unlabeled Metolachlor and $^{14}C$-ring labeled Metolachlor fed to different animals indicate clearly the identity and the amounts of the metabolites which result as residues in the excreta, tissues, milk, and eggs.

Although the exact metabolic pathway of Metolachlor in animals is not known, the available metabolic studies adequately delineate the fate of Metolachlor in animals for the purposes of establishing tolerances for corn grain and soybeans. (For an evaluation of rat metabolism data, please see Toxicology Chapter.)

## Analytical Methodology

*There must be available, before a tolerance may be granted, practicable analytical methods for the detection and measurement of the residue and its metabolites. Every commodity considered for a tolerance must have some applicable method. Such methods are often published and widely used; others may involve adaptations of common analytical procedures. In general, any analytical method suggested for consideration must be characterized in four ways: first, there should be some assurance as to the efficiency of the extraction procedure, so that the analysis is not carried out on partial samples; second, the method should afford a measure of the 'total toxic residue', including toxic degradation, metabolic, or other conversion products; third, the method must be thoroughly validated by analyses of representative samples in comparison to blank values significantly lower than the proposed tolerance; fourth, the validation should conclude with an estimate of sensitivity, i.e., the least concentration of pesticide which can be detected with a reasonable degree of assurance.*

*At least one method must be suitable as a regulatory enforcement method, in that it does not require the use of untreated crop samples for blanks, that it is rapid, that it makes use of commonly available equipment and reagents, and that it is sufficiently specific to identify and measure a specific pesticide in the presence of other residues likely to occur on the same commodity.*

Metolachlor in Corn and Soybeans

The residue data submitted for corn were obtained by the use of Methods AG-265 (Balasubramanian, Gold, and Ross, 1974) and AG-277 (Balasubramanian, Aziz, and Ross, 1975). The residue data for soybeans were obtained by Method AG-286 (Aziz and Ross, 1975). Most of the corn residue data were obtained by Method AG-265. This method utilizes HCl to hydrolyze Metolachlor and those metabolites which are capable of conversion to 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (HP-001).

In Method AG-265, fifty grams of ground or chopped sample is refluxed with 250 ml of 6N HCl for 16 hours. The aqueous extract is filtered off, neutralized, and made basic with NaOH solution and extracted twice with hexane. The combined hexane extracts are chromatographed on an alumina column. The residues of HP-001 are eluted using 5% ether in hexane. The eluate is evaporated and the residues are taken up in 0.5 ml of benzene. An aliquot of the sample solution is injected into a gas chromatograph equipped with a Coulson eletrolytic conductivity detector. Known amounts of HP-001 are used for standardization. Peak heights are compared with those of the standard for quantification. Residues are expressed as parent Metolachlor equivalents using the 1.47 factor.

The method was validated by the petitioner in three ways: (1) fortification with the determined compound, HP-001; (2) fortification with parent Metolachlor, (COM-001); and (3) comparison of GLC analyses of $^{14}C$-labeled residues from metabolism study samples with total $^{14}C$-combustion analyses of duplicate samples.

Recovery for samples of grain, forage, silage, and stover fortified at levels of 0.05-2.0 ppm with HP-001 averaged 81%. All control samples were determined to have <0.03 ppm (the method sensitivity). Fortification studies using parent Metolachlor averaged 63% for levels of 0.05-0.2 ppm in stover.

The total $^{14}C$-activities in samples of corn plants taken from both the field and greenhouse studies were determined by combustion (Hermes, 1972). The combustion technique determined all residues (both extractible and nonextractible) after conversion to $^{14}CO_2$. The residues (expressed as COM-001) determined by Chemical Method AG-265 ranged from 12% (mature crop) to 27% (immature forage or silage) of the total residues found by combustion techniques. Comparisons were also made of the total extractible residues by the chemical method vs. the $^{14}C$-combustion method using two extraction solvent systems, HCl, and combined chloroform-methanol solvent. About 50-60% of the $^{14}C$-residues in mature corn were extractable using either method. The chemical method determined 20-30% of the total extractable $^{14}C$-residues.

Except as stated directly below, method AG-265 (Balasubramanian, Gold, and Ross, 1974) was found to be specific in the presence of other pesticides with established tolerances on corn. Six pesticides were not available for testing: EPN, Vegadex, Avadex, Landrin, 4-amino pyridine, and 2-(thiocyanomethylthio)-benzotriazole. An alternate column liquid phase is available and provides additional specificity for residues of Metolachlor.

Method AG-277 (Balasubramanian, Aziz, and Ross, 1975) is a modification of AG-265 which includes partitioning, clean-up, derivatization, and micro-coulometric GLC steps determining two hydrolysis products: 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (HP-001) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (HP-002).

Residues of Metolachlor (COM-001) in corn grain, ears, forage, fodder and stover are converted to a mixture of HP-001 and HP-002 by refluxing 16 hours with 6N HCl. The filtered acid extract is partitioned with dichloromethane to extract the HP-002 into the organic phase. The aqueous phase containing HP-001 is made strongly basic with 50% sodium hydroxide and subjected to distillation-partition into isooctane using a Bleidner apparatus. The isooctane phase containing HP-001 is cleaned up by using an alumina column. HP-001 is determined with a gas chromatograph equipped with a Coulson electrolytic conductivity nitrogen detector. It is quantified by comparing it with the peak height of a standard amount of HP-001 and then calculated as COM-001 using the 1.47 equivalence factor.

The dichloromethane phase containing HP-002 is washed with 5% sodium carbonate solution and further cleaned up using an alumina column. The chloroethanol derivative of HP-002 is formed by reaction with boron trichloride/2-chloroethanol at 90°C for 15 minutes. The derivative is partitioned into hexane and an aliquot is cleaned up using silica gel and alumina columns. A gas chromatograph equipped with Dohrmann microcoulometric chloride detector is used for analysis. For quantification, the peak area is compared to that of peak areas of derivatized standard HP-002. Residues are calculated as COM-001 using the conversion factor 1.14.

Controls for HP-001 usually ranged from less than 0.02 ppm to 0.05 ppm. In some samples, the controls ranged up to 0.1 ppm due to an interfering peak. We consider the sensitivity of the method for HP-001 to be 0.05 ppm or less. Recoveries for 69 samples of fodder, forage, grain, or ears, fortified at 0.02 and 0.20 ppm, ranged from 57-115% with an average of 65%. Typical recovery data residues of HP-002 for samples fortified at 0.05-0.20 ppm ranged from 45-102% with an average of 62%. The method sensitivity is considered to be 0.10 ppm for HP-002 when calculated as COM-001.

The method used for the soybean residue data is Method AG-286 (Aziz and Ross, 1975). This method, "Analytical Method for the Determination of Residues of Metolachlor Soybean Metabolites (as HP-001 and HP-002) by Acid Hydrolysis," is the method for regulatory enforcement which will be incorporated in the FDA pesticide Analytical Methods, Vol. II. Method AG-286 was tried out in one of EPA's laboratories and found to be acceptable.

Method AG-286 was tested for specificity with 54 of the 58 pesticides registered on soybeans. DC-200 and Carbowax 20 M are available as alternate liquid phases to enhance the specificity of the GLC determinative steps.

Metolachlor in Animal Tissues

Analyses of meat, milk, and egg samples were conducted by methods reported in Basle REM 5/74 (Hormann, Guth, Formica, and Schenker, 1974) and Basle REM 2/75 (Ramsteiner and Karlhuber, 1975). Analytical method (REM 2/75) accounts for "combined residues" of Metolachlor, determined as HP-001 and HP-002.

In the first method (REM 5/74), the herbicide and the potential metabolites and/or conjugates in animal products are subjected to acidic hydrolysis. The resulting solution is made alkaline before steam-

distillation; extraction of residues into isooctane is effected by means of a steam distillation-extraction head. The HP-001 fraction is cleaned up by using an alumina column and, if necessary, by TLC.

The HP-001 "residues" are detected by gas chromatography/mass spectrometry. This method is a minor modification of AG-265 and was used for the gas chromatographic analysis of milk, blood, meat, fat, liver, kidney, egg white and egg yolk. The limits of detection for HP-001 are 0.006 ppm for milk, 0.015 ppm for eggs and chicken tissues, and 0.02 ppm for cow tissues.

The second method (REM 2/75) determines all residues which are hydrolyzed by acid to HP-001 and HP-002. HP-002 is converted to a derivative which is determined by gas chromatography. This method for animal tissues involves minor modifications of Method AG-286. The reported limits of detectibility are 0.01 ppm in milk, and 0.04 in for meat, liver, and kidney.

Method REM 2/75, COM-001, "Determination of Total Residues in Material of Animal Origin" (Ramsteiner and Karlhuber, 1975), was tried on beef liver in one of EPA's laboratories. Samples fortified in duplicate with HP-001 gave 99% and 100% recovery. Samples fortified in duplicate with HP-002 showed 43% and 45% recovery.

Methods AG-286 and REM 2/75 were found to have adequate specificity and are judged satisfactory for enforcement purposes.

## Residue Data

*In addition to provisions for analytical methodology, a second prerequisite to the granting of tolerances is the generation of supporting data. Residue experiments generally consist of:*

1) *Data about the stability of extracted residues under storage;*
2) *An examination of raw consumable commodities for residues of the pesticide chemical after treatment corresponding to the proposed uses.*

*These commodities should include both the treated organism and any plants, livestock, or consumable wildlife that may be expected to acquire residues by feed, forage, or unintentional exposure. Where residues are likely to occur in plant parts which are used for animal feeds, it is necessary to have experimental evidence that such levels in feeds do not contribute non-tolerated residues to meat, poultry, eggs, or milk. Information about the fate and persistence of the pesticide in representative soil types would determine whether a residue could exist when 'rotational' crops are subsequently planted in treated fields. And information about the general environmental fate of the pesticide would ensure against non-tolerated residues in such consumable wildlife forms as fish and estuarine mollusks.*

*Residue data generally disclose: the nature of the residue (i.e., parent compound or transformation product); the level of the residue as it occurs in the whole raw agricultural commodity, the commodity being in the form in which it moves in interstate commerce; the distribution of the residue in the commodity; and sometimes also the effect on the residue caused by the processing of the commodity for consumption, including washing, brushing, trimming, curing, drying, cooking, or canning. Some data may be available*

*comparing various methods for the intentional removal of residues. Residue data can be obtained by field experiments, by animal treatment studies, by soil persistence studies, or by the monitoring of actual residues in marketed food or feed products, by which tolerances can be enforced or reassessed.*

Field residue data for Metolachlor should reflect the proposed use with respect to dosage, mode of application, number and timing of treatments, formulations used and geographical areas represented. Pre-plant soil treatments for grain crops should include examination of foliar parts of the plant during the growing season as well as analyses of the harvested grain.

The analytical methods used to generate the residue data involve a conversion of residues of Metolachlor and its metabolites (through hydrolysis) to 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (HP-001) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (HP-002). The resulting residues from the application of Metolachlor are accordingly expressed as HP-001 and HP-002, or combined as the total residue and calculated as Metolachlor.

A storage stability study of Metolachlor residues in corn fodder and grain was performed to ensure that results obtained for samples stored prior to analysis are valid (Gold and Kahrs, 1975b). Samples of corn fodder and corn grain were fortified with Metolachlor at 1.0 ppm and 0.2 ppm, respectively. The samples were kept frozen at -15°C and analyzed at pre-determined intervals up to 13 months after storage. The recoveries for the corn fodder ranged from 92-115% of the fortified amount and the corn grain samples ranged from 92-119%.

Several samples of field-treated corn fodder were also monitored during the 13-month storage period. Residues in one sample varied from 0.43-0.39 ppm and residues in another sample ranged from 0.29-0.26 ppm over the 13-month period.

Residues in Corn

The majority of the residue studies on field and sweet corn were performed by the use of a formulation of Metolachlor called 250 EC. No data were submitted regarding the composition of 250 E.C. formulation. The residues of COM-001 in these studies are determined as HP-001 alone. The HP-002 breakdown product was not determined. The studies were performed in 13 states representing major corn-producing areas. (Tweedy, 1974; Tweedy and Mattson, 1974; Mattson and Kahrs, 1975b).

Nine studies with field corn, at 2 lbs. and 4 lbs. ai/acre of 250 E.C., reported residues less than 0.03 ppm of Metolachlor (as HP-001) in grain at intervals of 111-162 days between pre-emergent application and harvest. Three studies with sweet corn at 2 lbs. and 4 lbs. ai/acre of 250 E.C. reported residues of Metolachlor (as HP-001) in ears as less than 0.03 ppm at 61, 67, and 138 days after the pre-emergent application. Two additional studies with field corn and one with sweet corn using the 6E formulation (at 3 and 6 lbs. ai/acre ) indicated no detectable combined residues of HP-001 (as Metolachlor) (less than 0.03 ppm) and HP-002 (less than 0.10 ppm) in the grain and fresh ears respectively 62, 92 and 129 days after the application. At a later date two additional studies at 2 lbs. and 4 lbs.ai/acre of 250 E.C. formulation on sweet corn were performed. No detectable residues of Metolachlor as HP-001 (less than 0.03 ppm) or HP-002 (less than 0.10 ppm) were found in the fresh ear sample at 60 and 67 days after the application.

Seventeen residue studies where Metolachlor was measured as HP-001 show forage residues were less than 0.03 ppm at intervals of 34 and 72 days

following 1.5 lbs. ai/acre. Residues resulting from 2 lbs. and 3 lbs. ai/acre applications (at 26 to 72 days) range from less than 0.03 ppm to 0.14 ppm, and less than 0.03 ppm to 0.10 ppm, respectively. At intervals of 26 to 64 days, 4 lbs. ai/acre resulted in residues of less than 0.03 to 0.43 ppm; 6 lbs. ai/acre rates showed HP-001 residues were 0.03 ppm to 0.19 ppm.

Silage stage forage residues of Metolachlor (measured as HP-001) resulting from 2 lbs. and 4 lbs. ai/acre range from less than 0.03 ppm to 0.16 ppm, and less than 0.03 ppm to 0.43 ppm, respectively, at intervals from 71 to 112 days after application.

Mature fodder and stover residues ranged from less than 0.03 ppm to 0.44 ppm (measured as HP-001) for both the 2 lbs. and 4 lbs. ai/acre rates.

Eleven studies in which Metolachlor was later measured as combined residues of HP-001 and HP-002 show residues in early forage of less than 0.03 ppm to 0.24 ppm and less than 0.03 ppm to 0.08 ppm for 2 lbs. and 3 lbs. ai/acre treatments, respectively; 4 lbs. and 6 lbs. ai/acre applications resulted in forage residues ranging from 0.04 ppm to 0.64 ppm and 0.03 to 0.19 ppm, respectively.

Silage stage forage showed combined HP-001 and HP-002 residues (as Metolachlor) of 0.08 to 0.14 ppm, 0.04 ppm to 0.12 ppm, and 0.05 ppm to 0.28 ppm for treatments at 1.5 lbs., 2.0 lbs., and 3.0 lbs., respectively. Combined residues from 4 lbs. and 6 lbs. ai/acre treatments were 0.14 to 0.63 ppm and 0.13 to 0.34 ppm, respectively.

Fodder and stover residues for 1.5 lbs., 2.0 lbs., and 3.0 lbs., ai/acre treatments were less than 0.03 to 0.06 ppm, less than 0.03 to 0.23 ppm, and 0.07 to 0.30 ppm.

Combined residues of HP-001 and HP-002 (as Metolachlor) in mature fodder and stover reported in six studies at 4 lbs. ai/acre ranged from 0.07 ppm to 0.90 ppm. Three studies at 6 lbs. ai/acre reported combined residues in fodder ranging from 0.14 to 0.53 ppm.

Because no detectable residues were found in corn grain, no residue data are needed for corn grain by-products (corn oil, corn meal, etc.).

Residues in or on Soybeans

Twenty-three residue studies were performed in ten states representing the major soybean growing areas. Application rates were from 2 to 6 lbs. ai/acre (Mattson and Rolla, 1975; Texas A & M Cottonseed Products Research Laboratory, 1966; Houseworth and Rolla, 1976).

Analyses involved the determination of both HP-001 and HP-002. No detectable residues (less than 0.05 ppm) of HP-002 were found in any of the soybean samples. Residues of HP-001 in the soybeans which ranged from less than 0.03 to 0.09 ppm resulted from application rates of up to 5 lbs. ai/acre; the maximum reported residue was from a 3 lb. ai/acre application. At 6 lbs. ai/acre, residues of HP-001 ranged from less than 0.03 to 0.21 ppm.

Three fractionation studies showed no detectable residues of HP-001 (less than 0.03 ppm) or HP-002 (less than 0.05 ppm) in any fraction (meal, crude and refined oil, soapstock) from soybeans treated at rates of 2 to 5 lbs. ai/acre. At 6 lbs. ai/acre, the only finite residue was found in the soybean meal where 0.04 ppm HP-001 was detected. In one of the three tests, soybean hulls (pods) contained 0.03 and 0.06 ppm HP-001 from treatment rates of 2.5 and 5 lbs. ai/acre.

Total residues (sum of residues converted to HP-001 and HP-002) of Metolachlor in soybean forage ranged from 0.20 to 0.36 ppm at a 2 lbs. ai/

acre application rate. Total residues in soybean forage at the 3 lbs. ai/acre ranged from 0.15 to 1.01 ppm. At exaggerated rates of 4 lbs. and 6 lbs. ai/acre, total residues ranged from 0.34 to 1.76 ppm. These residue studies represented pre-harvest intervals of 30-92 days.

Total residues in soybean hay at pre-harvest intervals of 122-194 days ranged from less than 0.10 to 0.84 ppm at rates of up to 3 lbs. ai/acre. At exaggerated rates of 4 to 6 lbs. ai/acre, total residues ranged from 0.14 to 2.46 ppm.

The above residue data for soybeans allow for an adequate range of geographical variation.

Residues in Meat, Milk, Poultry, and Eggs

*For this section, data should show whether residues will result in meat (muscle, liver, kidney, fat), poultry, eggs, or milk. The toxicant fed should correspond to the aged residues found in the item of feed, which may or may not be the parent pesticide. The studies should be performed at several dosage levels, including exaggerated dosages, preferably threefold and tenfold.*

Residues in meat and milk were studied in a three-level feeding study (Mattson, 1975). In this study, eleven cows were fed unlabeled Metolachlor at levels of zero, 0.02 ppm, 1.0 ppm, and 5.0 ppm of the total diet. Milk samples were collected at zero, 1, 2, 7, 14, 21, and 28 days. Animals were sacrificed and samples of tissues taken at 14, 21, and 28 days. Only milk and tissue samples from the two highest feeding levels (1.0 and 5.0 ppm) were analyzed.

In this study, the analytical method determined "total" residues of Metolachlor, (i.e., parent compound and all metabolites yielding HP-001 and HP-002 after hydrolysis with 6N HCl). All residues in milk samples were less than the method sensitivity of 0.006 ppm for HP-001 and 0.01 ppm for HP-002. All residues in the muscle, fat, kidney, and liver were less than the method sensitivity of 0.02 ppm for HP-001 and 0.04 ppm for HP-002.

Total $^{14}C$-residues (calculated as Metolachlor) were determined in the goat metobolism study where 4.7 ppm of $^{14}C$-labeled Metolachlor was fed for 10 days (Roger and Cassidy, 1974a). Activity levels were equivalent to 0.01 ppm in milk, 0.003 ppm in kidney, 0.07 ppm in liver, and less than .006 ppm in other tissues. The activity was not characterized. When $^{14}C$-labeled corn biosynthesized metabolites were fed to goats, no detectable $^{14}C$-residues resulted in milk or tissues (Roger and Cassidy, 1974b).

Residues in poultry and eggs were determined in a feeding study involving 112 laying hens (Mattson, 1975). The birds were fed unlabeled Metolachlor at levels of zero, 0.1, 0.5, and 2.0 ppm in the dry diet. Egg samples were taken on days 1, 3, 7, 10, 14, and 21. Birds were sacrificed after 7, 14, 21, and 28 days for tissue analysis. Only tissue and eggs samples from the two highest feeding levels (0.5 and 2.0 ppm) were analyzed. Residues as HP-001 in eggs, muscle, and fat were reported as less than 0.02 ppm. Residues of 0.02 ppm and 0.03 ppm as HP-001 were reported for the livers from birds fed at 0.5 and 2.0 ppm feeding levels, respectively. No detectable residues (less than 0.04 ppm) of HP-002 were found in eggs nor in any tissues.

From the feeding of soybean meal, hulls, and soap-stock bearing residues of 0.1 ppm, the dietary residue level could approach 0.04 ppm for cattle and 0.03 ppm for poultry. The feeding levels at which barely

detectable residues were found in the feeding studies represent exaggerations of ca. 100x for cows and 25x for poultry.

A restriction against the feeding of soybean forage or hay, including the fodder or straw from the bean harvest, precludes dietary residues for poultry and cattle except for the fractions of soybeans. Although the livestock feed use of soybean fractions may lead to small residues in meat, milk, poultry, and eggs, these residues, if present, would be at levels below the sensitivity of the analytical methods.

## Present Tolerances

A permanent tolerance of 0.1 ppm in corn grain (except popcorn) has been established for residues of Metolachlor and its metabolites pursuant to 40 CFR 180.368 (FR 41:178, 9/13/76). Temporary tolerances were granted on 4/23/76 for residues of Metolachlor and its metabolites at 0.1 ppm for soybeans, 1.25 ppm for soybean hay and forage, and 0.02 ppm for meat, eggs, poultry, and milk. (These were renewed on 2/9/78.)

Presently there is a proposal pending for a permanent tolerance of 0.1 ppm for residues of Metolachlor and its metabolites in soybeans. A restriction against the feeding or grazing of soybean hay or forage is on the label. The temporary tolerances for Metolachlor and its metabolites of 0.02 ppm for eggs, milk, meat, fat, and meat by-products are enforced for the following animals: cattle, goats, hogs, horses, poultry, and sheep. The permanent petition for these tolerances, in addition to the tolerance of 0.1 ppm in soybeans, is presently in abeyance because Toxicology reviewers are requiring additional toxicology studies as a prerequisite for permanent tolerances for meat, milk, eggs, and poultry.

## Regulatory Incidents

*Though EPA sets tolerances for pesticides, it is up to the Food and Drug Administration to enforce them. When reviewing Residue Chemistry for Registration Standards, EPA will routinely search regulatory records for incidents in which the tolerances for the chemical under review were exceeded. Such incidents can indicate problems in either the practicability of the tolerances or in the accurate detection of residues, and may suggest the re-evaluation of current tolerances.*

First, EPA has no record in their files concerning any regulatory action taken by FDA with respect to the registered uses of Metolachlor. Second, Metolachlor is a relatively new compound, and the method for regulatory compliance has not yet been edited and incorporated into the PAM II.

## Disciplinary Review

Residue Chemistry Profile
Tolerance Reassessment
Generic Data Gaps
Registration Requirements
Suggested Labeling

## Residue Chemistry Profile

When Metolachlor was applied as a pre-emergence treatment at 2 lbs./acre to corn and soybeans, total residues later found in plants parts were higher in soybeans than in corn. In corn, the residues were primarily metabolites conjugated with polar plant molecules such as amino acids or sugars. The major pathway of metabolism appears to be conjugation with glutathione, breakage of the thioglycoside bond to form mercaptan, conjugation of mercaptan with glucuronic acid, hydrolysis of methyl ether, and conjugation of the alcohol with a neutral sugar. Metabolic pathways in soybeans were similar to those observed in corn.

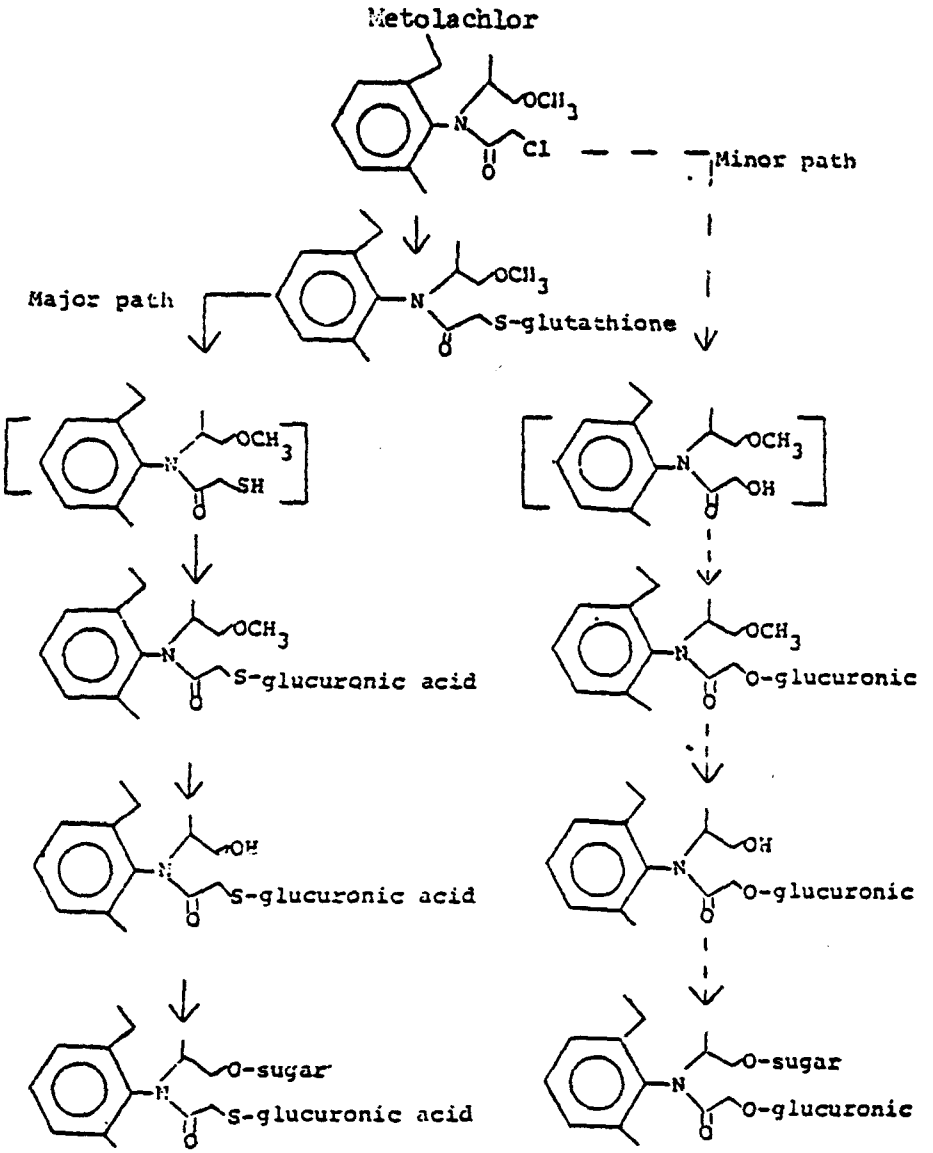
The metabolism of Metolachlor in animals appears to be similar to and as complex as that in plants. But whereas plants retain their metabolic products, animals eliminate their Metolachlor metabolic products almost completely. The parent compound was rapidly metabolized and almost totally eliminated in the urine and feces of goats, rats, and poultry, and no residues or only trace amounts could be detected in the tissues, kidneys, liver, blood, or milk of animals, or in the eggs, meat, or fat samples of laying chickens. The most significant residue detected was 0.02 to 0.03 ppm in the liver of chickens.

Adequate Metolachlor-specific and metabolite-specific analytical methods are available for the detection of residues in corn, soybeans, meat, milk, and eggs, and data were available on actual residues in these commodities. No detectable residues were found in corn grain, though small amounts of residues were found in corn forage, fodder, and stover. Residue data for soybeans were adequate to allow for the wide range in the geographical characteristics of the U.S. soybean crop, and detectable residues were found in the beans, soybean meal, hulls, forage, and hay, though all were in small quantities. The highest soybean residues (0.14 to 2.46 ppm) were in hay from plants treated with exaggerated rates of 4 lbs. and 6 lbs. ai/acre. Residues at just above or below the sensitivity of the analytical method were reported for cattle meat and milk, for goat meat and milk, and for poultry eggs, meat, and fat. The feeding levels at which barely detectable residues were found represent exaggerations of approximately 100 times for cows and 25 times for poultry.

Present tolerances for Metolachlor are set permanently for corn grain at 0.1 ppm, and temporarily at 0.1 ppm for soybeans, 1.25 ppm for soybean hay and forage, and 0.02 ppm for meat, eggs, poultry, and milk. There are no records of regulatory incidents involving the enforcement of these tolerances.

METABOLIC PATHWAYS OF METOLACHLOR

IN CORN AND SOYBEANS



## Tolerance Reassessment

*The exposure of humans to pesticide residues from registered uses and via the food chain is a function of several factors:*

*a) The established tolerance for a commodity (in ppm).*
*b) The percentage of a commodity in the daily diet.*
*c) The assumed amount of food consumption by an average person, which is 1.5 kg per day.*
*d) The assumed body weight of an average person, which is 60 kg.*

*When these factors are substituted into a toxicological formula [i.e., (a x b x c) divided by d], the human exposure to those pesticide residues in a commodity is found in terms of mg of pesticide per kg of body weight per day.*

*A tolerance is re-assessed by comparing this potential daily exposure with an 'Allowable Daily Intake', which is set on the basis of a toxicological 'No Observable Effect Level', plus a margin of safety factor of 100x, to allow for a 10x greater sensitivity of humans over test animals, and to allow for the possibility of an individual who is 10x more sensitive than the average person. In order to determine the 'No Observable Effect Level' for a pesticide chemical, the Toxicology reviewers must have a full complement of acute and chronic studies.*

For Metolachlor the following tolerances have been established: A permanent tolerance of 0.1 ppm in corn grain, and temporary tolerances of 0.1 ppm for soybeans, 1.25 ppm in soybean hay, and 0.02 ppm in meat, milk, poultry, and eggs. Based on these established permanent and temporary tolerances, the theoretical human exposure to Metolachlor residues is calculated to be <.0003 mg/kg/day. But because certain necessary chronic studies are not presently available (see Toxicology Chapter) a Tolerance Reassessment is not possible at this time, and will instead be performed when the chronic data have been supplied and reviewed.

## Generic Data Gaps

none

## Registration Requirements

The proposed guidelines for Residue Chemistry have not been published, and accordingly, there are no citations for Guidelines corresponding to the types of Residue Chemistry data normally required to support individual registrations. In general, however, the Residue Chemistry reviewers must have enough data for each proposed product to be assured that the residues of the parent chemical and its metabolites have been adequately identified, quantitatively and qualitatively.

## Suggested Labeling

For Emulsifiable Concentrate Metolachlor (8 lbs. or less per gallon):

for corn: Do not graze or feed forage and fodder to livestock or use for silage.

for soybeans: Do not graze or feed soybean hay or forage.

BIBLIOGRAPHY
(Reserved)

*In order for the provisions of FIFRA concerning data compensation (Section 3(c)(1)(d)) to be effective under Registration Standards, data used in direct support of the Standard for each type of product must be accurately listed, enabling applicants and their arbitrators to determine what data do and do not support the registrations of individual pesticide products. Thus, for each disciplinary chapter, studies used to evaluate hazard and establish Standards for the manufacturing-use chemical and for each type of end-use formulation will be listed separately.*

To protect present and potential applicants for the registration or re-registration of products containing Metolachlor, the citations appropriate to each disciplinary chapter will not be published in this Sample Standard, though a complete Bibliography is provided at the end of the document.

## ECOLOGICAL EFFECTS

*INTRODUCTION*

*The environment as a whole is a closed system that uses energy from the sun to constantly recycle its water, air, mineral, plant, and animal resources. Natural mechanisms recognized by ecologists to be essential to this system include: biogeochemical cycling, host/parasite relations, competition for habitat and food, predator/prey relationships, food chains, symbioses, community diversity and succession, and natural selection.*

*Man's activities form a significant subsystem of the earth's overall environment. When man utilizes the power of technology to support, defend, or enrich his existence, his activities can have a great enough impact to significantly disrupt ecological mechanisms, or to deplete and damage ecological resources. Sometimes the depleted resources are ones that man values for his own use, such as sport and commercial fisheries, shellfish populations, recreational areas, or agricultural land. Other times, there occurs a depletion of natural resources which man does not utilize directly, but which form an integral part of the ongoing process of ecological recycling.*

*As a technological intervention of significant magnitude, the release of pesticides into the environment influences both natural and man-modified ecosystems. The study of pesticide effects on ecological systems is difficult to carry out because of the complexity of the interactions involved. Testing begins with a selection of biological 'indicators', including single species of microbes, vertebrates, invertebrates, and plants, that provide for wide taxonomic representation and include a range of biological processes. Then, if single species show effects, true 'ecological effects' are determined by systemic studies of the environment's natural mechanisms.*

TOPICAL DISCUSSIONS

Corresponding to each of the Topical Discussions listed below is the number of the sections in the 'Proposed Guidelines' of July 10, 1978 (40 CFR Part 163) which explain the minimum data that the Agency usually requires in order to adequately assess a pesticide's Ecological Effects. Where no section number is listed, a minimum requirement has not been set for such information.

| | Guidelines Sections |
|---|---|
| Microbes | 163.62-8(f) and (g) |
| Algae | 163.122-2, .123-2. .124-2, and .125-4 |
| Aquatic Macrophytes | 163.122-2, .123-2, .124-2, and .125-4 |
| Terrestrial Plants | 163.121-1, .122-1, .123-1, .124-1, and .125 |
| Soil and Surface Invertebrates | |
| Birds | 163.70-1, .71-1, .71-2, .71-4, and .71-5 |
| Reptiles and Amphibians | |
| Wild Mammals | 163.70-1, .71-3, and .71-5 |
| Aquatic Invertebrates | 163.70-1, .72-2, .72-4a(1), .72-5, and .72-6 |
| Fish | 163.72-1, .72-4, .72-5, and .72-6 |
| Estuarine and Marine Organisms | 163.72-3, .72-5, and .72-6 |
| Effects on Nonbiological Components of the Environment | |
| Ecosystem Effects | 163.71-5 and 163.72-6 |

Microbes

*Bacteria and fungi are among the principal agents of decay and transformation, reducing plant, animal, and other organic remains to their component compounds. Cellulose decomposition by microbes forms nutrient-rich humus from decomposing plants on the soil surface, recycling large amounts of organically bound carbon. Microorganisms are also the primary actors in the nitrogen cycle, fixing gaseous nitrogen, and causing the ammonification of organically bound nitrogen, which reintroduces the element into the soil from protein wastes and remains. Sulfur salts from volcanic rock and hydrogen sulfide from the anaerboic microbial decomposition of plant and animal wastes are oxidized by other microorganisms to sulfates, which are taken up by plants as primary nutrients. The cyclic movements of chemical elements such as carbon, nitrogen, and sulfur through soil, air, and living tissue could not proceed without microbes, and the effect of pesticides on microbes is a potential impairment of these most basic ecological cycles.*

*Effects on microbes can also have serious consequences for resources used or modified by man. The fertility of natural farmland depends upon the presence of nitrogen-fixing bacteria as well as microorganisms which can degrade dead plant material. Reductions in particular populations of microbes might even interfere with the degradation of other pesticides applied to the same area. Some pesticides, which may be rinsed off into drains or sewer waters, can end up harming the populations of microorganisms responsible for normal wastewater treatment.*

Data on the effects of pesticides on microbes are obtained from laboratory studies employing non-radioisotopic analytical techniques. These studies determine effects on either microbial functions or microbial populations. The study of effects on microbial functions constitutes a more direct approach, but some effects cannot be measured directly and population studies may be the only recourse. Studies should be conducted over a long enough period to demonstrate whether there is a temporary or long-lasting effect on microbes. Three studies were submitted for Metolachlor. Two of the studies used the population approach and one used the functional approach.

In the first population study (Houseworth, 1973a), reviewers noted variations in tabulated results, and raised questions about the aggregation, dilution, dispersal, enumeration, and identification of selected soil microorganisms (such as Bacillus, Pseudomonas, Arthrobacter, Cellulomonas, Cytophaga, Flavobacterium, Achromobacter, Aspergillus, Chaetomium, Fusarium and Penicillium). These issues will require clarification before this study can be used to support regulatory decisions.

In the other population approach study (Ercegovich, Bogus, and Buly, 1978), a diverse selection of microorganisms with 27 species representing the family Actinomycetes and the following genera: Bacillus, Cellulomonas, Cytophaga, Flavobacterium, Pseudomonas, Archromobacter, Aspergillus, Chaetomium, Fusarium, Penicillium, and Tricoderma, were evaluated against three concentrations of Metolachlor; 5, 25, and 125 ppm. At 5 ppm, 6 of 27; at 25 ppm, 9 of 27; and at 125 ppm, 19 of 27 species were inhibited with a static not cidal effect shown. At 5 ppm, 4 of 27 species had increased counts and 1 species did not show any effect at all three concentrations. Potential degraders could be estimated and 10 of 27 species could have this potential. Data for oxygen consumption, carbon dioxide evolution, nitrogen cycling, dehydrogenase activity, and phosphatase activity were not supplied. Because

application rates normally used for Metolachlor are 1-3 lbs ai/A, the slight inhibitory/static effect on soil commensal populations would not be as significant as the laboratory study indicates, would be alleviated with time, and would allow populations to recover. The effect would be further minimized by reduction of the pesticide concentration by physico-chemical means, of which photolysis is a major pathway. Based on these actions, the fact that dehydrogenase or phosphatase activity data were not submitted does not invalidate the use of this study.

In a study by Ercegovich, Vallejo, and Bogus (1978), the effect of 5, 25, and 125 ppm concentrations of Metolachlor was evaluated on the soil function processes of nitrification in two soil types: Morrison sandy loam and Hagerstown silt loam. Morrison sandy loam did not show any inhibitory effects at any of the three concentrations evaluated. Hagerstown silt loam did not show any inhibitory effects at 5 or 25 ppm, but did show an inhibitory effect at 125 ppm. The rate of nitrification was inhibited for seven weeks, with a recovery starting at eight weeks and continuing until the end of the experiment (at ten weeks). Rates between the two soils varied considerably.

Though this latter study does not by itself fully explore the potential effects of Metolachlor on microbial functions (for example, effects on the degredation of cellulose, starch, and protein), it does support the data in Ercegovich, Bogus, and Buly (1978), and together these studies provide sufficient information about potential effects on naturally occurring microorganisms.

The activated sludge process used in wastewater treatment plants utilizes the metabolic degredation activity of certain microbes to break down raw sewage into a form acceptable for discharge in environmental waters. Because Metolachlor rinsate or irrigation mix may inadvertently make its way into municipal sewage systems, studies on its potential effects on wastewater treatment microorganisms is important. Not only may this cause unprocessed sewage to be released into the aquatic environment, but it may also impede the degradation of other toxics that are disposed of in sewer system drains.

Activated sludge metabolism data are not presently available for Metolachlor.

## Algae

*As aquatic plants utilizing light energy for photosynthesis, algae function as the primary aquatic producers of biomass upon which the higher levels of food chain are dependent. Inhibition of algal growth can reduce available biomass, while changes in algal size, content, or nutritive content can make it less accessible to higher-level feeders. The artificially stimulated growth of an algal population can suffocate a body of water by eutrophication. Information about the inhibition or stimulation of natural algal growth thus indicates the extent to which a chemical substance may interfere with such essential ecological functions as primary productivity, nitrogen fixation, oxygen production, and nutrient cycling in lakes, streams, estuaries, and oceans.*

*The atmospheric oxygen produced by marine algae is of course of direct importance to all animal life, including man. Algae are also a major source of food for zooplankton, which are fed upon by commercially and recreationally important fish and shellfish.*

Studies on Metolachlor's toxicity to algae are not presently available. But because residues of Metolachlor are expected to reach the freshwater aquatic environment, if such studies were available, they would be reviewed and assessed for information on potential effects to freshwater aquatic ecology.

## Aquatic Macrophytes

*Like algae, aquatic macrophytes transform light energy and simple molecules into biomass for consumers in the aquatic food chain. Decaying aquatic plants form a large part of fish and shellfish diets. Aquatic macrophytes also provide important microhabitats for aquatic organisms. Pesticides which can impair the growth of higher plants may shift relative populations of macrophytes and algal species, thus altering community composition, possibly upsetting habitat, food-chain, and productivity balances.*

*In addition to their contribution to aquatic microhabitats while alive and their contribution to the detritus food web upon decomposition, aquatic macrophytes may also participate in nutrient recycling. Aquatic plants which are rooted in aquatic sediment are particularly active in recycling nutrients from settled and decaying biomass and aquatic-bed minerals. These plants may unfortunately also face a greater exposure to pesticide residues sorbed to soil or organic matter, when this material enters bodies of water and settles to the bottom.*

Studies about Metolachlor's effect on aquatic plants are not available. But because residues of Metolachlor are expected to reach the freshwater aquatic environment, if such studies were available, they would be reviewed and assessed for information on potential effects to freshwater aquatic ecology.

## Terrestrial Plants

*One of the primary concerns of an Ecological Effects assessment, particularly for agricultural-use pesticides, is the toxicity of the chemical to non-target plants. This includes those plants within the pesticide application area which are subject to direct exposure, such as crop plants, as well as plants outside the target area which may be exposed to residues, such as adjacent crop plants, ornamentals, wildlife food and cover species, forests, and marshland plants. The potential risk to terrestrial plants is first an ecological threat, and secondly an economic threat.*

*The ecological impact of phytotoxicity ranges from soil disruptions to bioaccumulation. Because both roots and aerial plant parts contribute to soil structure and nutrient retention, toxic effects on terrestrial plants, either wild or cultivated, annual or perennial, may cause erosion, destabilizing terrestrial and aquatic ecosystems. Phytotoxic effects to forest vegetation can cause nutrient loss, the erosion of forest soils, and loss of wildlife habitat. Chemicals that do not visibly affect the normal growth, development, and reproduction of plants may, nevertheless, bioaccumulate to a degree that would cause hazard to primary or secondary consumers.*

*Phytotoxic effects of economic importance to man primarily concern the impaired growth of crop plants, and adverse effects to plants capable of nitrogen fixation, upon which crop plants depend. Diminished terrestrial*

*plant growth can sometimes lead to erosion into rivers and streams, which can in turn greatly diminish the useful life of dams, degrade the waters impounded by them and disable agricultural irrigation systems. If widespread, the inadvertent destruction of terrestrial plants can lead to the loss of forest and agricultural land by desertification.*

Studies on the ecological effects of Metolachlor on non-target terrestrial plants are not presently available. However, efficacy tests which examine the effects of an herbicide on protected crops can often supply sufficient information to conduct an ecological effects review of phytotoxicity. Nevertheless, in accordance with present Agency policy, which requires an efficacy review for pesticides only when the chemical's use has a direct impact on public health, efficacy data was not reviewed for the Metolachlor Standard.

## Soil and Surface Invertebrates

*Soil and surface invertebrates such as arthropods and earthworms play a number of important ecological roles, but are especially vital to the stability of the artificial ecosystems induced by agriculture.*

*In the natural environment, many species of mammals, birds, reptiles, and amphibians depend upon terrestrial invertebrates for their food supply, and their numbers may be adversely affected by reductions in invertebrate populations. The use of pesticides, especially insecticides, can subject non-target invertebrates to unnatural selection pressures and can create shifts in predator/prey relationships. Pesticide use may also result in a loss of insects important to flowering-plant pollination and soil aeration.*

*In an agricultural ecosystem, these effects may be manifested in the development of pesticide-resistant strains of insects, in a reduction in the number of parasitic and predaceous arthropods such as spiders, mites, and centipedes (which can exert a natural control over injurious insect populations), and in outbreaks of secondary pests. Likewise, pesticide use may result in a reduction in populations of earthworms, nematodes, insect larvae, and other organisms which are important in improving soil fertility through aeration and nutrient cycling. Finally, the use of certain pesticides may adversely affect such insects as honey bees, wild bees, silkworms, or lac insects, which perform functions directly useful to man.*

Studies concerning Metolachlor's effects on soil and surface invertebrates are not presently available. Though the Agency does not routinely require these data, because Metolachlor is applied to and mixed with the soil, if such studies were available, they would be reviewed and assessed for information on potential effects to terrestial invertebrates which affect the fertility of agricultural soil, and which keep potential insect pests in ecological check.

## Birds

*Both the ecological and economic importance of birds are partially dependent upon their functions as predators and prey. Birds may be exposed to pesticide chemicals by feeding on contaminated plants or animals, and by dermal contact and inhalation when in the proximity of outdoor sprays and dusts. A common route of exposure is the ingestion of contaminated water,*

*plants, seeds, invertebrates, fish, or rodents. Higher food chain carnivores, which include many endangered bird species, may be particularly susceptible to poisoning by pesticide chemicals which enter the environment at low concentrations but which are biomagnified through aquatic and terrestrial food chains. Also, birds themselves may bioaccumulate, and then pass on their stored residues to other predators. And as has been discovered in connection with certain now cancelled pesticides, chemicals that may be innocuous in terms of direct mortality may nevertheless threaten the survival of a bird population by impairing reproductive success.*

*Pesticide effects on birds as predators may have direct consequences for man. Insectivorous birds often help control insect populations which consume crops, while carnivorous birds such as owls help regulate rodent populations. In addition, birds are of aesthetic and recreational value, and many are considered to be significant food sources and popular targets for game.*

Data on the effects of single oral doses of Metolachlor to avian wildlife are reported by Fink (1976): the acute LD-50 for mallards (Anas platyrhynchos) was 4640 (3000-7200, 95% confidence limits) mg/kg, indicating that Metolachlor is practically non-toxic, acutely, to waterfowl. But due to deviations from recommended protocols, such as discrepancies in body weights, these data are unacceptable for use in the regulatory process. An avian single dose oral LC-50 determination is thus a data gap for Metolachlor.

However, acceptable data on the dietary LC-50 of Metolachlor for avian wildlife are reported on the mallard (Anas platyrhynchos) (Fink, 1974a), and the bobwhite quail (Colinus virginianus) (Fink, 1974b). The 5-day dietary LC-50 (with 3 days observation) for both species was greater than 10,000 ppm, indicating that Metolachlor is practically non-toxic, subacutely, to upland gamebirds and waterfowl.

Because, as was seen in the Environmental Fate chapter, Metolachlor is persistent under certain conditions and is stored in plant and rotational crop tissue, information on avian reproduction effects is needed. Avian reproduction studies are not presently available for Metolachlor, which constitutes a data gap.

## Amphibians and Reptiles

*As with birds, amphibians and reptiles can function as natural or introduced regulators of insect and rodent populations. Amphibians and reptiles most susceptible to pesticide residue exposure are those such as snakes, turtles, frogs, and lizards, which live near the shallow margins of streams and ponds, and those which live on the exposed surface of the ground. Shallow waters often collect residues from runoff without adequately diluting them, and some oil-based pesticides tend to concentrate at the water surface, where amphibians can be repeatedly exposed. Snakes which themselves feed on amphibians may be subject to poisoning by bioaccumulation.*

Studies concerning Metolachlor's potential effects on amphibians or reptiles are not presently available. Though the Agency does not routinely require these tests, because residues of Metolachlor are expected to reach the freshwater aquatic habitats of certain snakes, frogs, and lizards, if such studies were available, they would be reviewed and assessed for information on potential hazards to these species or to freshwater ecology.

## Wild Mammals

*Wild mammal food habits are extemely diverse, ranging from grazing on field plants to seed gathering to predation. Mammals such as ground squirrels, rabbits, racoons, bobcats, deer, and moose may be exposed to pesticide residues in food and forage as well as on plant surfaces. Occasionally such exposure may result in acute poisoning and death, though more commonly the hazard is chronic or indirect, due to such effects as a toxic bioaccumulation of residues, an increased susceptibility to capture by predators, lowered resistance to weather and disease, loss of food supply or inability to reach it, abandonment of habitat, bacterial upset in ruminants, or widespread population effects. For man, these effects can mean a loss of game, fur-bearing, and aesthetic resources.*

These data are not needed for Metolachlor because the data on laboratory animals reviewed in the Toxicology Chapter are generally sufficient for an estimation of toxicity to wild mammals. Based on the data in Metolachlor's Toxicology review, there do not appear to be any unusual hazards to wild mammals that arise with the use of the herbicide, and so no special precautions need be recommended.

## Aquatic Invertebrates

*Aquatic invertebrates, including crustaceans, zooplankton, and aquatic insect larvae, take a wide variety of forms in the aquatic environment, and occupy most of the vital niches of the food web. Many invertebrate species function as primary consumers, as predators and even as decomposers. In their role as primary consumers, herbivorous zooplankton consume phytoplankton which have converted solar energy into chemical energy.*

*Zooplankton are in turn consumed by higher animals and are thus the link between phytoplankton, the chemical energy base of aquatic ecosystems, and higher aquatic animals. Because invertebrates are so basic to ecosystem function, impacts on invertebrate populations can have major effects on the stability and viability of the aquatic ecosystem as a whole. The effects of pesticides on aquatic invertebrates is therefore a good indicator of the possibility of broader effects on the aquatic ecology.*

Data are available on the acute toxicity of Metolachlor in the water flea (Daphnia magna Straus) (Vilkas 1976). The 48-hour no-effect level was 5.6 ppm. The 48-hour LC-50 at 95% confidence limits is 25.1 (21.6-29.2) ppm. These data are sufficient to characterize Metolachlor as being slightly toxic to aquatic invertebrates, but less so than to fish. No precautionary labeling regarding aquatic invertebrates appears necessary.

## Fish

*Fish may be exposed to pesticide active ingredients or solvents by the migration of residues from terrestrial sites, by accumulation in the aquatic invertebrates they feed upon, by effluent discharge, or by direct pesticide*

*applications. Toxic effects to fish may include changes in behavior, physiology, and reproduction. Adult fish and fry are susceptible to poisoning by several routes of exposure, including ingestion, direct adsorption from water, and gill absorption. Fry are susceptible to poisoning by the absorption of a yolk sac carrying accumulated lipid soluble residues from the female's ovum. Because aquatic food chains have many links, and because fish at all levels tend to accumulate lipid soluble chemicals, some poisoning to fish and fish consumers may occur by bioaccumulation. As predators or grazers, fish aid in controlling the populations of organisms at lower trophic levels. As prey, they are crucial to the survival of various birds, terrestrial mammals, and other fish. The role of fish as predators, grazers, and prey can be significantly affected by pesticide poisoning. With ecological damage may come a threat to the economic uses of fish as food and recreational resources for man, either by population losses or through contamination.*

The acute toxicity of Metolachlor to fish is examined in two studies conducted by Buccafusco (1978), and in a study by Sachsse and Ullman (1974).

Cold-Water Fishes

Due to various deviations from the proposed recommended protocol, the data by Sachsse and Ullman are not adequate for regulatory use in establishing a 96-hour LC-50 to rainbow trout. Buccafusco (1978b) demonstrated a 96-hour LC-50 at 95% confidence limits of 3.9 (3.3-4.6) ppm. The acceptable rainbow trout study indicates that Metolachlor is moderately toxic to cold water fish.

Warm Water Fishes

Sachsse and Ullman tested four species of warm water fish to determine their respective 96-hour LC-50's for Metolachlor.

| Species | 96-Hour LC-50 (ppm) | 95% Confidence Limits |
|---|---|---|
| Crucian Carp (Carassius carasius) | 4.9 | 3.6 - 6.8 |
| Channel Catfish (Ictaluris punctatus) | 4.9 | 3.6 - 6.8 |
| Bluegill (Lepomis macrochirus) | 15.0 | --- |
| Guppy (Lebistes reticulatus) | 8.6 | 7.4 - 10.5 |

Buccafusco (1978a) derived a bluegill 96-hour LC-50 at 95% confidence limits of 10 (8.6-12) ppm. The acute LC-50 data from both studies are adequate to establish that Metolachlor is moderately toxic to warm water fish.

On the basis of available acute toxicity information, no precautionary labeling regarding hazards to fish appears necessary. But as was seen in the Environmental Fate chapter, Metolachlor is resistant to hydrolysis and metabolism in soil, and has a tendency to leach. Because of this significant potential for residues to migrate to freshwater aquatic habitats, a chronic fish study was recommended, and is currently underway, though it was initiated prior to a satisfactory "state of the art" success with the fish embryolarvae bioassay.

## Estuarine and Marine Organisms

*Marine and estuarine organisms, including clams, oysters, shrimp, crabs, seals, and gulls, have well-recognized economic and recreational importance, but also serve essential functions in coastal habitats. Coastal organisms are adapted to constantly changing climatic and tidal conditions. In the coastal food chain, clams, oysters, and other shellfish are filter feeders that extract nutrients and plankton from water passed through their gills. Crabs may feed on small fish and marine invertebrates. Fish, birds, and crabs search out the soft immature forms of oysters and clams. Seals and other marine mammals feed upon fish and invertebrates. And various marine invertebrates break down wastes from these higher organisms.*

*Coastal marine and estuarine organisms also protect themselves and each other against turbulence in tide or weather by physical modifications of the environment. Oyster beds are formed because the soft immature forms of these animals need the hard surface offered by the adults before they can mature. The calcareous secretions of many coastal invertebrates are also known to build up rock-like barriers which protect other organisms from extremes of weather.*

*The introduction of pesticide chemicals into the coastal or estuarine environment from terrestrial residue runoff and drift, direct discharge, waste disposal, or industrial spills, can have an adverse effect upon any of these organisms and their ecological functions. Filter feeders may filter out residues, while birds and seals may be indirectly exposed by the ingestion of other contaminated organisms.*

Data on Metolachlor's impact on estuarine and marine organisms are not presently available, and need not be provided, considering its present and proposed uses, which provide for application primarily in inland regions, and not near coastal or estuarine waters.

## Nonbiological Components of the Environment

*Studies of ecological effects must also focus on the non-living components of the environment. The abiotic portion of the natural biosphere can be divided into the solid earth or lithosphere, liquid water or hydrosphere, and the atmosphere.*

*Bodies or currents of water can be contaminated by spill, runoff, or direct discharge, rendering them toxic to man, plants, animals, or microorganisms. An ecosystem's water phase can also be modified by the presence of a foreign chemical so as to alter water's unique ecologically important properties, such as its viscosity, its thermal properties, its latent heat of evaporation or fusion, its properties as a solvent, or its surface tension.*

*An ecosystem can also be threatened by pesticide chemicals affecting sediments and soils. This can occur by the reaction of chemicals with minerals and nutrients, by reactions that inhibit the normal weathering of rocks, by effects on the lichens that help break rock down into soils, and by chemical effects upon the permeability and absorption potential of soils.*

*The troposphere is the segment of the earth's atmosphere upon which living organisms most depend, for it is the medium of our weather, the medium in which animals or microorganisms fly or float, and the medium which supplies life with its gaseous nutrients. The presence of certain chemicals in*

*significant concentrations could conceivably have an impact upon any of these functions. But the higher strata of the atmosphere also has certain features which, if altered by chemical reaction, could adversely affect the ecosystem. For instance, the ozone layer is of vital importance because its absorption of ultraviolet radiation prevents the latter from reaching the surface of the earth, where it would be lethal to most living organisms.*

Though the Agency does not routinely require information about the effects of a pesticide information on the nonbiological components of the environment, such information may be available in the open literature or through research involving the non-pesticidal aspects of the chemical. No such data were found in the world-wide literature search for Metolachlor.

## Ecosystem Effects

*An understanding of how the presence of a pesticide chemical may affect the operation of natural ecosystems often requires a systemic approach, in which the emphasis is placed on the way in which the various components of the ecosystem operate together as a unit. An alteration produced in any part of the ecosystem may have repercussions throughout the entire system as it responds and adapts to the change.*

*Several methods have been devised to create experimental 'microcosms', or assemblages of organisms and abiotic components that approximate a particular ecosystem. One method is to take into the laboratory a small functional segment of a natural setting, such as a soil core with its natural stratification preserved, or a sample of pond water, including some of the bottom sediment and macroorganisms. Another method would recreate simple food chains under controlled and monitorable conditions. But because microcosms are isolated, they are subject to a restricted capacity for the exchange of energy and materials, and therefore cannot consistently model the behavior of actual ecosystems.*

*Another approach to the study of ecosystem effects involves the monitoring of a measured test substance applied to an actual field site, and the correlation of the presence of the substance with observations of organism toxicity, reproductive success, predator/prey relationships, competition for food and habitat, symbioses, community diversity, and biogeochemical cycling. Observations of animal behavior can indicate ecological perturbations that may otherwise remain hidden. Many species of invertebrates, birds, mammals, and fish possess highly formalized behavioral repertoires. Changes in feeding, defense, mating, grooming, and nest building can disrupt the life-cycles of individual species, but may also indicate the need for a more detailed assessment of the effects of sublethal concentrations.*

*A third approach to the study of ecosystem functions and reactions is the development of computer models that mathematically simulate energy and material flows and exchanges. Though such models study environmental manipulations through many generations or seasonal cycles without additional risk or expense, the effects observed can only occur along the parameters and functions already anticipated by the programmer.*

No data on ecosystem effects are presently available for Metolachlor, though the results of ecological effects studies yet to be performed may later suggest the need for field tests under actual use conditions.

DISCIPLINARY REVIEW

Ecological Effects Profile
Ecological Effects Hazard Assessment
Generic Data Gaps
Suggested Labeling

## Ecological Effects Profile

Technical Metolachlor: The available studies suggest that Technical Metolachlor's toxicity to microbes and acute toxicity to certain species of wildlife is relatively mild. Of the organisms tested, only fish appear susceptible to adverse effects.

A diverse selection of soil microorganisms were evaluated against three concentrations of Metolachlor: 5, 25, and 150 ppm. Only static, not cidal, effects were noted (Ercegovich, Bogus, and Buly, 1978). Another study using the same concentrations showed no effects on nitrification at the two lower levels, and only temporary inhibition at the high level (Ercegovich, Vallejo, and Bogus, 1978). Effects on wastewater treatment microorganisms has not yet been investigated.

The toxicity of Technical Metolachlor to birds was shown to be low in one dietary LC-50 test, though adequate data were not available to determine single-dose toxicity nor reproductive effects. Based on the data reviewed in the Toxicology Chapter, Metolachlor appears to present a low toxicity to wild mammals. Metolachlor is slightly toxic to aquatic invertebrates, but less so than to fish. Both cold water and warm water fishes showed moderate toxic effects, and a chronic fish study is forthcoming.

Emulsifiable Concentrate Metolachlor: Because wildlife is not expected to sustain significant direct exposure to the Emulsifiable Concentrate, but only occasional exposures to residues of the active ingredient or its degradation products and metabolites, information on the toxicity of the Emulsifiable Concentrate to non-target wildlife organisms is effectively supplied by the studies on the Technical chemical.

## Ecological Effects Hazard Assessment

Technical Metolachlor: For wildlife in the proximity of Technical Metolachlor manufacture, storage, shipping, or disposal, intentional discharges of the chemical into the environment, such as by the disposal or drainage of effluent, as well as unintentional discharges, such as by spillage or fire, could result in significant wildlife exposures. Because of the stability of Metolachlor to hydrolysis and its potential resistance to metabolic degredation, and because of the moderate sensitivity of fish to Metolachlor poisoning, the hazard to fish is the most serious in this regard. Considering Metolachlor's potential for rotational uptake, a secondary exposure could conceivably result for herbivores in areas

proximate to the aquatic habitats contaminated with effluent, but the studies in the Toxicology chapter suggest that acute effects from such small exposures would be highly unlikely.

Ecological Effects data are available to EPA officials responsible for issuing a discharge permit should one become necessary.

Emulsifiable Concentrate: According to Metolachlor's common use patterns, certain non-target terrestrial and aquatic organisms in midwestern agricultural regions may be expected to encounter finite residues, between April and June of each year, from the pre-planting or pre-emergent application of E.C. Metolachlor (USDA #283, 1972).

We will consider first the hazard to aquatic organisms. As was discussed in the Fate Profile of the Environmental Fate chapter, assuming field application and climatic conditions result in a loss of 2.5% of Metolachlor applied at the maximum rate of 3 lbs. ai/acre, each acre of treated field would contribute 0.075 lbs. to an adjacent aquatic site. This amount of active ingredient in an acre foot of water would yield Metolachlor residues of .055 ppm in 6 inches of water and .0176 ppm in 12 inches of water. The lowest LC-50 to aquatic organisms was 3.9 ppm to rainbow trout; therefore, each treated acre within a watershed potentially contributes 1/70 of the LC-50 to an adjacent aquatic site which remains at an area of 1 acre and a depth of six inches of water regardless of the amount of runoff in one incident. Because 0.075 lbs ai. in a 6 inches acre of water is less than 1/10 the LC-50, E.C. Metolachlor is not considered an acute hazard to aquatic organisms which requires any restriction of use.

However, the persistence of Metolachlor in water will vary principally with microbial activity, as the compound has a hydrolysis half life of 200 days at 20°C and photodegredation rate of less than 10% in 30 days. Metolachlor's potential for persistence suggests the need for a chronic aquatic organism study (Criteria and Rationale for Decision making in Aquatic Hazard Evaluation, 1978), and indeed, as has been mentioned, a chronic fish study is presently underway.

The wildlife hazard assessment could also benefit from more precise information on Metolachlor's persistence in the aquatic environment. First, should the estimated environmental concentration residues levels due to a particular use pattern be equal to or exceed 1/10 of the 'no effect level' in the chronic study, aquatic field monitoring would be necessary to determine if the use pattern was acceptable. Secondly, there are approximately 40 species of fish within the 48 continental States listed as Federal Endangered Species. The future intent of EPA (in conjunction with USDI) will be to determine if any of these species are potentially exposed to residues of at least 1/10 the LC-10 of rainbow trout. The LC-10 value for Metolachlor is 2.6 ppm (Buccafusco, 1978b). Therefore, the critical residue level would be 0.26 ppm. Theoretically, an endangered species in an acre foot of water, receiving runoff from five acres of Metolachlor-treated land, could receive this amount of residue, resulting in a potentially hazardous condition.

Other non-target organisms of potential concern include microbes, plants, soil and surface invertebrates, mammals, amphibians and reptiles, and birds. Soil microbes and the nitrification process do not appear to be threatened. Despite the resistance of Metolachlor to hydrolysis and metabolism, and the possibility of plant uptake with later ingestion by herbivores, the application of E.C. Metolachlor should pose no, or at

most a highly unlikely, acute hazard to mammalian wildlife. Data are presently unavailable on toxicity to non-target plants themselves, to soil and surface invertebrates, and to amphibians and reptiles. As concerns the potential hazard to birds, taking into account E.C. Metolachlor's acceptable uses, its environmental fate, its metabolism, its persistence in soil under certain conditions, and its uptake by rotational crops, a long-term exposure of birds to finite levels of Metolachlor is expected. Yet considering Metolachlor's low dietary toxicity to birds, the acute hazard to birds is minimal, though the long-term effect of Metolachlor-use on avian wildlife cannot be determined until an acceptable avian reproduction study has been submitted and reviewed.

In conclusion, the most serious wildlife concern for Metolachlor was with aquatic organisms, and it is determined that presently registered use patterns of Emulsifiable Concentrate Metolachlor do not appear to pose an acute hazard to non-endangered aquatic species. Further investigation will be required to determine if target fields located in drainage basins, bordering streams inhabited by endangered aquatic species, should be prohibited from being treated with Metolachlor at any application rate. Finally, Metolachlor's quantified potential for persistence in the aquatic environment, and for causing chronic effects to aquatic organisms, have yet to be determined.

## Generic Data Gaps

The following are gaps in the Ecological Effects data base needed to adequately support a Registration Standard for Metolachlor. After each gap is listed the section in the Proposed Guidelines of July 10, 1978 (40 CFR Part 163) which describes that type of test and when it is required. The following studies would test the Technical in order to assess the hazard associated with the use of the Emulsifiable Concentrates.

For Technical Metolachlor:

| | | |
|---|---|---|
| 1) | Activated sludge metabolism study. | 163.62-8(g) |
| 2) | The avian acute oral LD-50 for one species of waterfowl (preferably the mallard) or one species of upland game bird (preferably the bobwhite, other native quail, or the ring-necked pheasant). | 163.71-1 |
| 3) | Avian reproduction studies on bobwhite quail and mallard ducks. | 163.71-4 |
| 4) | A freshwater fish (fathead minnow, preferably) life-cycle test. | 163.72-4 |

For Emulsifiable Concentrate Metolachlor (8 lbs./gallon or less): none

Suggested Labeling

In order to reduce the risk of the chemical reaching aquatic sites when an effluent occurs during the manufacturing of Metolachlor, or when Metolachlor is applied in the field, the following precautionary labeling is required:

For Technical Metolachlor:

"Do not discharge into lakes, streams, ponds, or public waters unless in accordance with an NPDES permit. For guidance, contact your Regional Office of the EPA."

For Emulsifiable Concentrate Metolachlor:

"Avoid direct application to any body of water. Do not apply where runoff is likely to occur. Do not contaminate water by cleaning of equipment or disposal of wastes. Do not apply when weather conditions favor drift from target area."

## BIBLIOGRAPHY
(Reserved)

*In order for the provisions of FIFRA concerning data compensation (Section 3(c)(1)(d)) to be effective under Registration Standards, data used in direct support of the Standard for each type of product must be accurately listed, enabling applicants and their arbitrators to determine what data do and do not support the registrations of individual pesticide products. Thus, for each disciplinary chapter, studies used to evaluate hazard and establish Standards for the manufacturing-use chemical and for each type of end-use formulation will be listed separately.*

To protect present and potential applicants for the registration or re-registration of products containing Metolachlor, the citations appropriate to each disciplinary chapter will not be published in this Sample Standard, though a complete Bibliography is provided at the end of the document.

## REGULATORY RATIONALE

*The purpose of the 'Regulatory Rationale' is to summarize the salient factors supporting the Agency's regulatory decisions, and to show how the regulatory position is logically derived from the evaluation of hazard in the Disciplinary Chapters. Because a manufacturing-use pesticide product presents different hazards from an end-use pesticide product, and because different types of end-use products can themselves present different hazards, each will have its own 'regulatory rationale'. The discussions are further divided between hazards to man and hazards to wildlife. The goal of each discussion is to determine how hazards may be lessened, mitigated, or prevented by regulatory actions which are appropriate to the severity of the problem and which preserve, to the greatest extent possible, the efficacy and benefits of the pesticide.*

### TECHNICAL METOLACHLOR

The only risks used to determine the conditions of a technical chemical's registerability are those which arise in the production, packaging, shipping, handling, re-formulating, and disposing of the chemical - that is, in the various aspects of its manufacture as a pesticide active ingredient.

Technical Metolachlor, at least ninety-five percent the pure compound, is an off-white, odorless liquid, soluble in water, and miscible with several organic solvents.

#### The Mitigation of Hazards to Humans

Technical Metolachlor's acute toxicity to humans appears to be mild: it has a low acute oral toxicity, it is not readily absorbed by the skin, it has a very low inhalation toxicity, and no eye irritation effects are observable. The only significant acute effect is skin sensitization. Once an exposure occurs, Metolachlor is rapidly absorbed, metabolized, and excreted. Though the available oncogenicity and chronic feeding studies were not adequate for a complete evaluation of these effects in humans, the long-term tests that were available showed no evidence of teratogenic, fetotoxic, reproductive, or mutagenic effects.

For persons involved in the manufacture, handling, storage, or shipment of Technical Metolachlor, there is little likelihood of oral exposure, and because of the low vapor pressure of the viscous liquid, there is also little chance of inhalation exposure. The most likely human exposure is a repeated dermal exposure, and occasionally, by accident, an occular exposure.

Though there is presently no evidence of teratogenic, fetotoxic, reproductive, or mutagenic effects due to Metolachlor, the chronic hazard to humans caused by repeated dermal exposure to a Technical Metolachlor solution cannot be concluded, for lack of sufficient chronic studies. Available studies do indicate a potential dermal sensitization problem for factory, transport, or re-formulation workers.

Two regulatory actions are available for helping to preclude repeated dermal exposures: a label warning to "Wear protective clothing while handling or using this product"; and a registration requirement for manufacturers that calls for the documentation of the lack of dermal exposures in manufacturing facilities or the monitoring and submission of skin sensitization data from such exposure.

For a Technical Metolachlor with a 'Category IV' toxicity by oral, dermal, and inhalation routes, and a 'Category IV' rating with regard to eye irritation, the label need only bear the following precautions: "CAUTION", followed by "Keep out of reach of children", "Harmful if swallowed", and the first-aid statement, "If swallowed, induce vomiting. Flush exposed eyes and skin with water."

The Mitigation of Hazards to Wildlife

The available wildlife studies suggested similarly mild ecological hazards. The toxicity of Technical Metolachlor to birds was shown to be low in one dietary LC-50 test, though adequate data were not available to determine single-dose toxicity nor reproductive effects. The data used to evaluate human acute toxicity were sufficient to indicate a low acute toxicity to wild mammals. Though the chronic fish study has not yet been completed, Technical Metolachlor was shown to have a moderate acute toxicity to cold and warm water fishes, and a somewhat lower acute toxicity to aquatic invertebrates.

For wildlife in the proximity of Technical Metolachlor manufacture, storage, shipping, or disposal, intentional discharges of the chemical into the environment, such as by disposal or drainage, as well as unintentional discharges, such as by spillage or fire, could result in significant wildlife exposures. The pathway of exposure which is the most direct concern is the discharge of effluent into freshwater aquatic habitats. The organisms most susceptible to exposure by route of freshwater aquatic discharge are fish, amphibians, and, because of plant uptake, certain local mammalian herbivores.

The stability of the Metolachlor compound to hydrolysis and its potential resistance to metabolic degredation, together with its moderate toxicity to both cold and warm water fishes, indicates a potential hazard to fish, if the Technical chemical or effluent from its manufacture were disposed of, spilled, or allowed to drain into freshwater aquatic habitats. Toxicity to mammals is low enough that an occasional exposure for mammalian herbivores is not of concern. Toxicity to amphibians is not known, and testing on amphibians and reptiles is not usually required. Though the required long-term studies on fish and birds, and the acute oral test for waterfowl, may later disclose a greater wildlife sensitivity to exposure, in the meantime, the label for Technical Metolachlor should bear the precaution: "Do not discharge into lakes, streams, ponds, or public waters unless in accordance with NPDES permit. For guidance, contact your Regional Office of EPA."

EMULSIFIABLE CONCENTRATES of METOLACHLOR

The only formulations of Metolachlor which are registered, and which therefore provide the standards of formulation for this chemical, are two Emulsifiable Concentrates: one formulated with six pounds active ingredient per gallon; and the other with eight pounds per gallon. Thus this Standard will cover all Emulsifiable Concentrates with eight pounds per gallon or less of the active ingredient. The currently registered products are in the form of viscous liquids of neutral pH. The more concentrated formulation is more viscous and slightly corrosive to steel and tin.

The Mitigation of Hazards to Humans

The Emulsifiable Concentrate formulations with eight pounds active ingredient per gallon have the potential for relatively serious acute

effects. Though they would not be readily absorbed through human skin, they could produce severe irritation and burns on contact, and like the active ingredient, may produce skin sensitization with repeated exposures. The formulations also have a moderate inhalation toxicity, and can cause serious eye irritation, including irreversible corneal opacity.

Though all chemical products present some possibility of accidental ingestion, for persons involved in the dilution, mixing, and application of Metolachlor formulations, there is little chance of oral exposure. But there is a significant possibility of dermal and eye exposure from the splashing that may occur while diluting and tank mixing, and in the loading of spray equipment. Due to the Emulsifiable Concentrate's high vapor pressure, an unprotected mixer or diluter who is handling an open container without adequate ventilation will be subject to fumes. Of greater concern is that the spray droplets generated by the application of end-use Metolachlor may result in an inhalation exposure for applicators and other agricultural workers who may be in the proximity of the spraying. Chronic dietary exposures for the general population, due to residues on food (and in feed given to livestock subsequently consumed by humans), are expected to occur at finite levels determined by the temporary tolerances.

Though there is presently no evidence of teratogenic, fetotoxic, reproductive, or mutagenic effects due to Metolachlor, chronic hazards to humans cannot be determined until further studies on the chronic effects of Metolachlor are completed. But we can presently conclude that there are acute hazards involved in the end-use of Emulsifiable Concentrate formulations of eight pounds or less active ingredient per gallon. The acute hazards to humans caused by the pre-application handling of these Emulsifiable Concentrate formulations consist primarily in the potential for skin and eye burns from accidental splashing, the potential for skin sensitization from repeated dermal contact, and the danger of fume inhalation from mixing or loading in a closed area. All of these 'risks' are routine safety considerations that arise in the mixing and loading of many an agricultural chemical, and do not suggest that Metolachlor is an unusually hazardous one, but only that common safety practices are in order. The greatest risk arising from the actual application of these formulations is the potential for toxic effects from the inhalation of spray droplets, and this too is a 'risk' that with proper safety precautions would be unlikely to occur.

There are several general label requirements that are routinely imposed to help ensure proper safety practices and thereby reduce the acute end-use risks of agricultural pesticides. To 'Keep out of reach of children' is the most effective prevention of accidental poisonings from ingestion. Certain signal words, such as 'Danger', 'Warning', and 'Caution', when used to reflect the level of a chemical's toxicity, can incite the user of a chemical product to follow written intructions more precisely so as to avoid accidental exposures. When accidental exposures do occur, their effects can often be diminished with appropriate first aid. In the case of E.C. Metolachlor, the first aid statement should instruct: 'If swallowed, promptly drink egg white or gelatin solutions; or if these are not available, water. Call a physician immediately. Do not induce emesis as a chemical pneumonitis may occur if aspirated.'

Other more specific label requirements, with stronger warnings for the more toxic formulations, are available to modify the user's behavior and thereby reduce the risks by particular routes of exposure: 'Harmful if swallowed' for oral exposure; 'Avoid contact with skin', 'Causes skin irritation', and/or 'May cause skin sensitization. Wear protective clothing when handling this product' for dermal exposure; 'Do

not breathe vapors' or 'Avoid breathing vapors' and 'Do not apply when weather conditions favor drift from target area' for inhalation exposure; 'Corrosive, causes eye damage. Wear goggles or face shield when handling', 'Causes eye irritation', or 'Avoid contact with eyes' for occular exposure. Emulsifiable Concentrates with acute hazards equivalent to or less than those set out by this Standard, as determined by the toxicity categories into which they fall, can generally be made safer for use by means of the appropriate statements of precaution, as set forth in the Agency's regulations on labeling (40 CFR 162.10).

Until more chronic data become available for the assessment of the hazards of a dietary exposure to Metolachlor, the temporary tolerances granted for Metolachlor will not be re-assessed. Because there are presently no tolerances for Metolachlor on them, corn forage or fodder or soybean hay or forage treated with Metolachlor should not be grazed or fed to livestock or used for silage.

The Mitigation of Hazards to Wildlife

The potential hazards to wildlife posed by the use of the Emulsifiable Concentrates arise from the toxicity of the active ingredient rather than the toxicity of any particular formulation, and the toxicity of the active ingredient is approximated in the toxicity studies on the Technical. To repeat the results of those studies: the toxicity of Technical Metolachlor to birds was shown to be low in one dietary LC-50 test, but adequate data were not available to determine single-dose toxicity nor reproductive effects. The data used to evaluate human acute toxicity were sufficient to indicate a low acute toxicity to wild mammals. Though the chronic fish study has not yet been completed, Technical Metolachlor was shown to have a moderate acute toxicity to cold and warm water fishes, and a somewhat lower acute toxicity to aquatic invertebrates.

As was discussed in the Ecological Effects Hazard Assessment, the 0.075 lbs. active ingredient that would collect in a 6 inches acre of water as a result of a normal application rate of 3 lbs. ai/acre would not pose an acute hazard to aquatic organisms. However, until the results of the chronic fish study are in, to reduce the chance of harm to an Endangered Species of freshwater fish, to help protect untested species such as amphibians and local herbivores, and to ensure that sludge treatment microbes are not affected, every effort should be made to keep the compound out of the natural aquatic environment and the sewer system, and the following label restrictions are recommended: "Avoid direct application to any body of water. Do not apply where runoff is likely to occur. Do not contaminate water by cleaning of equipment or disposal of wastes." To help protect other organisms which still require testing, particularly birds, from potential harmful exposures, the following additional label statement is recommended: "Do not apply when weather conditions favor drift from target area."

## REGULATORY POSITION

*The 'Regulatory Position' represents the Agency's final decision on how to best mitigate the hazards to humans and the environment which may arise as the result of the proposed uses of the pesticide chemical. It is based on the full consideration of all the available hazard information as presented in the Disciplinary Chapters, on the means for hazard mitigation discussed in the Regulatory Rationale, and on the public comments received in the course of the development of the Standard. The 'Position' may be expected to comply with the rules and regulations (40 CFR Parts 162.10 and 162.11) used to implement the Federal Insecticide, Fungicide, and Rodenticide Act, and with the Agency's present regulatory policies. The 'Regulatory Position' is a primary output of the 'standard-setting' function of a Registration Standard in that it represents the 'standards' of packaging, labeling, and usage which help to ensure the safe use of the pesticide chemical.*

*A separate position is reached for the manufacturing-use chemical and for each type of end-use formulation which presents a significantly different set of hazards.*

### Technical Metolachlor

Section 162.11(a) of the Regulations states that the Agency shall presume against the registration of a pesticide product which meets or exceeds certain specific risk criteria set forth therein. Because the available data do not indicate that any of these risk criteria have been met or exceeded for Technical Metolachlor, the Agency shall presume that the Technical Metolachlor described in this Standard is conditionally registerable for sale, distribution, and reformulation in the United States.

The following 'Sample Label' includes all those labeling statements which the Agency has determined will provide an adequate mitigation of those hazards to man and the environment which may result from the manufacture, packaging, transport, handling, reformulation, storage, or disposal of Technical Metolachlor.

PRODUCT NAME
For Formulation of Herbicides Only

Active Ingredient:
Metolachlor: 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide .....%
Inert Ingredients: .....%
Total: 100%

CAUTION
Keep Out of Reach of Children

PRECAUTIONARY STATEMENTS:

Hazards to Humans and Domestic Animals

Harmful if swallowed. May cause skin sensitization. Wear protective clothing (coveralls and gloves) while handling and using this product. If swallowed, induce vomiting. Flush exposed eyes and skin with water.

Hazards to Wildlife

Do not discharge into lakes, streams, ponds, or public waters unless in accordance with an NPDES permit. For guidance, contact your regional office of EPA.

Directions for Use

It is a violation of federal law to use this product in a manner inconsistent with its labeling. Refer to technical bulletin.

Storage and Disposal

For bulk shipments - holding tanks, tank cars, storage tanks, etc.:
Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited. Pesticide or rinsate that cannot be used or chemically re-processed should be disposed of in a landfill approved for pesticides or buried in a safe place away from water supplies. Thoroughly clean container before re-use. Consult federal, state, or local disposal authorities for approved alternative measures.

For metal drums, cans, etc.:
Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited. Pesticide or rinsate that cannot be used or chemically re-processed should be disposed of in a landfill approved for pesticides or buried in a safe place away from water supplies. Re-seal container and offer for re-conditioning; or triple rinse (or equivalent) and offer for recycling, re-conditioning, or disposal in approved landfill; or bury in a safe place. Consult federal, state, or local disposal authorities for approved alternative procedures.

Note to Formulators: formulators are responsible for providing data to support the registration of products formulated from this Technical.

EPA Registration No. _____ Net Wt. or Measure _____
Establishment No. _____
Name and Address of the producer, registrant, or person for whom produced.

Emulsifiable Concentrates of Metolachlor

(In order to be registerable under this Registration Standard, an end-use pesticide product containing Metolachlor must contain Metolachlor as the sole pesticide active ingredient. End-use products containing other pesticide active ingredients in addition to Metolachlor must be registered under a separate Registration Standard that covers the mixture. A Standard on a mixture of active ingredients will not routinely be set until the Agency has completed a Registration Standard for each of the active ingredients alone.)

Section 162.11(a) of the Regulations states that the Agency shall presume against the registration of a pesticide product which meets or exceeds certain specific risk criteria set forth therein. Because the available data do not indicate that any of these risk criteria have been met or exceeded for the proposed uses of Emulsifiable Concentrate Metolachlor of eight pounds per gallon or less, the Agency shall presume that the Emulsifiable Concentrates of Metolachlor described in this Standard are conditionally registerable for sale, distribution, and use in the United States.

Section 162.11(c) of the Regulations states that the Agency may classify for 'general use', that is, for use by any member of the general public, any end-use pesticide product which meets certain specific criteria set forth therein. An end-use pesticide product which does not meet all these criteria is considered a candidate for 'restricted use', that is, for use only by certified applicators. Because the available data adequately demonstrate that these criteria have been met for the Emulsifiable Concentrates of Metolachlor of eight pounds per gallon or less, the Agency shall conditionally classify for 'general use' the Emulsifiable Concentrates of Metolachlor described in this Standard.

The following two 'Sample Labels' are for Emulsifiable Concentrates of Metolachlor: the first 'Sample Label' is for an Emulsifiable Concentrate Metolachlor of six pounds per gallon, and the second is for one of eight pounds per gallon. These 'Sample Labels' include all those statements which the Agency has determined will provide an adequate mitigation of those hazards to man and the environment which may result from the packaging, handling, transport, application, storage, or disposal of the currently registered formulations, as investigated in the disciplinary chapters.

In order to be registered under this Standard, an Emulsifible Concentrate of eight pounds or less Metolachlor per gallon must be shown to have acute hazards which fall in the same or numerically higher toxicity categories (see the chart in 40 CFR 162.10) than those identified in the Toxicology chapter, and equivalent or lesser wildlife hazards than those identified in the Ecological Effects chapter. Thus, no end-use Emulsifiable Concentrate Metolachlor product may be registered under this Standard if its toxicity to humans or wildlife requires more stringent precautions than those appearing in either of the 'Sample Labels' that follow. Or in other words, the following 'Sample Labels' contain, between them, the most stringent precautions that will be needed for any end-use product registerable under this Standard.

PRODUCT NAME

PRODUCT NAME contains 6 lbs.
active ingredient per gallon

For weed control in soybeans
and in corn grown for grain (excluding popcorn)

| | | |
|---|---|---|
| Active Ingredient: | | |
| Metolachlor: | 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide | 68.5 % |
| Inert Ingredients: | | 31.5 % |
| Total: | | 100 % |

DANGER
Keep Out of Reach of Children
See additional danger statements on ____ side of container.

PRECAUTIONARY STATEMENTS:

Hazards to Humans and Domestic Animals

Corrosive - causes eye damage. Wear goggles or face shield when handling. Do not get on clothing. Harmful if swallowed. The active ingredient, metolachlor, may cause skin sensitization reactions in certain individuals. Wear protective clothing when handling, and wash thoroughly after handling. Avoid contamination of food. Remove and wash contaminated clothing before re-use.

FIRST AID: In case of contact with eyes, immediately flush with plenty of water for at least 15 minutes. Call a physician. If inhalation occurs, the victim should be moved to fresh air, and medical attention should be immediately sought. If swallowed, promptly drink egg white or gelatin solutions; or if these are not available, water. Call a physician immediately. (Note to physician: if swallowed, there is no specific antidote. Do not induce emesis as a chemical pneumonitis may occur if aspirated. Lavage stomach. Deposit 50 grams of activated charcoal in a water slurry in the stomach. Give a saline laxative and supportive therapy as needed.)

Hazards to Wildlife

Avoid direct application to any body of water. Do not apply where runoff is likely to occur. Do not contaminate water by cleaning of equipment or disposal of wastes. Do not apply when weather conditions favor drift from target area.

Physical/Chemical Hazards

Do not use or store near heat or open flame.

(sample label continued)

(sample label continued)

## Directions for Use

PRODUCT NAME (6 lbs. ai/gal.) is a selective herbicide recommended as a preplant incorporated or preemergence surface-applied treatment for control of most annual grasses and certain broadleaf weeds.

Corn: Use only on corn grown for grain. Do not use on sweet corn or popcorn. Do not graze or feed forage and fodder to livestock or use for silage.

Soybeans: Do not graze or feed soybean hay or forage.

It is a violation of federal law to use this product in a manner inconsistent with its labeling.

## Rotational Crops

1) If corn treated with PRODUCT NAME (6 lbs. ai/gal.) is lost due to poor germination, hail, flood, insects, etc., corn may be replanted immediately. Do not make a second broadcast application. If the original application was banded and the second crop is planted in the untreated row middles, a second band treatment may be applied. 2) Do not plant rotational crops other than corn or soybeans within 18 months after application.

## Storage and Disposal

Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited. Pesticide, spray mixture, or rinsate that cannot be used or chemically reprocessed should be disposed of in a landfill approved for pesticides or buried in a safe place away from water supplies. Triple rinse (or equivalent) empty containers, re-seal, and offer for recycling, re-conditioning, or disposal in an approved landfill or bury in a safe place. Consult federal, state, or local disposal authorities for approved alternative procedures.

EPA Registration No. _____ Net Wt. or Measure _____

Establishment No. _____

Name and Address of the producer, registrant, or person for whom produced.

PRODUCT NAME

PRODUCT NAME contains 8 lbs.
active ingredient per gallon.

For weed control in soybeans
and in corn grown for grain (excluding popcorn)

| | |
|---|---|
| Active Ingredient: | |
| Metolachlor: 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide | 86.4 % |
| Inert Ingredients: | 13.6 % |
| Total: | 100 % |

W A R N I N G
Keep Out of Reach of Children
See additional danger statements on ____ side of container.

PRECAUTIONARY STATEMENTS:

Hazards to Humans and Domestic Animals

Causes eye irritation. Do not get in eyes or on clothing. Causes skin irritation. Wear gloves and protective clothing when handling. Harmful if swallowed. Do not breathe vapors. The active ingredient, metolachlor, may cause skin sensitization in certain individuals. Wash thoroughly after handling. Avoid contamination of food. Remove and wash contaminated clothing before re-use.

FIRST AID: In case of contact with eyes, immediately flush with plenty of water for at least 15 minutes. Call a physician. If inhalation occurs, the victim should be moved to fresh air, and medical attention should be immediately sought. If swallowed, promptly drink egg white or gelatin solutions; or if these are not available, water. Call a physician immediately. (Note to Physician: If swallowed, there is no specific antidote. Do not induce emesis as a chemical pneumonitis may occur if aspirated. Lavage stomach. Deposit 50 grams of activated charcoal in a water slurry in the stomach. Give a saline laxative and supportive therapy as needed.)

Hazards to Wildlife

Avoid direct application to any body of water. Do not apply where runoff is likely to occur. Do not contaminate water by cleaning of equipment or disposal of wastes. Do not apply when weather conditions favor drift from target area.

Physical/Chemical Hazards

Do not place in unlined metal containers or tanks.

(sample label continued)

(sample label continued)

Directions for Use

PRODUCT NAME (8 lbs. ai/gal.) is a selective herbicide recommended as a preplant incorporated or preemergence surface-applied treatment for control of most annual grasses and certain broadleaf weeds.

Corn: Use only on corn grown for grain. Do not use on sweet corn or popcorn. Do not graze or feed forage and fodder to livestock or use for silage.

Soybeans: Do not graze or feed soybean hay or forage.

It is a violation of federal law to use this product in a manner inconsistent with its labeling.

Rotational Crops

1) If corn treated with PRODUCT NAME (8 lbs. ai/gal.) is lost due to poor germination, hail, flood, insects, etc., corn may be replanted immediately. Do not make a second broadcast application. If the original application was banded and the second crop is planted in the untreated row middles, a second band treatment may be applied. 2) Do not plant rotational crops other than corn or soybeans within 18 months after application.

Storage and Disposal

Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited. Pesticide, spray mixture, or rinsate that cannot be used or chemically reprocessed should be disposed of in a landfill approved for pesticides or buried in a safe place away from water supplies. Triple rinse (or equivalent) empty containers, re-seal, and offer for recycling, re-conditioning, or disposal in an approved landfill or bury in a safe place. Consult federal, state, or local disposal authorities for approved alternative procedures.

EPA Registration No. _____ Net Wt. or Measure _____

Establishment No. _____

Name and Address of the producer, registrant, or person for whom produced.

## REGISTRATION UNDER THIS STANDARD

### Registration Procedures

For a full understanding of pesticide testing guidelines and registration procedures, please refer to 40 CFR 162.1 - 162.23 and 40 CFR 162.40 - 162.96.

Briefly, however, to register or re-register a pesticide product under this Registration Standard for Metolachlor, an applicant must submit the appropriate application forms and other information, as specified below, to the following address:

Registration Division (WH-567)
Office of Pesticide Programs
Environmental Protection Agency
Washington, D.C. 20460

(All forms may be obtained by request from the same address. Please request forms with EPA Form Numbers by the number, and all other forms by title.)

I. Your application must include the following forms:

| | EPA Form Number |
|---|---|
| 1) Application for (Re-)Registration | 8570-1 |
| 2) Confidential Statement of Formula | 8570-4 |
| 3) Label Technical Data | 8570-10 |
| 4) Offer to Pay Statement | |
| 5) Certification Statement | |

II. Your application must also include:

1) Certification of Upper and Lower Limits of Components (See 40 CFR 163.61-6(a))
2) Proposed Label (2 copies) (see 'Sample Labels' in 'Regulatory Position')
3) Dermal Sensitization Data (see 40 CFR 163.81-6) - Applicants are required to document the lack of dermal exposure in manufacturing facilities or to monitor and submit skin sensitization data from such exposure.

III. In order to establish the equivalence of the composition of a proposed formulation to the composition of formulations covered by the Standard, applicants for the registration or re-registration of Emulsifiable Concentrate (8 lbs. or less/gallon) must also supply or cite Acute Toxicology Data which demonstrate that the proposed product meets the following criteria:

1. Acute Oral Toxicity
   Any E.C. Metolachlor of 8 pounds or less per gallon which falls into Category III or Category IV will be considered within the scope of this Standard with regard to acute oral toxicity.
2. Acute Dermal Toxicity
   Any E.C. Metolachlor of 8 pounds or less per gallon which falls into Category III or Category IV will be

considered within the scope of this Standard with regard to acute dermal toxicity.

3. Acute Inhalation Toxicity
   Any E.C. Metolachlor of 8 pounds or less per gallon which falls into Category II or a numerically higher category will be considered within the scope of this Standard with regard to acute inhalation toxicity.
4. Primary Eye Irritation
   Any E.C. Metolachlor of 8 pounds or less per gallon which falls into Category I or a numerically higher category will be considered within the scope of this Standard with regard to primary eye irritation.
5. Primary Dermal Irritation
   Any E.C. Metolachlor of 8 pounds per gallon or less which falls into Category II or a numerically higher category will be considered within the scope of this Standard with regard to primary dermal irritation.

## Generic Data Requirements

This document is currently a Conditional Registration Standard. That is, the registerability of a pesticide product under this Standard is 'conditional' upon each applicant's agreement to generate, or compensate other applicants for generating, certain missing but required data, within a specific schedule to be determined by the Agency at the time of application. Registrations or re-registrations which take place under this 'Conditional Standard' are termed 'conditional registrations'. When this required data is supplied to the Agency and has been determined to be sufficient for the support of a Final Registration Standard, the potential hazards will be re-assessed, the appropriate Disciplinary Chapters will be revised, and the regulatory position (and labels) will be modified to reflect the new information.

The data which are currently required in order to adequately support a Final Registration Standard for Metolachlor are listed below. After each requirement is listed the section in the Proposed Guidelines (40 CFR) which describes that type of data and when it is required.

For Technical Metolachlor:

| | | |
|---|---|---|
| **Product Chemistry** | | |
| 1) | Octanol/water partition coefficient | 163.61-8(c)6 |
| 2) | Flammability | 163.61-8(c)13 |
| 3) | Oxidizing or reducing action | 163.61-8(c)14 |
| 4) | Explosiveness | 163.61-8(c)15 |
| 5) | Viscosity | 163.61-8(c)17 |
| 6) | Corrosion characteristics | 163.61-8(c)18 |
| 7) | An analytical method (or reference to a method) for detecting and measuring each identifiable impurity (associated with the manufacturing of the technical grade of the active ingredient) in the formulated products of Metolachlor. | 163.61-7 |
| **Environmental Fate** | | |
| 8) | Adsorption/desorption studies | 163.62-9 |

Toxicology

| | | |
|---|---|---|
| 9) | Subchronic Oral Dosing - Acceptable pathology evaluation is required for both the rat and dog studies. | 163.82-1 |
| 10) | Oncogenicity - Completion of the mouse study and testing on a mammal other than the mouse (the laboratory rat is preferred) is required. | 163.83-2 |
| 11) | Chronic Feeding - A chronic feeding study using the laboratory rat is required. | 163.83-3 |

Ecological Effects

| | | |
|---|---|---|
| 12) | Activated sludge metabolism study | 163.62-8(g) |
| 13) | The avian acute oral LD-50 for one species of waterfowl (preferably the mallard) or one species of upland game bird (preferably the bobwhite, other native quail, or the ring-necked pheasant). | 163.71-1 |
| 14) | Avian reproduction studies on bobwhite quail and mallard ducks. | 163.71-4 |
| 15) | A freshwater fish (preferably the fathead minnow) life-cycle test. | 163.72-4 |

For Emulsifiable Concentrate Metolachlor (6 lbs./gallon):

Product Chemistry

| | | |
|---|---|---|
| 1) | Color | 163.61-8(c)1 |
| 2) | Odor | 163.61-8(c)2 |

For Emulsifiable Concentrate Metolachlor (8 lbs./gallon):

Product Chemistry

| | | |
|---|---|---|
| 1) | Color | 163.61-8(c)1 |
| 2) | Odor | 163.61-8(c)2 |
| 3) | Explosiveness | 163.61-8(c)15 |

## Amending the Standard

Applicants for the registration of a pesticide product which contains Metolachlor as the sole pesticide active ingredient, but which does not fall within the parameters of product composition, use, or toxicity as defined in this Standard, must petition the Agency to 'amend the Standard'. The Agency will consider the petition, and determine what studies are needed to assess the potential adverse effects of this new composition, new use, or higher toxicity to man or the environment. When the applicant has satisfactorily supplied the needed data, and providing that the data do not indicate the potential for unreasonable adverse effects, the Agency will then consider amending the Standard to cover the new type of product. Amendments to the Standard will involve the incorporation of the new information into the Disciplinary Chapters, the appropriate revision of the Regulatory Rationale and Position, and any needed modification of Registration Procedures.

The actual procedure to be used for petitioning the Agency to amend a Registration Standard will be forthcoming in future Regulations.

# APPENDICES

# APPENDIX A. CHEMICAL DATA SHEETS

Chemical Data Sheets have been prepared for the components, hydrolysis products, and known metabolites of manufacturing-use Metolachlor. The Data Sheets are divided into Components COM001 through COM011, Hydrolysis Products HP001 and HP002, and Metabolites MET001 through MET024. Chemical Data Sheets are not available for MET025 and MET026, though their structures are given in the Environmental Fate chapter.

COMPONENT NUMBER COM001

01. Chemical Abstracts Chemical names;

01 Acetamide, 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-(CA9)

02 o-Acetotoluidide, 2-chloro-6'-ethyl-N-(2-methoxy-1-methylethyl)-(CA8)

02. Other Chemical Names;

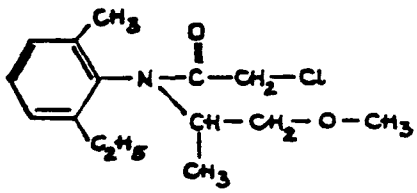
01 2-Chloro-N-(2-ethyl-6-methylphenyl)-N-(2'-methoxy-1'-methylethyl)-acetamide

02 Acetanilide, 2-chloro-2'-ethyl-N-(2-methoxy-1-methylethyl)-6'-methyl-

03 N-(2'-Methoxy-1'-methylethyl)-2-ethyl-6-methyl-chloroacetanilide

04 N-(Chloroacetyl)-6-ethyl-N-(2-methoxyisopropyl)-o-toluidine

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{15}H_{22}ClNO_2$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name;

01 Metolachlor

07. Other Common Names, Trade Names, or Codes;

01 Dual

02 CGA No. 24705

Chemical Data Sheets COM-002 through COM-011 have been omitted in this Sample Registration Standard because of confidentiality claims by the manufacturer.

HYDROLYTIC PRODUCT NUMBER HP001

01. Chemical Abstracts Chemical Names;

01 1-Propanol, 2-[(2-ethyl-6-methylphenyl)amino]- (CA9)

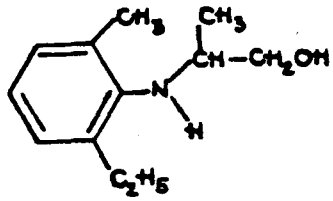
02 1-Propanol, 2-(6-ethyl-o-toluidino)- (CA8)

02. Other Chemical Names;

01 1-Propanol, 2-(2-ethyl-6-methylanilino)-

02 2-[(2-Ethyl-6-methyl)amino]-1-propanol

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{12}H_{19}NO$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 37913

02 PHP (Propanol hydrolytic product)

HYDROLYTIC PRODUCT NUMBER HP002

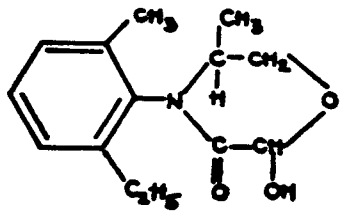
01. Chemical Abstracts Chemical Names;

01 3-Morpholinone, 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-

02 3-Morpholinone, 4-(6-ethyl-o-tolyl)-2-hydroxy-5-methyl-

02. Other Chemical Names;
01 4-(2-Ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{14}H_{19}NO_3$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 49751

02 MHP (morpholinone hydrolytic product)

METABOLITE NUMBER MET001

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-hydroxy-N-(2-methoxy-1-methylethyl)- (CA9)

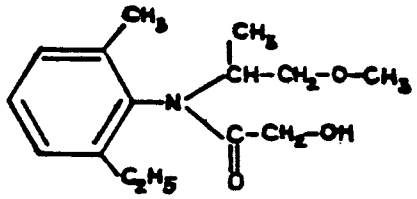
02 o-Acetotoluidide, 6'-ethyl-2-hydroxy-N-(2-methoxy-1-methylethyl)- (CA8)

02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-hydroxy-N-(2-methoxy-1-methylethyl)-6'-methyl-

02 N-(2-Ethyl-6-methylphenyl)-2-hydroxy-N-(2-methoxy-1-methylethyl)acetamide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{15}H_{23}NO_3$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 40172

METABOLITE NUMBER MET002

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-hydroxy- (CA9)

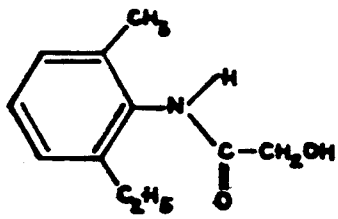
02 o-Acetotoluidide, 6'-ethyl-2-hydroxy-(CA8)

02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-hydroxy-6'-methyl-

02 N-(2-Ethyl-6-methylphenyl)-2-hydroxyacetamide

Structural Formula;




04. Molecular (Empirical) Formula;

$C_{11}H_{15}NO_2$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 37735

METABOLITE NUMBER MET003

01. Chemical Abstracts Chemical Names;

01 Acetamide, 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)- (CA9)

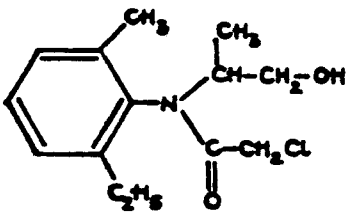
02 o-Acetotoluidide, 2-chloro-6'-ethyl-N-(2-hydroxy-1-methylethyl)- (CA8)

02. Other Chemical Names;

01 Acetanilide, 2-chloro-2'-ethyl-N-(2-hydroxy-1-methylethyl)-6'-methyl-

02 2-Chloro-N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)acetamide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{14}H_{20}ClNO_2$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 41638

METABOLITE NUMBER MET004

01. Chemical Abstracts Chemical Names;

01 DL-Alanine, N-(2-ethyl-6-methylphenyl)-N-(hydroxyacetyl)- (CA9)

02 DL-Alanine, N-(6-ethyl-o-tolyl)-2-(hydroxyacetyl)- (CA8)

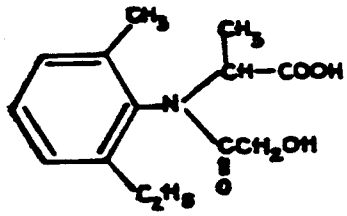
02. Other Chemical Names;

01 Propanoic acid, 2-[N-(2-ethyl-6-methylphenyl)-2-hydroxyacetamido]-

02 Propionic acid, 2-[N-(6-ethyl-o-tolyl)-2-hydroxyacetamido]-

03 N-(2-Ethyl-6-methylphenyl)-N-(hydroxyacetyl)alanine

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{14}H_{19}NO_3$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 46129

METABOLITE NUMBER MET005

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)- (CA9)

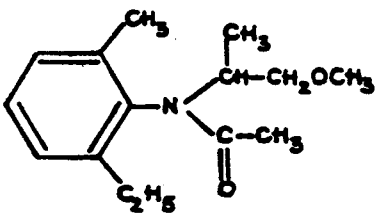
02 o-Acetotoluidide, 6'-ethyl-N-(2-methoxy-1-methylethyl)- (CA8)

02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-N-(2-methoxy-1-methylethyl)-6'-methyl-

02 N-(2-Ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{15}H_{23}NO_2$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Dechlorometolachlor

02 CGA No. 41507

METABOLITE NUMBER MET006

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)- (CA9)

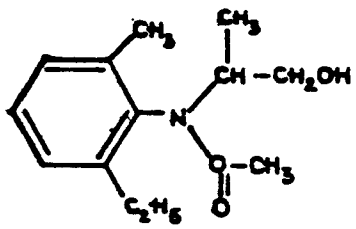
02 o-Acetotoluidide, 6'-ethyl-N-(2-hydroxy-1-methylethyl)- (CA8)

02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-N-(2-hydroxy-1-methylethyl)-6'-methyl-

02 N-(2-Ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)acetamide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{14}H_{21}NO$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 42446

METABOLITE NUMBER MET007

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)- (CA9)

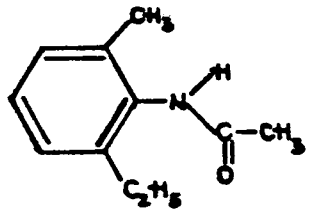
02 o-Acetotoluidide, 6'-ethyl- (CA8)

02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-6'-methyl-

02 N-(2-Ethyl-6-methylphenyl)acetamide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{11}H_{15}NO$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 42444

METABOLITE NUMBER MET008

01. Chemical Abstracts Chemical Names;

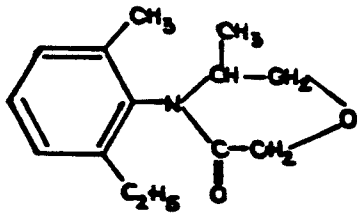
01 3-Morpholinone, 4-(2-ethyl-6-methylphenyl)-5-methyl- (CA9)

02 3-Morpholinone, 4-(6-ethyl-o-tolyl)-5-methyl- (CA8)

02. Other Chemical Names;

01 4-(2-Ethyl-6-methylphenyl)-5-methyl-3-morpholinone

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{14}H_{19}NO_2$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 40919

METABOLITE NUMBER MET009

01. Chemical Abstracts Chemical Names;

01 Acetamide, 2-chloro-N-(2-ethyl-6-methylphenyl)- (CA9)

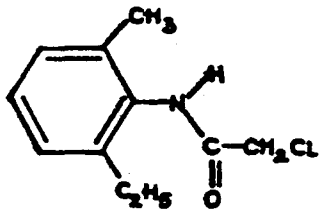
02 o-Acetotoluidide, 2-chloro-6'-ethyl- (CA8)

02. Other Chemical Names;

01 Acetanilide, 2-chloro-2'-ethyl-6'-methyl

02 2-Chloro-N-(2-ethyl-6-methylphenyl)acetamide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{11}H_{14}ClNO$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 13656

METABOLITE NUMBER MET010

01. Chemical Abstracts Chemical Names;

01 Benzenamine, 2-ethyl-N-(2-methoxy-1-methylethyl)-6-methyl- (CA9)

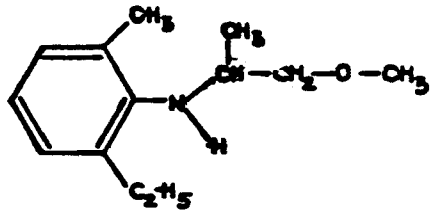
02 o-Toluidine, 6-ethyl-N-(2-methoxy-1-methylethyl)- (CA8)

02. Other Chemical Names;

01 Aniline, 6-ethyl-N-(2-methoxy-1-methylethyl)-6-methyl-

02 2-Ethyl-N-(2-methoxy-1-methylethyl)-6-methylbenzenamine

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{13}H_{21}NO$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 CGA No. 38502

METABOLITE NUMBER MET011

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-mercapto-N-(2-methoxy-1-methylethyl)-,S-conjugate with Glutathione

02 o-Acetotoluidide, 2'-ethyl-2-mercapto-N-(2-methoxy-1-methylethyl)-, S-conjugate with Glutathione

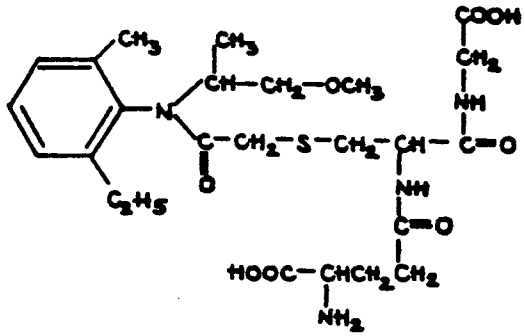
02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-mercapto-N-(2-methoxy-1-methylethy)-6'-methyl-,S-conjugate with Glutathione

02 Glutathione, sulfide with 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide

03 Glutathione, sulfide with 2-chloro-6'-ethyl-N-(2-methoxy-1-methylethyl)-o-acetotoluidide

03. Structural Formula;




04. Molecular (Empirical) Formula;

$C_{25}H_{38}N_4O_8S$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Metolachlor glutathione conjugate

02 CGA No. 43826

METABOLITE NUMBER MET012

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-mercapto-N-(2-methoxy-1-methylethyl)-,S-conjugate with Glucuronic acid (CA9)

02 o-Acetotoluidide, 2'-ethyl-2-mercapto-N-(2-methoxy-1-methylethyl)-, S-conjugate with Glucuronic acid (CA8)

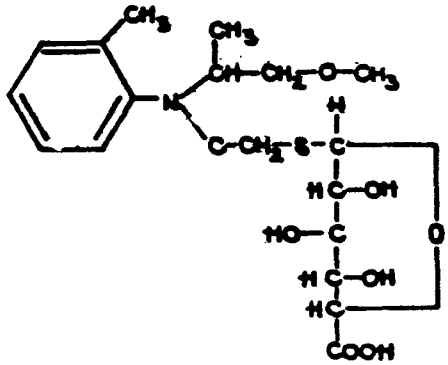
02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-mercapto-N-(2-methoxy-1-methylethyl)-6'-methyl-,S-conjugate with Glucuronic acid

02 Glucuronic acid, 1-S-[[[(2-ethyl-6-methylphenyl)(2-methoxy-1-methylethyl)-amino]carbonyl]methyl]-1-thio-

03 Glucuronic acid, 1-S-[[(6-ethyl-o-tolyl)(2-methoxy-1-methylethyl) carbamoyl]methyl]-1-thio-

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{21}H_{30}NO_8S$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Metolachlor glucuronic acid conjugate

02 Compound N

METABOLITE NUMBER MET013

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl)-2-mercapto-, O-glucoside, S-conjugate with Glucuronic acid (CA9)

02 o-Acetotoluidide, 6'-ethyl-N-(2-hydroxy-1-methylethyl)-2-mercapto-, O-glucoside, S-conjugate with Glucuronic acid (CA8)

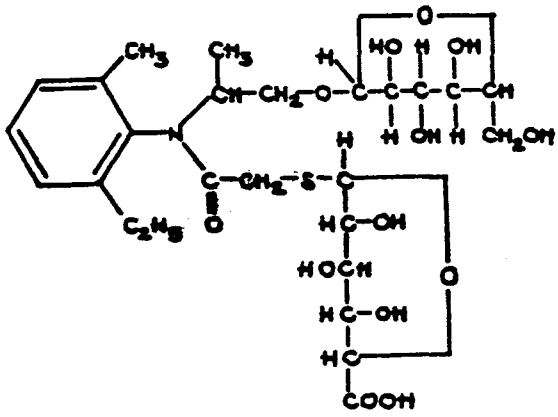
02. Other Chemical Names;

01 Acetanilide, 2'ethyl-N-(2-hydroxy-1-methylethyl)-2-mercapto-6'-methyl-, O-glucoside, S-conjugate with Glucuronic acid

02 Glucuronic acid, 1-S-[[(6-ethyl-o-tolyl)(2-glucosyl(1)-1-methylethyl)carbamoyl]methyl]-1-thio-

03 Glucuronic acid, 1-S-[[[(2-ethyl-6-methylphenyl)(2-glucosyl(1)-1-methylethyl)amino]carbonyl]methyl]-1-thio-

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{26}H_{39}NO_{13}S$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Compound No. 0

METABOLITE NUMBER MET014

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methoxyethyl)-2-mercapto-, S-conjugate with Glucuronic acid (CA9)

02 o-Acetotoluidide, 2'-ethyl-N-(2-hydroxy-1-methylethyl)-2-mercapto-, S-conjugate with Glucuronic acid (CA8)

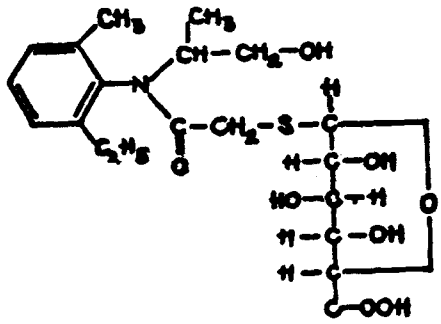
02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-N-(2-hydroxy-1-methylethyl)-2-mercapto-6'-methyl-, S-conjugate with Glucuronic acid

02 Glucuronic acid, 1-S-[[[(2-ethyl-6-methylphenyl)(2-hydroxy-1-methylethyl)amino]carbonyl]methyl]-1-thio-

03 Glucuronic acid, 1-S-[[(6-ethyl-o-tolyl)(2-hydroxy-1-methylethyl)carbamoyl]methyl]-1-thio-

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{20}H_{28}NO_8S$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Demethylmetolachlor glucuronic acid conjugate

METABOLITE NUMBER MET015

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-hydroxy-N-(2-methoxy-1-methylethyl)-, O-conjugate with Glucuronic acid (CA9)

02 o-Acetotoluidide, 2'-ethyl-2-hydroxy-N-(2-methoxy-1-methylethyl)-, O-conjugate with Glucuronic acid (CA8)

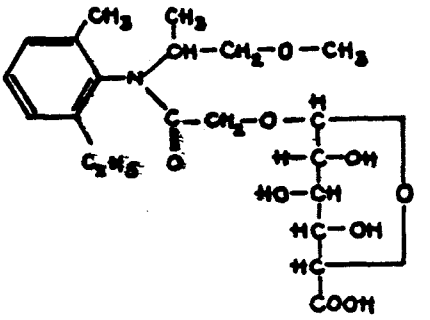
02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-hydroxy-N-(2-methoxy-1-methylethyl)-6'-methyl-, O-conjugate with Glucuronic acid

02 Glucuronic acid, 1-O-[[[(2-ethyl-6-methylphenyl)(2-methoxy-1-methylethyl)amino]carbony]methyl]-

03 Glucuronic acid, 1-O-[[(6-ethyl-o-tolyl)(2-methoxy-1-methylethyl)-carbamoyl]methyl]-

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{21}H_{31}NO_9$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Metolachlor glucuronic acid conjugate

METABOLITE NUMBER MET016

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-hydroxy-N-(2-hydroxy-1-methylethyl)-, O-conjugate with Glucuronic acid

02 o-Acetotoluidide, 2'-ethyl-2-hydroxy-N-(2-hydroxy-1-methylethyl)-, O-conjugate with Glucuronic acid

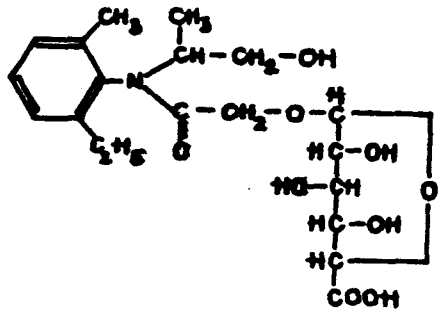
02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-hydroxy-N-(2-hydroxy-1-methylethyl)-6'-methyl-, O-conjugate with Glucuronic acid

02 Glucuronic acid, 1-O-[[[(2-ethyl-6-methylphenyl)(2-hydroxy-1-methylethyl)amino]carbonyl]methyl]-

03 Glucuronic acid, 1-O-[[(6-ethyl-o-tolyl)(2-hydroxy-1-methylethyl)-carbamoyl]methyl]-

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{20}H_{29}NO_9$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes;

01 Desmethylmetolachlor glucuronic acid conjugate

METABOLITE NUMBER MET017

01. Chemical Abstracts Chemical Names;

01 Acetamide, N-(2-ethyl-6-methylphenyl)-2-hydroxy-N-(2-hydroxy-1-methylethyl)-, O-glucoside, O-conjugate with Glucuronic acid (CA9)

02 o-Acetotoluidide, 6'-ethyl-2-hydroxy-N-(2-hydroxy-1-methylethyl)-, O-glucoside, O-conjugate with Glucuronic acid (CA8)

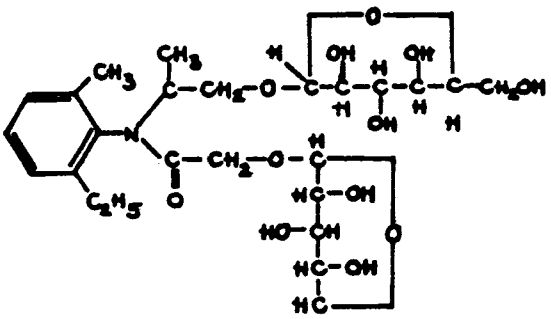
02. Other Chemical Names;

01 Acetanilide, 2'-ethyl-2-hydroxy-N-(2-hydroxy-1-methylethyl)-6'-methyl-,O-glucoside, O-conjugate with Glucuronic acid

02 Glucuronic acid, 1-O-[[(6-ethyl-o-tolyl)(2-glucosyl(1)-1-methylethyl)-carbamoyl]methyl]

03 Glucuronic acid, 1-O-[[[((2-ethyl-6-methylphenyl)(2-glucosyl(1)-1-methylethyl)amino]carbonyl]methyl]-

03. Structural Formula;



04. Molecular (Empirical) Formula;

$C_{26}H_{39}NO_{14}$

05. Chemical Abstracts (CAS) Registry Number;

06. Approved Common Name; None

07. Other Common Names, Trade Names, or Codes; None

METABOLITE NUMBER: 018

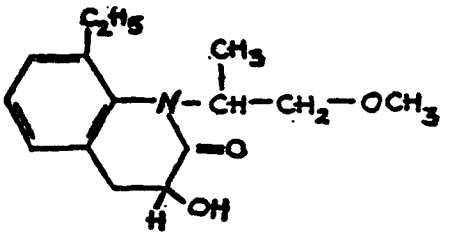
01. Chemical Abstracts Chemical Names:

01 Quinoline, N-(2-methoxy-1-methylethyl)-8-ethyl-3-hydroxy-2-oxo-1,2,3,4-tetrahydro-

02. Other Chemical Names:

01 8-Ethyl-3-hydroxy-N-(2-methoxy-1-methylethyl)-2-oxo-1,2,3,4-tetrahydroquinoline

03. Structural Formula:




04. Molecular (Empirical) Formula:

$C_{15}H_{21}NO_3$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names, Trade Names, or Codes:

METABOLITE NUMBER: 019

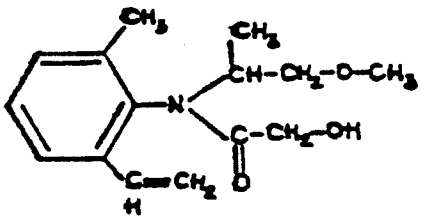
01. Chemical Abstracts Chemical Names:

01 Acetamide, 2-hydroxy-N-(2-methyl-6-vinylphenyl)-N-(2-methoxy-1-methylethyl)-

02. Other Chemical Names:

01 2-hydroxy-N-(2-mothyl-6-vinylphenyl)-N-(2-methoxy-1-methylethyl) acetamide

03. Structural Formula:



04. Molecular (Empirical) Formula:

$C_{15}H_{21}NO_3$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names: None

07. Other Common Names, Trade Names, or Codes:

METABOLITE NUMBER: 020

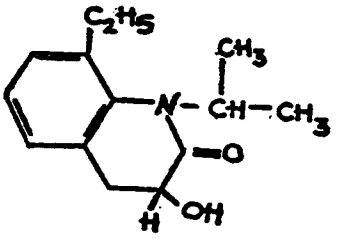
01. Chemical Abstracts Chemical Names:

01 Quinoline, N-isopropyl-8-ethyl-3-hydroxy-2-oxo-1,2,3,4,-tetrahydro-

02. Other Chemical Names:

01 8-Ethyl-3-hydroxy-N-isopropyl-2-oxo-1,2,3,4-tetrahydroquinoline

03. Structural Formula:




04. Molecular (Empirical) Formula:

$C_{14}H_{19}NO_2$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names: None

07. Other Common Names, Trade Names, or Codes:

METABOLITE NUMBER: 021

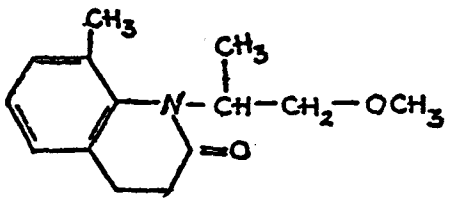
01. Chemical Abstracts Chemical Names:

01 Quinoline, 8-methyl-N-(2-methoxy-1-methylethyl)-2-oxo-1,2,3,4-tetrahydro

02. Other Chemical Names:

01 8-Methyl-N-(2-methoxy-1-methylethyl)-2-oxo 1,2,3,4-tetrahydroquinoline

03. Structural Formula:




04. Molecular (Empirical) Formula:

$C_{14}H_{19}NO_2$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names: None

07. Other Common Names, Trade Names, or Codes:

METABOLITE NUMBER: 022

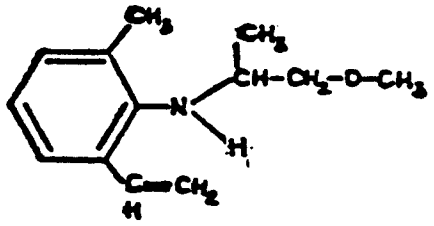
01. Chemical Abstracts Chemical Names:

01 Aniline, N-(2-methoxy-1-methylethyl)-2-methyl-6-vinyl-

02. Other Chemical Names:

01 N-(2-methoxy-1-methylethyl)-(2-methyl-6-vinyl) aniline

03. Structural Formula:



04. Molecular (Empirical) Formula:

$C_{13}H_{19}NO$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names: None

07. Other Common Names, Trade Names, or Codes:

METABOLITE NUMBER: 023

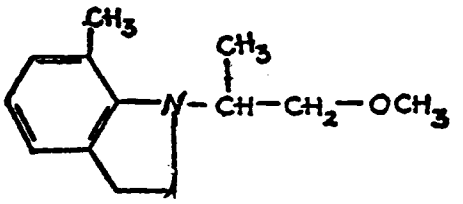
01. Chemical Abstracts Chemical Names:

01 Indole, 2,3-dihydro-N-(2-methoxy-1-methylethyl)-7-methyl-

02. Other Chemical Names:

01 N-(2-methoxy-1-methylethyl)-7-methyl-2,3-dihydroindole aniline

03. Structural Formula:




04. Molecular (Empirical) Formula:

$C_{13}H_{19}NO$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names: None

07. Other Common Names, Trade Names, or Codes:

METABOLITE NUMBER: 024

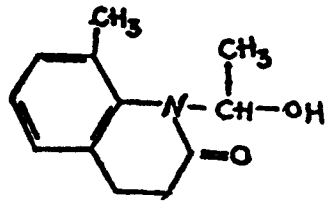
01. Chemical Abstracts Chemical Names:

01 Quinoline, N-(1-hydroxyethyl)-8-methyl-2-oxo-1,2,3,4-tetrahydro-

02. Other Chemical Names:

01 8-Methyl-N-(1-hydroxyethyl)-2-oxo-1,2,3,4-tetrahydroquinoline

03. Structural Formula:




04. Molecular (Empirical) Formula:

$C_{12}H_{15}NO_2$

05. Chemical Abstracts (CAS) Registry Number:

06. Approved Common Names: None

07. Other Common Names, Trade Names, or Codes:

## APPENDIX B. SIGNIFICANT HISTORICAL EVENTS

| | |
|---|---|
| March, 1975 | Receipt of application for pesticide registration. |
| May, 1977 | Registration of Technical Metolachlor. |

# APPENDIX C. INDEX OF ACCEPTABLE USES

RESERVED

## APPENDIX D. INDEX OF TOLERANCES
(as of February 9, 1978)

| Chemical | Commodity | PPM |
|---|---|---|
| Metolachlor | Corn Grain (except popcorn) | 0.1 |
| | Soybeans | 0.1 (temporary) |
| | Soybean Hay and Forage | 1.25 (temporary) |
| | Meat, Eggs, Poultry, Milk (for cattle, goats, hogs, horses, poultry, and sheep) | 0.02 (temporary) |

# APPENDIX E. COMPANY DATA CHRONOLOGY

RESERVED

# APPENDIX F. ANALYTICAL METHODS

RESERVED

## APPENDIX G. INFORMATION SEARCH STRATEGY

Technical literature used in the compilatiion of this standard was derived from an exhaustive search of world-wide literature sources using both manual and on-line automated search techniques.

Search completion date: November 1977

Update performed: N.A.

Chemical identification profile:

RN 51218-45-2
RN 55762-76-0
Dual
Metolachlor
CGA 24705
CGA24705
CGA-24705

Name Fragments
Acetamide and chloro and ethyl and methylphenyl and methoxy and methylethyl

Data bases searched
Automated (on-line) search
Agricola
Aquatic Abstracts
Biosis Previews
CAB Abstracts
Cancerline (NLM)
Cancerproj (NLM)
Chemical Abstracts 1970-1977
Dissertation Abstracts
Enviroline
Epilepsy (NLM)
Hayes (US EPA)
Medline/Medback (NLM)
NTIS (US Dept. Comm.)
Oceanic Abstracts
Pesticides Abstracts (U.S. EPA)
Pollution Abstracts
RTECS (Registry of Toxic Effects of Chemical Substances) (NIOSH)
Scisearch
Toxline/Toxback (NLM)
USDA CRIS

Manual Search

| | |
|---|---|
| Biological Abstracts | 1950-1970 |
| Chemical Abstracts | 1950-1970 |

Excerpta Medica:

| | | |
|---|---|---|
| Pharmacol. Toxicol. | 18:1965-41 | (2):1977 |
| Cancer | 1:1953-35 | (10:1977 |
| Devel. Biol. | 1:1961-17 | (7):1977 |

# APPENDIX H. TREATMENT OF CHEMICAL INTOXICATION

RESERVED

# APPENDIX I. MANAGEMENT OF ENVIRONMENTAL CONTAMINATION

RESERVED

# APPENDIX J. DISPOSAL INFORMATION

RESERVED

# BIBLIOGRAPHY

Affiliated Medical Research, Incorporated (1974a) Acute Dermal $LD_{50}$ of CGA-24705 - Technical in Rabbits: Contract No. 120-2255-34. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-E)

Affiliated Medical Research, Incorporated (1974b) Acute Dermal $LD_{50}$ of CGA-24705-6E: Contract No. 12-2255-34. Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-F)

Affiliated Medical Research, Incorporated (1974c) Acute Inhalation Study of CGA-24705-6E for Albino Rats: Contract No. 121-2253-34. Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-M)

Affiliated Medical Research, Incorporated (1974d) Acute Oral Toxicity in Rats of CGA-24705-6E: Contract No. 121-2255-34. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-B)

Affiliated Medical Research, Incorporated (1974e) Emetic Dose 50 in Beagle Dogs with CGA-24705-Technical: Contract No. 120-2255-34. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-C)

Affiliated Medical Research, Incorporated (1974f) Emetic Dose 50 in Beagle Dogs with CGA-24705-6E: Contract No. 121-2255-34.(Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-D)

Affiliated Medical Research, Incorporated (1974g) Evaluation of CGA-24705 Technical (FL740408) as a Potential Skin Sensitizer in the Guinea Pig: Contract No. 120-2255-34. (Unpublished study received Sep 26, 1977 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-K)

Affiliated Medical Research, Incorporated (1974h) Primary Dermal Irritation of CGA-24705-6E in Albino Rabbits: Contract No. 121-2255-34. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-J)

Affiliated Medical Research, Incorporated (1974i) Primary Eye Irritation of CGA-24705-6E in Albino Rabbits: Contract No. 121-2255-34. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-H)

Affiliated Medical Research , Incorporated (1974j) Twenty-One Day Repeated Dermal Toxicity of CGA-24705-6E in Rabbits: Contract No. 120-2255-34. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-Q)

Ahrens, J.F.; Cubanski, M. (1977) Herbicides for hemlock seedbeds. Pages 315-319, In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6, 1977, Baltimore, Maryland. Salisbury, Md.: [University of Maryland?].

American Institute of Biological Sciences, Aquatic Hazards of Pesticides Task Group (1978) Criteria and Rationale for Decision Making in Aquatic Hazard Evaluation: Report to the Environmental Protection Agency. Washington, D.C.: U.S. E.P.A. (EPA Contract No. 68-01-2457)

American National Standards Institute (1976). Common name for the pest control chemical 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide "metolachlor." In American National Standard: ANSI K62,198-1976. New York: ANSI.

Anon. (1976) 2-Chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) Acetamide: Tolerances for Residues. Federal Register 41(226):51400.

Arni, P.; Miller, D. (1976) Salmonella/Mammalian-Microsome Mutagenicity Test with CGA 24705 (Test for Mutagenic Properties in Bacteria): PH 2.632. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy, Ltd., Basle, Switzerland; CDL:95768-B)

Ashley, R.A. (1976) Varietal response of sweet corn to Procyazine and CGA-24705. Pages 193-196, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976, Boston, Massachusetts Salisbury, Md: University of Maryland, Vegetable Research Farm.

Aziz, S.A. (1974) Photolysis of CGA-24705 on Soil Slides under Natural and Artificial Sunlight Conditions: GAAC-74102. (Unpublished study received Mar 26, 1975 under 5F1606 prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-J)

Aziz, S.A.; Kahrs, R.A. (1974) Photolysis of CGA-24705 in Aqueous Solution under Natural and Artificial Sunlight Conditions: GAAC-74041.(Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94222-A)

Aziz, S.A.; Kahrs, R.A. (1975) Photolysis of CGA-24705 in Aqueous Solution -- Additional Information: GAAC-75021. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-M)

Aziz, S.A; Ross, J.A. (1975) Analytical Method for the Determination of Residues of CGA-24705 Soybean Metabolites as CGA-37913 and CGA-49751 by Acid Hydrolysis. Method AG-286 dated Jun 10, 1975. (Unpublished study received Nov 6, 1975 under 4G1469; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95190-E)

Aziz, S.A.; Ross, J.A. (1976) Specificity of Analytical Method AG-286 for the Determination of Residues of Metolachlor and Its Metabolites in Soybeans: ABR-76083. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95748-AC)

Bailey, G.W.; Leonard, R.A.; Livank, R.R., Jr. (1976) Land Application of Waste Materials: Transport, Detoxification, Fate, and Effects of Pesticides in Soil and Water Environment. Ankeny, Iowa: Soil Conservation Society of America. (p.48-78)

Balasubramanian, K.; Aziz, S.A.; Ross, J.A. (1975) Analytical Method for the Determination of Residues of CGA-24705 Corn Metabolites as CGA-37913 and CGA-49751 by Acid Hydrolysis. Method AG-277 dated Jan 9, 1975. (Unpublished study received Nov 6,1975 under 4G1469; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:95190-D)

Balasubramanian, K.; Gold, B.; Ross, J.A. (1973?) Gas Chromatographic Determination of Residues of CGA-24705 Metabolites in Corn as CGA-37913. Method AG-265 undated. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94380-P)

Balasubramanian, K.; Gold, B.; Ross, J.A. (1974) Validation of Method AG-265 for the Determination of CGA-24705 Metabolites Which are Converted to the CGA-37913 Moiety: GACC-74043. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94216-I)

Ballantine, L.G. (1975) CGA-24705: Environmental Impact Statement: GAAC-75011. (Unpublished study that includes studies AG-A 2929 I-IV 1st Rept., Ag-A 2929 I-IV 2nd Rept., AG-A 2969 I-III 1st Rept., AG-A 2969 I-IV 2nd Rept., AG-A 2973, AG-A 3105, AG-A 3133 1st Rept., Ag-A 3133 2nd Rept., AG-A 3150 I-II, AG-A 3244 II, AG-A 3282 I (2nd)-II, AG-A 3554; received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:94385-A, 94376)

Ballantine, L.G. (1976a) Metolachlor plus Atrazine Tank Mix Soil Dissipation: ABR-76076. (Unpublished study that includes the reports AG-A 3493 I-IV, and AG-A 3573 I-II; received Feb 18, 1977 under 100-583; prepared by Ciba Geigy Corp.; CDL:228125-A

Ballantine, L.G. (1976b) Metolachlor plus Linuron Tank Mix Soil Dissipation: ABR-76079. (Unpublished study that includes AG-A 3706 I-V, AG-A 3719 I-IV, and AG-A 4139 I, II; received Jan 19, 1977 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95763-D)

Ballantine, L.G. (1976c) Metolachlor plus Metribuzin Tank Mix Soil Dissipation: ABR-76092. (Unpublished study that includes studies AG-A 3807 I-V, AG-A 3722 I-IV, and AG-A 4140; prepared by Ciba-Geigy Corp. and studies no. 50842 and 50843 received Jan 19, 1977 under 100-583; prepared by Chemagro Agricultural Division, Mobay Chemical Corp. [Kansas City, MO.] for Ciba-Geigy Corp., Greensboro, N.C.; CDL:95763-A]

Ballantine, L.G. (1978) Metolachlor: Update of Environmental Impact Statement. ABR-78011. Unpublished study that includes studies AG-A 2929 I-IV 1st Rept., AG-A 2969 I-III 1st Rept., AG-A 3133 1st Rept., AG-A 3706 I-V, AG-A 3707 I-V, AG-A 3722 I-IV, AG-A 4140; received Feb 6, 1978 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:232789-A, 232789-N, 232789-O, 232789-P, 232789-Q, 232789-R, 232789-S, 232789-T)

Ballantine, L.G.; Herman, M.M. (1977a) Metalochlor Plus Atrazine Plus Paraquat Tank Mix Soil Dissipation: ABR-77068. (Unpublished study containing studies Ortho T-4088, Ortho T-4089, AG-A 4084 I-IV, AG-A 4085 I-IV; received Nov 8, 1977 under 100-EUP-59; CDL:232193-G, 232193-J, 232193-K, 232193-L, 232193-M)

Ballantine, L.G.; Herman, M.M. (1977b) Metolachlor Plus Dicamba Tank Mix Soil Dissipation Studies: ABR-77067. (Unpublished study including studies AG-A 4141 I-III, AG-A 4156 I-IV, Craven Lab 76-1-D; CDL:232193-A, 232193-D, 232193-E, 232193-F) received Nov 8, 1977 under 100-EUP-59 prepared by Ciba-Geigy Corp., Greensboro, N.C.;

Barrows. M.E. (1974) Exposure of fish to $^{14}$C-CGA-24705. Accumulation Distribution, and Elimination of $^{14}$C Residues. Report No.:73019-3. (Unpublished study received Mar 27, 1975 under 5F1606; prepared by Bionomics E G & G Environmental Consultants for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94376-E)

Bathe, R. (1973) Acute Oral $LD_{50}$ of Technical CGA-24705 in the Rat: Project No. Siss 2979. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Ltd., Basle, Switzerland; CDL:112840-A)

Bayer, G.H. (1977) Herbicide combinations for soy, snap, and kidney beans in New York. Pages 34-38, In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6, 1977, Baltimore, Maryland. Salisbury Md: [University of Maryland.]

Bing, A. (1977) 1976 pre-emergence weed control in nursery liners. Pages 320-325, In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6, 1977, Baltimore, Maryland. Salisbury, Md. [University of Maryland?]

Biometric Testing Incorporated (1973) Metabolism $^{14}$C-CGA-24705 Corn Biosynthesized Metabolites in a Lactating Goat: A-1004. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94217-J)

Bleidner, W.E.; Baker, H.M.; Levitsky, M.; Lowen, W.K. (1954) Determination of 3-(p-chlorophenyl)-1, 1-dimethylurea in soils and plant tissues. Journal of Agricultural and Food Chemistry 2(9): 476-479. (Also In unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.: CDL:94221-A)

Bohn, J.A.; Price, J.H.; Rieck, C.E. (1976). Comparison of the herbicidal activity of chloro-acetamides. Pages 30- , Page 150, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975, Milwaukee, Wisconsin. Omaha, Neb.; by Stauffer Chemical Company for the North Central Weed Control Conference:

Brashears, A.D.; Abernathy, J.R.; Schrib, J.V. (1976) An evaluation of yellow nutsedge control techniques in West Texas cotton: Abstract. In Proceedings of the 29th Annual Meeting of the Southern Weed Science Society; Jan 27-29, 1976, Dallas, Texas. Raleigh, N.C.: Glover Printing for the Southern Weed Science Society:

Buccafusco, Robert J. (1978a) Acute Toxicity Test Results of CGA-24705 to Bluegill Sunfish (Lepomis macrochirus): Report #BW-78-6-181. (Unpublished study received Jul 13, 1978 under 100.597; prepared by E G & G,Bionomics, Submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL:234396)

Buccafusco, Robert J. (1978b) Acute Toxicity Test Results of CGA-24705 to Rainbow Trout (Salmo gairdneri): Report #BW-78-6-186. (Unpublished study received Jul 13,1978 under 100-597; prepared by E.G. & G., Bionomics, submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL:234396)

Buckhard, N. (1974) CGA-24705: Hydrolysis of CGA Under Laboratory Conditions: AC 2.5.53; SPR 2/74. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94222-H)

Cannizzaro, R.D.: Hofberg, A. (1972) Analysis of Water in Soils and Column Adsorbants Using the Aquatest II Electronic Karl-Fischer Titration System. Method AG-192 dated Mar 9, 1972. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94216-K)

Centre de Recherche et d'Elevage des Oncins (1974) Toxicite De 3 Mois chez le Rat par Voie Orale du Produit CGA 24 705. [Three-Month Dietary Feeding Study in Rats: CGA 24 705]: IC-DREB-R 741009. (Unpublished study received Mar 26, 1975 under 5F1606; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94377-C)

Chalmers, A.H. (1974) Studies on the mechanism of formation of 5-mercapto-1-methyl-4-nitroimidazole, a metabolite of the immunosuppressive drug Azathioprine. Biochemical Pharmacology 23: 1891-1901. (Also In unpublis report received Mar 27, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94382-A)

Ciba-Geigy Corporation (1974) Section A, CGA-24705: Name, Chemical Identity and Composition of CGA-24705. (Unpublished study; received Sep 26, 1974 under 100-EUP-44; CDL:96505:A)

Ciba-Geigy Corporation (1975a) CGA-24705 Efficacy and Crop Safety Summary: 1973-1974. (Unpublished study that includes efficacy and crop safety reports 1-51 and rotational bioassay reports 52-71; received Mar 27, 1975 under 5F1606; CDL; 94383-A, 94384)

Ciba-Geigy Corporation (1975b) Biological Summary: Dual™ 6EC Applied Alone. (Unpublished study that includes reports 1-99; received Nov 25, 1975 under 100-EUP-43; CDL:94832-A; 94831)

Ciba-Geigy Corporation (1975c) Biological Summary: Dual 6EC + Lorox Tank Mix. (Unpublished study that includes reports 1-21; received Nov 25, 1975 under 100-EUP-43; CDL:94832-B; 94829)

Ciba-Geigy Corporation (1975d) Biological Summary: Dual 6EC + Sencor 50% W.P. or Lexone Tank Mix. (Unpublished study that includes reports 1-49; received Nov 25, 1975 under 100-EUP-43; CDL:94832-C; 94830)

Ciba-Geigy Corporation (1975e) Efficacy and Crop Safety Summary GA-2-686 15G Herbicide for Corn. (Unpublished study including summary tables and efficacy tests 1-6, 8-14L; received Feb 9, 1976 under 100-EUP-44; CDL:96496-B)

Ciba-Geigy Corporation (1975f) Name, Chemical Identity and Composition of CGA-24705. (Unpublished study received Nov 25, 1975 under 100-EUP-43; CDL:94879-A)

Ciba-Geigy Corporation (1975g) Results of Dual™ 6E and Cycle™ 80W Experimental Permits. (Unpublished study; received Dec 29, 1975 under 100-EUP 36; CDL:95053-A)

Ciba-Geigy Corporation (1975?h) Section A, CGA-24705: Name, Chemical Identity and composition of CGA-24705. (Unpublished study; received Nov 25, 1975 under 6G1708; CDL:96439-A)

Ciba-Geigy Corporation (1976a) CGA-24705: Name, Chemical Identity and Composition of CGA-24705. (Unpublished study received Nov 23, 1976 under 100-587; prepared by Ciba-Geigy Corp., Greensboro, N.C.: CDL:226955-A)

Ciba-Geigy Corporation (1976b) Aerial Application. (Unpublished study that includes reports Dual/PPI, Dual/PRE, Dual & Lorox, III.1 - III.10; received Jan 19, 1977 under 100-583; CDL:95738-E; 95757)

Ciba-Geigy Corporation (1976c) Dual(R) + Sencor(R) Pre-emergence. (Unpublished study that includes reports I.1 - I.78 with a summary, II.1 - II.62 with a summary and III.1 - III.33 with a summary, and received Jan 19, 1977 under 100-583; CDL:95738-C:95744; 95765; 95756; 95769; 95741)

Ciba-Geigy Corporation (1976d) Dual(R) 6E + Lorox(R) Pre-emergence. (Unpublished study that includes reports I.1 - II.27 with a summary, and III.1 - III.28 with a summary; received Jan 19, 1977 under 100-583; CDL:95738-D; 95740; 95760; 95759; 95758)

Ciba-Geigy Corporation (1976e) Dual(R) 6E Preemergence. (Unpublished study that includes reports I.1 - I.139 with a summary, II.1-II.94 with a summary, and III.1 - III.33 with a summary; received Jan 19, 1977 under 100-583; CDL:95738-B; 95742; 95766; 95743; 95752; 95751; 95762; 95761)

Ciba-Geigy Corporation (1976f) Dual(R) 6E Preplant Incorporated. (Unpublished study that includes reports I.1 - I.40 with a summary, II.1-II.21 with a summary and III.1-III.19 with a summary; received Jan 19, 1977 under 100-583; CDL:95738-A; 95755; 95754; 95753)

Ciba-Geigy Corporation (1976g) Compatibility of Dual(R) 6E with Fertilizers and Other Herbicides. (Unpublished study received Jan 19, 1977 under 100-583; CDL:95738-H)

Ciba-Geigy Corporation (1976h) Liquid Fertilizer. (Unpublished study that includes reports Dual/PPI, I.1 - I.8, III.1-III.5; Dual/PRE, I.1 -I.4, III.1 - III.5: received Jan 19, 1977 under 100-583; CDL:95738-F; 95746)

Ciba-Geigy Corporation (1976i) Rotational Crops. (Unpublished study that includes reports Dual/PRE, I. - I.48 with a summary; DUAL/PPI, I.1 - I.11 with a summary; Dual + Sencor/PRE, I.1-I.9 with a summary; Dual + Lorox/PRE, I.1 - 1.5 with a summary; received Jan 19, 1977 under 100-583; CDL:95738-G; 95745; 95739)

Ciba-Geigy Corporation (1977a) Aerial Application. (Unpublished study that includes reports ID-9D with a summary; received Feb 18, 1977 under 100-583; CDL:228101-F;228122)

Ciba-Geigy Corporation (1977b) Aerial Application. (Unpublished study containing reports ID - 10D with a summary; received Jun 20, 1977; CDL:230672-D, 230683)

Ciba-Geigy Corporation (1977c) Aerial Application. (Unpublished study received Nov 8, 1977 under 100-EUP-59; CDL:232194-G)

Ciba-Geigy Corporation (1977d) Application in Liquid Fertilizers. (Unpublished study that includes reports 1-18 with a summary; received Feb 18, 1977 under 100-583; CDL:228101-E; 228121)

Ciba-Geigy Corporation (1977e) Application in Liquid Fertilizers. (Unpublished study containing reports 1-9 with a summary, ID - 4D with a summary; received Jun 20, 1977 under 100-590; CDL:230672-C, 230682)

Ciba-Geigy Corporation (1977f) Application in Fertilizers. (Unpublished study received Nov 8, 1977 under 100-EUP-59; CDL:232194-F)

Ciba-Geigy Corporation (1977g) Application in Fertilizers. (Unpublished study received Nov 14, 1977 under 100-EUP-61; CDL:96624-C)

Ciba-Geigy Corporation (1977h) Application-to-Planting interval. (Unpublished study received Nov 1, 1977 under 100-583; CDL:232134-BB)

Ciba-Geigy Corporation (1977i) Ciba-Geigy Rating System. (Unpublished study received Nov 1, 1977 under 100-583; CDL:232134-C)

Ciba-Geigy Corporation (1977j) Dual(R) 6E + AAtrex(R)--Preemergence. (Unpublished study that includes reports 1-35 with a summary and 1C-32C with a summary; received Feb 18, 1977 under 100-583; CDL:228101-C; 228114; 228115)

Ciba-Geigy Corporation (1977k) Dual(R) 6E + AAtrex(R) --Preplant Incorporated. (Unpublished study that includes reports 1-96 with a summary, 1C-32C with a summary, and 1D-10D with summary; received Feb 18, 1977 under 100-583; CDL:228101-D; 228116; 228117; 228118; 228119; 228120)

Ciba-Geigy Corporation (1977l) Dual 6E Alone --Preemergence. (Unpublished study that includes reports 1-139 with a summary, 1C-70C with a summary, and 1D-12D with summary; received Feb 18, 1977 under 100-583; CDL;228101-A: 228102; 228103; 228104; 228105; 228106; 228107; 228108)

Ciba-Geigy Corporation (1977m) Dual(R) 6E Alone -- Preplant Incorporated. (Unpublished study that includes reports 1-82 with a summary, 1C-52C with a summary, and 1D-11D with summary; received Feb 18, 1977 under 100-583; CDL:228101-B; 228109; 228110; 228118; 228111; 228112; 228113)

Ciba-Geigy Corporation (1977n) Dual(R) 8E + AAtrex(R) + Paraquat or Roundup. (Unpublished study containing reports 1-22 with a summary, 1C-27C with a summary; received Nov 8, 1977 under 100-EUP-59; CDL:232194-D, 232200, 232201)

Ciba-Geigy Corporation (1977o) Dual(R) 8E + AAtrex(R) Early Post. (Unpublished study containing reports 1-47 with a summary, 1C-15C with a summary; received Nov 8, 1977 under 100-EUP-59; CDL:232194-E, 232202, 232203)

Ciba-Geigy Corporation (1977p) Dual(R) 8E Alone. (Unpublished study including reports 1-43 with a summary; received Nov 8, 1977 under 100-EUP-59; CDL:232194-A, 232195)

Ciba-Geigy Corporation (1977q) Dual(R)8E Alone. (Unpublished study that includes reports 1-32 with a summary; received Nov 14, 1977 under 100-EUP-61; CDL:96624-A; 96618)

Ciba-Geigy Corporation (1977r) Dual(R)/Atrazine Prepack: Chemistry Data Section. (Unpublished study; received June 20, 1977 under 100-590; CDL:230686-A)

Ciba-Geigy Corporation (1977s) Dual(R) 8E + Banvel(R). (Unpublished study containing reports 1-21, with a summary, 1C-9C with a summary; received Nov 8, 1977 under 100-EUP-59; CDL:232194-C, 232198, 232199)

Ciba-Geigy Corporation (1977t) Dual(R) 8E + Bladex(R). (Unpublished study containing reports 1-37 with a summary, 1C-10C; received Nov 8, 1977 under 100-EUP-59; CDL:232194-B, 232196, 232197)

Ciba-Geigy Corporation (1977u) Dual + Lorox PRE. (Unpublished study received Nov 1, 1977 under 100-583; CDL:232134-P)

Ciba-Geigy Corporation (1977v) Dual + Lorox -- Soybeans Preemergence: Phyto Summary or 1/13/77 Submission. (Unpublished study received Nov 1, 1977 under 100-583; CDL:232134-Q)

Ciba-Geigy Corporation (1977w) Dual + Lorox -- Soybeans Preemergence: Phyto Summary of 1/13/77 Submission. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-R)

Ciba-Geigy Corporation (1977x) Dual + Lorox PRE Yield Data. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-T)

Ciba-Geigy Corporation (1977y) Dual Preemergence. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-D)

Ciba-Geigy Corporation (1977z) Dual(R) PRE Yields. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-G)

Ciba-Geigy Corporation (1977aa) Dual PRE Yield Data (1977). (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-H)

Ciba-Geigy Corporation (1977ab) Dual(R) PRE Yield Questions. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-I)

Ciba-Geigy Corporation (1977ac) Dual(R) + Lorox(R) Yields. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-S)

Ciba-Geigy Corporation (1977ad) Dual + Lorox Yields. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-U)

Ciba-Geigy Corporation (1977ae) Dual Preplant Incoroporated. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-J)

Ciba-Geigy Corporation (1977af) Dual(R) PPI Yields. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-M)

Ciba-Geigy Corporation (1977ag) Dual PPI Yield Data. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-N)

Ciba-Geigy Corporation (1977ah) Dual(R) PPI Yield Questions. (Unpublished study; received Nov 1,1977 under 100-583; CDL:232134-O)

Ciba-Geigy Corporation (1977ai) Dual + Sencor PRE. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-V)

Ciba-Geigy Corporation (1977aj) Dual + Sencor/Lexone -- Soybeans Preemergence: Phyto Summary of 1/13/77 Submission. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-W)

Ciba-Geigy Corporation (1977ak) Dual + Sencor/Lexone -- Soybeans Preemergence: Phyto Summary of 1/13/77 Submission. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-X)

Ciba-Geigy Corporation (1977al) Dual + Sencor PRE Yield Data. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-Z)

Ciba-Geigy Corporation (1977am) Dual(R) + Sencor(R) Yields. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-Y)

Ciba-Geigy Corporation (1977an) Dual(R) + Sencor(R) Yields. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-AA)

Ciba-Geigy Corporation (1977ao) Dual - Soybeans Preemergence Phyto and Yield review of 1/13/77 Submission. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-E)

Ciba-Geigy Corporation (1977ap) Dual - Soybeans Preemergence Phyto and Summary of 1/13/77 Submission. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-F)

Ciba-Geigy Corporation (1977aq) Dual -- Soybeans Preplant Incorporated: Phyto Summary of 1/13/77 Submission. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-K)

Ciba-Geigy Corporation (1977ar) Dual -- Soybeans Preplant Incorporated: Phyto Summary of 1/13/77. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-L)

Ciba-Geigy Corporation (1977as) Foxtail Millet. (Unpublished study that includes 3, 7, 8, 19, 35, and 52 with a summary; received Nov 1, 1977 under 100-583; CDL:232134-A)

Ciba-Geigy Corporation (1977at) M+A 4.5L - Preemergence. (Unpublished study containing reports 1-71 with a summary, 1C-12C with a summary, and 1D -16D with a summary; received Jun 20, 1977 under 100-590; CDL:230672-A, 230673, 230674, 230675, 230676).

Ciba-Geigy Corporation (1977au) M+A 4.5L - Preplant Incorporated. (Unpublished study containing reports 1-50 with a summary, 1C-9C with a summary, and 1D-12D with a summary; received Jun 20, 1977 under 100-590; CDL:230672-B, 230678, 230679, 230680, 230681)

Ciba-Geigy Corporation (1977av) Response to EPA Comments Concerning Marginal Soybean Tolerance to Dual(R) PPI or PRE, Dual + Lorox(R) or Dual + Sencor(R) Application. (Unpublished study; received Nov 1, 1977 under 100-583; CDL:232134-B)

Ciba-Geigy Corporation (1977aw) Rotational Crops. (Unpublished study containing reports 1-13 with a summary; received Jun 20, 1977 under 100-590; CDL:230672-E 230684)

Ciba-Geigy Corporation (1977ax) Rotational Crops. (Unpublished study including reports Vol. 2 - Report 40 and Vol. 9 - Report 46; received Nov 8, 1977 under 100-EUP-59; CDL:232194-H, 232195, 232202)

Ciba-Geigy Corporation (1977ay) Tank Mixtures. (Unpublished study; received Nov 14, 1977 under 100-EUP-61; CDL:96624-B)

Ciba-Geigy Corporation (1977az). Rotational Crops. (Unpublished study that includes reports 1-49 with a summary, 1-39 with a summary; received Feb 18, 1977 under 100-583; CDL:228101-G; 228123; 228124)

Ciba-Geigy Corporation (1977ba) Section A General Chemistry. (Unpublished study; received Jan 19, 1977 under 7F1913; CDL:95764-A)

Ciba-Geigy Limited (1973?) CGA 24 705 Feeding Study in Milk Cows: Methods. (Unpublished study; received Sep 26, 1974 under 5G1553; CDL:94216-G)

Ciba-Geigy Limited (1973?) CGA 24 705 Feeding Study in Milk Cows: Methods. (Unpublished study prepared by Ciba-Geigy Ltd.; St. Aubin, Switzerland; received Nov 14, 1977 under 8G2019; CDL:96626-C)

Ciba-Geigy Limited (1974) CGA 24705: Hydrolysis of CGA-24705 under Laboratory Conditions. AC 2.53/NB/cr; SPR 2/74. (Unpublished study; received Mar 27, 1975 under 5F1606; CDL:94376-J)

Ciba-Geigy Limited (1976a) Dominant Lethal Study on CGA 24705 Technical: Mouse (Test for Cytotoxic or Mutagenic Effects on Male Germinal Cells) PH 2.632. (Unpublished study including Addendum; received Jan 18, 1978 under 7F1913; CDL:96717-C; 96717-D)

Ciba-Geigy Limited (1976b) Reproduction Study CGA 24705 Tech.: Rat: Seg. II (Test for Teratogenic or Embryotoxic Effects) PH 2.632. (Unpublished study including Addendum; received Jan 18, 1978 under 7F1913; CDL: 96717-A; 96717-B)

Ciba-Geigy Limited (1977) Skin Sensitizing (Contact Allergenic) Effect in Guinea Pigs of Technical CGA 24705: Siss 5726. (Unpublished study; received Jan 18, 1978 under 7F1913; CDL:96717-E)

Coquet, B.; Galland L.; Guyot, D.; Fouillet, X.; Rouaud, J.L. (1974a) Essai de Toxicite de 3 Mois chez Le Chien par Voie Orale du Produit CGA 24 705. [Three-Month Oral Toxicity Trial of CGA 24 705 in Dog]: IC-DREB-R-740119. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by the Oncins Research and Breeding Center for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94223-B)

Coquet, B.; Galland L.; Guyot, D.; Fouillet, X.; Rouaud, J.L. (1974b) Essai de Toxicite de 3 Mois chez Le Rat par Voie Orale du Produit CGA 24 705. [Three month oral Toxicity Trial of CGA 24 705 in Rats]: IC-DREB-R-740120. (Unpublished study received Mar 1, 1974 under 5G1553; prepared by the Oncins Research and Breeding Center for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94219-B)

Coquet, B.; Galland L.; Guyot, D.; Fouillet, X.; Rouaud, J.L. (1974c) Three-Month Oral Toxicity Test of CGA 24 705 in Dog. A translation of: Essai de Toxicite de 3 Mois chez Le Chien par Voie Orale du Produit CGA 24 705: IC-DREB-R-740119. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by the Oncins Research and Breeding Center for Ciba-Geigy Corp., Greensboro, N.C.; CDL;94223-A)

Coquet, B.; Galland, L.; Guyot, D.; Fouillet, X.; Rouaud, J.L. (1974d) Three-Month Oral Toxicity Test of CGA 24 705 in Rats. A translation of: Essai de Toxicite de 3 Mois chez Le Rat par Voie Orale du Produit CGA 24 705: IC-DREB-R-740120. (Unpublished study received Mar 1, 1974 under 5G1553; prepared by the Oncins Research and Breeding Center for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94219-A)

Counselman, C.J.; Roger, J.C. (1973) Biological Report, Goat Metabolism Study with ø-$^{14}$C-CGA-24705 and ø-$^{14}$C-CGA-17020. (Unpublished study received Nov 25, 1975 under 6G1708; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94984-K)

Cullen, T.; Balu, K. (1973) Determination of CGA-18762 Residues in Corn Forage, Stover, and Grain by Microcoulometric Gas Chromatography. Method AG-249 dated Jun 20, 1973. (Unpublished study received Nov 6, 1975 under 4G1469; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:95190-B)

Davis, T.W. (1976) Report to Ciba-Geigy Corporation: Eye Irritation Test with CGA-24705 + Atrazine (2.5:2.0) 4.5L:IBT No. 601-08061. (Unpublished study received Jun 20, 1977 under 100-590; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp.; Greensboro, N.C.; CDL:230687-A)

Derot, P. (1976) Desherbage du maise: L' association metetlilachlor + atrazine.[Weed control in maize: A mixture of metetilachlor (CGA24705) and atrazine] La Defense des Vegetaux 30(177): 39-48.

Dest, W.M.; Peters, R.A., Barrett, M. (1976) The control of crabgrass and redroot pigweed in the silage corn. Pages 55-58, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976, Boston, Massachusettes. Salisbury, Md.: University of Maryland, Vegetable Research Farm:

Dietz, W.P.; Jennings, V.M. (1976) 1975 No-till corn herbicide results in northeast Iowa. Pages 151-152, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975, Milwaukee Wisconsin. Omaha, Neb.; by the Stauffer Chemical Company for the North Central Weed Control Conference:

Diner, A.M.; Davis, D.E.; Truelove, B. (1977) Absorption and translocation of root and foliar-applied $^{14}$C-metolachlor in soybean: Abstract. Pages - , In Proceedings of the Thirtieth Meeting of the Southern Weed Science Society; Jan 19-21, 1977, Dallas, Texas. Raleigh, N.C.: Glover Printing for the Southern Weed Science Society.

Donald A. Willigan, Incorporated (1975) Supplementary Report to Contract No.: 120-2255-34: Histopathological Evaluation: Twenty-One day Repeated Dermal Toxicity of CGA 24705-6E in Rabbits. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Affiliated Medical Research, Inc., Princeton, N.J. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94377-A)

Draize, J.H. (1959) The Appraisal of Chemicals in Food, Drugs, and Cosmetics. Austin, Texas: Association of Food and Drug Officials of the United States.

Dreier, H. (1977) Report to Ciba-Geigy Corporation: Acute Aerosal Inhalation Toxicity Study with Dual(R) 8E (FL-770350) in Albino Rats: IBT 8562-10823. (Unpublished study received Nov. 8, 1977 under 100-EUP-059; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C., including Addendum C — Validation by Ciba-Geigy Corp.; CDL:232191-C)

Dupre, G.D. (1974a) Abbreviated Anaerobic Metabolism of $^{14}$C-CGA-24705 in Silt Loam Soil under Greenhouse Conditions: Report No. 73019-3. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Bio/dynamics Inc. for Ciba-Geigy Corp., Greensboro, N.C. CDL:94222-B)

Dupre, G.D. (1974b) Leaching Characteristics of $^{14}$C-CGA-24705 and its Degradation Products Following Aging in Sandy Loam Soil under Greenhouse Conditions: Report no. 73021-6. (Unpublished study received by Sep 26, 1974 under 5G1553; prepared by Bio-dynamics Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94222-C)

Dupre, G.D. (1974c) Runoff Characteristics of $^{14}$C-CGA-24705 Applied to Sandy Loam Soil under Greenhouse Conditions: Report no. 73022-1. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Bio-dynamics Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94222-D)

Elkins, D.M.; Vandeventer, J.W.; Briskovich, M.A. (1977). Effect of chemical growth retardants on turfgrass morphology. Agronomy Journal 69(3): 458-461.

Ellegehausen, H. (1976a) Project Report 48/76: A Model system for Estimating the Uptake, Transfer and Degradation of Agrochemicals by Aquatic Organisms. AC 2.52. (Unpublished study received Feb 6, 1978 under 100-583; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:232789-B)

Ellegehausen, H. (1976b) Project Report 4/76: Degradation of CGA 24 705 in Aerobic, Anaerobic and Autoclaved Soil. AC 2.52. (Unpublished study received Feb 6, 1978 under 100-583; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:232789-D)

Ellegehausen, H. (1976c) Project Report 5/76: Addendum to Project Report 4/76: Degradation of CGA 24 705 in Aerobic, Anaerobic and Autoclaved Soil. AC 2.52. (Unpublished study received Feb 6, 1978 under 100-583; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:232789-E)

Ellegehausen, H. (1977) Project Report Project Report 32/77: Uptake, Transfer and Degradation of CGA 24705 (Dual$^{(R)}$) by Aquatic Organisms. AC 2.52. (Unpublished study received Feb 6, 1978 under 100-583; prepared by Ciba Geigy Ltd., Basle, Switzerland; CDL:232789-C)

Environmental Protection Agency (1977) 2-Chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl-acetamide): Extension of Temporary Tolerances. Federal Register 42 (67): 18426.

Ercegovich, C.D.; Bogus, E.R.; Buly, R.L. (1978) The Effects of 5, 25, and 125 PPM of Metolachlor, [2-Chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide] on Actinomycetes, Bacteria and Fungi in Laboratory Culture Tests. E-2/1-CG78. received Feb 6, 1978 under 100-583; (Unpublished report received Feb 6, 1978 under 100-583; prepared by Pesticide Research Lab., Pennsylvania State University for Ciba-Geigy Corp., Greensboro, N.C.; CDL:232789-F)

Ercegovich, C.D.; Vallejo, R.P.; Bogus, E.R. (1978) The Effects of 5, 25, and 125 PPM of Metolachlor, [2-Chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-

methylethyl) acetamide], on Soil Nitrification. E-3/2-CG78. (Unpublished study received Feb 6, 1978 under 100-583; prepared by Pesticide Research Lab., Pennsylvania State University for Ciba-Geigy Corp., Greensboro, N.C.; CDL:232789-G)

Eschiapati, D.; Dachler, C. (1976) Metetilachlor + Atrazine, a new herbicide for corn crops. Resumos XI Seminario Brasileiro de Herbicidas e Ervas Daninhas, Londrina, 1976: 44-45.

Fink, R. (1974a) Eight-Day Dietary $LC_{50}$--Mallard Ducks Technical CGA-24705: Project No. 108-111. Received Sep 26, 1974 under 5G1553. (Unpubli report Truslow Farm Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-O)

Fink, R. (1974b) Eight-Day Dietary $LC_{50}$--Bobwhite Quail Technical CGA-24705: Project No. 108-111. (Unpublished study received Sep 26, 1974 under 5G1553.; Truslow Farm Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-P)

Fink, R. (1976) Acute Oral $LD_{50}$ - Mallard Duck: CGA-24705 Technical: Final Report. (Unpublished study received Nov 23, 1976 under 100-587; prepared by Truslow Farms Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:226955-D)

Frans, R.E.; Richardson, J.T.; Gordon, E.C. (1977) Herbicide Field Evaluation Trials on Field Crops, 1976. Fayetteville, Ark.: University of Arkansas, Department of Agronomy. (Arkansas Agricultural Experiment Station, Mimeograph Series 249)

Frans, R.E.: Blythe, T.O.; Richardson, J.T. (1976). Herbicide Field Evaluation Trials on Field Crops, 1975. Fayetteville, Ark.: University of Arkansas, Department of Agronomy. (Arkansas Agricultural Experiment Station, Mimeograph Series, 240)

Fritz, H. (1976) Reproduction Study CGA 24705 Tech. Rat: Seg. II: (Test for Teratogenic or Embryotoxic Effects): PH 2.632. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:95768-A)

Gerber, H.R.; Mueller, G.; Ebner, L. (1974) CGA 24705, A new grasskiller herbicide. Pages 787-794, In Proceedings of the 12th British Weed Control Conference; Nov 18-12, 1974 Brighton, England. Begbroke Hill, Oxford, England:ARC Weed Research Organization.

Gesme, J.; Albanese, E.; Marias, A.J. (1977) Report to Ciba-Geigy Corporation: Carcinogenicity Study with CGA-24705 Technical in Albino Mice: IBT No. 622-07925 (8532-07925). (Unpublished study received Jan 18, 1978 under 7F1913; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp.; including Validation report prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:96719-A; 96720-A; 96720-B)

Gfeller, W. (1974) Tolerability Trial in Milk Cows with CGA 24 705: 14, 21 and 28 day Feeding Study: AC 9.26; T73/23. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., St. Aubin, Switzerland; CDL:94216-F)

Gold, B.; Kahrs, R.A. (1975a) DC-200: An Alternate Gas Chromatographic Column for the Determination of CGA-37913: GAAC-75026. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-X)

Gold, B.; Kahrs, R.A. (1975b) Freeezer Storage Stability of CGA-24705 Residues in Corn Fodder and Grain: GAAC-75062. (Unpublished study received Nov 25, 1975 under 6G1708; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94877-Y)

Gross, D. (1974a) Project Report No. 8/74: Uptake, Translocation and Degradation of CGA 24 705 in Corn Grown under Controlled Conditions. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94217-F)

Gross, D. (1974b) Project Report No. 13/74: Addendum to Project Report No. 8/74: Uptake, Translocation and Degradation of CGA 24 705 in Corn Grown under Controlled Conditions: AC 2.52. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94378-H)

Guth, J.A. (1974) CGA 24705: Total Residues in Chicken Tissues and Eggs, 1974: AC 2.53; RVA 88/74. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94216-D)

Hack, H., Schmidt, R.R. (1976). Use of Metamitron in weed control systems in sugar beets. Pages 197-204, In Proceedings 1976 British Crop Protection Conference, Bayer AG, Pflanzenschutz Anwendunstechnik, Leverkusen, Federal Republic of Germany.

Hambock, H. (1974a) Project No. 7/74: Metabolism of CGA 24 705 in the Rat. (Status of Results Gathered up to June 10, 1974): AC 2.52. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94217-L)

Hambock, H. (1974b) Project Report 12/74: Addendum to Project Report 7/74: Metabolism of CGA 24 705 in the Rat: AC 2.52; (Unpublished study received Nov 25, 1975 under 6G1708; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94984-P)

Hambock, H. (1974c) Project Report No. 1/74: Distribution, Degradation and Excretion of CGA 24 705 in the Rat. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94217-K)

Harrison, W.A.; (1975) Report to Ciba-Geigy Corporation: Acute Toxicity Studies with CGA 24705 + Atrazine: IBT No. 601-07539. (Unpublished study received Dec 29, 1975 under 100-EUP-45; prepared by Industrial Bio-Test Laboratories, Inc., For Ciba-Geigy Corp., Greensboro, N.C.; CDL:224074-B; 231913)

Harvey, R.G.; Baker, C.R. (1974?) Annual Weed Control in Corn Study: Project No. 755. (Unpublished study received Feb 9, 1976 under 100-EUP-44; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:96496-C)

Heinrichs, L. (1975) Determination of CGA-24705 and Procyazine in GA-2-686 15G by Gas Chromatography: Method PA-71 T dated Oct 9, 1975. (Unpublished study received Feb 9, 1976 under 100-EUP-44; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:96496-A)

Heinrichs, L. (1976) The Determination of Metolachlor in Dual(R) 6E by Gas Liquid Chromatography. Method PA-9A dated Dec 16, 1976. (Unpublished study received Nov 14, 1977 under 100-EUP-61; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:96623-A)

Helseth, J.; Cole, G. (1973) The Determination of CGA-24705 in Emulsifiable Concentrates by Gas Liquid Chromatography. Method PA-9 dated Nov 14, 1973. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:96666-A)

Hermes, P. (1970) Extraction of Radioactive Metabolites from Sorghum Treated with $^{14}C$ GS-13529. Method AG-141 dated Jun 23, 1970. (Unpublished study received Mar 26, 1975 under 5F160; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-A)

Hermes, P. (1972) Biphasic Extraction of Radioactive Metabolites from Treated Biological Material. Method AG-214 dated Aug 15, 1972. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94216-M)

Hermes, P. (1973) Radioassay of $^{14}C$ in Biological Materials by Combustion using the Harvey Biological Material Oxidizer (BMO). Method AG-252 dated Aug 14, 1973. (Unpublished study received Sep 26, 1974 under 5G1553.; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94216-R)

Higgins, E.R.; Schnappinger, M.G.; Pruss, S.W. (1975) Yellow nutsedge control with CGA-24705 in corn and soybeans. Pages 9-16, In Proceedings of the Twenty-Ninth Annual Meeting of the Northeastern Weed Science Society; Jan 7-9, 1975; New York City. Salisbury, Md.: University of Maryland, Vegetable Research Farm.

Higgins, E.R.; Schnappinger, M.G.; Pruss, S.W. (1976) CGA-24705 plus atrazine yellow nutsedge control in corn. Pages 65-70, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976; Boston, Massachusettes. Salisbury, Md.: University of Maryland, Vegetable Research Farm.

Hofberg, A.; Balu, K. (1972a) Preparation of a Model System to Study Aqueous Solution Photolysis in a Laboratory Environment. Method AG-208 dated Aug 11, 1972. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94216-L)

Hogenboom, P.W. (1976) Metetilachlor - a new grass herbicide. Resumas XI Seminario Brasileir de Herbicidas e Eruas Daininhas, Londrina, 1976: 127-128.

Holliday, W.K. (1975) Report to Ciba-Geigy Corporation: Acute Aerosol Inhalation Toxicity Study with CGA-24705 + Atrazine (2.5:2.0) 4.5F in Albino Rats: IBT No. 633-07540. (Unpublished study received Dec 29, 1975 under 100-EUP-45; prepared by Industrial Bio-Test Laboratories, Inc., for Ciba-Geigy Corp., Greensboro, N.C.; CDL:224074-C)

Hormann, W.D.; Guth, J.A.; Formica, G.; Schenker, M. (1974) CGA 24705: Gas Chromatographic Determination of Total Residues in Material of Animal Origin. (Provisional): AC 2.53; REM 5/74. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94216-E)

Houseworth, L.D. (1973?a) Effect on CGA-24705 on Microbial Populations in Two Soils: Report No. 2. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by University of Missouri--Columbia, Department of Plant Pathology for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94222-F)

Houseworth, L.D. (1973?) Report on Parent Leaching Studies for CGA-24705: Report No. 1. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by University of Missouri--Columbia, Department of Plant Pathology for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94222-E)

Houseworth, L.D. (1977) Residues of Metolachlor and Atrazine in or on Corn Grain Resulting from Preemergence and Preplant Incorporated Application of a Liquid Prepack Formulation of Metolachlor and Atrazine with and without Liquid Fertilizer. (Unpublished study including reports AG-A-3298 II, III, AG-A-3325 II, AG-A-3326 II, AG-A-3372 II, AG-A-3406 II, AG-A-3674 II, III, AG-A-3745 I, II, III, with a summary ABR-77028; received Jun 20, 1977 under 100-590; prepared by Ciba-Geigy Corp.; Greensboro, N.C.; CDL:230685-A)

Houseworth, L.D. (1977) Residues of Metolachlor and Dicamba in or on Corn Grain Resulting from Preemergence Tank Mix Applications: ABR-77071. (Unpublished study containing reports AG-A 4253, AG-A 4264, AG-A 4270 received Nov 8, 1977 under 100-EUP-59; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:232192-A)

Houseworth, L.D.; Rolla, H. (1976) Residues from Metolachlor Alone and in Tank Mix with Linuron, Metribuzin and Liquid Fertilizer in Soybeans: ABR-76077. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95767-A)

Houseworth, L.D.; Rolla, H. (1977a) Residues of Metolachlor and Atrazine in or on Corn Grain Resulting from Tank Mix Applications with and without Liquid Fertilizer-Preplant Incorporated and Preemergence Applications: ABR-77017. (Unpublished study that includes studies AG-A-3325 II, AG-A-3406 II, AG-A-3672 II-III, AG-A-3673 I, II, III, AG-A-3704 I, II, AG-A-3735 I, II, III, AG-A-3799 II, III, AG-A-3858 with a summary; received Feb 18, 1977 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C., CDL:228126-A)

Houseworth, L.D.; Rolla, H. (1977b) Residues of Metolachlor in or on Sorghum Resulting from Preplant Incorporated and Preemergence Applications: ABR-77086. (Unpublished study, that includes studies AG-A-4413, AG-A-4418, AG-A-4503, and AG-A-4753, received Nov 14, 1977 under 8G2019; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:96625, 96626-A, 96626-B, 96626-C, 96626-D)

Iggo, G.A. (1975) Results of screening preemergence herbicides for sugarcane. Pages 11-14, In Proceedings of the South African Sugar Technologists' Association Forty-Ninth Meeting; Jun 30-Jul 4, 1975; Durban, South Africa. Durban, South Africa: Hayne and Gibson Ltd. for the Society and the South African Sugar Association Experiment Station:

Industrial Bio-Test Laboratories, Incorporated (1975) Report to Ciba-Geigy Corporation: Acute Dust Inhalation Toxicity Study with CGA-24705 + CGA-18762 (1:1) 15G(FL-751873) in Albino Rats: IBT No. 663-07826. (Unpublished study received Feb 9, 1976 under 100-EUP-44; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:96495-B)

Industrial Bio-Test Laboratories, Incorporated (1975) Report to Ciba-Geigy Corporation: Acute Toxicity Studies with CGA-24705 + CGA-18762 (1:1) 15G: IBT No. 601-07825. (Unpublished report received Feb 9, 1976 under 100-EUP-44; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:96495-A)

Jagschitz, J.A. (1976) Response of Kentucky bluegrass to growth retardant chemicals. Pages 327-333, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976; Boston, Massachusettes. Salisbury, Md. University of Maryland, Vegetable Research Farm.

Jordan, L.; Harvey, G. (1976) Comparison of acid aralid herbicides for canning pea weed control. Page 30, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975; Milwaukee, Wisconsin. Omaha, Neb.; by Stauffer Chemical Company for the North Central Weed Control Conference.

Jooste, J. v.d. W.; Van Biljon, J.J. (1976). Metolachlor + Atrazine a combination pre-emergence herbicide for broad spectrum weed control in maize. Gewasproduksie/crop production 5:85-90.

Kahrs, R.A. (1977) Tank Mixes of Metolachlor Plus Atrazine Plus Paraquat - Corn: No and Minimum Tillage Applications: Summary of Residue Data: ABR-77074. (Unpublished study containing reports AG-A-4167 II, AG-A-4187 II, III, AG-A-4198 II, III, AG-A-4247 II, III, AG-A-4288 I, II received Nov 8, 1977 under 100-EUP-59; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:232192-H)

Kaiser, F. (1974) Soil Degradation Study of Ciba-Geigy $^{14}C$-CGA-24705. (Unpublished study received Mar 27, 1975 under 5F1606; prepared by Analytical Biochemistry Laboritories, Inc., Submitted by Ciba-Geigy Corp., Greensboro, N.C.; CDL: 94376-A)

Karlhuber, B.; Ramsteiner, K. (1973) CGA 24705: Gas Chromatographic Residue Determination in Plant Material, Grains and Soil. (Provisional): AG 2.53; REM 2/73. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94222-G)

Keezer, W. (1971) Ion-Exchange Characterization of Metabolites of Radioactive Pesticides. Method AG-156 dated Mar 3, 1971. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-C)

Kennedy, G.L. (1975) 28-Day Mouse Pilot Study with CGA-24705 (Technical). dated Nov 21. 1975; IBT No. 622-07857. (Unpublished study received Feb 16, 1978 under 100-583; prepared by Industrial Biotest Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL-232855-B)

Kennedy, G.L. (1976a) Letter [dated Dec 10, 1976, relative to the results of the first generation of a three generation reproduction study in albino rats with the chemical CGA 24705 (IBT No. 8533-07928)] to George Rolofson. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Industrial Bio-Test Laboratory, Inc., for Ciba-Geigy Corp., Greensboro, N.C.; CDL:95768-E)

Kennedy, G.L. (1976b) Letter [dated Dec 13, 1976, interim report on IBT No. 8531-07926, 2 year chronic toxicity of CGA 24705 in albino rats] to George Rolofson. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Industrial Bio-Test Laboratory, Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:95768-D)

Kennedy, G.L. (1976c) Letter [dated Dec 13, 1976, relative to the 2 year carcinogenicity study of CGA 24705 in albino mice (IBT No. 8531-07925)] to George Rolofson. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Industrial Bio-Test Laboratories, Inc., for Ciba-Geigy Corp., Greensboro, N.C.; CDL:95768-C)

Knaak, J.B.; Tallant, M. J.; Bartley, W.J.; Sullivan, L.J. (1965) The metabolism of carbaryl in the rat, guinea pig, and man. Journal of Agricultural and Food Chemistry. 13(6): 537-542. (Also In unpublished report received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94221-C)

Kurtz, L.; Stroube, W. (1976). Control of yellow nutsedge by various herbicides. Page 59, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975; Milwaukee, Wisconsin. Omaha, Neb.; by the Stauffer Chemical Company for the North Central Weed Control Conference.

Lazzara, K.; Paa, H. (1975) Report to Ciba-Geigy Corporation: Acute Dermal Toxicity Study with 1:4 Aqueous Suspension of CGA-24705 + Atrazine (2.5:2.0) 4.5L in Albino Rabbits: IBT No. 601-08061. (Unpublished study received Jun 20, 1977 under 100-590; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:230687-B)

Lee, T.; Kaldon, H. (1974) [Tank-Mix Compatabilities Test Report for CGA-24705-6E, GA-2-621, with other Herbicides]: AG Request No. 4349. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94384-A)

Lorenzi, H.J. (1976j). Herbicide tests on corn crops. Resumes XI Seminario Brasileiro de Herbicidas e Eruas Daninhas, Londrina, 1976: 38:39

Maher, J.; Heinrichs, L. (1975a) Analysis of Atrazine and CGA-24705 in GA-2-622 4.5 L Formulation. Method Pa-72-T dated Oct 9, 1975. (Unpublished study received Dec 29, 1975 under 100-EUP-45.; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:224074-A)

Maher, J.; Heinrichs, L. (1975b) Analysis of Atrazine and CGA-24705 in Ultrex™ 4.5L Formulation by Gas Chromatography. Method PA-72-T dated Oct 9, 1975. (Unpublished study received Jun 20, 1977 under 100-590; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:230686-B)

Marco, G. (1974) Summary of Section D: CGA-24705-Corn: Residues Observed and Metabolism Data Including the Analytical Methods Used: GAAC-74062. (Unpublished study that includes reports AG-A-2929, AG-A-2969, AG-A-2973, AG-A-3105, AG-A-3133; received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:94217-A; 94222)

Marco, G. (1975) Summary of Section D: CGA-24705 Corn: Residues Observed and Metabolism Data Including the Analytical Methods Used: GAAC-75001. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94378-A)

Mattson, A.M. (1969) Quantitative Determination of Triazine Herbicides in Soils by Chemical Analysis: GAAC-69014. (Unpublished study received Feb 18, 1977 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:228125-B)

Mattson, A.M. (1974) CGA-24705 Residues in Milk, Meat, Eggs and Chickens (Three Level Feeding Studies): GAAC-74064. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94216-B)

Mattson, A.M. (1975) CGA-24705 Residues in Milk, Meat, Eggs and Chickens (Three Level Feeding Studies): GAAC-75059. (Unpublished study received Nov 25, 1975 under 6G1708; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94878-A)

Mattson, A.M.; Kahrs, R.A. (1969) Quantitative Determination of Triazine Herbicides in Soils by Chemical Analysis: GAAC-69014. (Unpublished study received Nov 8, 1977 under 100-EUP-59; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:232193-H)

Mattson, A.M.; Kahrs, R.A. (1975a) Procyazine -- Corn: Tank Mixes with CGA-24705 with and without Fertilizers, Preemergence and Preplant Incorporated Applications: Procyazine Plus CGA-24705-15% Granule: GAAC-75077.

(Unpublished study that includes reports AG-A-3638, AG-A-3671, AG-A-3716, AG-A-3731, AG-A-3741, AG-A-3798, AG-A-3703, AG-A-3726, AG-A-3784, AG-A-3817; received Nov 26, 1975 under 4G1469; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:95190-A)

Mattson, A.M.; Kahrs, R.A. (1975b) Residues in Field Grown Corn Following Use of CGA-24705 Determined as CGA-37913 and CGA-49751: GAAC-75015. (Unpublished study that includes reports AG-A-2967, AG-A-2982, AG-A-3255, AG-A-3289, AG-A-3299, AG-A-3328, AG-A-3383, AG-A-3501, AG-A-3005, AG-A-3153, AG-A-3446; received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:94379-B)

Mattson, A.M.; Kahrs, R.A. (1975c) Summary of Residue Data CGA-24705-Atrazine Combinations as Corn Herbicides Tank Mixes-Dual™ 6EC Plus AAtrex(R) 80W or AAtrex(R) 4L Flowable Combination Formulation-GA-2-6-622 4.5L Preemergence and Preplant Incorporated Applications: GAAC-75081. (Unpublished study including reports AG-A-2974; AG-A-3057; AG-A-3070; AG-A-3288; AG-A-3298; AG-A-3325; AG-A-3326; AG-A-3372; AG-A-3406; received Dec 29, 1975 under 100-EUP-45; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:224074-D)

Mattson, A.M.; Rolla, H. (1975) Summary of Section D: CGA-24705-Soybeans: Residues Observed and Metabolism Data Including the Analytical Methods Used: GAAC-75057. (Unpublished study that includes reports AG-A-3268, AG-A-3466, AG-A-3523, AG-A-3570, AG-A-3650 I & II, AG-A-3702, AG-A-3724, AG-A-3743, AG-A-3776, AG-A-3780, AG-A-3803; received Nov 25, 1975 under 6G1708; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:94984-A; 94878)

Mattson, A.M.; Kahrs, R.A.; Schneller, J. (1965) Use of Microcoulometric gas chromatograph for triazine herbicides. Journal of Agricultural and Food Chemistry 13(2): 120-122. (Also In unpublished study received Feb 18, 1977 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:228126-K)

McCohen, L.L.; Tiedje, J.M. (1978). Metabolism of two new acylanilide herbicides, Antor Herbicide (H-22234) and Dual (Metolachlor) by the soil fungus Chaetomium globosum. Journal of Agricultural and Food Chemistry 26(2):414-419.

McGahen, L.L.; Tiedje, J.M. (1978). Metabolism of two new acylanilide herbicides, Antor Herbicide (H-22234) and Dual (Metolachlor) by the soil fungus Chaetomium globosum. Journal of Agricultural Food Chemistry 26(2): 414-419.

McLaughlin, J.P.; Hartwig, N.L. (1976) Yellow nutsedge control in conventional, minimum, and no-tillage corn, Pages 7il-76, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976; Boston, Massachusettes. Salisbury, Md: University of Maryland, Vegetable Research Farm.

Michieka, R.W.; Ilnicki, R.D.; Somody, J. (1976). The response of corn and annual weeds to some new herbicides used alone and in combination with atrazine or alachlor. Pages 46-47, In Proceedings of the Northeastern Weed Science Society.

Michieka, R.W.: Ilnicki, R.D.: Somody, J. (1977). Weed control in potatoes with preplant incorporated herbicides applied alone, in combination, and with follow-up preemergence herbicides. Pages 197-198 In Proceedings of the Northeastern Weed Science Society.

Miyazaki, S. (1976) Gas Chromatographic Residue Determination of CGA-24705 in Soil. Method AG-303 dated Oct 15, 1976. (Unpublished study received Jan 19, 1977 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95763-B)

Miyazaki, S. Kahrs; R.A. (1974) Specificity of the Residue Determination of CGA-24705 Metabolic Residues in Corn (AG-265): GAAC-74063. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94216-J)

Miyazaki, S.; Kahrs, R.A. (1975) Specificity of the Residue Determination of CGA-24705 Residues in Corn (AG-277): GAAC-75014. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-W)

Murphy, H.J.; Gajewski, T. (1977). Effect of several herbicides applied preemergence, at drag-off and layby on weed control in white potatoes. Pages 176-179, In Proceedings of the Northeastern Weed Science Society.

Murphy, H.J.; Goven, M.J. (1976). A comparison of AC 92,553, CGA-24705, and FMC 25213 in combination with metribuzin for weed control in potatoes. Pages 256-261, In Proceedings of the Northeastern Weed Science Society.

Nham, Dan; Harrison, W.A. (1977a) Report to Ciba-Geigy Corporation: Acute Oral Toxicity Study with Dual(R) 8E in Albino Rats: IBT No. 8530-10822. (Unpublished study received Nov 8, 1977 under 100-EUP-59; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C., including Addendum A — Validation by Ciba-Geigy Corp.; CDL:232191-A)

Nham, Dan; Harrison, W.A. (1977b) Report to Ciba-Geigy Corporation: Acute Dermal Toxicity Study with Dual(R) 8E in Albino Rabbits: IBT 8530-10822. (Unpublished study received Nov 8, 1977 under 100-EUP-59; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C.; including Addendum B--Validation by Ciba-Geigy Corp; CDL:232191B)

Noll, C.J.(1976). Chemical weed control on snap beans. Pages 202-204, In Proceedings of the Northeastern Weed Science Society 30:202-204.

Norton, J.A. (1978) Letter Sent to George LaRocca data Aug 28, 1978. Dual 8E Herbicide [Request for Acceptance of Finished Labeling to Allow Use on Corn Grown for Grain, Excluding Popcorn.] Received May 1978 under 100-597. (Submitted by Ciba-Geigy Corp., Greensboro, N.C.)

Norton, J.A. (1978) [Letter on Dual(R) 6E Herbicide -EPA Reg. No. 100-583 Ciba-Geigy follow-up to requests from Mr. James Skaptason, Metolachlor Generic Standard] to Mr. Henry M. Jacoby, dated Feb 21, 1978. (Unpublished

letter from the files of the Office of Pesticide Programs, Technical Services Division. Received Feb 22, 1978 under 100-583 prepared by Ciba-Geigy Corp., Greensboro, N.C; CDL:232898)

Norton, J.A. (1977) Letter sent to Henry Jacoby dated May 20, 1977. [Relative to the May 17, 1977, meeting between H. Craven, R. Felthausen, and H. Jacoby of EPA and J. Barnett, L. Newly, and J. Norton of Ciba-Geigy. Conclusions reached on text protocols, data requirements, and timetables relating both to Ciba-Geigy's petition for residue tolerances for metolachlor in soybeans and to its application for registering Dual 6E for selective weed control]. (Submitted by Ciba-Geigy and on file in Generic Standards Branch, OPP)

Norton, J.A. (1978) Letter sent to Henry Jacoby dated March 23, 1978. [Dual 6E Herbicide - Follow-up to questions raised by Mr. Harry. Craven, Efficacy and Ecological Effects Branch, During Reviews for Metolachlor Generic Standard.] Received May 1978 under 100-583. (Submitted by Ciba-Geigy Corp., Greensboro, N.C., and on file in Generic Standards Branch, OPP)

Norton, J.A. (1978) Letter sent to Henry Jacoby dated February 3, 1978. [Dual 6E Herbicide - Binomial Nomenclature - Channel Catfish.] Received Feb 27, 1978 under 100-583. (Submitted by Ciba-Geigy Corp., Greensboro, N.C. and on file in Generic Standards Branch, OPP)

Norton, J.A. (1978) Letter sent to Henry Jacoby dated March 8, 1978. [Dual 6E Herbicide - Regarding Norton's February 3, 1978 Letter on Binomial Nomenclature for Channel Catfish]. Received Mar 1978 under 100-853. (Submitted by Ciba-Geigy Corp., Greensboro, N.C. and on file in Generic Standards Branch, OPP)

Oncins Research and Breeding Center (1974) Three-Month Dietary Feeding Study in Rats: CGA 24 705. A translation of: Toxicite de 3 Mois chez le Rat par Voie Orale du Produit CGA 24 705, translated by F. Roulet: IC-DREB-R 741009. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94377-B)

Paa, H. (1976a) Report to Ciba-Geigy Corporation: Acute Dermal Toxicity Study with an Aqueous Herbicide Use Dilution Containing a Combination of Dual(R) 6EC (FL-760205) and Lorox(R) 50 W (FL-761533) in Albino Rabbits: IBT No. 8530-09780. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL;95768-G)

Paa, H. (1976b) Report to Ciba-Geigy Corporation: Acute Dermal Toxicity Study with an Aqueous Herbicide Use Dilution Containing a Combination of Dual(R) 6EC (FL-760205) and Sencor(R) 50W (FL-761088) in Albino Rabbits: IBT No. 8530-09781. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Industrial Bio-Test Laboratory Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:95768-H)

Parker, C.; Dean, M.L. (1976) Control of wild rice in rice. Pesticide Science 7(4):403-416.

Parochetti, J.V. (1975) Weed control in soybeans with metribuzin and combinations with other herbicides.Pages 28-35, In Proceeding of the Twenty-Ninth Annual Meeting of the Northeastern Weed Science Society; Jan 7-9, 1975; New York City. Salisbury, Md: University of Maryland, Vegetable Research Farm.

Parochetti, J.V. (1977). Herbicides for no-tillage double cropped soybeans, Pages 54-60, In Proceedings of the Northeastern Weed Science Society.

Parochetti, J.V. (1977). Residual herbicides on no-tillage corn in a rye cover crop. Pages 24-29 In Proceedings of the Northeastern Weed Science Society.

Parochetti, J.V.; Burt, G.W.; Bell, A.W. (1976). Triazines, acetanilides, and several other herbicides for weed control in corn. Pages 48-54, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976; Boston, Massachusettes. Salisbury, Md.: University of Maryland Vegetable Research Farm.

Peek, J. W. (1976) Dual(R) Experimental Use Permit for Weed Control in Sorghum Grown for Seed. (Unpublished report received Dec 14, 1976 under 100-EUP-54; prepared by Ciba-Geigy Corp., Greensboro, N.C. that includes reports 1-38 with summary; CDL:229062-A; 229063)

Peek, J.W. (1977) Biological Research Report on Herbicide Efficacy and Crop Safety: Bicep™ 4.5 L Experimental Use Permit for Weed Control Evaluation in Grain Sorghum. (Unpublished study received Nov 8, 1977 under 100-EUP-60; prepared by Ciba-Geigy Corp., Greensboro, N.C.; including studies 1-8 with a summary; CDL:96615-A, 96616)

Peters, R.A.; Dest, W.M. (1975) Evaluation of herbicides for use on no-tillage corn in a rye cover crop. Pages 74-77, In Proceedings of the Twenty-Ninth Annual Meeting of the Northeastern Weed Science Society; Jan 7-9, 1975; New York City. Salisbury, Md: University of Maryland, Vegetable Research Farm.

Pillai, G.G.P., Davis, D.E. (1975) Mode of action of CGA-18762, CGA-17020, and CGA-24705. In Proceedings of the Twenty-Eighth Annual Meeting of the Southern Weed Science Society.

Pillai, C.G.P., Davis, D.E., Truelove, B. (1976) CGA-24705 effects on germination, growth, leucine uptake, and incorporation: Abstract. Page 403, In Proceedings of the Twenty-Ninth Annual Meeting of the Southern Weed Science Society; Jan 27-29, 1976; Dallas, Texas. Raleigh, N.C.; Glover Printing for the Southern Weed Science Society.

Pillai, G.G.P., Davis, D.E., Truelove, B. (1977) Site of uptake and mode of action of metolachlor: Abstract. Page 367, In Proceedings of the Thirtieth Annual Meeting of the Southern Weed Science Society; Jan 19-21, 1977; Dallas, Texas. Raleigh, N.C.; Glover Printing for the Southern Weed Science Society.

Pruss, S.W.; Higgins, E.R.; Schnappinger, M.G. (1976). CGA-24k705 plus triazine herbicides for annual grass and broadleaf weed control in corn.

Pages 40-45, In Proceedings of the Thirtieth Annual Meeting of the Northeasten Weed Science Society; Jan 6-8, 1976; Boston, Massachusettes. Salisbury, Md.: University of Maryland Vegetable Research Farm.

Ramsteiner, K; Karlhuber, B. (1975) CGA-24705: Determination of Total Residues in Material of Animal Origin: AC 2.53; REM 2/75. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:94379-I)

Remos, M. (1976). Chemical weed control in growing soybeans planted with minimum soil preparation. Resumos XI Seminario Brasileiro de Herbicidas e Ervas Daninhaus, Londrina, 1976: 91-92.

Richter, W.; Alt, K.O.; Blum, W.; Winkler, T. (1974) Structure Elucidation of 'Metabolite X', a Degradation Product of CGA 24705: AC 2.53. (Unpublished study received March 26, 1975 under 5F1606; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL: 94380-S.)

Robbins, J.D.; Bakke, J.E. (1967) Sheep and goat metabolism unit for the collection of excreta and expired $C^{14}O_2$. Journal of Animal Science 26(2): 424-429. (Also In unpublished report received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94221-E)

Roger, J.C. (1973) Addendum to AG-218 — Total Organic $^{14}C$ Contents in Rumen and Intestinal Wash Using Lindberg Combustion Furnace. Method AG-251 dated Aug 16, 1973. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-K)

Roger, J.C.; Cassidy, J.E. (1974a) Metabolism and Balance Study of $\phi$-$^{14}C$-CGA-24705 in a Lactating Goat: GAAC-74020. (Unpublished study received Sep 25, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94217-G)

Roger, J.C.; Cassidy, J.E. (1974b) Metabolism and Balance Study of $\phi$-$^{14}C$-CGA-24705 Corn Biosynthesized Metabolites in a Goat: M6-68-2A: GAAC-74046. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94217-I)

Roger, J.C. (1973?) Radioassay of $C^{14}O_2$ by Acid Neutralization and Subsequent Counting by Liquid Scintillation. Method AG-250 undated. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94216-Q)

Roger, J.C.; Counselman, C.J. (1973) Goat Metabolism Study with $^{14}C$-CGA-24705 and $^{14}C$-CGA-17020. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94378-J)

Roger, J.C.; Counselman, C.J. (1973) Goat Metabolism Study with $^{14}C$-CGA-24705 and $^{14}C$-CGA-17202. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94217-H)

Ross, J.A.; Balasubramanian, K. (1975) Validation of Method AG-277 for the Determination of Corn CGA-24705 Metabolites as CGA-37913 and CGA-49751: GAAC-

75013. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-V)

Rowe, G.R.; O'Connor, B.P.; Patterson, T.M. (1976). Metolachlor for control of 'summer grasses' in maize. Pages 135-137, In Proceedings of the Twenty-Ninth New Zealand Weed and Pest Control Conference; Aug 3-5, 1976; Christchurch, New Zealand. Hamilton, N.Z.: Ruakura Agricultural Research Center for the New Zealand Weed and Pest Control Society, Inc.

Ruscoe, A. W.; Harvey, R. G. (1976) Annual weed control in sweet corn. Page 182, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975; Milwaukee, Wisconsin. Omaha, Neb.; by the Stauffer Chemical Company for the North Central Weed Control Conference.

Ruttiman, J.; Gfeller, W. (1974) Tolerability Trial in Laying-Hens with CGA 24' 705: 28 Day Feeding Study: AC 9.26/9.24; LH 10 CRA. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., St. Aubin, Switzerland; CDL:94216-H)

Sachsse, K. (1973a) Irritation of Technical CGA-24705 in the Rabbit Eye: Project No. Siss 2979. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:112840-G)

Sachsse, K. (1973b) Skin Irritation in the Rabbit after Single Application of Technical CGA-24705: Project No. Siss 2979. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:112840-I)

Sachsse, K. (1977) Skin Sensitizing (Contact Allergenic) Effect in Guinea Pigs of Technical CGA-24705. Project No. Siss 5726. [Unpublished study received Oct 17, 1977; prepared by Ciba-Geigy Ltd., Basle, Switzerland]

Sachsse, K.; Ullman, L (1974a) Acute Inhalation Toxicity of Technical CGA-24705 in the Rat: Project No. Siss 3516. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:112840-L)

Sachsse, K.; Ullman, L. (1974b) Acute Toxicity to Rainbow Trout, Crucian Carp, Channel Catfish, Bluegill, and Guppy of Technical CGA-24705: Project No. Siss 3516. (Unpublished study received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Ltd., Basle, Switzerland; that includes a cable from Ciba-Geigy Corp., Greensboro, N.C. on fish name change; CDL:112840-N)

Sarpe, N.; Tomoroga, P.; Segarceanu, O.; Apostol, V. (1975). The effect of Triflurolin, Butylate, Nitroaniline (Profuralin) and Metetilachlor combined with Metribuzin, Chlorbromuran and other herbicides in controlling weeds in soybeans and sunflowers. Compte Rendu de la 8th Conference du Columa 1975:599-610.

Schenker, M. (1974) CGA 24705: Total Residues in Milk and Tissues of Swiss Cows: Switzerland 1973: AC 2.53 RVA 81/74. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:95747-F)

Schenker, M. (1975a) CGA 24705: Determination of the Degradation Product CGA 49751 in Chicken Liver: Switzerland 1973: RVA 02/75. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:95747-I)

Schenker, M. (1975) CGA 24705: Determination of the Degradation Product CGA 49751 in Cow Tissues and Milk: Switzerland 1973: AC 2.53; RVA 01/75. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Ltd., Basle, Switzerland; CDL:95747-H)

Schnappinger, M.G.; Higgins, E.R.; Pruss, S.W. (1975) Annual grass and broadleaf control in corn and soybeans with CGA-24705. Pages 44-48, In Proceedings of the Twenty-Ninth Annual Meeting of the Northeastern Weed Science Society; Jan 7-9, 1975; New York City. Salisbury, Md.: University of Maryland, Vegetable Research Farm.

Schnappinger, M.G.; Pruss, S.W.; Higgins, E.R. (1976). CGA-24705 combinations for annual grass and broadleaf weed control in soybeans. Pages 7-12, In Proceedings of the Northeastern Weed Science Society.

Schroter, R. (1963) Reductions with Raney nickel catalysts. Translated and revised by I. Salminen. In Newer Methods of Preparative Organic Chemistry. New York: Interscience Publishers. pp. 61-101. (A translation of: Neuere Methoden der Praparativen Organischen Chemie. Weinheim, [Germany]: Verlag Chemie.) Also In unpublished report received Mar 27, 1975 under 5F1606; Prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94382-G)

Scibor, G. (1977a) Report to Ciba-Geigy Corporation: Eye Irritation Tests with Dual(R) 8E in Albino Rabbits: IBT No. 8530-10822. (Unpublished study received Nov 8, 1977 under 100-EUP-59; prepared by Industrial Bio-Test Laboratories Inc., for Ciba-Geigy Corp., Greensboro, N.C.; including Addendum D — Validation by Ciba-Geigy Corp.; CDL:232191-D

Scibor, G. (1977b) Report to Ciba-Geigy Corporation: Primary Skin Irritation Test with Dual(R) 8E in Albino Rabbits: IBT No. 8530-10822. (Unpublished study received Nov 8, 1977 under 100-EUP-059; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C., including Addendum E — Validation by Ciba-Geigy Corp.; CDL:232191-E)

Sein, A.L.; Jennings, V.M. (1976). Soybean herbicide evaluations across Iowa in 1975. Pages 54-58, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975; Milwaukee, Wisconsin. Omaha, Neb.; by the Stauffer Chemical Company for the North Central Weed Control Conference.

Selleck, G.W.; Sanok, W.J. (1977). Herbicides for weed control in sweet corn and cabbage. Pages 256-260, In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6; Baltimore, Maryland. Salisbury, Md.

Selleck, G.W.; Weber, L.E. (1976). Herbicide trials for yellow nutsedge in potatoes on Long Island. In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976; Boston, Massachusettes

Selleck, G.W.; Weber, L.E.; Sanok, W.J. (1977). Herbicides for control of yellow nutsedge in potatoes. In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6; Baltimore, Maryland, Salisbury, Md.

Simoneaux, B. (1972a) Extraction of CGA-10832 Residues from Soil. Method AG-219 dated Oct 5, 1972. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:95748-H)

Simoneaux, B. (1972b) Measurement of Total Organic $^{14}C$ in soils by Combustion. Method AG-218 Dated Oct 5, 1972. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Ardsley, N.Y.; CDL:95748-G)

Simoneaux, B.; Hermes, P. (1973a) Extraction of CGA-10832 Residues from Soil. Method AG-254 dated Aug 10, 1973. (Unpublished study received Nov 25, 1975 under 6G1708; prepared for Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94877-M)

Simoneaux, B.; Hermes, P. (1943b) Extraction of Triazine Residues from Soil. Method AG-255 Dated Aug 10, 1973. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Ardsley, N.Y.; CDL:94216-S)

Simoneaux, B.; Roger, J.C. (1972) Blending of Soils and Homogenization of Biological Materials for Radioassay and Extraction. Method AG-223 dated Oct 5, 1972. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Ardsley,N.Y.; CDL:94216-P)

Skipper, H.D.; Gossett, B.J.; Smith, G.W. (1976) Field evaluation and soil residual characteristics of CGA-24705 and Alachlor. Pages 418-422, In Proceedings of the Twenty-Ninth Annual Meeting of the Southern Weed Science Society; Jan 27-29, 1976; Dallas, Texas. Raleigh, N.C. Glover Printing for the Southern Weed Science Society.

Smith, K.S. (1977) Report: Catfish Bioaccumulation Study Following Exposure to $^{14}C$-Metolachlor in a Soil/Water/Fish Ecosystem. 7E-6506; (Unpublished study received Feb 6, 1978 under 100-583; prepared by Cannon Laboratories, Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:232789-U)

Smith, S.H.; Adler, G.L. (1978) Final Report to Ciba-Geigy Corporation: Three-Generation Reproduction Study with CGA-24705 Technical in Albino Rats: IBT No. 8533-07928. (Unpublished study received Jan 18, 1978 under 7F1913; prepared by Industrial Bio-Test Laboratories, Inc. for Ciba-Geigy Corp.; including Audit Report No. 6 prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:96718-A; 96718-B)

Studt, D.M.; Jennings, V.M. (1976). Corn herbicide evaluations across Iowa in 1975. In Proceedings of the North Central Weed Control Conference; Dec 9-11, 1975; Milwaukee, Wisconsin. Omaha, Neb.; by the Stauffer Chemical Company for the North Central Weed Control Conference: Vol 30: 146-150.

Sumner, D.D. (1978a) Audit Report Dated Nov 21, 1975: 28-Day Mouse Pilot Study with CGA-24705 (Technical). (Unpublished study received Feb 16, 1978 under 100-583; IBT No. 622-07857; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:232855-C)

Sumner, D.D. (1978b) Addendum to Audit Report Dated Jan 12, 1978: Carcinogenic Study with CGA-24705 Technical in Albino Mice. (Unpublished study received Feb 16, 1978 under 100-583;IBT No. 622-07925; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:232855-A)

Sumner, D.D. (1974) Extraction of Humic Acid and Fulvic Acid Fractions from Soil Containing Non-extractable $^{14}C$ - Residues. Method AG-268 dated Aug 13, 1974. (Unpublished study received Mar 26. 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-Y)

Sumner D.D.; Cassidy, J.E. (1974a) A Comparison of $\phi^{14}C$-CGA-24705 Corn Biosynthesized Metabolites with Those in the Excreta of Goats Fed the $^{14}C$-Corn:GAAC-74055. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95750-D)

Sumner, D.D.; Cassidy, J.E. (1974b) The Metabolism of CGA-24705 in Corn: GAAC-74050. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95750-C)

Sumner, D.D.; Cassidy, J.E. (1974c) The Uptake and Distribution of $\phi^{14}C$-CGA-24705 from Soil in Greenhouse Grown Corn: GAAC-74015. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:95750-A)

Sumner, D.D.; Cassidy, J.E. (1974d) The Uptake and Distribution of $\phi$-$^{14}C$-CGA-24705 in Field Grown Corn: GAAC-74022. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-C)

Sumner, D.D.; Cassidy, J.E. (1974e) The Uptake of $\phi$-$^{14}C$-CGA-24705 and Its Aged Soil Degradation Products in Rotation Carrots: GAAC-74112. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-K)

Sumner, D.D.; Cassidy, J.E. (1974f) The Uptake of $\phi$-$^{14}C$-CGA-24705 and Its Aged Soil Degradation Products in Rotation Oats: GAAC-74085. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-I)

Sumner, D.D.; Cassidy, J.E. (1974g) The Uptake of $\phi$-$^{14}C$-CGA-24705 and Its Aged Soil Degradation Products in Rotation Soybeans: GAAC-74113. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.: CDL:94385-L)

Sumner, D.D.; Cassidy, J.E. (1974h) The Uptake of Ø-$^{14}$C-CGA-24705 and Its Aged Soil Degradation Products in Rotation Wheat: GAAC-74071. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-H)

Sumner, D.D.; Cassidy J.E. (1974i) Uptake of Nonextractable Soil Metabolites of Ø-$^{14}$C-CGA-24705 by Carrots: GAAC-74057. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-F)

Sumner, D.D.; Cassidy J.E. (1974j) Uptake of Nonextractable Soil Metabolites of Ø-$^{14}$C-CGA-24705 by Soybeans: GAAC-74056. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-E)

Sumner, D.D.; Cassidy J.E. (1974k) Uptake of Nonextractable Soil Metabolites of Ø-$^{14}$C-CGA-24705 by Winter Wheat: GAAC-74058. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-G)

Sumner, D.D.; Cassidy, J.E. (1975a) The Degradation of CGA-24705 in a Field Soil: GAAC-75022. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94385-N)

Sumner, D.D.; Cassidy, J.E. (1975b) The Uptake and Distribution of Ø-$^{14}$C-CGA-24705 from Soil in Greenhouse Grown Soybeans: GAAC-75039. (Unpublished study received Nov 26, 1975 under 6G1708; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94984-G)

Sumner, D.D., Szolics, I.M.; Cassidy, J.E. (1976) Degradation of CGA-24705 In Soil Report No. ABR-76057, Biochemistry Dept. Agricultural Chem. Division, Ciba-Geigy Corp., Greensboro, N.C., Issue Date: Oct 15, 1976.

Sumner, D.D., Szolics, I.M.; Cassidy, J.E. (1976) Degradation of CGA-24705 in Soil. ABR-76057. (Unpublished study received Feb 6, 1978 under 100-583; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:232789-V)

Sumner, D.D.; Thomas, R.D.; Cassidy, J.E. (1975) Structure Elucidation of the Metabolites of CGA-24705 in Corn: GAAC-75012. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94378-F)

Taylor, T.D. (1974) Duration of Biological Activity of CGA-24705. (Unpublished study received Mar 27, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94376-D)

[Texas A & M] Cottonseed Products Research Laboratory (1966) Description of Bench Scale Solvent Extraction Process for Soybeans. (Unpublished study received Nov 26, 1975 under 6G1708; prepared by the Texas Engineering Experiment Station, College Station, Tex.; for Ciba-Geigy Corp., Greensboro, N.C.; CDL:94877-U)

Thompson, L. Jr. (1976). New herbicides. Weeds Today 7(1): 27-28.

Thompson, L. Jr.; Taylor, T.D. (1976). CGA-24705 plus procyazine--a new combination for weed control in corn. Page 153, In Proceedings of the North Central Weed Control Conference; December 9-11, 1975; Milwaukee, Wisconsin. Omaha, Neb.; by the Stauffer Chemical Company for the North Central Weed Control Conference.

Tin, M.; Heinrichs, L. (1975) Complete Analysis of CGA-24705 Technical by Gas Chromatography. Method PA-69 dated Sep 23, 1975. (Unpublished study received Nov 23, 1976 under 100-587; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:226955-B)

Truslow Farms Incorporated (1974a) Eight-Day Dietary $LC_{50}$--Bobwhite Quail Technical CGA-24705: Project No. 108-110. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-P)

Truslow Farms Incorporated (1974b) Eight-Day Dietary $LC_{50}$--Mallard Ducks Technical CGA-24705: Project No. 108-111. (Unpublished study received Sep 26, 1974 under 5G1553; prepared for Ciba-Geigy Corp., Greensboro, N.C.; CDL:112840-0)

Tryzna, E.; Paa, H. (1976) Report to Ciba-Geigy Corporation: Acute Dermal Toxicity Study with CGA-24705 6E (1:10 dilution) in Albino Rabbits: IBT 8530-0859. (Unpublished study received Jan 19, 1977 under 7F1913; prepared by Industrial Bio-Test Laboratory, Inc. for Ciba-Geigy Corp., Greensboro, N.C.; CDL:95768-F)

Tweedy, B.B. (1974) CGA-24705-Corn: Summary of Residues Observed and Analytical Methods Used: GAAC-74061. (Unpublished study that includes tests number AG-A 2967, AG-A 2982. AG-A 3132, AG-A 2972, AG-A 3057, AG-A 3005, AG-A 3083, AG-A 3153, AG-A 3141, AG-A 3103, AG-A 3137, AG-A 3070, AG-A 3255, AG-A 2974, AG-A 3057 II, AG-A 3288, AG-A 3289, AG-A 3327, AG-A 3328; received Sep 26, 1974 under 5G1553; prepared by Ciba-Geigy Corp., Greensboro, N.C., CDL:94216-A)

Tweedy, B.G.; Mattson, A.M. (1974) CGA-24705: Corn Summary of Residues Observed and Analytical Methods Used: GAAC-74067. (Unpublished study that includes studies AG-A-2967, AG-A-2972, AG-A-2982, AG-A-3057, AG-A-3103, AG-A-3132, AG-A-3137, AG-A-3141, AG-A-3255, AG-A-3289, AG-A-3299, AG-A-3327, AG-A-3005, AG-A-3083, AG-A-3153, AG-A-2974, AG-A-3057 II, AG-A-3070, AG-A-3288, AG-A-3298, AG-A-3325, AG-A-3326, AG-A 3406; received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C. CDL:94379-A)

Ueda, A. (1976). The use of Metetilachlor-Metribuzin in soybean cultivation. XI Seminario Brasileiro De Herbicides E Ervas Daninhas, Resumos, Londrina, Parana, 1976: 81-82.

U.S. Department of Agriculture (1941) Climate and Man. Washington, D.C. U.S. Government Printing Office.

U.S. Department of Agriculture's Statistical Reporting Service (1972) Usual Planting and Harvesting Dates. Washington, D.C.: U.S. Government Printing Office. (Report contains information on usual planting and harvesting dates for major field and seed crops.)

U.S. Department of Agriculture (1975) Control of Water Pollution from Cropland: Vol. I. A Manual for Guideline Development. By the Agricultural Research Service. Washington, D.C.: U.S. Government Printing Office.

U.S. Food and Drug Administration (1975) Paraquat: 1,1'dimethyl 4,4'bipyridinium ion. In Pesticide Analytical Manual: Vol. II: Methods for Individual Pesticides Residues. [Rockville, Md.]: U.S. Department of Health,Education, and Welfare. Sec. 180.205 (Also In unpublished report received Nov 8, 1977 under 100-EUP-59 prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL: 232192-Q)

Vengris, J. (1975) Annual Weed control in field corn 1974: Abstract. Pages 68-70, In Proceedings of the Twenty-Ninth Annual Meeting of the Northeastern Weed Science Society; Jan 7-9, 1975; New York City. Salisbury, Md: University of Maryland, Vegetable Research Farm.

Vengris, J. (1977a) Annual weed control in alfalfa new seedlings. Pages 99-103, In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6, 1977; Baltimore, Maryland. Salisbury, Md.

Vengris, J. (1977b) Annual weed control in field corn. Pages 1-5, In Proceedings of the Thirty-First Annual Meeting of the Northeastern Weed Science Society; Jan 4-6, 1977; Baltimore, Maryland. Salisbury, Md.

Venturella, L.R.C.; Filho, O.R.; Davis, G.G. (1976). Various herbicides tested for control of weeds with soybeans (Glycine maxmerril). XI Seminario Brasileirio De Herbicides E Erauas Danimhas, Resumos, 20-22 July 1976, Londrina, Parana: 71.

Vial, J.; Ostrousky, V; Metz, F.X. (1975). Weed control in maize fields, combination of Metetilachlor + Atrazine - a new solution to the problem of controlling Graminacae and dicotyledons in maize fields. Compte Rendu de la 8e Conference du Columa, 1975: 487-497 (comite francais de lutte contre las mauvaises herbes).

Vilkas, A.G. (1976) Acute Toxicity of CGA-24705 Technical to the Water Flea Daphnia magna. Received Nov 23, 1976 under 100-587. (Unpublished study prepared by Aquatic Environmental Sciences, Union Carbide Corp. for Ciba Geigy Corp., Greensboro, N.C.; CDL:226955-C)

Vogel, C.; Aebi, R., inventors; Ciba-Geigy Corp., Assignee (1976). Plant growth regulating agent. U.S. patent 3, 937, 730. Feb 10: 8 p. Int. $CI^2$. C07C 103.34.

Vogel, C.; Aebi, R; inventors; Ciba-Geigy Corp., Assignee (1973) Haloacetanilides acting on plant growth. German patent 2, 328, 340. Dec 20: 50 p. Int. CI. C07C 103.38.

Watschke, T.L.; Waddington, D.V.; Forth, C.L. (1975) Growth regulation in tall fescue. Pages 397-402, In Proceedings of the Twenty-Ninth Annual Meeting of the Northeastern Weed Science Society; Jan 7-9, 1975; New York City. Salisbury, Md.: University of Maryland, Vegetable Research Farm.

Watschke, T.L.; Wehner, D.J.; Duich, J.M. (1976) Pre and postemergence crabgrass control in turf. Pages 358-366, In Proceedings of the Thirtieth Annual Meeting of the Northeastern Weed Science Society; Jan 6-8, 1976; Boston, Massachasetts. Salisbury, Md: University of Maryland. Vegetable Research Farm.

Watts, R. (July 1976) Memo from Chemist, Chemistry Branch, RD, OPP, to Cummings, J., Chief, Chemistry Branch, RD, OPP, concerning Method Trial for Metabolites of Metolachlor and Their Hydrolytic Products CGA-37913 and CGA-49751 in Corn and Beef Liver [PP#5F1606] July 28, 1976.

Wills, G.D. (1976) Effect of soil incorporated herbicides on cotton and purple nutsedge. Pages 110-114, In Proceedings of the Twenty-Ninth Annual Meeting of the Southern Weed Science Society; Jan 27-29, 1976; Dallas, Texas. Raleigh, NC; Glover Printing for the Southern Weed Science Society.

Wolf, M. (1974) [Letter on Synthesis of ø-$^{14}$C-CGA-37913] to Dr. J.A. Ross, Dated Jun 3, 1974. (Unpublished letter received Feb 6, 1978 under 100-583; CDL:232789-W)

Wolf, M.; Sumner, D.D. (1974a) Statistical Methods in the Measurement of Radioactivity. Method AG-276 dated Jan 31, 1974. (Unpublished study received Mar 26, 1975 under 5F1606; prepared by Ciba-Geigy Corp., Greensboro, N.C.; CDL:94380-Q)

Wolf, M.: Sumner, D.D. (1974b) Statistical Methods in the Measurement of Radioactivity. Method AG-260 dated. (Unpublished study prepared by Ciba Geigy Corp., Greensboro, N.C.; CDL:94380-0)

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