738R93010

REJECTION RATE ANALYSIS

ENVIRONMENTAL FATE

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REJECTION RATE ANALYSIS

I. INTRODUCTION

This rejection rate analysis was undertaken by the Special Review and Reregistration Division (SRRD), the Health Effects Division (HED), and the Environmental Fate and Effects Division (EFED) in the Office of Pesticide Programs (OPP) of the Environmental Protection Agency (EPA). The decision to analyze these factors was made after a FIFRA Reregistration recosting analysis conducted in the Spring of 1991. This analysis indicated that studies rejected during the review process posed the most significant potential for delays in the production of Reregistration Eligibility Documents (REDs). The purpose of this guideline-by-guideline survey is to identify those factors that most frequently cause studies required for pesticide registration to be rejected. This information will allow OPP to provide registrants with information to minimize rejection of future studies, assess and improve current guidelines if necessary, and change processes or procedures deemed appropriate.

Following review, environmental fate studies are classified as acceptable, supplemental (upgradeable or ancillary), or unacceptable (invalid). An acceptable study provides scientifically valid information that is fully documented and which clearly addressed the study objectives as outlined in Subdivision N. Studies that are less than fully acceptable may be classified upgradeable or ancillary. Upgradeable studies provide scientifically valid information that address the study objectives as outlined in Subdivision N, but are missing certain critical data necessary for complete verification. The study may be upgraded to acceptable with the submission of additional information. Ancillary studies provide data which appears to be scientifically sound, but cannot be verified under EPA's criteria. An ancillary study is not upgradeable and a new study may be required. The data from these two studies can be used as supplemental information but does not satisfy the registration requirement. Finally, studies that do not provide scientifically valid information are unacceptable or invalid. A new study is required. The studies that must be repeated are "rejected" studies and were the ones examined during this analysis because they represent the greatest potential for reregistration delays and expenditure of additional resources.

Reregistration eligibility decisions require that relevant human health and ecological risk assessments be performed for each chemical. OPP uses registrant submitted data to make these risk assessments and to estimate the degree of certainty of its decisions. This cannot be done if the quality or completeness of the data is questionable. The entire dataset from acceptable and

supplemental studies must be sufficient to support a decision concerning the potential of a compound to pose unreasonable risk to the environment or human health. Sound scientific study design provides a solid basis for development of a comprehensive data base from which decisions can be made.

II. SCOPE OF ANALYSIS

The scope of this analysis for environmental fate is limited to an examination of rejected studies that were submitted for high priority pesticides (List A and a few list B chemicals). This focus was chosen because the extent of the deficiencies in rejected studies often requires that they be repeated, which is both expensive and time consuming. In addition, studies submitted to support these high priority pesticides represent the largest dataset of reviewed studies.

The initial examination included a comparison of the number of supplemental versus the number of unacceptable studies. This was done because, even if the number of unacceptable studies is small, a large number of supplemental studies may indicate a problem that needs attention. In the case of environmental fate, 17% (135/789) of the studies reviewed were classified as supplemental. A little more than half (78/135) of these supplemental studies were submitted to satisfy the terrestrial or aquatic field dissipation guidelines. Upon examination of these studies it was discovered that 56 of the 78 field dissipation studies dealt with copper compounds for which no additional data were required. Consequently, these supplemental studies did not require any new work or cause time delays in the reregistration process. When these are subtracted, only 10% (79/789) of the environmental fate studies reviewed were classified as supplemental, which is consistent with the supplemental rates in other disciplines, 8% overall. Since the number of studies classified as supplemental did not contribute excessively to the overall rejection rate for environmental fate, the remainder of the analysis was performed on rejected studies that were classified as unacceptable.

List A chemicals have the highest priority in reregistration because they are high-volume, food-use chemicals which pose the greatest potential risk to human health and the environment. These chemicals, therefore, have generated the most extensive data requirements. With the exception of a few chemicals from Lists B, chemicals from Lists B, C and D were not included in this analysis because they do not yet have an adequate pool of reviewed studies for each guideline.

This rejection rate analysis produced an **estimate** of the number and types of factors that cause environmental fate studies to be rejected. This assessment may have over- or underestimated the rejection factors that could be identified in future assessments. A variety of circumstances contribute to the uncertainty of this estimation and it, therefore, may not be applicable to all of the chemicals on Lists B, C, and D.

First, List A contains the largest number of chemicals that are wide-use, agricultural chemicals and therefore, have the most environmental fate data requirements. Chemicals on the other lists contain decreasing numbers of agricultural chemicals, therefore, a decreasing number of data requirements for environmental fate will be imposed. Another factor that may reduce the number of rejection factors for chemicals on other lists is that some studies for List A chemicals were initiated prior to the development of the Phase 3 acceptance criteria (1989). These studies could, therefore, have been rejected based upon criteria that was not in place when they were initiated. Data Call-Ins for List B, C, and D chemicals were issued subsequent to OPP's publication of the guidelines and acceptance criteria. Factors that caused studies for List A chemicals to be rejected would likely not be repeated for List B, C, and D chemicals. On the other hand, this assessment may have missed some rejection factors because some of the current studies that were classified as acceptable were actually studies performed to replace rejected studies.

The Chemistry Branches of Health Effects Division (HED) have taken over the responsibility for review of studies which determine whether pesticide residues of concern are observed in rotational crops as a result of uptake from soil of previously treated fields (Guideline Nos. 165-1 and 165-2). This transfer was performed because the concern over residues in these situations is chiefly dietary.

III. PROCESS OF ANALYSIS

The Agency reviewed the data evaluation records (study reviews) on a guideline-by-guideline basis in order to:

(1) identify those factors which most frequently caused each guideline study to be rejected; and

(2) determine the rejection rates and possible trends for each guideline requirement.

A draft of this analysis was provided to an industry workgroup of scientists for review and comment. This opened a dialogue concerning the reasons for rejection of submitted studies and allowed OPP to obtain feed-back on guidance documents

from a user's perspective. Industry and EPA scientists met on September 23 and 24, 1992 to discuss the problem areas in order to develop a better understanding of them. The revised Environmental Fate chapter includes industry comments on each rejection factor and EPA's response to them. Industry comments on scientific matters outside the scope of the rejection rate document are also included with EPA's response.

Primary development of the environment fate rejection rate analysis was performed by Emil Regelman, Dana Spatz, Mah Shamim, Stephanie Syslo (Environmental Fate and Ground Water Branch, EFED). In addition to this core group of individuals, many others worked to make this project a success. Rosemary Kearns and Jean Holmes (Science Analysis and Coordination Staff, EFED) conducted the initial survey of EFGWB files to compile the data on rejection rate based on the results reported in the DERs. Henry Jacoby, Elizabeth Leovey, Akiva Abramovitch, Paul Mastradone, Henry Nelson, Elizabeth Behl, Constance Hoheisel, Jim Hetrick, Arnet Jones, and David Edelstein provided significant input toward the development of the final document, including participating in meetings with NACA and providing thoughtful and constructive recommendations on the "EPA Response" portion of the text. Peter Caulkins, Lois Rossi and Moana Appleyard (SRRD) initiated the Rejection Rate effort and actively facilitated all phases of the project, including coordination of meetings with NACA and interchange of documents.

The industry workgroup included Jim Clark (BASF); Paul Hendly (ICI), Gene Burnett (CIBA-GEIGY); Val Clay (Miles); Alec McGibbon (Dow-Elanco); Paula Paul and Iain Kelly (Nor-Am); Al Barefoot (Dupont); Dick Heintzelman (Rhone-Poulenc); Karen Erstfeld (Hoechst-Roussel); Robert Larkin and Berni Chong (Rohm and Haas).

IV. DESCRIPTION OF DISCIPLINE

The philosophy of the Environmental Fate and Ground Water Branch (EFGWB) is one of chemical stewardship. For environmental fate, stewardship requires that, prior to a pesticide's release into the environment, the registrant be able to account for the pesticide, its major degradates, and their whereabouts under actual use conditions. This includes a knowledge of the major route(s) of dissipation, as well as the ability to trace the degradation pathway through the metabolic/degradation steps.

EFGWB relies upon industry to meet the goal of stewardship through submission of sound data and objective estimates of a compound's environmental fate based on that data. The environmental fate dataset describes a compound's potential to move outside of its orbit of application into various segments of the environment. The submitted data must be of a quality and completeness that will allow the EFGWB reviewer to integrate it

and form a comprehensive scientific assessment of the fate of the compound in the environment under actual use conditions.

Environmental fate data requirements include both laboratory and field studies. Controlled laboratory studies are required to examine the persistence, mobility and accumulation potential of a pesticide and its major degradates. Persistence studies examine a pesticide's behavior as it interacts with water, soil, air, sunlight and microorganisms. Mobility studies attempt to predict the potential of the pesticide to volatilize into the atmosphere, move into ground or surface waters or bind to the soil. Accumulation studies examine the potential of a pesticide to accumulate in rotational crops and fish. These studies are designed to help identify which dissipation processes are likely to occur when the pesticide is released into the environment and characterize the significant degradates likely to result from these processes. From the results of these studies OPP develops a preliminary, qualitative environmental fate and transport assessment. The data are then used to design and/or trigger appropriate field studies and to provide parameters needed in simulation modelling.

Field studies are required to provide a more realistic picture of the dissipation of the parent compound and those degradates determined to be significant. Under field conditions pesticides are exposed simultaneously to the individual dissipation processes examined separately in the laboratory. Thus, in field studies, some dissipation processes may be altered due to competition or interaction.

The field and laboratory data are integrated to characterize the persistence and transport of the pesticide and its degradates in the environment. From these data a quantitative environmental fate assessment is developed. Model-estimated environmental concentrations of the pesticide in different media under various pesticide application and site scenarios are also calculated. These estimates of exposure are used in conjunction with toxicity data to assess the risks to non-target species associated with the use of the pesticide. Computed risks are used by the Agency to determine the degree of regulatory action required. Regulatory action may include label advisories, use restrictions, use under a State Management plan, suspension, or cancellation. If the data warrant, a pesticide may also be placed in the Special Review process to undergo a more extensive examination of specific problems uncovered by review of data submitted to address reregistration data requirements.

There are 24 guideline requirements for environmental fate, a complete list of which is provided in Appendix B. The following discussion of the environmental fate requirements is divided into groups of related guidelines.

Two of the environmental fate guidelines, accumulation in rotational crops (165-1 and -2) have been transferred to HED since the concern over residues in these situations is chiefly dietary.

Physicochemical Degradation (Guidelines 161-1, 161-2, 161-3, 161-4). These data requirements include hydrolysis (161-1), photodegradation in water (161-2), photodegradation in soil (161-3), and photodegradation in air (161-4). The hydrolysis study determines the potential of the parent pesticide to degrade due to the influence of water alone. Photodegradation studies determine the potential of the parent pesticide to degrade in water, soil or air as it interacts with sunlight. During these studies data are also collected concerning the identity, formation and persistence of significant degradates.

Biological Degradation (Guidelines 162-1, 162-2, 162-3, 162-4). These data requirements include aerobic soil metabolism (162-1), anaerobic soil metabolism (162-2), anaerobic aquatic metabolism (162-3), and aerobic aquatic metabolism (162-4). The soil metabolism studies determine the persistence of the parent pesticide when it interacts with soil microorganisms living under aerobic and anaerobic conditions. The aquatic metabolism studies produce similar data that are generated by pesticide interaction with microorganisms in a water/sediment system. These studies also identify the significant degradates that result from biological degradation.

Mobility (Guidelines 163-1, 163-2, 163-3). These data requirements include leaching and adsorption/desorption (163-1), laboratory volatility (163-2), and field volatility (163-3). The leaching study assesses the mobility of the parent pesticide and its degradates through columns packed with various soils. The adsorption/desorption study determines the potential of the parent pesticide and its degradates to bind to soils of different types. The potential mobility of the parent pesticide and each degradate is determined by examining the data from both of these studies and may range from immobile to highly mobile.

Volatility studies determine the potential of a pesticide to move into the air and off-site. The laboratory volatility study provides a rate of volatilization and the resulting air concentration under confined conditions. The field volatility study is performed to provide more realistic estimates of volatility when the pesticide is applied as it is intended to be used.

Field Dissipation (Guidelines 164-1, 164-2, 164-3, 164-4, 164-5). These data requirements include terrestrial field dissipation (164-1), aquatic (sediment) dissipation (164-2), forestry dissipation (164-3), combination products and tank mix

use dissipation (164-4) and long term field dissipation (164-5). These field dissipation studies are performed to provide more realistic estimates of the persistence and transport of a pesticide and its degradates when the parent pesticide is applied under actual use conditions.

Accumulation (Guidelines 165-1, 165-2, 165-3, 165-4, 165-5). These data requirements include accumulation in confined rotational crops (165-1), accumulation in field rotational crops (165-2), accumulation in irrigated crops (165-3), accumulation in fish-lab (165-4) and field accumulation in aquatic nontarget organisms (165-5). The results from the rotational crop studies are used to estimate biomagnification of the parent and major degradates in the food chain, to establish crop rotation interval restrictions and, where necessary, to determine if tolerances may be needed for residues on rotational crops (Note: The responsibility for review of these two guideline topics has been assumed by the Chemistry Branches of HED.). Accumulation in fish studies are used to estimate the bioconcentration potential of the parent pesticide under controlled laboratory conditions.

Ground Water Monitoring (Guidelines 166-1 and 166-2). These data requirements include small-scale prospective ground water monitoring (166-1) and small-scale retrospective ground water monitoring (166-2). Ground water monitoring studies are designed to determine whether a pesticide applied under various conditions reaches ground water and in what concentrations.

Spray Drift (Guidelines 201-1, 202-1) These data requirements include droplet size spectrum (201-1) and field drift evaluation (202-1). The objective of pesticide spray drift evaluations is to determine the potential of a pesticide to drift off-site during or immediately after it is applied according to label directions. The droplet size spectrum test provides information on the effects of pesticide application equipment and formulations on droplet sizes. Droplet size influences how readily the pesticide droplets are carried by air currents. The field drift evaluation test determines the effects of environmental conditions and application equipment on the extent of off-target transport immediately following release of the pesticide from the application equipment.

V. STUDY INTERDEPENDENCE

Chart 1 depicts the general sequence and interdependence of studies performed to meet the environmental fate data requirements. Studies are performed in a general sequence starting with laboratory studies and proceeding to field studies, which are designed using the data from the laboratory studies. In addition, requirements for certain studies can be triggered by the results of laboratory or field studies.

Some laboratory studies (hydrolysis, photolysis, soil metabolism) are routinely required for all outdoor use pesticides while requirements for others (e.g., photodegradation in air, volatility, and droplet size) are triggered by use/application patterns and basic product chemistry data. Laboratory studies primarily generate the following crucial pieces of information:

* the half-life of the parent
* the identity of significant degradates
* rates of formation and decline of degradates
* mobility of the parent and significant degradates.

These data along with product chemistry data are used to design the field studies.

For the rejection rate analysis, the terrestrial field dissipation study was considered a keystone study, since it depends upon the results of the laboratory studies for proper design and its results can trigger additional field studies. Since the field dissipation study is conducted under actual field conditions, the individual degradation processes identified in the laboratory studies may be enhanced or abated because of competitive interactions. The results of this study may trigger a long-term terrestrial field study although, in practice, most registrants continue the original field dissipation study until a half-life is reached, thereby precluding the need to start over with the long-term field dissipation study. The terrestrial field dissipation study in combination with other data may trigger a ground water study. If these data indicate that the parent and/or degradates are both persistent and mobile, then a small-scale, prospective ground water study may be required.

The basic triggering criteria are:

* combined weight of the evidence from the laboratory studies and the field dissipation study indicates that the pesticide has properties and characteristics similar to pesticides that have been detected in ground water (see Table 1); and

* a field dissipation study demonstrates movement of the parent or degradates 75-90 centimeters through the soil profile; or

* other monitoring studies report that the pesticide has been detected in ground water;

In addition, use patterns, application rates, timing of application, potential acreage to be treated, depth to ground water, soil types, hydraulic gradient, and climate are evaluated as part of the triggering criteria. The results of a ground water study are used to develop label restrictions, require State

Management plans and/or to place a pesticide in the Special Review process.

Some laboratory and field studies, such as, volatility, rotational crop, bioaccumulation, and spray drift are triggered by the integration of basic product chemistry, product formulation, the results of laboratory studies and other information such as toxicity data and use patterns.

If significant pesticide residues of concern are detected in the confined rotational crop study (study usually conducted in a lab or greenhouse), then an accumulation in field rotational crop study (165-2) may be triggered. If a confined study indicates persistence of a real, identifiable residue, then an attempt is made to establish an acceptable rotational interval (up to one year) at which the representative crop (small grain, leafy vegetable or root crop) does not contain residues of concern. If residues of concern are observed in the confined study such that no acceptable rotational interval can be established, Registrants should conduct the limited field studies, where weathering and other effects may act to reduce crop residues. Alternatively, the Registrant may choose to reduce application rates, or petition the Agency for the establishment of rotational crop tolerances for all crops to be rotated.

The laboratory volatility study is triggered for pesticides with vapor pressures greater than 10^{-4} Torr. This study is generally not triggered by pesticides with vapor pressures below 10^{-6} Torr. Vapor pressures between these two levels trigger the laboratory volatility data requirement on a case-by-case basis, usually tied to specific use patterns. The results of this laboratory study are then used to determine the need for a field volatility study. The results of the laboratory and field volatility studies are used to characterize volatility as a route of dissipation and identify potential exposure to non-target organisms near the site.

The registrant may request that the requirement for the laboratory accumulation in fish study be waived on the basis that the parent and/or major degradates cannot reach water, or will not persist in water longer than 4 days, or have a very low potential to bioaccumulate. These determinations are based upon use patterns, the hydrolysis half-life and the octanol/water partition coefficient ($K_{ow} << 1000$). If this study is required, the data that it provides concerning the levels of parent pesticide residues in whole body, viscera, and edible tissue of the fish can trigger a field accumulation in non-target species study. The information from these two studies can be used to develop label restrictions or action levels for human consumption.

If the spray drift data requirement was triggered by use patterns and non-target organism toxicity, two spray drift studies would normally be required. For those registrants who are participating in the Spray Drift Task Force (SDTF), EFGWB has previously decided to hold this requirement in reserve pending the work done by the task force, which is conducting a long-term analysis of spray drift in order to develop a predictive model that can be used to satisfy these data requirements. The decision is made on a case-by-case basis for each chemical. For those companies not participating in the SDTF effort, the conventional requirements would be imposed.

VI. SUMMARY

From a rejection rate perspective, studies with the most potential to delay the completion of a RED are those that are performed in sequence or trigger longer term field studies, such as the ground water monitoring study. High rejection rates in laboratory studies will effect not only the initially rejected study, but also all studies that were designed using its data. This could result in a cascade effect that would result in significant delays in reregistration. Since the field dissipation study plays an essential role in both characterizing dissipation under actual field conditions, as well as triggering other studies, its rejection rate is especially critical.

The Chemistry Branches of Health Effects Division (HED) have taken over the responsibility for review of studies which determine whether pesticide residues of concern are observed in rotational crops as a result of uptake from soil of previously treated fields (Guideline Nos. 165-1 and 165-2). This transfer was performed because the concern over residues in these situations is chiefly dietary.

From a scientific perspective, the environmental fate dataset is developed to form a comprehensive understanding of the environmental fate of a pesticide under actual use conditions. The guidelines, therefore, are used most effectively in conjunction with the study director's critical judgement. Compounds vary considerably in their chemistry, use patterns, and fate in the environment. The guidelines cannot address all possible issues which might arise in a given study. Studies are sometimes rejected, not for failure to meet guideline standards, but for a failure in reporting. Study reports must adequately communicate the scientific rationale for departing from the guidelines and demonstrate that the study has produced reliable data concerning the fate of the pesticide.

Deciding how strictly to follow study guidelines should be directed towards clarification of the pesticide's fate in the environment. Study authors should consider the results of their

studies in light of the rest of the available data set, and indicate how the process(es) observed in the study contribute to the dissipation of the compound in the environment. The results must fit into a complete environmental fate profile, including the chemical's likely degradation products, dissipation routes, persistence. Explanations should be offered for all major trends, issues, and anomalies. The study author should offer a hypothesis for the environmental fate of the test compound, and show how the data collected in the study support that hypothesis.

EFGWB uses registrant submitted data to characterize the fate of a pesticide in the environment and to estimate the degree of certainty of this characterization. EFGWB cannot do this if the quality or completeness of the data set is questionable. Sound scientific judgement and comprehensive reporting provide a solid basis for discussion of study acceptance or rejection. The total environmental fate dataset must be sufficient to support a decision concerning the potential of the compound to pose unreasonable or excessive exposure to the environment or humans. This is only possible when individual studies are designed, performed and reported with the goal of this complete dataset in mind.

Table 1. Ground Water Study Triggers

Characteristic	Guideline	Description	Ground-Water Trigger
Water Solubility	63-1	The amount of a pesticide that can be dissolved in water. Pesticides with higher water solubilities have a greater potential to be carried in solution to surface and/or ground waters.	>30 ug/L
Volatility	63-1	Volatility expressed using Henry's Constant describes the solubility of a gas in a liquid in relationship to pressure.	$<10^{-2}$ atm-m^3/mol
Speciation	63-1	The ability of the pesticide to ionize and the resultant charge on the ion.	Full or partial negative charge at ambient pH
Hydrolysis	161-1	Degradation in water.	Half-life > 25 weeks
Photolysis	161-2 161-3	Degradation due to sunlight	Half-life > 1 week
Aerobic and anaerobic soil metabolism	162-1 162-2	Degradation due to the biological and physical/chemical properties of soil	Half-life > 2-3 weeks
Soil Adsorption/ Desorption	163-1	K_d is the soil/water partition coefficient. K_{oc} is the organic carbon/water partition coefficient. These values vary from soil to soil for a given pesticide.	K_d < 5 (usually < 1) K_{oc} < 500
Field Dissipation	164-1	The rate of dissipation of the pesticide after application	Half-life > 2-3 weeks Leaching 75-90 cm deep

VII. CURRENT REJECTION RATE

The following bar charts demonstrate the current and historical rejection rates for each of the environmental fate guidelines. The historical rate does not include studies that were submitted prior to the publication of the Registration Standards. None of the results reported in this section have been tested for statistical significance, and therefore caution should be exercised in their interpretation. The purpose here is not to develop an empirically defensible rejection rate value. Rather, the intent is to use rejection rates as the best indicator available of where additional Agency/Registrant attention and efforts are warranted to improve the quality of the studies. Further caution is warranted since not all rejected studies were required to be repeated. In some cases, the submission of additional, supporting data (e.g. soil characteristics) was sufficient to upgrade the study to acceptable.

Figure 1 illustrates the overall rejection rate for environmental fate guidelines, which is now estimated at approximately 28 percent. This is down from the overall rate of approximately 54 percent prior to 1986. As indicated in Figure 1, the overall rejection rate for environmental fate guidelines has decreased by about 25 to 30 percent every two years since 1986. While the rejection rate from pre-1986 to post-1988 has been virtually cut in half, the post-1988 rate still remains high. (Note: SRRD has a goal of reducing all rejection rates to 10% or less. Consequently, any rejection rate greater than 10% is considered high.)

Figure 2 illustrates what EPA believes is the current rejection rate within each guideline. The current rate refers to all post-1988 studies that were reviewed by the EPA. The rejection rate (percentage of rejected studies) is given at the top of each guideline bar and the number of rejected studies over the number of studies reviewed are listed inside each bar. Some environmental fate guidelines with an insufficient number of studies were omitted. These guidelines include 161-4, 162-3, 162-4, 163-2, 163-3, 164-4, 164-5, 165-2, 165-3, 165-5, 166-1, 201-1, 202-1.

Figure 3 illustrates the rejection rates over time for each guideline. For each guideline, the rejection rates from three time frames are listed for comparison. The time frames include: (a) pre-1986 (not including information received for Registration Standards); (b) from 1986 to 1988; and (c) post 1988. In this figure, some guidelines have showed a continuous drop in rejection rates over all three time periods - 164-1, 164-2, 161-2, 161-3 and 163-1. Others have shown a drop from pre-1986 to the present but the trend has not been a continuously downward one - 165-4, 161-1. Since no clear trend is evident, it is less

certain whether these data represent improved performance in providing acceptable quality studies for those guidelines. Three guidelines show rejection rates that appear to have remained relatively constant over time - 162-1, 162-2 and 165-1.

Figure 4 portrays the trend in the photodegradation - water (161-2), photodegradation - soil (161-3), leaching and adsorption/desorption (163-1), terrestrial field dissipation (164-1), and aquatic field dissipation (164-2) guidelines, all of which have experienced a continuous drop in the rate of rejection since pre-1986.

Figure 5 illustrates rejection rates that have remained relatively constant or increased over time. The guidelines in this category are aerobic soil metabolism (162-1), anaerobic soil metabolism (162-2), and confined rotational crop (165-1).

Summary

Key implications that can be drawn from the following graphs include:

(1) overall rejection rates in environmental fate appear to have gone down significantly;

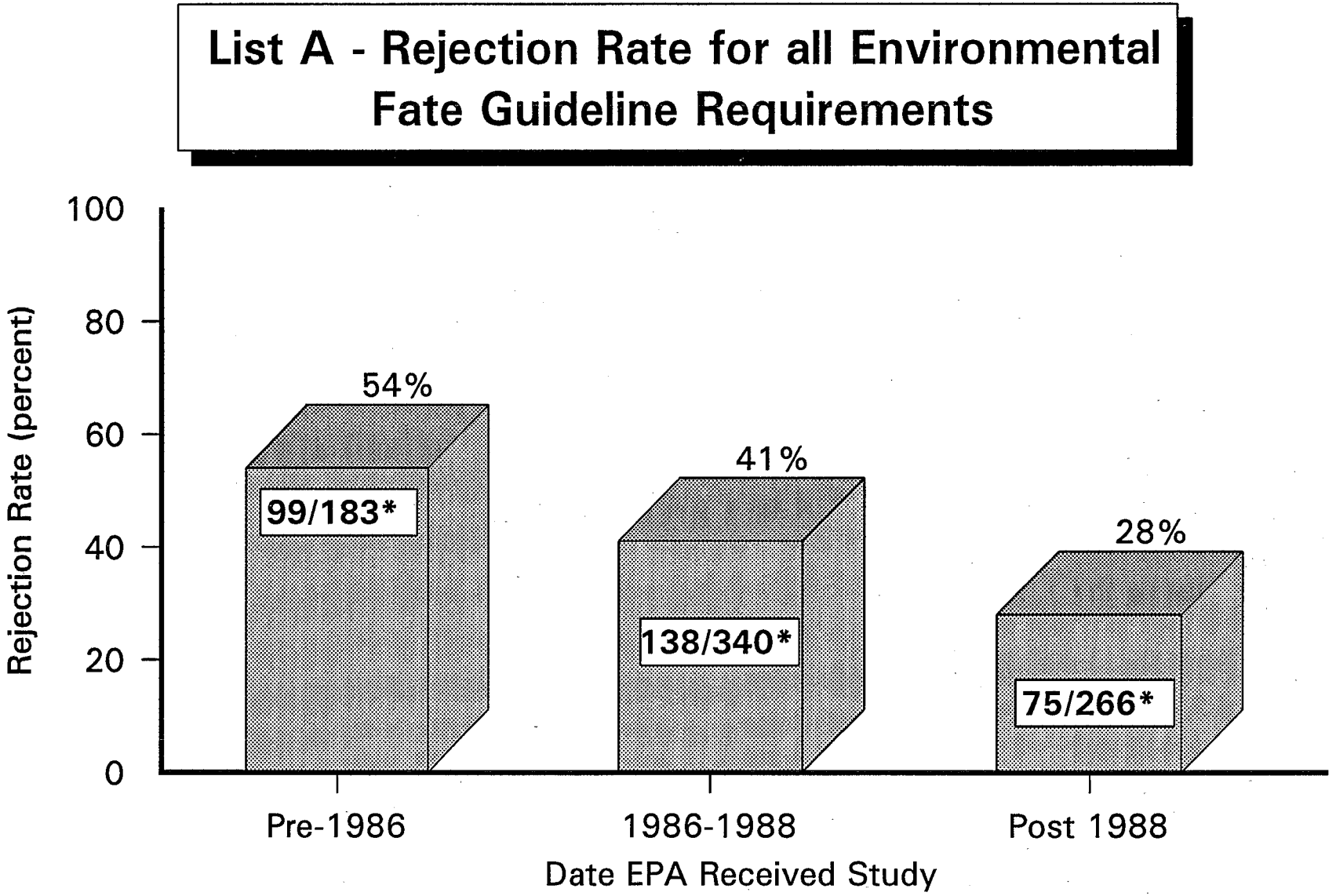
(2) the photodegradation - water (161-2), photodegradation - soil (161-3), leaching (163-1), terrestrial field dissipation (164-1) and aquatic field dissipation (164-2) guidelines have shown a continuous and substantial decline in their rejection rates;

(3) for the aerobic soil metabolism (162-1), anaerobic soil metabolism (162-2), confined crop rotation (165-1) and bioaccumulation in fish (165-4) guidelines, the rejection rate trends do not indicate substantial improvement;

(4) all of the guidelines examined still have high rejection rates when compared to the goal of reducing all rejection rates to 10% or less;

(5) none of the implications discussed above are based on statistically significant results, and therefore caution should be exercised in interpreting them.

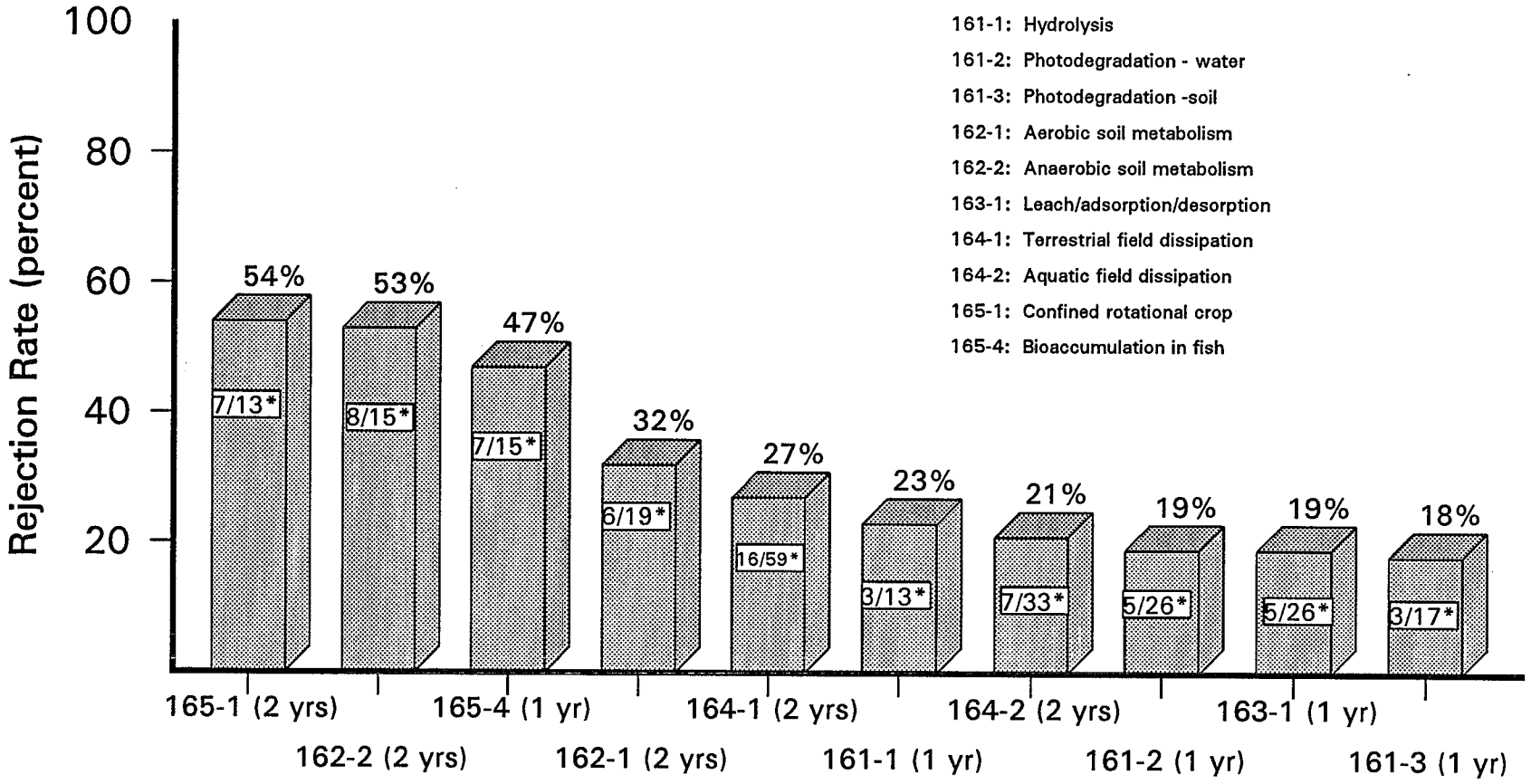
Figure 1



* - number of rejected studies/total number of studies reviewed

Figure 2

List A - Current (Post-1988) Rejection Rate by Environmental Fate Guideline

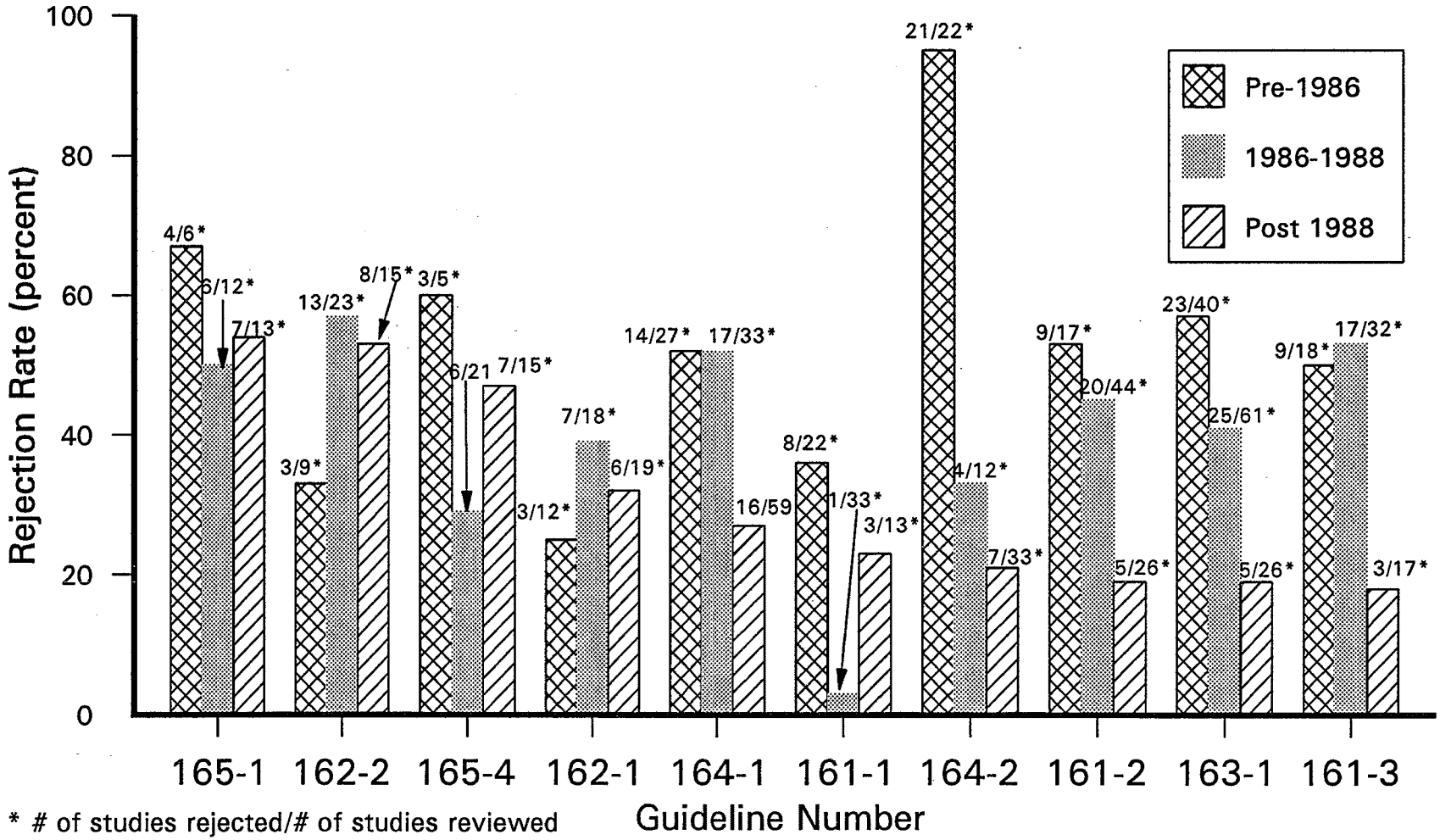


* - # of studies rejected/# of studies reviewed
( ) # of years to complete study

Note: Insufficient data to evaluate:161-4,162-3,162-4,163-2,163-3,164-3,164-4, 165-5,165-2,165-3,165-5,166-1,166-2,166-3,167-1,167-2,201-1,202-1

Figure 3

List A - Environmental Fate Rejection Rate Prior to 1986 to Post 1988

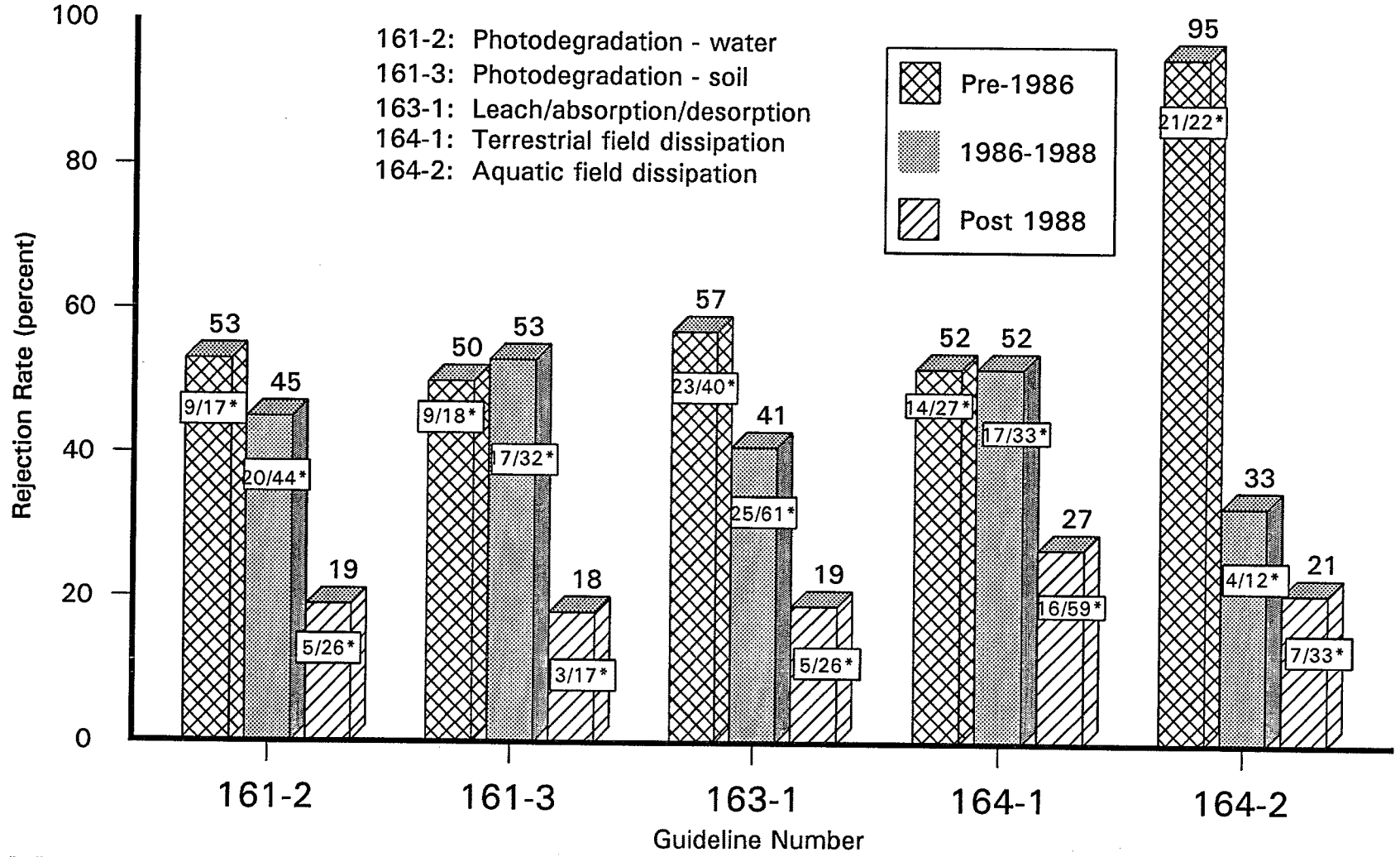


* # of studies rejected/# of studies reviewed

Note: Insufficient data to evaluate:161-4,162-3,162-4,163-2,163-3,164-3,164-4, 165-5,165-2,165-3,165-5,166-1,166-2,166-3,167-1,167-2,201-1,202-1

Figure 4

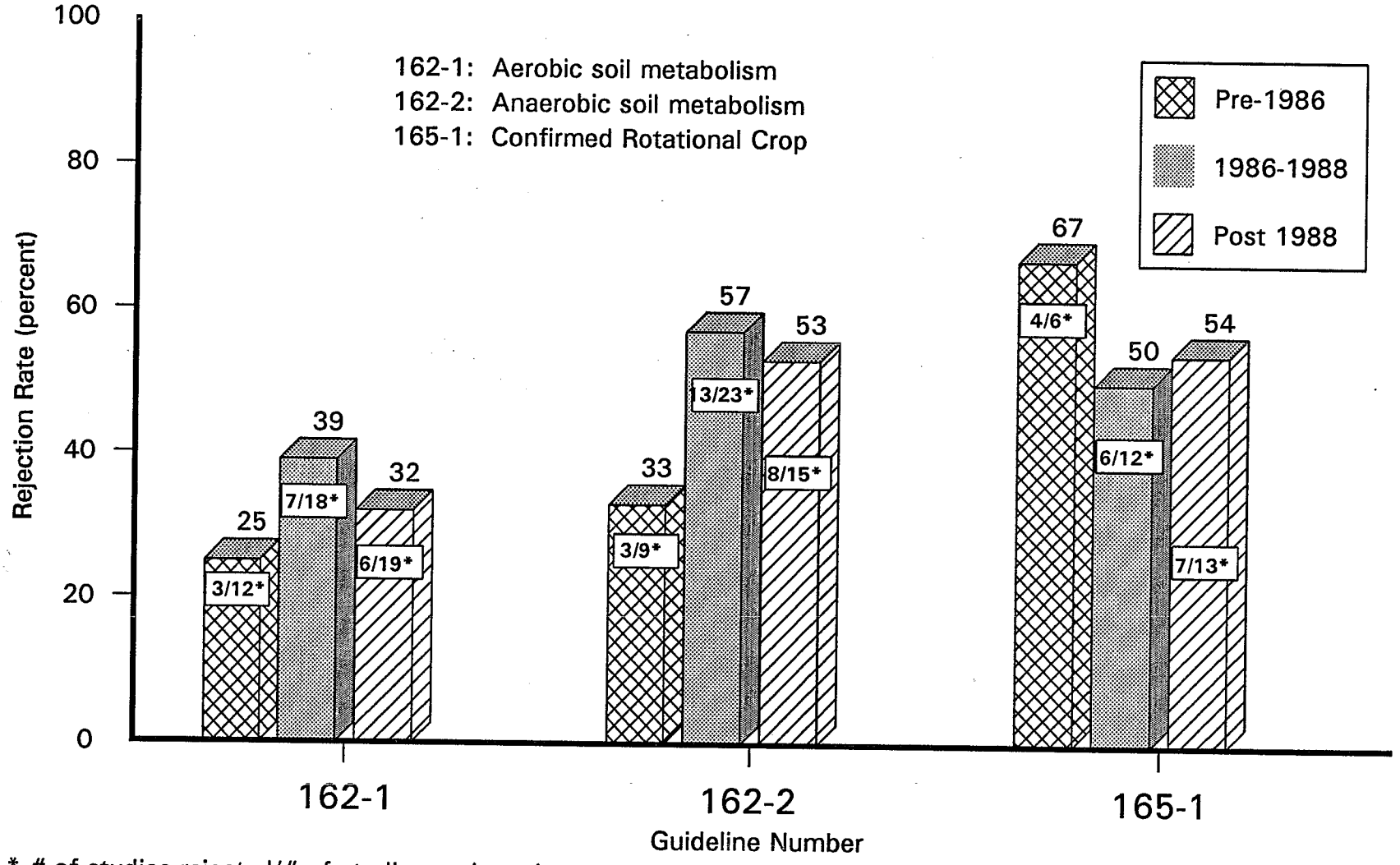
List A - Environmental Fate Guidelines With Lower Rejection Rates Over Time



* # of studies rejected/# of studies reviewed

Figure 5

List A - Environmental Fate Rejection Rates that Have Increased or Remained Constant Over Time



* # of studies rejected/# of studies reviewed

VIII. REJECTION FACTORS

Rejected studies, that were submitted to fulfill Environmental Fate data requirements, were analyzed to determine the most common reasons for rejection of studies. To accomplish this, EFED scientists catalogued the rejection factors, then explained why each study deficiency was critical, causing the study to be found unacceptable. The rejection factors for each guideline are listed according to the frequency of their occurrence.

Specific references to EPA guidance documents addressing each rejection factor are given. The guidance documents were also analyzed to determine if the registrants had sufficient available information to avoid the specified deficiency. A list of all guidance documents available for environmental fate studies is provided in the Appendix.

GUIDELINE 161-1 HYDROLYSIS STUDY

1. Rejection Factor: A material balance was not provided.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 44.
- Standard Evaluation Procedure (SEP) for Hydrolysis Studies. (June 1985), pages 11 & 12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-280.

The term "material balance" measures the quantity of a chemical and its degradates in a defined system based on total radioactivity and/or other recognized analytical methodology. The material balance is a measure of how completely the applied radioactivity was recovered in the end products. This study is designed to measure the hydrolysis of a pesticide in water and the formation and decline of the degradates. This is achieved by measuring the test substance applied at the beginning of the experiment and then accounting for it at the end of the experiment. The purpose of this measurement is to verify that all degradates formed are isolated and that an accurate rate of hydrolysis is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

Industry agrees that acceptable mass balance is needed for a study to be considered valid. If there is no attempt to provide

a mass balance or if a significant amount of the starting activity is not accounted for, the study should be rejected. The EPA should be flexible on the definition of acceptable mass balance, however. For example, an extremely low solubility compound which is stable under the conditions of the hydrolysis study, may well show a reduced mass balance over the period of the study due to adsorption to surfaces of the test vessel which can be difficult to quantify precisely. Hence, rejection should only occur when there is a gross loss of mass balance.

Industry Recommendation: The EPA should be flexible on the definition of acceptable mass balance. Rejection should only occur when there is a gross loss of mass balance without adequate explanation.

EPA Response

The Agency continues to believe that 90-110 % accountability should be viewed as an ideal target range. However, the Agency recognizes that in many cases this is not possible and, therefore, has assessed the material balance within the context of the entire study, and has not routinely rejected studies solely on the basis of low material balance.

2. Rejection Factor: The study was not conducted in the dark.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 44.
- Standard Evaluation Procedure (SEP) for Hydrolysis Studies. (June 1985), pages 8 & 10.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-280.

The hydrolysis study is designed to provide the rate of hydrolysis of the parent compound, rates of formation and decline of hydrolysis products, and the identity of the hydrolysis products. Since photolysis of organic compounds can occur under normal laboratory lighting conditions, the hydrolysis study should be conducted in darkness.

Industry Comment

Industry agrees that the elimination of photolysis as a potential source of degradation in the hydrolysis study is a basic requirement.

EPA Response

No comment.

3. Rejection Factor: **The study duration and number of sampling intervals were insufficient to establish the decline and half-life.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 45.
- Standard Evaluation Procedure (SEP) for Hydrolysis Studies. (June 1985), pages 8 & 12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-280.

Data should be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for a duration of 30 days, whichever comes first. The purpose of this is to assess the kinetics of pesticide degradation and the formation and degradation of its metabolites. This information is used to calculate a half-life for the pesticide and predict how long the pesticide and its metabolites will persist in the environment. If the duration of the study is not long enough and does not have sufficient sampling points, the confidence in the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified.

Industry Comments

Industry believes that appropriate sampling intervals are not well defined for the hydrolysis study. We suggest that the study should continue through two half-lives or 30 days, which ever is shorter. Samples should be taken at initiation of the experiment and at least 6 other intervals. If less than 10% of the chemical has hydrolyzed after 30 days, then it should be considered stable to hydrolysis and analysis of samples from the earlier intervals should not be required.

Industry Recommendation: Industry recommends that the Agency clarify the sampling intervals required for the hydrolysis study. We suggest that the study should continue through two half-lives or 30 days, which ever is shorter. Samples should be taken at initiation of the experiment and at least 6 other intervals. If less than 10% of the chemical has hydrolyzed after 30 days, then it should be considered stable to hydrolysis and analysis of samples from the earlier intervals should not be required.

EPA Response

EPA agrees that if less than 10% of the chemical has hydrolyzed after 30 days, then it should be considered stable to hydrolysis. However, the occurrence of a clear single degradate would require identification at lower levels. Higher temperatures could also be used to demonstrate the stability of the chemical. With reference to sampling intervals, samples should be taken on a schedule defined by the nature of the chemistry involved (e.g., chemicals with short half lives may require that numerous early samples be taken, while more stable chemicals may require fewer early samples, but more intense later sampling). Where little or no degradation of the chemical occurs, three sampling points of 0, 15, and 30 days would be sufficient to determine the stability of the chemical.

4. Rejection Factor: It was not specified that the buffer solutions were sterile; therefore, it could not be determined if degradation was due to hydrolysis or biotic processes.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 45.
- Standard Evaluation Procedure (SEP) for Hydrolysis Studies. (June 1985), pages 5.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-280.

The hydrolysis study is conducted to determine the rate of hydrolysis of the active ingredient, rates of formation and decline of hydrolysis products and the identity of the hydrolysis products. It is therefore essential to ensure the sterility of

buffer solutions and glassware so that the results of the study are not affected by microbial degradation.

Industry Comments

Industry agrees that the equipment and solutions used in this study should be sterilized at the initiation of the study to prevent competing microbial degradation. It is impractical to require demonstration of sterility throughout the study period, however. In addition, if screening studies have shown that the chemical does not degrade microbially, then sterile conditions should not be required.

Industry Recommendation: The Agency should continue to require sterilization of the equipment and solutions used in this study but should not require demonstration of sterility throughout the study. Also, sterility should not be required where screening studies have shown that biodegradation does not to occur under the conditions of the study.

EPA Response

EPA agrees with industry. A study in which no degradation was observed should never be rejected solely on the basis of failure to prove sterile conditions. However, reasonable efforts should be made to assure that sterile conditions are maintained throughout the study.

5. Rejection Factors: The test substance was not characterized.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 44.
- Standard Evaluation Procedure (SEP) for Hydrolysis Studies. (June 1985), pages 5 & 7.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-280 & C-282.

Characterization of the test substance involves determining the identity and the purity of test substance to ensure that the right chemical is being tested and that the impurities in the test substance do not affect the results of the study.

Industry Comments

Industry agrees that adequate characterization of the test substance should be a requirement for a valid study. Industry suggests that a radiopurity of 95% should be acceptable in most cases and we would like the Agency to confirm this.

Industry Recommendation: No study should be initiated with a test substance which has not been adequately characterized. In using this rejection factor however, the Agency should be specific in delineating what exactly is deficient with respect to test substance characterization. Further, the Agency should specify what is acceptable radiochemical purity. Industry recommends that a radiopurity of 95% should be considered acceptable unless adequate justification for lower purity is provided by the registrant.

EPA Response

For laboratory studies conducted with radiolabeled chemicals, the use of a test substance with low radiopurity may unnecessarily complicate the identification of degradation products since the fate of the parent and its degradates is followed by monitoring the radioactivity.

Industry should strive for the highest possible radiopurity but not less than 95%. The Agency understands that achieving a high level of radiopurity may depend on the chemical characteristics of the specific compound and on the type of radioisotope used. The Agency further acknowledges that some chemicals may require extensive preparation in order to achieve this high level of radiopurity, and has previously concurred with time extensions for submission of data to allow for such preparation. The Agency has also previously accepted the use of lower purity radiochemicals with adequate justification as to why higher radiochemical purity could not be achieved.

6. Rejection Factor: The incubation temperature was not maintained.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 45.
- Standard Evaluation Procedure (SEP) for Hydrolysis Studies. (June 1985), pages 7 & 9.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-280 & C-282.

The temperature of the hydrolysis reaction must be precisely controlled, since one major purpose of the study is to determine the hydrolytic rate, which may vary unpredictably if the temperature is uncontrolled. A variation in the temperature of as little as 1°C may lead to an error in the measurement of the hydrolytic rate of as much as 10%.

Industry Comment

Industry agrees that the control of temperature in the hydrolysis study is critical to the validity of the study. The incubation temperature should be controlled to ±2-3°C as specified by the Agency. However, where there is slow, or no hydrolysis, this should not be sufficient reason to reject a study. In addition, if the decline curve is linear with a reasonable correlation coefficient (r^2), some minor temperature deviation should be acceptable.

Industry Recommendation: The Agency should continue to require careful temperature control for this study but should be flexible where deviations are minor and do not affect the determination of the hydrolysis rate. Careful temperature control is also much less important where the hydrolysis rate is very slow.

EPA Response

Industry should strive to maintain a constant temperature of ±1°C. Minor deviations from this range would not automatically be a cause for rejection of the study, but would be taken into account on a case-by-case basis (especially if little or no hydrolysis occurred). Since wide variations in temperature would almost certainly affect the measured rate of hydrolysis, the Agency continues to believe that this parameter must be well controlled in order for the study to generate reliable data.

7. Rejection Factor: Insufficient data were presented to support the reported conclusion.

This issue does not normally result in the rejection of a study, and it is usually repairable by the submission of additional data.

Industry Comment

Industry agrees that conclusions based on scientifically sound data should required.

EPA Response

No comment.

8. Rejection Factor: Degradation curves and regression analysis were not provided.

This issue does not normally result in the rejection of a study, and it is usually repairable by the submission of additional data.

Rejection factors (7 & 8) relate to basic information required by the agency. The information pertains to important study parameters that must be reported so that a technical evaluation of the data can be made.

Industry Comment

Industry agrees that degradation curves and regression analysis are important conclusions of the study and should be provided, except where extremely slow or no degradation was observed.

Industry Recommendation: The Agency should continue to require this information except in cases where hydrolysis did not reach 10% within 30 days, in which case the compound should be considered hydrolytically stable.

EPA Response

EPA agrees that if less than 10% of the chemical has hydrolyzed after 30 days, then it should be considered stable to hydrolysis. However, the occurrence of a clear single degradate would require identification at lower levels. Higher temperatures could also be used to demonstrate the stability of the chemical. With reference to sampling intervals, samples should be taken on a schedule defined by the nature of the chemistry involved (e.g., chemicals with short half lives may require that numerous early samples be taken, while more stable chemicals may require fewer early samples, but more intense later sampling). Where little or no degradation of the chemical occurs, three sampling points of 0, 15, and 30 days would be sufficient to determine the stability of the chemical.

Additional Industry Comments Hydrolysis Studies

Co-solvent concentrations sufficient to solubilize the test chemical should be permitted. Hydrophobic chemicals may not be sufficiently soluble in water to allow the experiment to be conducted with ≤1% co-solvent.

EPA Response

The Agency agrees that conducting a Hydrolysis study with extremely insoluble compounds may not always be feasible. However, the Agency is concerned that the use of extreme measures to solubilize the pesticide (greater than 1% co-solvent) may result in unreliable data due to pesticide-solvent interactions which may impact the hydrolysis rate as well as the types of degradates formed. Therefore, the use of co-solvents should be avoided when possible. Instead, the pesticide concentration selected for this study should be within the compound's solubility limit. In some cases, this will require that more sensitive analytical methods be developed.

GUIDELINE 161-2 PHOTODEGRADATION STUDIES IN WATER

1. **Rejection Factor:** **The light source was not adequately characterized and was not compared to sunlight.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 48.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 5, 8, 9, & 10.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-284 & C-286.

The light source used for sample irradiation may be either natural or simulated sunlight. If natural sunlight is used, a record of its intensity and wavelength distribution is required in addition to other major variables which affect incident light such as the time of exposure, latitude, time of year and atmospheric cover. If an artificial light source is used, its intensity, wavelength distribution and the length of exposure should be comparable to sunlight, as the rate of photolysis is dependent on these factors and will vary if the artificial light source is different from sunlight. It has been our observation that, of the currently available artificial light sources, the xenon arc lamp best simulates natural sunlight in both wavelength distribution and intensity. Therefore, the Agency currently prefers this light source over other artificial lamps. The Agency will consider the suitability of any future light sources as they become available.

Industry Comment

Industry agrees that adequate characterization of any light source and its comparison to natural sunlight is critical to photolysis studies. It would be helpful if "natural sunlight" could be defined more precisely. We suggest that sunlight be defined as the solar irradiance at 40° North Latitude, as shown in the EPA Mean Solar Data Table (EPA Chemical Fate Test Guidelines, 1983, Photolysis in Aqueous Solution in Sunlight, CG-6000, Office of Toxic Substances, Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency).

Irradiation equivalent to 30 days exposure to standard sunlight should be acceptable. For example, 420 hours of continuous irradiation from a source that simulates sunlight would be equivalent to a 30 day exposure to sunlight with a photoperiod of 14 hours.

Industry Recommendation: We would like the Agency to define standard sunlight and we suggest that sunlight be defined as the solar irradiance at 40° North Latitude. We also suggest that continuous irradiation equivalent to 30 days exposure to standard sunlight should be acceptable for the aqueous photolysis study.

EPA Response

Historically, guidance suggested that the light source parallel that in the intended use area, at the anticipated time of the year when the pesticide would normally be applied. As noted above, this may have led to inconsistent studies which could not be compared one to the other. This would seem to be in conflict with our goal to utilize "standardized" testing which would allow comparisons between chemicals.

Using standardized sunlight with solar irradiance at 40° North Latitude is an idea which, although not accounting for variations in season and natural lighting conditions, may nevertheless prove more consistent in predicting photolytic effects. The Agency is considering whether or not this should be implemented. In addition the Agency is also considering when quantum yield calculations may be used to allow the extrapolation of the laboratory results to other locations and times of year. Also the suggested continuous irradiation equivalent to 30 days exposure to natural sunlight or 420 hours of continuous irradiation from a source that simulates sunlight also appears to be a workable alternative to current practice.

2. Rejection Factor: Degradates were not identified.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 48.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), page 8.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-284.

Identification of residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the aqueous photolysis study. One primary purpose of this study is to identify the photodegradates formed after incubation of the active ingredient in water. Failure to identify one (or more) significant metabolites limits the understanding of the aqueous photolysis under actual use situations; hence the environmental fate of the pesticide is unclear.

Industry Comment

The Agency's comments (above) are not consistent with the referenced guidance documents. Failure to identify compounds present at 10% of applied should be a reason to reject a study unless the author can present valid reasons as to why this could not be achieved. There is NO valid justification for requiring registrants to identify compounds at greater than 0.01 ppm and there is no mention of this requirement in any of the guidance documents.

The purpose of this study is to identify the major photoproducts and these have been defined at those produced in yields of ≥10% of the applied test material. There is no justification for introducing a 0.01 ppm requirement.

Industry Recommendation: Photoproducts produced in yields of ≥10% of the applied test material should be identified in this study unless the registrant can present valid reasons as to why this could not be achieved.

EPA Response

The Agency agrees and will require the identification of all residues equal to or greater than 10% of the dose rate. The dose rate is defined as that applied concentration of the test substance which does not exceed the solubility limit of the pesticide in water and is <250 ppm. This level of residue identification should provide adequate information for most chemicals.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

3. Rejection Factor: The material balances were incomplete.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 48.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-284.

This study is designed to measure the photolysis of a pesticide in water and the formation and decline of the degradates. This is achieved by measuring the test substance applied at the beginning of the experiment and then accounting for it at the end of the experiment. The purpose of this test is to verify that all degradates formed are isolated and that an accurate rate of photolysis is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

Industry agrees that acceptable mass balance is needed for a study to be considered valid. If there is no attempt to provide a mass balance or if a significant amount of the starting activity is not accounted for, the study should be rejected. The EPA should be flexible on the definition of acceptable mass balance, however. For example, an extremely low solubility compound which is stable under the conditions of the aqueous photolysis study, may well show a reduced mass balance over the period of the study due to adsorption to surfaces of the test vessel which can be difficult to quantify precisely. Hence, rejection should only occur when there is a gross loss of mass balance.

Industry Recommendation: The EPA should be flexible on the definition of acceptable mass balance. Rejection should only occur when there is a gross loss of mass balance without adequate explanation.

EPA Response

The Agency continues to believe that 90-110% accountability should be viewed as an ideal target range. However, the Agency recognizes that in many cases this is not possible and,

therefore, has assessed the material balance within the context of the entire study, and has not routinely rejected studies solely on the basis of low material balance.

4. Rejection Factor: The test solutions were not buffered and the pH of the water was not reported.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), pages 47 & 48.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 12 & 7.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-284 & C-286.

The aqueous photolysis study should be conducted at a pH of greatest hydrolytic stability to minimize hydrolysis of the test substance. Therefore, the test solutions should be buffered and their pH maintained throughout the study.

Industry Comment

Industry agrees that the pH of the test solutions should be reported. Buffers should not be required unless needed to control hydrolytic stability.

Industry Recommendation: The pH of the test solutions in the aqueous photolysis study should be reported. Buffers should not be required unless needed to control hydrolytic stability.

EPA Response

Buffers are normally required to maintain constant pH in order to reduce contributions from hydrolysis in an aqueous photolysis study; therefore, a non-buffered photolysis study of a chemical which is hydrolytically stable at pH 5, 7, & 9 would normally not result in the rejection of the study.

5. Rejection Factor: The analytical methodology was incomplete and no raw data was provided to support the conclusions.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 6, 8, 13 & 14.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-287.

The guidelines specifically require that method validation data, recovery and method detection limit, quality control procedures and results should be provided. In addition, raw data, sample chromatograms and sample calculations should be included to determine how the photolysis rates were derived and how the photolysis products were identified.

Industry Comment

Industry agrees that the information specified in the guidelines should be included in the study report. We are not certain what is meant by "raw data". It would be helpful if the Agency defined the minimum raw data required for inclusion in the study report.

Industry Recommendation: The Agency should define the minimum raw data required for inclusion in the study report.

EPA Response

Raw data usually consist of laboratory worksheets, records, memoranda, notes, or exact copies thereof, which are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. The registrant should submit a representative sampling of the raw data (particularly chromatograms and spectra), to enable the reviewer to confirm the reported results. The Agency expects to issue further guidance on raw data requirements in the near future.

6. Rejection Factor: The sampling protocol was inadequate.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 48.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), page 12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-284.

Data should be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for a duration of 30 days, whichever comes first. The purpose of this is to assess the kinetics of pesticide degradation and the formation and degradation of its metabolites. This information is used to calculate a half-life for the pesticide and predict how long the pesticide and its metabolites will persist in the environment.

If the duration of the study is not long enough and does not have sufficient sampling points, the confidence in the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified. Also, if insufficient sampling occurred early in a study with a rapid decline curve, then statistical evaluation of the data might lead to the conclusion that the data are unreliable, and a new study would be required.

Industry Comment

Industry agrees that the Agency's guidance on this factor is adequate. Samples must be taken at the initiation of the study and at four or more sampling time intervals, with at least one observation made after one-half of the test substance is degraded or after the equivalent of 30 days natural sunlight (12 hours of light per day), whichever comes first. If less than 10% of the chemical has degraded after the equivalent of 30 days of exposure, then it should be considered stable to photolysis and analysis of samples from the earlier intervals should not be required.

Industry Recommendation: There is no need for the Agency to change the required sampling protocol. However, if less than 10% of the chemical has degraded after the equivalent of 30 days of

exposure, then it should be considered stable to photolysis and analysis of samples from the earlier intervals should not be required.

EPA Response

EPA agrees that if less than 10% of a chemical is found to photodegrade within 30 days, then the pesticide should be considered photolytically stable in water. However, the occurrence of a clear single degradate would require identification at lower levels. The UV-VIS spectrum (290-800) of the test substance and potential degradates in the medium/media used in the study should provide guidance as to the potential for a pesticide to undergo direct photolysis (see attached EFGWB Policy Note 1-2 dated 3/9/92). In accordance with the OECD guidelines, the Agency would consider a waiver request for the Photodegradation in Water data requirement if the molar absorption (extinction) coefficient of the pesticide in water was less than 10 l $mole^{-1}$ cm^{-1}. With reference to sampling intervals, samples should be taken on a schedule defined by the nature of the chemistry involved (eg., chemicals with short half lives may require that numerous early samples be taken, while more stable chemicals may require fewer early samples, but more intense later sampling). Where little or no degradation of the chemical occurs, three sampling points of 0, 15, and 30 days would be sufficient to determine the stability of the chemical.

7. **Rejection Factor:** **The temperatures of the test solutions were not reported.**

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 5 & 7.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-284 & C-286.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. The temperature of aqueous photolysis study should be monitored and maintained at 25 ±1 °C to simulate the actual use conditions and to avoid contributions from thermal reactions such as hydrolysis and oxidation.

Industry Comment

The temperature of the photolysis study should be reported but control at 25 ± 1° is not critical unless hydrolysis is also occurring at a competing rate under the conditions of the study.

Industry Recommendation: The EPA should not invalidate photolysis studies for failure to control temperature unless hydrolysis is occurring at a competing rate under the conditions of the study.

EPA Response

Industry should strive to maintain a constant temperature range of ±1°C. Minor deviations from this range would not automatically be a cause for the rejection of the study, but would be taken into account on a case-by-case basis. Although a 1°C rise in temperature does not affect the rate of photolysis, it may increase the rate of hydrolysis and other thermal reactions by 10%, thereby increasing contributions from such processes. Since wide variations in temperature would almost certainly increase contributions from thermal processes, the Agency continues to believe that this parameter must be well controlled in order for the study to meet one of its major intended purposes (eg. to follow the photolytic degradation of the pesticide in water and its correlation with other competitive degradation processes such as hydrolysis, microbial degradation...etc.).

8. Rejection Factor: Volatilization was neither measured nor controlled.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 47.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), page 12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-284.

This deficiency is only critical in situations with demonstrated poor material balances. It is needed under these circumstances to demonstrate that no radioactivity was lost

through volatilization. Therefore, traps must be used to monitor production of volatile photolytic products.

Industry Comment

Industry agrees that acceptable mass balance is vital to the validity of a study and where collection and analysis of volatile materials is needed to achieve this, it should be required.

EPA Response

No comment.

9. Rejection Factor: A photosensitizer was used as the co-solvent.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 47.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 7 & 12.

A photolytic process involves transfer of energy directly from the light to the affected compound. This energy transfer can also occur indirectly from the light to another compound, which then transfers this energy to the affected compound. This process is called photosensitized energy transfer and the compound responsible for this type of energy transfer is called a photosensitizer. The co-solvent used to increase the solubility of the test substance must not be a photosensitizer, because it will erroneously increase the rate of photolysis.

Industry Comment

Industry agrees that photosensitizers should not be used as co-solvents in photolysis studies. It was helpful that the Agency recommended the use of methanol and acetonitrile in the Standard Evaluation Procedure for this study. It would also be helpful if the Agency could provide a list of co-solvents which they have determined are not acceptable for this study.

Industry Recommendation: It would be helpful if the Agency could provide a list of co-solvents which they have determined are not acceptable for this study.

EPA Response

The Agency neither maintains a list nor has the resources to develop a comprehensive list of all possible solvents and substances which could conceivably act as photosensitizers. However, Industry could develop such a list.

10. Rejection Factor: It was not specified that the test solutions were sterile.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 47.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages ?
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-284.

The aqueous photolysis study is conducted to determine the rate of photolysis of the active ingredient, rates of formation and decline of the photodegradates and the identity of the photolysis products. Photolysis competes in nature with biological metabolism. Therefore, it is important that the study is conducted under sterile conditions to eliminate interference from biological degradation.

Industry Comment

Industry agrees that the equipment and solutions used in this study should be sterilized at the initiation of the study to prevent competing microbial degradation. It is impractical to require demonstration of sterility throughout the study period, however. In addition, if screening studies have shown that the chemical does not degrade microbially, then sterile conditions should not be required.

Industry Recommendation: The Agency should continue to require sterilization of the equipment and solutions used in this study but should not require demonstration of sterility throughout the study. Also, sterility should not be required where screening studies have shown that biodegradation does not to occur under the conditions of the study.

EPA Response

EPA's agrees that a study in which no degradation was observed should never be rejected solely on the basis of failure to prove sterile conditions. However, reasonable efforts should be made to assure that sterile conditions are maintained throughout the study.

11. Rejection Factor: The study was terminated before the half-life of the test substance was established or before 30 days.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 48.
- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), pages 7 & 12.

Data should be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for a duration of 30 days, whichever comes first. The purpose of this is to assess the kinetics of pesticide degradation and the formation and degradation of its degradates. This information is used to calculate a half-life for the pesticide and predict how long the pesticide and its degradates will persist in the environment. If the duration of the study is not long enough and does not have sufficient sampling points, the confidence in the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified.

Industry Comment

Industry agrees that the study should be continued until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for a duration of 30 days, whichever comes first, as specified in the Agency's discussion above.

EPA Response

No comment.

12. Rejection Factor: The coefficients of determination for the data used to determine the half-lives were very poor.

EPA Guidance on this Factor

There is no specific EPA guidance on this rejection factor. However, it pertains to basic information relating to data analysis. It appears that the r^2 values were low and the data points for the regression analysis were highly scattered making the first order rate constant unreliable.

Industry Comment

Industry agrees that a reasonable correlation coefficient for the calculation of the photolytic half-life is important in cases where this route of degradation is competing with other degradation routes to define the overall dissipation rate of the compound. One may frequently encounter low r^2 values, however, where there is very slow or very fast degradation. In these cases, even without a precise calculation of the half-life, the contribution of aqueous photolysis to the dissipation of the test substance in the environment will have been adequately characterized. Low r^2 alone should not be sufficient reason to reject a study.

Industry Recommendation: There should be no specific requirement to meet a minimum correlation coefficient. Decisions on the validity of the study should be made on the basis of whether the data produced in the study answer the question of photolytic stability and allow for a calculation of the rate where it is needed.

EPA Response

With extremely rapid or extremely slow degradation, r^2 needs to be considered on a study basis. However, for the vast majority of these studies, the need to accurately define the reaction kinetics demands that the data have a good fit to the regression line; hence, the need for an "acceptable" coefficient of determination.

13. Rejection Factor: The stability of the pesticide under refrigeration was not addressed.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation in Water Studies. (June 1985), page 5.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-284 & C-287.

Even under ideal conditions chemicals may degrade during storage. Therefore, if samples are taken and stored before analysis, a storage stability study is required in order to assess the effects, if any, of storage on those samples. In many cases, studies rejected due to storage stability data problems may be upgraded by the registrant with the submission of additional data/information.

Industry Comment

Industry agrees that when samples are stored for a significant period before analysis their stability under the conditions of storage must be proved. Some reasonable, short period of storage, eg, 10 days at 5°C or 30 days frozen, should be acceptable, however.

Industry Recommendation: Storage stability data should only be required beyond 10 days at 5°C or 30 days frozen.

EPA Response

Note: The following discussion is consistent with the position of the Chemistry Branches in HED on the requirements for storage stability data (Health Effects Division memo dated January 14, 1993). The registrants are referred to that document for additional guidance. Industry may, at its option, propose an alternative guidance document for Agency consideration.

Chemicals may degrade during storage, even under ideal storage conditions. Therefore, storage stability data are essential in order to be confident that any degradation measured in the test system was due solely to the environment of that test system, and not due to handling and storage. Storage stability is chemical specific and a chemical's stability under storage can vary depending upon the matrix stored (e.g., soil, water, organic extract, plant tissue, fish tissue, etc.). The Agency does however agree that unless a pesticide/residue of concern is

otherwise known to be volatile or labile, storage stability data will not be needed for samples stored frozen for ≤30 days.

For frozen storage intervals >30 days, evidence must be provided confirming that the identity of residues did not change during the period between collection and final analysis. Ideally, storage stability data should be obtained concurrently with the particular environmental fate guideline study, not independent from it.

However, concurrent storage stability studies will not be required in many cases. Provided that the pesticide residues are found to be stable in the matrices of interest, a storage stability study run in a separate freezer at a different time period will be acceptable if the storage conditions (particularly temperature) are the same as those in the corresponding environmental fate guideline study. However, for pesticides whose residues are known or suspected to be unstable or volatile, concurrent studies may be needed. In fact, for such pesticides, it is advisable to run a storage stability study in advance to determine proper storage conditions and maximum storage times before treated samples are placed into storage.

Additional Industry Comments on Photodegradation in Water Studies

Co-solvent concentrations greater than 1% should be permitted if needed to solubilize the test material.

Conclusions from natural water photolysis studies are not necessarily applicable to all bodies of water but may give a better indication of the fate of the pesticide in the environment. Natural water photolysis studies should continue to be regarded as supplemental, to be conducted at the discretion of the registrant, but not required.

EPA Response

The Agency agrees that conducting a Photodegradation in Water study with extremely insoluble compounds may not always be feasible. However, the Agency is concerned that the use of extreme measures to solubilize the pesticide (greater than 1% co-solvent) may result in unreliable data due to pesticide-solvent interactions which may impact the photolysis rate as well as the types of degradates formed. Therefore, the use of co-solvents should be avoided when possible. Instead, the pesticide concentration selected for this study should be within the compound's solubility limit. In some cases, this will require that more sensitive analytical methods be developed.

The Agency agrees with Industry's comments regarding natural water photolysis studies. Currently, natural water photolysis studies are not required to satisfy the environmental fate data requirements; however, such studies conducted under special circumstances previously have been found valuable in evaluating the photolytic behavior of the pesticide under natural environmental conditions.

GUIDELINE 161-3 PHOTODEGRADATION ON SOIL

1. Rejection Factor: The material balance was incomplete.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 51.
- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 11 & 8.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-289.

This study is designed to measure the photolysis of a pesticide on the soil and the formation and decline of the degradates. This is achieved by measuring the test substance applied at the beginning of the experiment and then accounting for it at the end of the experiment. The purpose of this test is to verify that all degradates formed are isolated and that an accurate rate of photolysis is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comments

Industry agrees that acceptable mass balance is needed for a study to be considered valid. If there is no attempt to provide a mass balance or if a significant amount of the starting activity is not accounted for, the study should be rejected. The EPA should be flexible on the definition of acceptable mass balance, however. Rejection should only occur when there is a gross loss of mass balance.

Industry Recommendation: The EPA should be flexible on the definition of acceptable mass balance. Rejection should only occur when there is a gross loss of mass balance without adequate explanation.

EPA Response

The Agency continues to believe that 90-110 % accountability should be viewed as an ideal target range. However, the Agency recognizes that in many cases this is not possible and, therefore, has assessed the material balance within the context

of the entire study, and has not routinely rejected studies solely on the basis of low material balance.

2. **Rejection Factor:** **Volatilization was neither measured nor controlled.**

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 11 & 7.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-288.

The study must demonstrate that no radioactivity is lost through volatilization. Therefore, traps must be used to monitor production of volatile photolysis products. This issue connects directly with low material balances, where unaccounted-for components need to be identified (even if it is ultimately determined to consist of radiolabeled-CO_2 or Parent pesticide).

Industry Comment

Industry agrees that acceptable mass balance is vital to the validity of a study and where collection and analysis of volatile materials is needed to achieve this, it should be required.

EPA Response

No comment.

3. **Rejection Factor:** **Artificial light source was not similar to natural sunlight.**

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 12 & 7.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-288.

The light source used for sample irradiation may be either natural or simulated sunlight. If natural sunlight is used, a record of its intensity and wavelength distribution is required

in addition to other major variables which affect incident light such as the time of exposure, latitude, time of year and atmospheric cover. If an artificial light source is used, its intensity, wavelength distribution and the length of exposure should be comparable to sunlight, as the rate of photolysis is dependent on these factors and will vary if the artificial light source is different from sunlight. It has been our observation that, of the currently available artificial light sources, the xenon arc lamp best simulates natural sunlight in both wavelength distribution and intensity. Therefore, the Agency currently prefers this light source over other artificial lamps. The Agency will consider the suitability of any future light sources as they become available.

Industry Comment

Industry agrees that adequate characterization of any light source and its comparison to natural sunlight is critical to photolysis studies. It would be helpful if "natural sunlight" could be defined more precisely. We suggest that sunlight be defined as the solar irradiance at 40° North Latitude, as shown in the EPA Mean Solar Data Table (EPA Chemical Fate Test Guidelines, 1983, Photolysis in Aqueous Solution in Sunlight, CG-6000, Office of Toxic Substances, Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency).

Irradiation equivalent to 30 days exposure to standard sunlight should be acceptable. For example, 420 hours of continuous irradiation from a source that simulates sunlight would be equivalent to a 30 day exposure to sunlight with a photoperiod of 14 hours.

Industry Recommendation: We would like the Agency to define standard sunlight and we suggest that sunlight be defined as the solar irradiance at 40° North Latitude. We also suggest that continuous irradiation equivalent to 30 days exposure to standard sunlight should be acceptable for the soil photolysis study.

EPA Response

Historically, guidance suggested that the light source parallel that in the intended use area, at the anticipated time of the year when the pesticide would normally be applied. As noted above, this may have led to inconsistent studies which could not be compared one to the other. This would seem to be in conflict with our goal to utilize "standardized" testing which would allow comparisons between chemicals.

Using standardized sunlight with solar irradiance at 40° North Latitude is an idea which, although not accounting for variations in season and natural lighting conditions, may nevertheless prove more consistent in predicting photolytic effects. The Agency is considering whether or not this should be implemented. In addition the Agency is also considering when quantum yield calculations may be used to allow the extrapolation of the laboratory results to other locations and times of year. Likewise, the suggested continuous irradiation equivalent to 30 days exposure to natural sunlight or 420 hours of continuous irradiation from a source that simulates sunlight also appears to be a workable alternative to current practice. The Agency will consider Industry's suggestions in revising Subdivision N.

4. Rejection Factor: The test substance was not technical grade or purer.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 50.
- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 5 & 8.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-288.

The purity of the test substance is critical for accurate study results. Any impurities in the test substance may interfere with the results and may lead to erroneous conclusions about the instability of the test substance or the types of photoproducts formed.

Industry Comment

Industry agrees that the test substance purity should be a requirement for a valid study. We suggest that a radiopurity of 95% should be acceptable in most cases and we would like the Agency to confirm this.

Industry Recommendation: No study should be initiated with a test substance which is not sufficiently pure. The Agency should specify what is acceptable radiochemical purity. recommends that a radiopurity of 95% should be considered acceptable unless adequate justification for lower purity is provided by the registrant.

EPA Response

For laboratory studies conducted with radiolabeled chemicals, the use of a test substance with low radiopurity may unnecessarily complicate the identification of degradation products since the fate of the parent and its degradates is followed by monitoring the radioactivity.

Industry should strive for the highest possible radiopurity but not less than 95%. The Agency understands that achieving a high level of radiopurity may depend on the chemical characteristics of the specific compound and on the type of radioisotope used. The Agency further acknowledges that some chemicals may require extensive preparation in order to achieve this high level of radiopurity, and has previously concurred with time extensions for submission of data to allow for such preparation. The Agency has also previously accepted the use of lower purity radiochemicals with adequate justification as to why higher radiochemical purity could not be achieved.

5. Rejection Factor: Raw data were not provided.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 6 & 13.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. The guidelines specifically require that raw data, sample chromatograms and sample calculations be provided on how the photolysis rates were derived and how the photolysis products were identified.

Industry Comment

Industry agrees that the information specified in the guidelines should be included in the study report. We are not certain what is meant by "raw data". It would be helpful if the Agency defined the minimum raw data required for inclusion in the study report.

Industry Recommendation: The Agency should define the minimum raw data required for inclusion in the study report.

EPA Response

Raw data usually consist of laboratory worksheets, records, memoranda, notes, or exact copies thereof, which are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. The registrant should submit a representative sampling of the raw data (particularly chromatograms and spectra), to enable the reviewer to confirm the reported results. The Agency expects to issue further guidance on raw data requirements in the near future.

6. Rejection Factor: The incubation temperature was not provided.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), page 5.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-289 & 291.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. Soil temperatures in this study are important because soil surface temperature increases under sunlight and the heating may accelerate various nonphotochemical reactions such as hydrolysis and oxidation. Thus, if the soil is not cooled, thermal reactions are likely to increase pesticide loss in the soil.

Industry Comment

Industry agrees that the temperature of the test system should be reported and that cooling should be used in the study to control the heating caused by exposure to sunlight. Imperfect temperature control should not be sufficient reason to reject a study alone, especially if plus or minus 1°C is the qualifier. Exposure to intense light can lead to temporary fluctuations from the desired range. Normally, thin layers of soil are used, and it difficult to monitor and control the temperature in the test system. Temperature control of the irradiated soil should be within ± 5° C of the dark controls.

Industry Recommendation: The temperature of the test system should be reported and cooling should be used in the study to control the heating caused by exposure to light. Temperature

control of the irradiated soil should be within ± 5° C of the dark controls.

EPA Response

Industry should strive to maintain a constant temperature of ±1°C. Minor deviations from this range would not automatically be a cause for the rejection of the study, but would be taken into account on a case-by-case basis. Although a 1°C rise in temperature does not affect the rate of photolysis, it may increase the rate of hydrolysis and other thermal reactions by 10%, thereby increasing contributions from such processes. Since wide variations in temperature would almost certainly increase contributions from thermal processes, the Agency continues to believe that this parameter must be well controlled in order for the study to meet one of its major intended purposes (eg. to follow the photolytic degradation of the pesticide in water and its correlation with other competitive degradation processes such as hydrolysis, microbial degradation...etc.).

7. Rejection Factor: Degradates were not identified.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 51.
- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 12 & 7.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-289.

The identification of those residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the soil photolysis study. One primary reason this study is conducted is to identify the photodegradates on soil. Failure to identify one (or more) significant degradates inhibits a complete understanding of the soil photolysis. Hence prediction of the environmental fate under actual use situations becomes much more difficult.

Industry Comment

The Agency's comments (above) are not consistent with the referenced guidance documents. Failure to identify compounds present at 10% of applied should be a reason to reject a study

unless the author can present valid reasons as to why this could not be achieved. There is NO valid justification for requiring registrants to identify compounds at greater than 0.01 ppm and there is no mention of this requirement in any of the guidance documents.

The purpose of this study is to identify the major photoproducts and these have been defined at those produced in yields of ≥10% of the applied test material. There is no justification for introducing a 0.01 ppm requirement.

Industry Recommendation: Photoproducts produced in yields of ≥10% of the applied test material should be identified in this study unless the registrant can present valid reasons as to why this could not be achieved.

EPA Response

The Agency agrees that the identification of residues present at 0.01 ppm may not always be feasible, especially for those products with field application rates exceeding approximately 1 lb ai/A. The Agency will require the identification of all residues equal to or greater than 10% of the dose rate. This level of residue identification should provide adequate information for most chemicals. The dose rate is defined as that concentration of radiolabeled pesticide in soil equal to the maximum field application rate at a 1 cm depth. For example, if the maximum field application rate is 5 lbs ai/A, the dose rate should approximate 37.5 μg ai/g of soil in the test system. All residues present at ≥10% of this dose rate (i.e., 3.75 μg parent equivalents/g soil) must be identified.

In the event that the dose rate must exceed the maximum field application rate for residue identification purposes, (e.g., for technological, specific activity, or other limitations), a separate exaggerated dose rate study may be conducted. However, this exaggerated dose rate study cannot be used to provide kinetics information. The kinetics study must be conducted with the maximum dose rate as described above.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

8. Rejection Factor: The test was not performed on soil.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 50.
- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), pages 5, 9, & 11.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-288 & C-290.

This study is conducted to provide data on photodegradation of the active ingredient on soil surfaces. The supporting documents provide adequate guidance in soil selection and require specific information about the description of soil type, soil characteristics, and the test soil source including country and state of origin.

Some submitters have expressed an interest in conducting this study on glass beads instead of on soil. Glass beads however cannot mimic the many processes which take place in the soil matrix.

Industry Comment

Industry agrees that the soil photolysis study must be conducted on soil. Maintaining conditions suitable for microbial growth (i.e., moist), however, unnecessarily complicates the study and does not contribute to the overall purpose of providing data on soil surface-catalyzed photodegradation.

Industry Recommendation: The Agency should require that studies be conducted on well characterized soil, but it should not require that conditions suitable for microbial growth be maintained throughout the study. The soils should be permitted to dry.

EPA Response

The Agency agrees that maintaining soil moisture level in the laboratory studies may be difficult; however, a reasonable effort must be made (eg., humidification of the ventilation airstream) to keep the soil somewhat moist so as to prevent significant alteration of the soil structure and properties.

9. Rejection Factor: The treatment rate was not reported.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 50.
- Standard Evaluation Procedure (SEP) for Photodegradation on Soil Studies. (June 1985), page 5.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-288 & 291.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. The treatment rate is important in evaluating the soil photolysis study, because the amount of disappearance of the parent and the metabolites formed during the process are dependent on the initial concentration of the test substance applied to the soil.

In many experiments, results are reported as a percent recovered, rather than as percent of applied. Also, the amount of active ingredient used usually closely approximates the anticipated field use rate.

Industry Comment

Industry agrees that the treatment rate must be reported.

EPA Response

No comment.

Additional Industry Comments on Photodegradation on Soil Studies

Soil used for the dark controls should be treated similarly to the exposed samples. Dark controls should be used solely to evaluate degradation in the soil photolysis experiment. Comparison of degradation rates observed in the dark controls with rates from the aerobic soil metabolism study may not be appropriate. The rate of microbial degradation on a thin layer of air-dried soil is not likely to duplicate the results of the soil metabolism study. Comparing the products found in the soil photolysis study to those of the aerobic soil metabolism study should provide an adequate basis for determining any differences.

EPA Response

EPA agrees that comparing the products found in the soil photolysis study to those of the aerobic soil metabolism study should provide an adequate basis for identification of the actual photodegradates. However, the Agency remains concerned with the manner in which dark controls are maintained. In a vast majority of the Photolysis in Soil studies, the dark controls are wrapped in aluminum foil and set aside in the dark without making sufficient efforts to maintain the same conditions as in the exposed samples (e.g., moisture level, air flow, temperature). Ideally, the dark controls should represent all processes <u>except</u> photolysis. Every effort should be made to ensure that, except for light, the dark controls and irradiated samples are maintained under the same environmental conditions.

GUIDELINE 161-4 PHOTODEGRADATION IN AIR

1. Rejection Factor: **The pesticide degradation in the vapor phase could not be distinguished from degradation that occurred in material adsorbed to the sides of the glass container.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-292 & C-293.

Appropriate analytical methods are required to clearly distinguish between vapor phase and liquid phase photoproducts.

Industry Comment

There is extreme procedural difficulty in addressing this problem. The reference cited in the Subdivision N Guidelines (Crosby and Moilanen, 1974) employ a rather large vessel of 72 liters in an attempt to maximize volume to surface area ratio and thus minimize wall effects. Sampling the vapor phase in this type of apparatus is complicated by the extremely low concentrations of chemical present for many agricultural chemicals due to their low vapor pressures (typically $<10^{-3}$ mm Hg). Attempts with even larger vessels have been made (Teflon bags, etc.), but these studies suffer from low material balance.

Industry Recommendation: Industry needs significantly more guidance on this study.

EPA Response

It appears that the use of a large vapor-phase photoreactor which permits compensation for wall effects by maximizing volume to surface area ratio may present significant experimental difficulties. However, in the studies which were rejected, the experimenters cooled the reaction vessel, condensing all vapor-phase components with those already in solution or adherent to the vessel walls. This approach further confounded the study.

The Agency acknowledges that the test procedures for photodegradation in air could be improved, and welcomes suggestions on technical and/or procedural enhancements to the study protocol.

2. Rejection Factor: Air samples were never analyzed separately from nonvaporized pesticide.

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-292 & C-293.

Photodegradation in air is a vapor phase study which is significantly different from the photodegradation in water study. Appropriate analytical methods are required to clearly distinguish between vapor phase and liquid phase photoproducts.

Industry Comment

Achieving this objective is also difficult. The dish from which the chemical is vaporized can be analyzed separately without too much problem, but analysis of the vapor phase is fraught with pitfalls as described above (Rejection Factor 1.)

EPA Response

See EPA Response to factor #1.

3. Rejection Factor: The material balance was low.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 53.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-292 & C-294.

This study is designed to measure the photolysis of a pesticide in the air and the formation and decline of the degradates. Therefore, the test substance applied at the beginning of the experiment must be accounted for at the end of the experiment to be certain that all degradates formed are isolated and an accurate rate of photolysis is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

With the large incubation vessels, used to minimize surface interactions, difficulties in achieving good sealing can occur.

Flexibility is needed in assessing the acceptability of mass balance in an air photolysis study.

EPA Response

EPA agrees that the Agency should allow some flexibility in what constitutes an acceptable material balance for those studies conducted in large reaction vessels.

4. Rejection Factor: High percentages of unidentified material were reported.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 53.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-292.

The identification of those residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the photodegradation in air study. One primary reason this study is conducted is to identify the photodegradates in the air. Failure to identify one (or more) significant degradates may result in gaps in the data regarding the photodegradation in the vapor phase. Hence the understanding of the environmental fate under actual use situations will be unclear.

Industry Comment

The Agency's comments (above) are not consistent with the referenced guidance documents. Failure to identify compounds present at 10% of applied should be a reason to reject a study unless the author can present valid reasons as to why this could not be achieved. There is NO valid justification for requiring registrants to identify compounds at greater than 0.01 ppm and there is no mention of this requirement in any of the guidance documents.

The purpose of this study is to identify the major photoproducts and these have been defined at those produced in yields of ≥10% of the applied test material. There is no justification for introducing a 0.01 ppm requirement.

Industry Recommendation: Photoproducts produced in yields of ≥10% of the applied test material should be identified in this

study unless the registrant can present valid reasons as to why this could not be achieved.

EPA Response

The Agency agrees that the identification of residues present at 0.01 ppm may not always be feasible, especially for those products with field application rates exceeding approximately 1 lb ai/A. The Agency will require the identification of all residues equal to or greater than 10% of the dose rate. This level of residue identification should provide adequate information for most chemicals.

In the event that the dose rate must exceed the maximum field application rate for residue identification purposes, (e.g., for technological, specific activity, or other limitations), a separate exaggerated dose rate study may be conducted. However, this exaggerated dose rate study cannot be used to provide kinetics information. The kinetics study must be conducted with the maximum dose rate as described above.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

5. **Rejection Factor:** **The registrant did not measure the vapor pressure at the temperature the study was conducted.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 52.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-293.

The vapor pressure should be measured at the same temperature that the study is conducted, as a different temperature will affect the results of the study.

Industry Comment

There is no mention of the measurement of vapor pressure in either of the references cited.

EPA Response

Vapor pressure at the temperature of the experiment needs to be measured to calculate the amount of the test substance present in the vapor phase since the concentration of the test substance varies with the temperature and pressure in the reaction vessel.

6. **Rejection Factor:** **The analytical method was inadequate.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-292 & C-293.

Photodegradation in air is a vapor phase study which is significantly different from the photodegradation in water study. Therefore, it requires appropriate analytical methods which clearly distinguishes between vapor phase and liquid phase photoproducts.

Industry Comment

Industry needs significantly more guidance on this factor.

EPA Response

The Agency acknowledges the need for additional guidance, and would welcome Industry's support in the development of additional SEPs for the remaining guidelines for which no SEP currently exists.

The identification and quantification of both parent and major degradates requires the use of methods of analysis which will unequivocally distinguish between vapor phase and liquid phase photoproducts.

7. **Rejection Factor:** **The spectrum of the artificial light source was not similar to that of natural sunlight.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 52.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-292 & C-293.

The light source used for sample irradiation may be either natural or simulated sunlight. If natural sunlight is used, a record of its intensity and wavelength distribution is required. In addition, other major variables which affect incident light must be used such as the time of exposure, latitude, time of year and atmospheric cover. If an artificial light source is used, its intensity, wavelength distribution and the length of exposure should be comparable to sunlight, as the rate of photolysis is dependent on these factors and will vary if the artificial light source is different from the natural sunlight.

Industry Comment

Industry agrees that adequate characterization of any light source and its comparison to natural sunlight is critical to photolysis studies. It would be helpful if "natural sunlight" could be defined more precisely. We suggest that sunlight be defined as the solar irradiance at 40° North Latitude, as shown in the EPA Mean Solar Data Table (EPA Chemical Fate Test Guidelines, 1983, Photolysis in Aqueous Solution in Sunlight, CG-6000, Office of Toxic Substances, Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency).

Irradiation equivalent to 30 days exposure to standard sunlight should be acceptable. For example, 420 hours of continuous irradiation from a source that simulates sunlight would be equivalent to a 30 day exposure to sunlight with a photoperiod of 14 hours.

Industry Recommendation: Industry would like the Agency to define standard sunlight, and we suggest that sunlight be defined as the solar irradiance at 40° North Latitude. Industry also suggests that continuous irradiation equivalent to 30 days exposure to standard sunlight should be acceptable for the air photolysis study.

EPA Response

Historically, guidance suggested that the light source parallel that in the intended use area, at the anticipated time of the year when the pesticide would normally be applied. As noted above, this may have led to studies that could not be compared to one another because of differences in lighting conditions. This would seem to be in conflict with our goal to utilize "standardized" testing which would allow comparisons between chemicals.

Using standardized sunlight with solar irradiance at 40° North Latitude is an idea which, although not accounting for

variations in season and natural lighting conditions, may nevertheless prove more consistent in predicting photolytic effects. The Agency is considering whether or not this should be implemented. In addition the Agency is also considering when quantum yield calculations may be used to allow the extrapolation of the laboratory results to other locations and times of year. Also the suggested continuous irradiation equivalent to 30 days exposure to natural sunlight or 420 hours of continuous irradiation from a source that simulates sunlight also appears to be a workable alternative to current practice. The Agency will consider Industry's suggestions in revising Subdivision N.

8. Rejection Factor: A photosensitizer was present in the primary stock solution.

A photolytic process involves the transfer of energy directly from the light to the affected compound. This energy transfer can also occur indirectly from the light to another compound which is then transferred to the affected compound. This process is called photosensitized energy transfer and the compound responsible for this type of energy transfer is called a photosensitizer. A co-solvent used to increase the solubility of the test substance must not be a photosensitizer because it will erroneously increase the rate of photolysis.

Industry Comment

Industry agrees that photosensitizers should not be used in the test solution.

EPA Response

No comment.

9. Rejection Factor: No raw data was submitted.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. The guidelines specifically require that raw data, sample chromatograms and sample calculations be provided on how the photolysis rates were derived and how the photolysis products were identified.

Industry Comment

Industry agrees that the information specified in the guidelines should be included in the study report. We are not

certain what is meant by "raw data". It would be helpful if the Agency defined the minimum raw data required for inclusion in the study report.

Industry Recommendation: The Agency should define the minimum raw data required for inclusion in the study report.

EPA Response

Raw data usually consist of laboratory worksheets, records, memoranda, notes, or exact copies thereof, which are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. The registrant should submit a representative sampling of the raw data (particularly chromatograms and spectra), to enable the reviewer to confirm the reported results. The Agency expects to issue further guidance on raw data requirements in the near future.

Additional Industry Comments on Photodegradation in Air Studies

Although there was no rejection rate data on this study in your report, our internal evaluation of the rejection rate is high. There is insufficient guidance available for this very difficult study. Industry recommends that there be a moratorium on air photolysis studies until additional guidance can be provided.

This study is quite difficult to carry out and requires specialized equipment. We recommend additional discussions between academic, EPA, and industry scientists to determine if a practical laboratory study can indeed determine pesticide photolysis in air. Such a study should be focused on qualitative aspects, as there is no clear use for quantitative rates. It should be required only when there is demonstrated volatility in a laboratory volatility study.

Industry offers to establish a forum to address the study design.

EPA Response

The Agency agrees that there is insufficient guidance available for the Photodegradation in Air data requirement; the study is costly, complex and if not done extremely well generates results which are difficult to interpret. These observations were made by the Agency almost ten years ago, at which time we decided to dramatically reduce the instances where the

requirement would be imposed. Based on an informal poll, the requirement has only been imposed a few times each year.

Additionally, the thrust of the requirement has changed dramatically. When first promulgated, photodegradation in air was conducted to define possible exposure of workers to potentially toxic photoproducts, under certain specialty use situations (eg., greenhouse use sites). With the development of Subdivision K and U emphasis shifted to general atmospheric contamination and non-target risk (i.e., contribution to photochemical smog, or toxic fogs). The Agency continues to require this study on a very limited case-by-case basis.

The Agency would appreciate input from the industry in addressing the changing needs for air monitoring in general. The suggested forum may be an excellent mechanism to achieve this goal.

GUIDELINE 162-1 AEROBIC SOIL METABOLISM

1. Rejection Factor: Residue identification was incomplete.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 55.
- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), pages 9, 15-16.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-296.

The identification of residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the aerobic soil metabolism study. One primary reason this study is conducted is to identify the degradates that are formed after application of a pesticide to soil. The failure to identify one (or more) significant degradates leads to an incomplete understanding of the metabolism, and hence the environmental fate. The result is that the dissipation under actual use situations will be unclear.

Industry Comment

Residues occurring at a level of 10% of the applied radioactivity or greater should be identified when feasible. The criteria for identification of residues should be consistent with the 1982 Guidelines as stated in the purpose of the study [§ 162-1 (a)] and with § 162-1 (c)(2)(ii). The Guidelines state at § 162-1 (c)(2)(ii) that the concentration of the test substance should be ". . . sufficient to permit . . . identification of major degradates formed."

The identification level specified above is 0.01 ppm or 10% of applied. A residue present at 0.01 ppm may not be a major degradate, particularly when the normal field application rate of a product is greater than 1 lb./A. For a variety of reasons, e.g., specific activity limitations for radiolabeled test substances, technological limitations for detection/quantitation methodology, dose rates for soil metabolism studies may differ significantly from the field application rate. For products with lower field application rates, soil metabolism studies must be conducted at exaggerated rates to permit metabolite identification at the required level. However, for products with field application rates exceeding approximately 1 lb./A, the

requirement for identification at 0.01 ppm is excessive since each component at or exceeding 1% of the treatment dose should be identified. Identification of degradates which represent 0.01 ppm is not always technically possible nor practical, especially when considering that the starting materials may not be purer than 97%. Thus it may not necessarily be useful to identify degradates that represent less than 3% of the applied material.

b) On page C-296 of the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, guidance is provided on the extent of effort desired for extraction to remove residues from soil, i.e., ". . . a reasonable attempt was made - perhaps with multiple solvent systems - to extract metabolites/degradates." Guidance documents do not address the current desire to reduce the nonextractable residues to less than 10% of the dose rate, using harsh acid/base digestion if required. Further, guidance documents do not address the extent of effort desired to identify components of the bound residue removed by harsh digestion procedures. Although it may be feasible to achieve the identification level for residues extractable by conventional means, identification of components obtained following harsh digestion is generally considerably more difficult due to the large amounts of coextractives. Since these components may have been altered by the methods employed, it should be sufficient to provide only characterization of these components.

Industry Recommendations: a) The Agency should define 'major degradates' as degradates that represent 10% or greater of the applied radioactivity. Using this definition, all major degradates should be identified.

b) Identification of degradates should be limited to those components which are extractable by reasonable means, i.e., organic solvents and water, and not applied to components removed following harsh acid/base digestion procedures.

EPA Response

The Agency agrees that the identification of residues present at 0.01 ppm may not always be feasible, especially for those products with field application rates exceeding approximately 1 lb ai/A. The Agency will require the identification of all residues equal to or greater than 10% of the dose rate. This level of residue identification should provide adequate information for most chemicals.

In the event that the dose rate must exceed the maximum field application rate for residue identification purposes, (e.g., for technological, specific activity, or other

limitations), a separate exaggerated dose rate study may be conducted. However, this exaggerated dose rate study cannot be used to provide kinetics information. The kinetics study must be conducted with the maximum dose rate as described above.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

The Agency agrees that identification of degradates should be limited to those components that are extractable by reasonable means (e.g., organic solvents and water), and not necessarily include those components removed following harsh acid/base extraction procedures. These "bound" residues are generally not available for plant or animal uptake, leaching, or run off. Harsh extraction, which changes the nature of the residues, is not necessary.

2. Rejection Factor: The material balance was inadequate.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), page 3, 15.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-295.

This is a controlled laboratory experiment designed to measure the breakdown of a pesticide in the soil and the formation and decline of the metabolites. Therefore, the test substance applied at the beginning of the experiment must be accounted for at the end of the experiment to be certain that all degradates formed are isolated and that an accurate rate of degradation is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

Guidance is adequate on the necessity to maintain a good material balance. The guidance is interpreted to mean that an adequate mass balance maintained during the course of the study is necessary to assure that all significant degradates formed are isolated. A target material balance of 90-110% would be an adequate measure of a study's accountability of the applied radioactivity. It is possible that individual sample time points and/or sample replicates could fall outside of the stated (target) material balance range and not adversely effect interpretation of the results. The most prevalent example is for studies with test substances which rapidly degrade to volatile products, notably CO2.

Industry Recommendation: The Agency should continue to assess any material balance deviations from the desired target range (90-110%) within the context of the entire study and not on a single sampling interval.

EPA Response

The Agency agrees that the material balance should be assessed within the context of the entire study and not on a single sampling interval; the 90-110% accountability should be viewed as an ideal target range.

3. **Rejection Factor:** **The study was conducted for an inadequate length of time to establish the patterns of formation and decline.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 55.
- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), pages 11-12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-295.

Data are to be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for one year, whichever comes first. The reason for this is to ensure that the kinetics of degradation of the pesticide and of the formation and degradation of its metabolites are fully understood. This information is used to

calculate a half-life for the pesticide and predict how long it and its metabolites persist in the environment. If the duration of the study is not long enough or there are insufficient sampling points, confidence in the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified.

Industry Comment

The purpose of the Aerobic Soil Metabolism study is to determine the nature and extent of degradation of the parent chemical and not, necessarily, to determine the half-life of the parent chemical. An Aerobic Soil Metabolism test system is an artificial environment which exerts selection pressure on microbial populations. The populations after 12 months cannot be expected to resemble those in fresh soil. Six months is a sufficient time to characterize the metabolism and rate of degradation for all intended uses of the pesticide.

Industry Recommendation: A maximum sampling period of 6 months would be adequate to reliably determine degradation rates.

EPA Response

The Agency continues to believe that a major purpose of the Aerobic Soil Metabolism study is the determination of the half-life of the parent chemical, as indicated in each of the guidance documents. However, the determination of the nature and extent of the formation and decline of degradation products is also important in helping us understand the fate of the chemical and anticipate the likelihood that the compound (or its degradates) will persist in the environment, where it may become available to rotational crops, non-target organisms, ground water and surface water.

A 6-month timeframe may not be sufficient to characterize the degradation of chemicals which are more than moderately persistent. However, for those chemicals which are rapidly degraded, Subdivision N already allows for flexibility in terminating the study, (i.e., until patterns of decline of parent and patterns of formation/decline of degradates are established or for no more than one year, whichever comes first). This provides a timeframe sufficient to define the kinetic behavior of the chemical. Chemicals found not to degrade significantly after 6 months will be considered metabolically stable.

The Agency acknowledges the "artificial" nature of the Aerobic Soil Metabolism test system, but recognizes that a laboratory study is intended to provide preliminary information

about a pesticide (and its degradates) under well-controlled conditions, prior to the initiation of field studies. Variables such as moisture content and temperature are maintained to ensure viable microbial populations in the soil, with the understanding that, as in the field, microbial populations will fluctuate over time.

4. Rejection Factor: Purity of the test substance was not specified.

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 42, 54.
- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), pages 2, 8, 9.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-295, C-297.
- Addendum 5 on Data Reporting to Pesticide Assessment Guidelines: Aerobic Soil Metabolism Studies. (January 1988), page 6.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

A technical grade or purer test substance is required. A technical grade test substance is the active ingredient which does not contain inert ingredients other than one used for purification of the active ingredient. A technical grade or purer test substance is essential for this study as one objective of the study is to determine the fate of the pesticide and its degradates in a controlled laboratory setting. Impurities in the test material will likely confound the results.

Industry Comment

Industry agrees that adequate characterization of the test substance should be a requirement for a valid study. We suggest that a radiopurity of 95% should be acceptable in most cases and would like the Agency to confirm this.

Industry Recommendation: No study should be initiated with a test substance which has not been adequately characterized. In using this rejection factor however, the Agency should be

specific in delineating what exactly is deficient with respect to test substance characterization. Further, the Agency should specify what is acceptable radiochemical purity. Industry recommends that a radiopurity of 95% should be considered acceptable unless adequate justification for lower purity is provided by the registrant.

EPA Response

For laboratory studies conducted with radiolabeled chemicals, the use of a test substance with low radiopurity may unnecessarily complicate the identification of degradation products since the fate of the parent and its degradates is followed by monitoring the radioactivity.

Industry should strive for the highest possible radiopurity but not less than 95%. The Agency understands that achieving a high level of radiopurity may depend on the chemical characteristics of the specific compound and on the type of radioisotope used. The Agency further acknowledges that some chemicals may require extensive preparation in order to achieve this high level of radiopurity, and has previously concurred with time extensions for submission of data to allow for such preparation. The Agency has also previously accepted the use of lower purity radiochemicals with adequate justification as to why higher radiochemical purity could not be achieved.

5. Rejection Factor: The experimental design was inadequate to assess the metabolism in soil.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 54-55.
- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), pages 9-12.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-295.

This is a general criticism of the methodology employed by the study author to evaluate the rate of degradation of the pesticide in the soil and the rate of formation and decline of the degradation products. The aerobic soil metabolism study is a laboratory study conducted under controlled conditions designed to control as many variables as possible so that the data will reflect degradation in soil due to microorganisms as well as

chemical degradation by the soil constituents, including water. Other degradation processes, such as those caused by photolysis, are prevented from occurring so that the data will solely reflect soil metabolism under aerobic conditions and that the data may be compared to data on other pesticides. If the design of the experiment does not follow the general guidance as outlined in either Subdivision N or the SEP for aerobic soil metabolism, the data may not be useful for predicting the fate of the chemical and its degradates in the environment.

Industry Comment

Guidance for overall study design is adequate.

Industry Recommendation: The experimental design should be flexible; unnecessary requirements should be waived. For example, if a chemical has been shown to be photolytically stable on soil, it should not be a requirement to conduct the study in the complete absence of light.

EPA Response

The Agency agrees that the experimental design must have some flexibility. Requirements in Subdivision N pertaining to experimental design are generic and cannot possibly address the unique physical/chemical properties and behavior of each individual pesticide. In evaluating the experimental design, the Agency considers whether generally-accepted methods were used, whether sufficient numbers of measurements were made to achieve statistical reliability, and whether sufficient controls were built into all phases of the experiment. In the example given in the Recommendation, exclusion of light may still be necessary because of its effects on microbial behavior and the resulting impact on degradation.

6. Rejection Factor: The incubation temperature was not reported.

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 55.
- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), page 11.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-295, C-298.

- Addendum 5 on Data Reporting to Pesticide Assessment Guidelines: Aerobic Soil Metabolism Studies. (January 1988), pages 6, 7.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

This information is important because temperature will likely affect the metabolism rate. Guidance for this study requires that the study be conducted at a constant temperature within a specified range.

Industry Comment

Guidance is adequate for the reporting of incubation temperature. However, a constant temperature of ±1°C is technically difficult to maintain for a one-year incubation. A greater range, ±2-3°C, should be acceptable since it is doubtful that this wider range would effect either the rate of degradation or degradation pathway.

Industry Recommendation: The Agency should consider a wider range, ±2-3°C, as the definition of constant temperature.

EPA Response

Industry should strive to maintain a constant temperature of ±1°C. Minor deviations from this range would not automatically be a cause for rejection of the study, but would be taken into account on a case-by-case basis. Since variations in temperature will almost certainly affect the measured rate of metabolism, the Agency continues to believe that this parameter must be well-controlled in order for the study to meet one of its major intended purposes. Minor fluctuations may be tolerable when the results of the study are not adversely impacted and the study objectives are met.

7. Rejection Factor: The soil textures could not be confirmed because the soils were not classified using the USDA Soil Textural Classification System.

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 42-43, 55.

- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), pages 2, 8, 10.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989) pages C-295, C-297.

- Addendum 5 on Data Reporting to Pesticide Assessment Guidelines: Aerobic Soil Metabolism Studies. (January 1988), pages 6-7.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

Soil characteristics may affect the results of this study. The USDA Soil Textural Classification System is the standard method by which soils are classified. This classification provides important information about the soil which is then used in deriving conclusions from the results of the study.

Rejection factors 5-10 relate to basic information required to be included in any study submitted to the EPA. The information pertains to important study parameters that must be reported so that a technical evaluation of the data can be made. In most cases, studies rejected solely on these reporting deficiencies are likely to be upgraded by the registrant by the submission of the additional data/information.

Industry Comment

Guidance is adequate for reporting the soil textural classification. The Agency needs to specify any additional requirements for reporting soil characteristics.

Industry Recommendation: The Agency should specify the soil characteristics, i.e., percent organic matter, cation exchange capacity, percent content of sand, silt, and clay, bulk density, and pH, to be reported in addition to the USDA soil textural classification.

EPA Response

Soil characteristics are currently specified in the SEP and, with the exception of bulk density, also in the Phase 3 Technical Guidance Documents. Complete physical, chemical and mineralogical characteristics are necessary for a reasonable comparison of soils. When soil characteristics are reported in a nonstandard way (i.e., not according to the well established USDA

scheme), comparison of study results with those of other studies becomes more difficult.

8. **Rejection Factor:** **The analytical methodology was incomplete and no raw data were provided to support conclusions.**

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 55.
- Standard Evaluation Procedure (SEP) for Aerobic Soil Metabolism Studies. (June 1985), pages 2, 3, 13, 14.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-296, C-298.
- Addendum 5 on Data Reporting to Pesticide Assessment Guidelines: Aerobic Soil Metabolism Studies. (January 1988), pages 7-8, 9.

The analytical method needs to adequately identify all degradates that are formed after application of a pesticide to soil. Raw data are frequently needed in order for the reviewer to validate the registrant's reported results and conclusions.

Industry Comment

Guidance for methodology, presented in Appendix 3 of the Standard Evaluation Procedure, is adequate in specifying techniques for identification. However, the guidance does not specify the number and/or combinations of chromatographic techniques required to provide adequate identification by cochromatography.

Guidance documents do not specify the amount of raw data to include with the report.

Industry Recommendation: The Agency should specify, for the general case, the number of independent chromatographic techniques necessary to adequately support identity of a metabolite by cochromatography.

The Agency should define what raw data need to be included in the final report.

EPA Response

Identification of degradates must be established using two different analytical techniques except when unambiguous identification is made using a method such as GC/MS or NMR. In general, the Agency will not consider chromatographic techniques utilizing the same stationary phase with two different solvent systems (or the same solvent system with two different stationary phases), to be adequate two-method verification of degradate identity.

Raw data usually consist of laboratory worksheets, records, memoranda, notes, or exact copies thereof, which are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. The registrant should submit a representative sampling of the raw data (particularly chromatograms and spectra), to enable the reviewer to confirm the reported results. The Agency expects to issue further guidance on raw data requirements in the near future.

9. Rejection Factor: The raw data examined did not support the half-life reported by the registrant.

Industry Comment

Guidance is adequate in specifying methods for half-life determinations. However, degradation of pesticides in soil seldom follow first-order kinetics.

Industry Recommendation: The Agency should allow first-order and non-first-order determinations of the half-life. These methods may include, but are not limited to, DT50 determinations and multi-phasic first-order calculations of several half-lives.

EPA Response

The Agency agrees that the degradation kinetics should be correctly defined, based on statistical evaluation of the measured data using an appropriate degradation model. Some degradation patterns do not follow either first-order or multi-phasic first order kinetics very well. Therefore, non first-order determinations of the half-life should be utilized by data submitters when appropriate, to more reliably predict the dissipation characteristics of the compound under those conditions.

10. Rejection Factor: Degradate characterization data were presented as percent of recovered rather than percent of applied.

EPA Guidance on this factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-298.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

Results must be reported in terms of percent of applied radioactivity in order that a material balance may be calculated. Results reported in terms of percent of recovered radioactivity can not be used to determine if all the pesticide applied at the beginning of the study has been accounted for. It is important to be certain that all degradates formed are isolated and an accurate rate of degradation is calculated.

Industry Comment

Guidance is adequate for the presentation of data to support the reported material balance and amounts of degradates.

Industry Recommendation: If data are expressed as a percent of the recovered in an effort to resolve material balance problems, the Agency should review the study according to the criteria stated in Rejection Factor #2 above.

EPA Response

Data presented as "percent of recovered" tend to mask recovery problems (i.e., poor material balances). Interpretation of such data becomes more difficult, if not impossible. Such reporting of data does not help resolve material balance problems, but from our experience further confounds them.

GUIDELINE 162-2 ANAEROBIC SOIL METABOLISM

1. Rejection Factor: Residue identification was incomplete.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 58-59.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 9, 17.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-300.

The identification of those residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the anaerobic soil metabolism study. One primary reason this study is conducted is to identify the degradates that are formed after application of a pesticide to soil. The failure to identify one (or more) significant degradates leads to an incomplete understanding of the metabolism, and hence the environmental fate. The result is that the dissipation under actual use situations will be unclear.

NOTE: The original Subdivision N guidance for this requirement describes a significantly deficient approach to monitoring Anaerobic (terrestrial) Soil metabolism. As a consequence of later thinking, we have urged submitters to utilize the Anaerobic Aquatic (sediments) protocol, which is much more useful, using soil instead of sediments. Studies conducted under the original protocol are likely to have very inadequate sampling and consequently an unreliable degradation rate and metabolite estimation.

Industry Comments

a) The 1982 Guidelines require analysis, if feasible, of residues occurring at 0.01 ppm or greater when plants are treated at the nominal field rate. Industry recommends that individual compounds comprising 10% or greater of the applied radioactivity should be identified, when feasible. The criteria for identification of residues should be consistent with the 1982 Guidelines as stated in the purpose of the study [§ 162-2(a)] and with § 162-2(c)(2)(ii).

The identification level specified above is 0.01 ppm or 10% of applied. A residue present at 0.01 ppm may not be a major

degradate, particularly when the normal field application rate of a product is greater than 1 lb./A. For a variety of reasons, e.g., specific activity limitations for radiolabeled test substances, technological limitations for detection/quantitation methodology, dose rates for soil metabolism studies may differ significantly from the field application rate. For products with lower field application rates, soil metabolism studies must be conducted at exaggerated rates to permit metabolite identification at the required level. However, for products with field application rates exceeding approximately 1 lb./A, the requirement for identification at 0.01 ppm is excessive since each component at or exceeding 1% of the treatment dose should be identified. Identification of degradates which represent 0.01 ppm is not always technically possible nor practical, especially when considering that the starting materials may not be purer than 97%. Thus it may not necessarily be useful to identify degradates that represent less than 3% of the applied material.

b) On page C-300 of the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, guidance is provided on the extent of effort desired for extraction to remove residues from soil, i.e., "...a reasonable attempt was made - perhaps with multiple solvent systems - to extract metabolites/degradates." Guidance documents do not address the current desire to reduce the nonextractable residues to less than 10% of the dose rate, using harsh acid/base digestion if required. Further, guidance documents do not address the extent of effort desired to identify components of the bound residue removed by harsh digestion procedures. Although it may be feasible to achieve the identification level for residues extractable by conventional means, identification of components obtained following harsh digestion is generally considerably more difficult due to the large amounts of coextractives. Since these components may have been altered by the methods employed, it should be sufficient to provide only characterization of these components.

c) The NOTE above is clear in the direction the Agency has provided on use of the Anaerobic Aquatic (§ 162-3) rather than the Anaerobic Soil study design (§ 162-2). However, the Agency's direction has not been adequately communicated to registrants and the Agency's mechanism of communication is not known to Industry. The Anaerobic Aquatic (§ 162-3) study design cannot provide data to assess item II.A.(b) of the Standard Evaluation Procedure for Anaerobic Soil Metabolism Studies (§ 162-2), i.e., to provide information on "...the rate of formation and degradation of aerobic degradation products formed during aerobic preincubation; ..." Accordingly, Anaerobic Aquatic studies (§ 162-3) should not be required for terrestrial use products.

Industry Recommendations: a) The Agency should define 'major degradates' as degradates that represent 10% or greater of the applied radioactivity. Using this definition of major degradates, all major degradates should be identified.

b) Identification of degradates should be limited to those components which are extractable by reasonable means, i.e., organic solvent and water, and not applied to components removed following harsh acid/base digestion procedures. The Agency should also allow flexibility in metabolite identification based upon the efforts involved. For example, certain polar metabolites may not be amenable to separation, cleanup, and/or identification. In such cases, characterization should be sufficient, since polar metabolites usually tend to degrade further.

c) Guidance is requested from the Agency concerning the Agency's position that chemicals should be tested by the Anaerobic Aquatic study design (§ 162-3) and the use of field soil rather than sediment when using the Anaerobic Aquatic study design (§ 162-3) for Anaerobic Soil Metabolism studies (§ 162-2).

EPA Response

The Agency agrees that the identification of residues present at 0.01 ppm may not always be feasible, especially for those products with field application rates exceeding approximately 1 lb ai/A. The Agency will require the identification of all residues equal to or greater than 10% of the dose rate. This level of residue identification should provide adequate information for most chemicals.

In the event that the dose rate must exceed the maximum field application rate for residue identification purposes, (e.g., for technological, specific activity, or other limitations), a separate exaggerated dose rate study may be conducted. However, this exaggerated dose rate study cannot be used to provide kinetics information. The kinetics study must be conducted with the maximum dose rate as described above.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

The Agency agrees that identification of degradates should be limited to those components that are extractable by reasonable

means (e.g., organic solvents and water), and not necessarily include those components removed following harsh acid/base extraction procedures. These "bound" residues are generally not available for plant or animal uptake, leaching, or run off. Harsh extraction, which changes the nature of the residues, is not necessary.

The Agency agrees that a mechanism is needed to communicate new or changing Branch policies in a more timely fashion, and is currently developing a mechanism which involves capturing such changes as "Policy Note" documents; these would then be made available (via dial-in modem) from EFED's Pesticide Information Network (PIN) bulletin board system.

According to Subdivision N (162-2 (b) (2)), "data from an anaerobic soil metabolism study need not be submitted if data from the anaerobic aquatic metabolism study described in 162-3 of this subdivision have been submitted." Because of the inadequacy of the sampling protocol described in Subdivision N for the Anaerobic Soil Metabolism study (30 and 60 days of anaerobic incubation), the Agency is currently recommending that the Anaerobic Aquatic Metabolism (162-3) study protocol be followed when an Anaerobic Soil Metabolism (162-2) data requirement has been triggered. The Anaerobic Aquatic Metabolism study protocol provides for adequate sampling intervals to fully describe the patterns of decline of parent and formation and decline of degradates under anaerobic conditions.

The usefulness of the Anaerobic Soil Metabolism study as it is currently described in Subdivision N and the SEP is an issue for future guideline revision.

2. Rejection Factor: The material balance was inadequate.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 4, 16-17.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-299.

This is a controlled laboratory experiment designed to measure the breakdown of a pesticide in the soil and the formation and decline of the degradates. This is achieved by measuring the test substance applied at the beginning of the experiment and then accounting for it at the end of the experiment to be certain that all degradates formed are isolated

and that an accurate rate of degradation is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

Guidance is adequate on the necessity to maintain a good material balance. The guidance is interpreted to mean that an adequate mass balance maintained during the course of the study is necessary to assure that all significant degradates formed are isolated. A target material balance of 90-110% would be an adequate measure of a study's accountability of the applied radioactivity. It is possible that individual sample time points and/or sample replicates could fall outside of the stated (target) material balance range and not adversely effect interpretation of the results. The most prevalent example is for studies with test substances which rapidly degrade to volatile products, notably CO2. It is also noted that maintaining material balance can be more difficult with anaerobic than aerobic studies due to measurement and summing of residue in water and soil phases versus only soil for aerobic studies.

Industry Recommendation: The Agency should continue to assess any material balance deviations from the desired target range (90-110%) within the context of the entire study and not on a single sampling interval.

EPA Response

The Agency agrees that the material balance should be assessed within the context of the entire study and not on a single sampling interval; the 90-110% accountability should be viewed as an ideal target range.

3. **Rejection Factor:** **The purity of the test substance was not specified.**

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 42, 58.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 2, 10.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-299, C-301.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

A technical grade or purer test substance is required. A technical grade test substance is the active ingredient which does not contain inert ingredients other than one used for purification of the active ingredient. A technical grade or purer test substance is essential for this study as one objective of the study is to determine the fate of the pesticide and its degradates in a controlled laboratory setting. Impurities in the test material will likely confound the results.

Industry Comment

Industry agrees that adequate characterization of the test substance should be a requirement for a valid study. We suggest that a radiopurity of 95% should be acceptable in most cases and would like the Agency to confirm this.

Industry Recommendation: No study should be initiated with a test substance which has not been adequately characterized. In using this rejection factor however, the Agency should be specific in delineating what exactly is deficient with respect to test substance characterization. Further, the Agency should specify what is acceptable radiochemical purity. Industry recommends that a radiopurity of 95% should be considered acceptable unless adequate justification for lower purity is provided by the registrant.

EPA Response

For laboratory studies conducted with radiolabeled chemicals, the use of a test substance with low radiopurity may unnecessarily complicate the identification of degradation

products since the fate of the parent and its degradates is followed by monitoring the radioactivity.

Industry should strive for the highest possible radiopurity but not less than 95%. The Agency understands that achieving a high level of radiopurity may depend on the chemical characteristics of the specific compound and on the type of radioisotope used. The Agency further acknowledges that some chemicals may require extensive preparation in order to achieve this high level of radiopurity, and has previously concurred with time extensions for submission of data to allow for such preparation. The Agency has also previously accepted the use of lower purity radiochemicals with adequate justification as to why higher radiochemical purity could not be achieved.

4. Rejection Factor: **The storage stability data were not provided, although the raw data indicate that both soil samples and extracts were stored prior to analysis.**

EPA Guidance on this factor

- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), page 13.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-302.

Even under ideal conditions, chemicals may degrade during storage. Therefore, if samples are taken and stored before analysis, a storage stability study is required in order to assess the effects, if any, of storage on those samples. In many cases, studies rejected due to storage stability data problems may be upgraded by the registrant by the submission of additional data/information.

Industry Comment

Industry agrees that storage stability data must be provided (if the samples are stored for an extended period of time) for the parent and metabolites in tissue samples. Since the nature of the residue is unknown at the start of the study, flexibility is required on the means of obtaining the data.

Industry Recommendation: Industry recommends that EPA accept a 4- to 6-month grace period for sample storage during which no storage stability information would be required, provided that samples have been stored properly. If samples are

stored more than 6 months, the registrant should: a) Reference storage stability data already obtained from relevant sample types and storage conditions in other studies; or b) Analyze a representative substrate as soon as practicable (i.e., within 4 to 6 months of collecting the samples), and then repeat the analysis at the end of the study. The chromatographic profiles may be compared to insure that no gross changes have occurred during storage. This is consistent with the policy on plant metabolism studies currently in force in the Chemistry Branches of the Health Effects Division (P. Paul conversation with R. Loranger, 6/23/92).

EPA Response

Chemicals may degrade during storage, even under ideal storage conditions. Therefore, storage stability data are essential in order to be confident that any degradation measured in the test system was due solely to the environment of that test system, and not due to handling and storage. Storage stability is chemical specific and a chemical's stability under storage can vary depending upon the matrix stored (e.g., soil, water, organic extract, plant tissue, fish tissue, etc.). Therefore, the Agency is concerned that a blanket 4- to 6-month grace period for sample storage, during which no storage stability information would be required, may not be appropriate for environmental fate testing. The Agency does however agree that unless a pesticide/residue of concern is otherwise known to be volatile or labile, storage stability data will not be needed for samples stored frozen for ≤30 days.

For frozen storage intervals >30 days, it is recommended that evidence be provided confirming that the identity of residues did not change during the period between collection and final analysis. The Agency has agreed to let industry develop a draft storage stability guidance document to address this and other storage stability issues. Final Agency judgement on this issue will be reserved for the Storage Stability follow-up guidance.

Ideally, storage stability data should be obtained concurrently with the particular environmental fate guideline study, not independent from it. However, concurrent storage stability studies will not be required in many cases. Provided that the pesticide residues are found to be stable in the matrices of interest, a storage stability study run in a separate freezer at a different time period will be acceptable if the storage conditions (particularly temperature) are the same as those in the corresponding environmental fate guideline study.

However, for pesticides whose residues are known or suspected to be unstable or volatile, concurrent studies may be needed. In fact, for such pesticides, it is advisable to run a storage stability study in advance to determine proper storage conditions and maximum storage times before treated samples are placed into storage.

5. Rejection Factor: Degradates present in small concentrations were not identified.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 58-59.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 9, 17.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-300.

Identifying residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the anaerobic soil metabolism study. One primary reason this study is conducted is to identify the degradates that are formed after application of a pesticide to soil.

Industry Comment

a) The 1982 Guidelines require analysis, if feasible, of residues occurring at 0.01 ppm or greater when plants are treated at the nominal field rate. Industry recommends that individual compounds comprising 10% or greater of the applied radioactivity should be identified, when feasible. The criteria for identification of residues should be consistent with the 1982 Guidelines as stated in the purpose of the study [§ 162-2(a)] and with § 162-2(c)(2)(ii).

The identification level specified above is 0.01 ppm or 10% of applied. Residues present at 0.01 ppm may not be a major degradate, particularly when the normal field application rate of the product is greater than 1 lb/A. For a variety of reasons, e.g., specific activity limitations for radiolabeled test substances or technological limitations for detection/quantitation methodology, dose rates for soil metabolism studies may differ from the field application rate. For products with lower field application rates, soil metabolism studies need to be conducted at exaggerated rates to permit

metabolite identification at the required level. However, for products with field application rates exceeding approximately 1 lb./A, the requirement for identification at 0.01 ppm is excessive since each component at or exceeding 1% of the treatment dose should be identified. On the other hand, when the application rate is low, major degradates or the parent compound may be present at a concentration less than 0.01 ppm. Identification of degradates which represent 0.01 ppm is not always technically possible nor practical. Especially when considering that the starting materials may not be purer than 97% and thus will not necessarily be useful to identify degradates that represent less than 3% of the applied material.

b) On page C-300 of the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, guidance is provided on the extent of effort desired for extraction to remove residues from soil, i.e., "...a reasonable attempt was made - perhaps with multiple solvent systems - to extract metabolites/degradates." Guidance documents do not address the current desire to reduce the nonextractable residues to less than 10% of the dose rate, using harsh acid/base digestion if required. Further, guidance documents do not address the extent of effort desired to identify components of the bound residue removed by harsh digestion procedures. Although it may be feasible to achieve the identification level for residues extractable by conventional means, identification of components obtained following harsh digestion is generally considerably more difficult due to the large amounts of coextractives. Since these components may have been altered by the methods employed, it should be sufficient to provide only characterization of these components.

Industry Recommendations: a) The Agency should define 'major degradates' as degradates that represent 10% or greater of the applied radioactivity. Using this definition of major degradates, all major degradates should be identified.

b) Identification of degradates should be limited to those components which are extractable by reasonable means, i.e., organic solvent and water, and not applied to components removed following harsh acid/base digestion procedures.

EPA Response

The Agency agrees that the identification of residues present at 0.01 ppm may not always be feasible, especially for those products with field application rates exceeding approximately 1 lb ai/A. The Agency will require the identification of all residues equal to or greater than 10% of

the dose rate. This level of residue identification should provide adequate information for most chemicals.

In the event that the dose rate must exceed the maximum field application rate for residue identification purposes, (e.g., for technological, specific activity, or other limitations), a separate exaggerated dose rate study may be conducted. However, this exaggerated dose rate study cannot be used to provide kinetics information. The kinetics study must be conducted with the maximum dose rate as described above.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

The Agency agrees that identification of degradates should be limited to those components that are extractable by reasonable means (e.g., organic solvents and water), and not necessarily include those components removed following harsh acid/base extraction procedures. These "bound" residues are generally not available for plant or animal uptake, leaching, or run off. Harsh extraction, which changes the nature of the residues, is not necessary.

6. **Rejection Factor:** **The experimental design was inadequate to accurately assess the degradation under anaerobic conditions.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 58-59.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 10-13.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989) page C-299.

This is a general criticism of the methodology employed by the study author to evaluate the rate of pesticide degradation in the soil and the rate of formation and decline of the degradation products. The anaerobic soil metabolism study is a laboratory study conducted under controlled conditions designed to account for as many variables as possible so that the data will reflect

degradation in soil due to microorganisms as well as chemical degradation by the soil constituents, including water. Other degradation processes, such as those caused by photolysis, are prevented from occurring so that the data will solely reflect soil metabolism under anaerobic conditions and so that the data may be compared to data on other pesticides. If the design of the experiment does not follow the general guidance as outlined in either Subdivision N or the SEP for anaerobic soil metabolism, the data may not be useful for predicting the fate of the chemical and its degradates in the environment.

Industry Comment

The anaerobic metabolism of a chemical with a long aerobic half-life may be suitably characterized by a study which begins with anaerobic conditions. If the intent is to determine the fate of the parent compound, then the requirement for aerobic incubation is unnecessary. Since the Anaerobic Aquatic study may be submitted in lieu of an Anaerobic Soil study [see § 162-2(b)(2)], there is limited justification for an initial aerobic phase in the latter study.

Industry Recommendation: The experimental design should be flexible; unnecessary requirements should be waived. For example, if a chemical has been shown to be photolytically stable on soil, it should not be a requirement to conduct the study in the complete absence of light. Industry requests the Agency to allow the Anaerobic Soil Metabolism study to be conducted without aerobic incubation for chemicals with an aerobic half-life greater than 100 days.

EPA Response

The Agency agrees that the experimental design must have some flexibility. Requirements in Subdivision N pertaining to experimental design are generic and cannot possibly address the unique physical/chemical properties and behavior of each individual pesticide. In evaluating the experimental design, the Agency considers whether generally-accepted methods were used, whether sufficient numbers of measurements were made to achieve statistical reliability, and whether sufficient controls were built into all phases of the experiment. In the example given in the Recommendation, exclusion of light may still be necessary because of its effects on microbial behavior and the resulting impact on degradation.

The Agency agrees that the anaerobic metabolism of a chemical with a long aerobic half-life may be suitably characterized by a study which forgoes the aerobic preincubation.

The 100 day figure proposed by Industry for allowing the Anaerobic Soil Metabolism study to be conducted without aerobic incubation for chemicals seems reasonable, and its implementation will be considered. However, the aerobic preincubation would certainly be indicated for those compounds which degrade somewhat rapidly under aerobic conditions.

7. Rejection Factor: **The length of frozen storage was not specified. Frozen storage stability data are required to confirm that the residues were stable.**

EPA Guidance on this factor

- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), page 13.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-302.

Even under ideal conditions, chemicals may degrade during storage. Therefore, if samples are taken and stored for long periods of time prior to analysis, a storage stability study is required in order to assess the effects, if any, of storage on those samples. In many cases, studies rejected due to storage stability data problems may be upgraded by the registrant submitting additional data/information.

Industry Comment

Industry agrees that storage stability data must be provided (if the samples are stored for an extended period of time) for the parent and metabolites in tissue samples. Since the nature of the residue is unknown at the start of the study, flexibility is required on the means of obtaining the data.

Industry Recommendation: Industry recommends that EPA accept a 4- to 6-month grace period for sample storage during which no storage stability information would be required, provided that samples have been stored properly. If samples are stored more than 6 months, the registrant should: a) Reference storage stability data already obtained from relevant sample types and storage conditions in other studies; or b) Analyze a representative substrate as soon as practicable (i.e., within 4 to 6 months of collecting the samples), and then repeat the analysis at the end of the study. The chromatographic profiles may be compared to insure that no gross changes have occurred during storage.This is consistent with the policy on plant

metabolism studies currently in force in the Chemistry Branches of the Health Effects Division (P. Paul conversation with R. Loranger, 6/23/92).

EPA Response

Chemicals may degrade during storage, even under ideal storage conditions. Therefore, storage stability data are essential in order to be confident that any degradation measured in the test system was due solely to the environment of that test system, and not due to handling and storage. Storage stability is chemical specific and a chemical's stability under storage can vary depending upon the matrix stored (e.g., soil, water, organic extract, plant tissue, fish tissue, etc.). Therefore, the Agency is concerned that a blanket 4- to 6-month grace period for sample storage, during which no storage stability information would be required, may not be appropriate for environmental fate testing. The Agency does however agree that unless a pesticide/residue of concern is otherwise known to be volatile or labile, storage stability data will <u>not</u> be needed for samples stored frozen for ≤ 30 days.

For frozen storage intervals >30 days, it is recommended that evidence be provided confirming that the identity of residues did not change during the period between <u>collection and final analysis</u>. The Agency has agreed to let industry develop a draft storage stability document to address this and other storage stability issues. Final Agency judgement on this issue will be reserved for the Storage Stability follow-up guidance.

Ideally, storage stability data should be obtained concurrently with the particular environmental fate guideline study, not independent from it. However, concurrent storage stability studies will not be required in many cases. Provided that the pesticide residues are found to be stable in the matrices of interest, a storage stability study run in a separate freezer at a different time period will be acceptable if the storage conditions (particularly temperature) are the same as those in the corresponding environmental fate guideline study. However, for pesticides whose residues are known or suspected to be unstable or volatile, concurrent studies may be needed. In fact, for such pesticides, it is advisable to run a storage stability study in advance to determine proper storage conditions and maximum storage times before treated samples are placed into storage.

8. Rejection Factor: Method detection limits were not provided.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 3, 14, 15, 17

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-299.

This rejection factor relates to basic information required to be included in any study submitted to the EPA. The information pertains to an important study parameter that must be reported so that a technical evaluation of the data can be made. In most cases, studies rejected solely on this reporting deficiency are likely to be upgraded by the registrant by the submission of the additional data/information.

Industry Comment

Guidance is acceptable for the necessity to report method detection limits for quantitation.

Industry Recommendation: Method detection limits for quantitation will be reported.

EPA Response

No comment necessary.

9. Rejection Factor: Large discrepancies existed in the data for duplicate samples collected after anaerobic conditions were established. The data, therefore, cannot be used reliably to calculate the rate of degradation in soil under anaerobic conditions.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 3, 12.

In order for the data to be statistically significant, the soil treatments must be replicated. Replicate treatments should

provide similar, if not the same, results. If the results are dissimilar, a standard statistical methodology may then be used to disqualify the study as unreliable. Large discrepancies may be indicative of a major problem in the experimental design and/or analytical methodology.

Industry Comment

In test systems where microbial processes are occurring, it is not uncommon to observe variations of 10% or more in degradation rates even with study durations of 60 days or less. Especially at later sampling intervals when the level of parent may be minimal and bound residues may be significant, precision diminishes due to the summing of parent residues in the water and soil phases. It is unrealistic to expect that results would be 'the same'.

Industry Recommendation: Industry requests the Agency to be flexible recognizing the limitations of analyzing minute quantities of residues.

EPA Response

The Agency is aware of the limitations involved in analyzing small quantities of residues and strives to take these into account when interpreting such data.

10. Rejection Factor: The study was conducted for an inadequate length of time to establish the patterns of formation and decline of the pesticide under anaerobic conditions. The study should have been conducted for 60 days.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 58.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 12, 13
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-299.

In the case of a highly persistent compound, the time required to meet the intent of the guidance may exceed 60 days.

Data should have been collected for at least 60 days after anaerobic conditions were established for this particular active ingredient. This is to be certain that the kinetics of pesticide degradation and of the formation and degradation of its metabolites are fully understood. The data are used to calculate a half-life for the pesticide and predict how long it and its degradates will persist in the environment. If the duration of the study is not long enough or there are insufficient sampling points, the reliability of the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified.

Experimenters may fail to conduct the study for a sufficient length of time because they (inappropriately) choose to save all samples frozen until the conclusion of the study. They therefore might not be aware of the chemical's persistence. Ideally, samples should be analyzed soon after collection, and results compared throughout the course of the study.

Industry Comment

As noted under Rejection Factor 1, the Agency recognizes the deficiency of guidance documents for Anaerobic Soil Metabolism in specifying a study duration sufficient to observe formation and decline of degradates. The anaerobic metabolism of a chemical with a long aerobic half-life may be suitably characterized by a study which begins with anaerobic conditions. If the intent is to determine the fate of the parent compound, then the requirement for aerobic incubation is unnecessary. Since the Anaerobic Aquatic study may be submitted in lieu of an Anaerobic Soil study [see § 162-2(b)(2)], there is limited justification for an initial aerobic phase in the latter study.

Industry Recommendation: As recommended under Rejection Factor 1, guidance should be revised for Anaerobic Soil Metabolism to include at a minimum when required (if it is currently the Agency's position that all chemicals should be tested by the Anaerobic Aquatic protocol) and the use of field soil rather than sediment when using the Anaerobic Aquatic study design. The experimental design should be flexible; unnecessary requirements should be waived. For example, if a chemical has been shown to be photolytically stable, it should not be a requirement to conduct the study in the complete absence of light. Industry requests the Agency to allow the Anaerobic Soil Metabolism study to be conducted without aerobic incubation for chemicals with an aerobic half-life greater than 100 days.

EPA Response

According to Subdivision N (162-2 (b) (2)), "data from an anaerobic soil metabolism study need not be submitted if data from the anaerobic aquatic metabolism study described in 162-3 of this subdivision have been submitted." Because of the inadequacy of the sampling protocol described in Subdivision N for the Anaerobic Soil Metabolism study (30 and 60 days of anaerobic incubation), the Agency is currently recommending that the Anaerobic Aquatic Metabolism (162-3) study protocol be followed when an Anaerobic Soil Metabolism (162-2) data requirement has been triggered. The Anaerobic Aquatic Metabolism study protocol provides for adequate sampling intervals to fully describe the patterns of decline of parent and formation and decline of degradates under anaerobic conditions. The test media should always be sediments collected from areas predominantly under anaerobic conditions.

The usefulness of the Anaerobic Soil Metabolism study as it is currently described in Subdivision N and the SEP is an issue for future guideline revision.

The Agency agrees that there needs to be flexibility in designing this experiment. Requirements in Subdivision N pertaining to experimental design are generic and cannot possibly address the unique physical/chemical properties and behavior of each individual pesticide. In evaluating the experimental design, the Agency considers whether generally-accepted methods were used, whether sufficient numbers of measurements were made to achieve statistical reliability, and whether sufficient controls were built into all phases of the experiment.

11. Rejection Factor: No raw data were provided to support the conclusions.

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 59.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 3, 15.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

Raw data are frequently needed in order for EPA to validate the registrant's reported results and conclusions.

Industry Comment

Industry is not certain what is meant by "raw data." Guidance documents do not specify the amount of raw data to include with the report. It would be helpful if the Agency defined the minimum raw data required for inclusion in the study report.

Industry Recommendation: The Agency should define the minimum raw data required for inclusion in the study report.

EPA Response

Raw data usually consist of laboratory worksheets, records, memoranda, notes, or exact copies thereof, which are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. The registrant should submit a representative sampling of the raw data (particularly chromatograms and spectra), to enable the reviewer to confirm the reported results. The Agency expects to issue further guidance on raw data requirements in the near future.

12. Rejection Factor: **A complete description of the test water, including the pH and dissolved oxygen content, was not provided.**

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

A description of the test water is essential for the purpose of defining the conditions under which the study is conducted.

Industry Comment

Industry agrees that a description of the test water is essential for the purpose of defining the conditions under which the study is conducted.

Industry Recommendation: The Agency should specify that anaerobicity (pH and redox potential) should be demonstrated and reported.

EPA Response

The Agency agrees that pH and redox potential should be determined, and both the SEP and the Phase 3 Technical Guidance documents specify that these measurements are to be reported. The Agency welcomes additional discussion on a clear definition of "anaerobic conditions."

13. Rejection Factor: The soil was not classified according to the USDA Soil Textural Classification System.

EPA Guidance on this factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 42-43, 59.
- Standard Evaluation Procedure (SEP) for Anaerobic Soil Metabolism Studies. (August 1988), pages 2, 9, 11.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-299, C-301.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

Soil characteristics may affect the results of this study. The USDA Soil Textural Classification System is the standard method by which soils are classified. This classification provides important information about the soil which is then used in deriving conclusions from the results of the study.

Rejection factors 8 to 13 relate to basic information required to be included in any study submitted to the EPA. The information pertains to important study parameters that must be reported so that a technical evaluation of the data can be made. In most cases, studies rejected solely on these reporting deficiencies are likely to be upgraded by the registrant by the submission of the additional data/information.

Industry Comment

Guidance is adequate for reporting the soil textural classification. The Agency needs to specify any additional requirements for reporting soil characteristics.

Industry Recommendation: The Agency should specify the soil characteristics, i.e., percent organic matter, cation exchange capacity, percent content of sand, silt, and clay, bulk density, and pH, to be reported in addition to the USDA soil textural classification.

EPA Response

Soil characteristics are currently specified in the SEP and, with the exception of bulk density, also in the Phase 3 Technical Guidance Documents. Complete physical, chemical and mineralogical characteristics are necessary for a reasonable comparison of soils. When soil characteristics are reported in a nonstandard way (i.e., not according to the well established USDA scheme), comparison of study results with those of other studies becomes more difficult.

GUIDELINE 162-3 ANAEROBIC AQUATIC METABOLISM

1. **Rejection Factor:** **The sampling protocol was inappropriate because it contained too few sampling intervals and was inadequate to establish the half-life for the pesticide.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 60.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-303.

Data are to be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for one year, whichever comes first. This is to be certain that the kinetics of pesticide degradation and of the formation and degradation of its metabolites are fully understood. This information is used to calculate a half-life for the pesticide and predict how long it and its degradates will persist in the environment. If the duration of the study is not long enough or there are insufficient sampling points, the reliability in the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified.

Industry Comment

The purpose of the Anaerobic Aquatic Metabolism study is to determine the nature and extent of degradation of the parent chemical and not, necessarily, to determine the half-life of the parent chemical. An Anaerobic Aquatic Metabolism test system is an artificial environment which exerts selection pressure on microbial populations. The populations after 12 months cannot be expected to resemble those in fresh soil. Six months is a sufficient time to characterize the metabolism and rate of degradation for all intended uses of the pesticide.

Industry Recommendation: A maximum sampling period of 6 months would be adequate to reliably determine degradation rates.

EPA Response

The Agency continues to believe that a major purpose of the Anaerobic Aquatic Metabolism study is the determination of the half-life of the parent chemical, as indicated in each of the

guidance documents. However, the determination of the nature and extent of the formation and decline of degradation products is also important in helping us understand the fate of the chemical and anticipate the likelihood that the compound (or its degradates) will persist in aquatic environments, where it may become available to irrigated crops, non-target organisms, ground water and surface water.

A 6-month timeframe may not be sufficient to characterize the degradation of chemicals which are more than moderately persistent. However, for those chemicals which are rapidly degraded, Subdivision N already allows for flexibility in terminating the study (i.e., until patterns of decline of parent and patterns of formation/decline of degradates are established or for no more than one year, whichever comes first). This provides a timeframe sufficient to define the kinetic behavior of the chemical. Chemicals found not to degrade significantly after 6 months will be considered metabolically stable.

The Agency acknowledges the "artificial" nature of the Anaerobic Aquatic Metabolism test system, but recognizes that a laboratory study is intended to provide preliminary information about a pesticide (and its degradates) under well-controlled conditions, prior to the initiation of field studies. Variables such as redox potential and temperature are maintained to ensure viable microbial populations in the sediment, with the understanding that, as in the field, microbial populations will fluctuate over time.

2. **Rejection Factor:** **The pesticide residues were quantified using a chemically nonspecific analytical method. No attempt was made to characterize the pesticide residues in soil and water matrices.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 60-61.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-303.

One primary reason this study is conducted is to identify each and every significant degradate that is formed after application of a pesticide to the aquatic environment, if feasible. An analytical method that is chemically nonspecific cannot distinguish between different residues, as it can only

measure the total amount of those residues present with no regard to their individual identities. The identification of residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the anaerobic aquatic metabolism study.

Industry Comment

a) Although no Standard Evaluation Procedure or Pesticide Assessment Guideline has been issued for Anaerobic Aquatic Metabolism, guidance regarding identification of metabolites/degradates is presented in Subdivision N Guidelines and Phase 3 Technical Guidance.

b) Residues occurring at a level of 10% of the applied radioactivity or greater should be identified when feasible. The criteria for identification of residues should be consistent with the 1982 Guidelines as stated in the purpose of the study [§ 162-3 (a)] and with § 162-3 (c)(2)(ii). Guidelines state at § 162-3 (c)(2)(ii) that the test substance should be applied at a rate ". . . sufficient to permit . . . identification of major degradates."

The identification level specified above is 0.01 ppm or 10% of applied. A residue present at 0.01 ppm may not be a major degradate, particularly when the normal field application rate of a product is greater than 1 lb./A. For a variety of reasons, e.g., specific activity limitations for radiolabeled test substances, technological limitations for detection/quantitation methodology, dose rates may differ significantly from the field application rate. For products with lower field application rates, Anaerobic Aquatic Metabolism studies must be conducted at exaggerated rates to permit metabolite identification at the required level. However, for products with field application rates exceeding approximately 1 lb./A, the requirement for identification at 0.01 ppm is excessive since each component at or exceeding 1% of the treatment dose should be identified. Identification of degradates which represent 0.01 ppm is not always technically possible nor practical, especially when considering that the starting materials may not be purer than 97%. Thus it may not necessarily be useful to identify degradates that represent less than 3% of the applied material.

c) On page C-303 of the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, guidance is provided on the extent of effort desired for extraction to remove residues from soil, i.e., "...a reasonable attempt was made - perhaps with multiple solvent systems - to extract metabolites/degradates." Guidance documents do not address the current desire to reduce the nonextractable

residues to less than 10% of the dose rate, using harsh acid/base digestion if required. Further, guidance documents do not address the extent of effort desired to identify components of the bound residue removed by harsh digestion procedures. Although it may be feasible to achieve the identification level for residues extractable by conventional means, identification of components obtained following harsh digestion is generally considerably more difficult due to the large amounts of coextractives. Since these components may have been altered by the methods employed, it should be sufficient to provide only characterization of these components.

Industry Recommendation: a) Since the Agency is recommending the Anaerobic Aquatic protocol, using soil instead of sediment, for the Anaerobic Soil metabolism study, it is highly recommended that written guidance be issued, e.g., a Standard Evaluation Procedure. To the extent possible, it is recommended that study design, reporting requirements, etc. be consistent for the Anaerobic Soil and Anaerobic Aquatic requirements. If the Agency desires, Industry is willing to draft a Standard Evaluation Procedure for EPA.

b) The Agency should define 'major degradates' as degradates that represent 10% or greater of the applied radioactivity. Using this definition of major degradates, all major degradates should be identified.

c) Identification of degradates should be limited to those components which are extractable by reasonable means, i.e., organic solvent and water, and not applied to components removed following harsh acid/base digestion procedures.

EPA Response

The Agency acknowledges the need for additional guidance, and would welcome Industry's support in the development of additional SEPs for the remaining guidelines for which no SEP currently exists.

The issue of nonspecific analytical methods to quantitate residues was not addressed in Industry's response. The identification and quantification of both parent and major degradates requires the use of methods of analysis that will unequivocally distinguish between the various degradates and/or metabolites in an extract, as well as between these components and other substances which might interfere with the analysis. In some cases, methods used are simply too non-specific (e.g., One-Dimensional Thin Layer Chromatography with UV visualization,

total radioactivity), and cannot possibly distinguish/confirm components.

3. Rejection Factor: Material balances were incomplete.

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-303.

This is a laboratory experiment designed to measure the breakdown of a pesticide in the hydrosoil/water medium and the formation and decline of the metabolites. This is achieved by measuring the test substance at the beginning of the experiment and then accounting for it at the end of the experiment to ensure that all degradates formed are isolated and that an accurate rate of degradation is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

Guidance is adequate on the necessity to maintain a good material balance. The guidance is interpreted to mean that an adequate mass balance maintained during the course of the study is necessary to assure that all significant degradates formed are isolated. A target material balance of 90-110% would be an adequate measure of a study's accountability of the applied radioactivity. It is possible that individual sample time points and/or sample replicates could fall outside of the stated (target) material balance range and not adversely effect interpretation of the results. The most prevalent example is for studies with test substances which rapidly degrade to volatile products, notably CO_2. It is also noted that maintaining material balance can be more difficult with anaerobic than aerobic studies due to measurement and summing of residue in water and soil phases versus only soil for aerobic studies.

Industry Recommendation: The Agency should continue to assess any material balance deviations from the desired target range (90-110%) within the context of the entire study and not on a single sampling interval.

EPA Response

The Agency agrees that the material balance should be assessed within the context of the entire study and not on a single sampling interval; the 90-110% accountability should be viewed as an ideal target range.

4. **Rejection Factor: Degradates were not identified.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 61.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-303.

The identification of residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the anaerobic aquatic metabolism study. One primary reason this study is conducted to identify the degradates that are formed after application of a pesticide to the aquatic environment. Failure to identify one (or more) significant degradates may result in an unclear understanding of the metabolism, and hence the environmental fate. Thus the understanding of dissipation under actual use situations is uncertain.

Industry Comment

a) Although no Standard Evaluation Procedure or Pesticide Assessment Guideline has been issued for Anaerobic Aquatic Metabolism, guidance regarding identification of metabolites/degradates is presented in Subdivision N Guidelines and Phase 3 Technical Guidance.

b) Residues occurring at a level of 10% of the applied radioactivity or greater should be identified when feasible. The criteria for identification of residues should be consistent with the 1982 Guidelines, as stated in the purpose of the study [§ 162-3(a)], and with § 162-3(c)(2)(ii). Guidelines state at § 162-3(c)(2)(ii) that the test substance should be applied at a rate ". . . sufficient to permit . . . identification of major degradates."

The identification level specified above is 0.01 ppm or 10% of applied. A residue present at 0.01 ppm may not be a major degradate, particularly when the normal field application rate of a product is greater than 1 lb./A. For a variety of reasons, e.g., specific activity limitations for radiolabeled test substances, technological limitations for detection/quantitation methodology, dose rates may differ significantly from the field application rate. For products with lower field application rates, Anaerobic Aquatic Metabolism studies must be conducted at exaggerated rates to permit metabolite identification at the required level. However, for products with field application

rates exceeding approximately 1 lb./A, the requirement for identification at 0.01 ppm is excessive since each component at or exceeding 1% of the treatment dose should be identified. Identification of degradates which represent 0.01 ppm is not always technically possible nor practical, especially when considering that the starting materials may not be purer than 97%. Thus it may not necessarily be useful to identify degradates that represent less than 3% of the applied material.

c) On page C-303 of the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, guidance is provided on the extent of effort desired for extraction to remove residues from soil, i.e., ". . . a reasonable attempt was made - perhaps with multiple solvent systems - to extract metabolites/degradates." Guidance documents do not address the current desire to reduce the nonextractable residues to less than 10% of the dose rate, using harsh acid/base digestion if required. Further, guidance documents do not address the extent of effort desired to identify components of the bound residue removed by harsh digestion procedures. Although it may be feasible to achieve the identification level for residues extractable by conventional means, identification of components obtained following harsh digestion is generally considerably more difficult due to the large amounts of coextractives. Since these components may have been altered by the methods employed, it should be sufficient to provide only characterization of these components.

Industry Recommendation: a) Since the Agency is recommending the Anaerobic Aquatic protocol, using soil instead of sediment, for the Anaerobic Soil metabolism study, it is highly recommended that written guidance be issued, e.g., a Standard Evaluation Procedure. To the extent possible, it is recommended that study design, reporting requirements, etc. be consistent for the Anaerobic Soil and Anaerobic Aquatic requirements. If the Agency desires, Industry is willing to draft a Standard Evaluation Procedure for EPA.

b) The Agency should define major degradates as those that represent 10% or greater of the applied radioactivity. Using this definition of major degradates, all major degradates should be identified.

c) Identification of degradates should be limited to those components which are extractable by reasonable means, i.e., organic solvent and water, and not applied to components removed following harsh acid/base digestion procedures.

EPA Response

Industry's response does not seem to address the rejection factor issue of degradate identification. The intended purpose of these laboratory studies is the clear and unequivocal identification and quantification of both parent and major degradates. The submitted study(ies) were apparently rejected because no attempt was made to identify and quantify any of the degradates which occurred. Thus the intended purpose of the study could not be met. Studies such as these might be repairable if the submitter had retained frozen samples, which could be reanalyzed provided there was adequate storage stability data to support the results.

5. **Rejection Factor: The test substance was not technical grade or purer.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 60.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-303.

A technical grade or purer test substance is required. A technical grade test substance is the active ingredient which does not contain inert ingredients other than one used for purification of the active ingredient. A technical grade or purer test substance is essential for this study, as one objective of the study is to determine the fate of the pesticide and its degradates in a controlled laboratory setting. Impurities in the test material will likely confound the results.

Industry Comment

Industry agrees that adequate characterization of the test substance should be a requirement for a valid study. We suggest that a radiopurity of 95% should be acceptable in most cases and would like the Agency to confirm this.

Industry Recommendation: No study should be initiated with a test substance which has not been adequately characterized. In using this rejection factor however, the Agency should be specific in delineating what exactly is deficient with respect to test substance characterization. Further, the Agency should specify what is acceptable radiochemical purity. Industry recommends that a radiopurity of 95% should be considered

acceptable unless adequate justification for lower purity is provided by the registrant.

EPA Response

For laboratory studies conducted with radiolabeled chemicals, the use of a test substance with low radiopurity may unnecessarily complicate the identification of degradation products since the fate of the parent and its degradates is followed by monitoring the radioactivity.

Industry should strive for the highest possible radiopurity but not less than 95%. The Agency understands that achieving a high level of radiopurity may depend on the chemical characteristics of the specific compound and on the type of radioisotope used. The Agency further acknowledges that some chemicals may require extensive preparation in order to achieve this high level of radiopurity, and has previously concurred with time extensions for submission of data to allow for such preparation. The Agency has also previously accepted the use of lower purity radiochemicals with adequate justification as to why higher radiochemical purity could not be achieved.

6. **Rejection Factor:** **The test water was not characterized. Foreign soils were not completely characterized and may not have been typical of those in the United States. The soil must be representative of that found at an intended use site.**

EPA Guidance on These Factors

- Subdivision N: Environmental Fate Guidelines. (1982), pages 42-43, 61.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-303, C-305.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

Rejection factors 1 to 6 relate to basic information required to be included in any study submitted to the EPA. The information pertains to important study parameters that must be reported so that a technical evaluation of the data can be made. In most cases, studies rejected solely on these reporting

deficiencies are likely to be upgraded by the registrant by the submission of the additional data/information.

Industry Comment

a) Industry agrees that a description of the test water is essential for the purpose of defining the conditions under which the study is conducted.

b) Guidance is adequate for reporting the soil textural classification. The Agency needs to specify any additional requirements for reporting soil characteristics.

Industry Recommendation: a) The Agency should specify that anaerobicity (pH and redox potential) should be determined and reported.

b) The Agency should specify the soil characteristics, i.e., percent organic matter, cation exchange capacity, percent content of sand, silt, and clay, bulk density, and pH, to be reported in addition to the USDA soil textural classification. Guidance is requested from the Agency concerning the Agency's position that chemicals should be tested by the Anaerobic Aquatic study design (§ 162-3) and the use of field soil rather than sediment when using the Anaerobic Aquatic study design (§ 162-3) for Anaerobic Soil Metabolism studies (§ 162-2).

EPA Response

The Agency agrees that pH and redox potential should be determined, and the Phase 3 Technical Guidance document specifies that these measurements are to be reported. The Agency welcomes additional discussion on a clear definition of "anaerobic conditions."

With the exception of bulk density, soil characteristics are currently specified in the Phase 3 Technical Guidance Documents. Complete physical, chemical and mineralogical characteristics are necessary for a reasonable comparison of sediments and soils. When soil characteristics are reported in a nonstandard way (i.e., not according to the well established USDA textural scheme), comparison of study results with those of other studies becomes more difficult. Also, data from one or more laboratory studies may enable better prediction of real-world behavior if the soil characteristics in the laboratory are sufficiently similar to anticipated domestic use sites.

Because of the inadequacy of the sampling protocol described in Subdivision N for the Anaerobic Soil Metabolism study (30 and

60 days of anaerobic incubation), the Agency is currently recommending that the Anaerobic Aquatic Metabolism (162-3) study protocol be followed when an Anaerobic Soil Metabolism (162-2) data requirement has been triggered. The Anaerobic Aquatic Metabolism study protocol provides for adequate sampling intervals to fully describe the patterns of decline of parent and formation and decline of degradates under anaerobic conditions. The test media should always be sediments collected from areas predominantly under anaerobic conditions.

GUIDELINE 162-4 AEROBIC AQUATIC METABOLISM

NOTE: The usefulness of the Aerobic Aquatic Metabolism study as described in Subdivision N, when an aerobic soil metabolism study has already been conducted, and the question of what additional information this study provides are issues for further discussion.

1. **Rejection Factor: The sampling schedule was inadequate.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 63.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-307.

Data are to be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized or for 30 days, whichever comes first. The reason for this is to ensure that the kinetics of pesticide degradation and the formation and degradation of its degradates are fully understood. This information is used to calculate a half-life for the pesticide and predict how long it and its degradates will persist in the environment. If the duration of the study is not long enough or there are insufficient sampling points, the reliability of the calculated half-lives will be greatly diminished as will the certainty that all degradation products have been formed and identified.

Industry Comment

Guidance for study duration is adequate.

Industry Recommendation: Industry agrees that data should be collected until the decline of the test substance and the formation and decline of degradation products are clearly characterized, or for 30 days, whichever comes first.

EPA Response

No comment.

2. **Rejection Factor: Material balances were incomplete.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-307.

This is a controlled laboratory experiment designed to measure the breakdown of a pesticide in the hydrosoil/water medium and the formation and decline of the degradates. This is achieved by measuring the test substance at the beginning of the experiment and then accounting for it at the end of the experiment to be certain that all degradates formed are isolated and an accurate rate of degradation is calculated. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

Guidance is adequate on the necessity to maintain a good material balance. The guidance is interpreted to mean that an adequate mass balance maintained during the course of the study is necessary to assure that all significant degradates formed are isolated. A target material balance of 90-110% would be an adequate measure of a study's accountability of the applied radioactivity. It is possible that individual sample time points and/or sample replicates could fall outside of the stated (target) material balance range and not adversely effect interpretation of the results. The most prevalent example is for studies with test substances which rapidly degrade to volatile products, notably CO2. It also noted that maintaining material balance can be more difficult with aerobic aquatic than aerobic soil studies due to measurement and summing of residue in water and soil phases versus only soil for aerobic studies.

Industry Recommendation: The Agency should continue to assess any material balance deviations from the desired target range (90-110%) within the context of the entire study and not on a single sampling interval.

EPA Response

The Agency agrees that the material balance should be assessed within the context of the entire study and not on a single sampling interval; the 90-110% accountability should be viewed as an ideal target range.

3. Rejection Factor: **Residues were incompletely characterized.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 63.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-307.

Identification of residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the aerobic aquatic metabolism study. One primary reason this study is conducted is to identify the degradates that are formed after application of a pesticide to the aquatic environment. Failure to identify one (or more) significant degradates may leave gaps in the understanding of the metabolism, and hence the environmental fate. Thus, the understanding of dissipation under actual use situations is unclear.

Industry Comment

a) Although no Standard Evaluation Procedure or Pesticide Assessment Guideline has been issued for Aerobic Aquatic Metabolism, guidance regarding identification of metabolites/degradates is presented in Subdivision N Guidelines and Phase 3 Technical Guidance.

b) Residues occurring at a level of 10% of the applied radioactivity or greater should be identified when feasible. The criteria for identification of residues should be consistent with the 1982 Guidelines, as stated in the purpose of the study [§ 162-4(a)], and with § 162-4(c)(2)(i).

The identification level specified above is 0.01 ppm or 10% of applied. A residue present at 0.01 ppm may not be a major degradate, particularly when the normal field application rate of a product is greater than 1 lb./A. For a variety of reasons, e.g., specific activity limitations for radiolabeled test substances, technological limitations for detection/quantitation methodology, dose rates may differ significantly from the field application rate. For products with lower field application rates, Aerobic Aquatic Metabolism studies must be conducted at exaggerated rates to permit metabolite identification at the required level. However, for products with field application rates exceeding approximately 1 lb./A, the requirement for identification at 0.01 ppm is excessive since each component at

or exceeding 1% of the treatment dose should be identified. Identification of degradates which represent 0.01 ppm is not always technically possible nor practical, especially when considering that the starting materials may not be purer than 97%. Thus it may not necessarily be useful to identify degradates that represent less than 3% of the applied material

c) On page C-307 of the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, guidance is provided on the extent of effort desired for extraction to remove residues from soil, i.e., "...a reasonable attempt was made - perhaps with multiple solvent systems - to extract metabolites/degradates." Guidance documents do not address the current desire to reduce the nonextractable residues to less than 10% of the dose rate, using harsh acid/base digestion if required. Further, guidance documents do not address the extent of effort desired to identify components of the bound residue removed by harsh digestion procedures. Although it may be feasible to achieve the identification level for residues extractable by conventional means, identification of components obtained following harsh digestion is generally considerably more difficult due to the large amounts of coextractives. Since these components may have been altered by the methods employed, it should be sufficient to provide only characterization of these components.

Industry Recommendation: a) If the Agency desires, Industry is willing to draft a Standard Evaluation Procedure for EPA.

b) The Agency should define 'major degradates' as degradates that represent 10% or greater of the applied radioactivity. Using this definition of major degradates, all major degradates should be identified.

c) Identification of degradates should be limited to those components which are extractable by reasonable means, i.e., organic solvent and water, and not applied to components removed following harsh acid/base digestion procedures.

EPA Response

The Agency acknowledges the need for additional guidance, and would welcome Industry's support in the development of additional SEPs for the remaining guidelines for which no SEP currently exists.

The Agency agrees that the identification of residues present at 0.01 ppm may not always be feasible, especially for those products with field application rates exceeding

approximately 1 lb ai/A. The Agency will require the identification of all residues equal to or greater than 10% of the dose rate. This level of residue identification should provide adequate information for most chemicals. The dose rate is defined as that concentration of radiolabeled pesticide in the dissolved phase equal to the concentration expected when the maximum label rate is applied to a 1 hectare pond, 2 meters deep. All residues present at ≥10% of this dose rate must be identified.

In the event that the dose rate must exceed the maximum field application rate for residue identification purposes, (e.g., for technological, specific activity, or other limitations), a separate exaggerated dose rate study may be conducted. However, this exaggerated dose rate study cannot be used to provide kinetic information. The kinetics study must be conducted with the maximum dose rate as described above.

The 10% criterion is a general guideline. The registrant is expected to identify single degradates present at concentrations approaching 10% of the dose rate. In addition, degradates of known toxicological or ecotoxicological concern must certainly be identified and quantified even if they are present at <10% of the dose rate.

The Agency agrees that identification of degradates should be limited to those components that are extractable by reasonable means (e.g., organic solvents and water), and not necessarily include those components removed following harsh acid/base extraction procedures. These "bound" residues are generally not available for plant or animal uptake, leaching, or run off. Harsh extraction, which changes the nature of the residues, is not necessary.

4. **Rejection Factor: The test water was not characterized.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 63.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-307, C-309.

A description of the test water is essential for the purpose of defining the conditions under which the study is conducted.

This rejection factor relates to basic information required to be included in any study submitted to the EPA. The information pertains to an important study parameter that must be reported to ensure a technical evaluation of the data can be made. In most cases, studies rejected solely on this reporting deficiency are likely to be upgraded by the registrant by the submission of the additional data/information.

Industry Comment

Industry agrees that a description of the test water is essential for the purpose of defining the conditions under which the study is conducted.

Industry Recommendation: The Agency should specify that aerobicity (Ph and dissolved oxygen concentration) should be determined and reported.

EPA Response

The Phase 3 Technical Guidance document already specifies that pH and redox potential should be reported. Dissolved oxygen concentration should also be reported.

GUIDELINE 163-1 LEACHING AND ADSORPTION/DESORPTION

1. Rejection Factor: Degradates were not identified.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), pages 66-67.
- Addendum 6 on data reporting for Leaching and Adsorption/Desorption Studies. page 6.
- Standard Evaluation Procedure (SEP) for Soil Column Leaching Study. (June 1985), page 11.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-311.

Identification of residues present at levels greater than or equal to 0.01 ppm or 10% of applied, whichever is less, is a critical element of the Leaching and Adsorption/Desorption study. One reason this study is conducted is to determine the mobility of parent and its degradates in soil. Failure to identify one (or more) significant degradates results in gaps in the understanding of the mobility of the chemical and its degradation products in soil and their leaching potential in ground water.

Industry Comment

The identification of degradates has never been a requirement for batch equilibrium studies. The mobility of "major" degradates has been a testing requirement, however. The testing of degradates may be prepared from either 1) aging the test substance under aerobic conditions for 30 days or one half-life (whichever is shorter) in one soil type and performing soil column leaching or soil TLC studies, or 2) performing batch equilibrium studies on individual degradates.

Industry realizes that minor metabolites may be of interest.

Industry Recommendation: Industry recommends that a joint EPA/Industry work group set criteria for triggering degradate studies based on physical/chemical properties (K_{ow}), persistence, application rate of the active ingredient, as well as, "major" degradates from soil metabolism studies. (See also recommendations above under Rejection Factor 3).

EPA Response

Although the identification of degradates is best addressed in the degradation (abiotic, biotic) studies and is not a formal requirement for Leaching and Adsorption/Desorption studies, the Agency does require mobility information on all residues equal to or greater than 10% of the dose rate, as defined by the degradation and metabolism studies. In addition, the mobility of degradates of known toxicological or ecotoxicological concern must certainly be defined even if they are present at <10% of the dose rate.

The Agency agrees that the mobility of degradates of concern can be determined by aging the test substance under aerobic conditions for 30 days or one half-life (whichever is shorter) and performing soil column leaching studies using the aged soil. However, soil TLC studies using aged soil are no longer acceptable. At this time the Agency requests that batch equilibrium studies be performed using individual degradates in four soils each for each degradate; however, the Agency has agreed to further discussion with industry on this topic and will finalize its position at that time.

The Agency and Industry have agreed to form a joint workgroup to discuss and resolve the issues regarding the appropriate criteria for triggering and conducting mobility - adsorption/desorption (163-1) studies. These criteria will be incorporated into any future revisions of this guideline.

2. **Rejection Factor:** **The test soils were autoclaved prior to conducting the study.**

EPA Guidance on this Factor

EPA does not have any formal guidance on autoclaving of the test soils. However, it is well established that autoclaving the soils significantly changes their physical and chemical properties, which may affect the adsorption of pesticides by the soils.

Industry Comment

Industry agrees in principle. However, exceptions should be allowed for compounds that are rapidly degraded in soil. Soil sterilization techniques should be allowable in batch equilibrium studies for the exception noted above, and should not be allowed in the case of aged mobility studies. Moreover, the use of soil sterilization techniques has been mentioned in the Phase 3

Technical Guidance for summarizing Leaching and Adsorption/ Desorption studies.

Industry Recommendation: An exception should be allowed for compounds that are rapidly degraded in soil.

EPA Response

For those specific pesticides and/or degradates that degrade rapidly in soil (i.e., within hours of application), the Agency would consider requests for a waiver of the mobility requirement. However, the registrant would be required to demonstrate that the rate of degradation was such that equilibrium could not be established. If the parent compound degrades rapidly, information on the mobility of its degradates will be of primary importance.

If the registrant chooses to use sterilized soil to study the mobility of rapidly degraded compounds, the batch equilibrium studies must include reference chemicals of known mobility. The sterilization technique used must avoid, to the maximum extent possible, any alteration of the soil matrix which could distort the mobility characteristics.

3. Rejection Factor: The material balance was incomplete.

EPA Guidance on this Factor

- Standard Evaluation Procedure (SEP) for Soil Column Leaching Study. (June 1985), page 15.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-311, C-314 & C-315.

This experiment is designed to measure the adsorption and desorption of a pesticide. This is achieved by measuring the test substance applied at the beginning of the study and then accounting for it at the end of the experiment to monitor the disappearance of the parent and formation and decline of the degradates. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

1) In principle we agree with this concept, obtaining good material balances makes good analytical sense. However, in some instances special analytical techniques are required for which

there is no guarantee that a material balance of 90-110% can be achieved. The Agency should make allowance for these special circumstances (e.g., hydrophobic compounds), where additional efforts have been made endure a good material balance, but, due to the nature of the test chemical, material balance in the range of 90-110% is not achievable.

2) The study objective is to obtain partition coefficients/ mobility information. The requirement to measure the formation and decline of degradates appears to be a new requirement and is beyond the scope of the study objectives. Formation and decline of degradates is addressed in soil metabolism studies.

Industry Recommendation: Guidelines need to be revised to include material balance requirements. The issue of measuring the formation and decline of degradates has never been and should not be a requirement for leaching and adsorption/desorption studies, given the study objectives.

The larger issue of adsorption/desorption studies of degradates needs to be addressed. Industry recommends that a joint EPA/Industry work group set criteria for triggering degradate studies based on physical/chemical properties (K_{ow}), persistence, application rate of the active ingredient, as well as, "major" degradates from soil metabolism studies. (See additional comments under Rejection Factor 1).

EPA Response

Measuring the formation and decline of degradates is best addressed in the degradation studies (abiotic, biotic) studies and is not a formal requirement for Leaching and Adsorption/ Desorption studies. However, in situations where degradation of the test material occurs during the course of the study, it may be necessary to characterize and quantify the degradates. (For further discussion of which degradates to consider, see Rejection Factor 1 above). In these rare cases, an acceptable material balance should approach 90-110% of the applied test substance in order to permit defining the mobility characteristics of both parent and major degradates as clearly as possible.

The Agency and Industry have agreed to form a joint workgroup to discuss and resolve the issues regarding the appropriate criteria for triggering and conducting mobility - adsorption/desorption (163-1) studies. These criteria will be incorporated into any future revisions of this guideline.

4. Rejection Factor: Soils and sediments were incompletely characterized.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 65.
- Standard Evaluation Procedure (SEP) for Soil Column Leaching Studies. (June 1985), page 9.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-311 & C-313 .

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. Information on the soil class, texture, pH, and percent organic matter is necessary to verify that the soil is representative of agricultural soils. If foreign soils are used, such data on soil class, textural classification, and crop use are needed to indicate its similarity to U.S. soils.

Industry Comment

Industry agrees that soil/sediment characteristics should be provided, including soil class, texture, pH and percent organic matter, as representative of agricultural use or other appropriate uses.

Industry Recommendation: The Agency should specify the soil characteristics to be reported, in addition to the USDA soil texture classification.

EPA Response

Soil characteristics to be reported are currently specified in the SEP and, with the exception of bulk density, also in the Phase 3 Technical Guidance documents. Additional information concerning physical, chemical, and mineralogical characteristics may be reported if this information contributes to the understanding of the process(es) observed in the study.

5. Rejection Factor: Desorption of a major degradate was not addressed.

The purpose of leaching and adsorption/desorption study is to provide data on the mobility of the pesticide and its degradates and to determine their leaching potential in ground

water. Adsorption/desorption coefficients calculated from batch equilibrium study are used to determine the mobility of the test substance in different soil types. If no data is provided on the desorption of a major degradate, the information on the mobility of the degradate and its leaching potential in ground water is incomplete.

Industry Comment

See comments and recommendations in this section for Rejection Factors 1 and 3.

EPA Response

When using batch equilibrium techniques, a separate adsorption/desorption study must be conducted for the parent and for each degradate of concern. For further information on what constitutes degradates of concern, see the responses in this section for Rejection Factors 1 and 3.

6. **Rejection Factor: Foreign soils were used which may not be typical of soils in the United States.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 65.
- Standard Evaluation Procedure (SEP) for Soil Column Leaching Studies. (June 1985), page 9.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-311 & C-313.

Information on the soil class, texture, pH, and percent organic matter is necessary to verify that the soil is representative of agricultural soils. If foreign soils are used, such data on soil class, textural classification, and crop use are needed to indicate its similarity to U.S. soils, since mobility of pesticides in such soils may be dramatically different than in domestic soils (eg., in a volcanic ash).

Industry Comment

We agree that the information on soil class, texture, pH and percent organic matter is relevant for mobility considerations. However, information on crop use is irrelevant and should not be

required. The Agency should specify the soil characteristics to be reported in addition to the USDA soil textural classification.

Industry Recommendation: Information on crop use is irrelevant and should not be required. The Agency should specify the soil characteristics to be reported in addition to the USDA soil texture classification.

EPA Response

Soil characteristics to be reported are currently specified in the SEP and, with the exception of bulk density, also in the Phase 3 Technical Guidance documents. Additional information concerning physical, chemical, and mineralogical characteristics may be reported if this information contributes to the understanding of the process(es) observed in the study.

EPA strongly prefers that domestic soils be used in the mobility studies. However, the Agency will accept non-domestic/European soil for two of the four soils required if and only if the soils are characterized according to the USDA system. The soils selected should be representative of and appropriate for the use patterns being supported. All additional studies using non-domestic soil(s) would be considered supplemental.

7. Rejection Factor: Kd values (values of soil/water relationships) were not reported.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 66-67.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-312 & C-314.

Adsorption/Desorption coefficients (Kd) calculated from batch equilibrium studies are used to determine the mobility of the test substance in different soil types. If no data are provided on the rate of adsorption and desorption, the information on the mobility of the degradate and its leaching potential in ground water is incomplete.

Industry Comment

Information on K_d values should be supplied. However, the requirement on the "rate" of adsorption and desorption is beyond

the stated scope of these type of studies, as referenced in the Pesticide Assessment Guidelines.

Industry Recommendation: The requirement on the "rate" of adsorption and desorption is beyond the stated scope of these type of studies, and should be stricken as a study requirement.

EPA Response

EPA agrees that "rate" is beyond the scope of the current guidelines.

8. **Rejection Factor:** **The desorption phase was done serially, with incomplete removal of the supernatant at each step.**

This rejection factor relates to basic analytical techniques required for a sound scientific study. In an adsorption/ desorption (batch equilibrium) study, incomplete removal of supernatant from the desorption phase would result in an erroneous calculation of the amount of test substance desorbed from the soil. This results in an inaccurate assessment of the adsorption/desorption potential of the chemical and hence its mobility in the soil.

Industry Comment

Efforts to remove as much supernatant as possible is a reasonable approach to this issue. Moreover, serial desorption is a well documented method of performing this type of study. Provided the amount of residual radioactivity in the supernatant is accounted for, the resulting partition coefficient can be accurately determined.

Industry Recommendation: A calculated partition coefficient that takes into account residual radioactivity associated with the supernatant should be acceptable.

EPA Response

The Agency agrees that serial desorption is a well documented technique for Batch Equilibrium studies; however, the problem described here arose because it was apparent to the reviewer that a large portion of the supernatant was not removed. This would result in an underestimation of the amount of radioactivity desorbed and the appearance that the chemical is less mobile than it actually is. The Agency continues to believe that the additional work required for removal of the majority of

the supernatant during the desorption phases would yield a more accurate estimation of the desorption coefficient.

9. Rejection Factor: **The soil texture could not be confirmed because the soil was not classified using the USDA Soil Textural Classification System.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 65.
- Standard Evaluation Procedure (SEP) for Soil Column Leaching Studies. (June 1985), page 9.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-311 & C-313.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. Information on the soil class, texture, pH, and percent organic matter is necessary to verify that the soil is representative of agricultural soils. If foreign soils are used, such data on soil class, textural classification, and crop use are needed to indicate its similarity to U.S. soils.

Industry Comment

The soil information mentioned above in Rejection Factor 9 should be provided.

Industry Recommendation: See Rejection Factor 9 above.

EPA Response

Soil characteristics to be reported are currently specified in the SEP and, with the exception of bulk density, also in the Phase 3 Technical Guidance documents. Additional information concerning physical, chemical, and mineralogical characteristics may be reported if this information contributes to the understanding of the process(es) observed in the study.

10. Rejection Factor: It was not established that the time used allowed sufficient for the soil:solution slurries to reach equilibrium.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 67.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-312 & C-314.

Sufficient time must be allotted for the equilibration of the test substance with the soils so that they achieve an equilibrium and the adsorption/desorption coefficients are accurately determined.

Industry Comment

In principle we agree. However, exceptions should be allowed for compounds that rapidly degrade and for classes of compounds that exhibit very low adsorptive properties.

Twenty-four (24) hours should be maximum equilibration time required for adsorption and desorption studies.

Industry Recommendation: Exceptions should be allowed for compounds that rapidly degrade and for classes of compounds that exhibit very low adsorptive properties.

Twenty-four (24) hours should be maximum equilibration time required for adsorption and desorption studies.

EPA Response

The Agency agrees that chemicals which fall outside of the 'norm' (eg., compounds which degrade rapidly or which exhibit very low adsorptive properties) should be granted wider latitude.

The Agency concurs with establishing a standard 24-hour maximum equilibration time for all chemicals as a consistent experimental parameter. However, if preliminary studies indicate that 24 hours is insufficient for complete equilibration to occur, the registrant may chose to equilibrate for a longer time to more accurately determine the mobility characteristics. It should be noted that failure to allow sufficient time for full equilibration may underestimate the adsorption coefficient of the chemical and hence, overestimate mobility.

11. Rejection Factor: **The bioassay methods used in the study were not acceptable analytical techniques.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), pages 64-71.

- Standard Evaluation Procedure (SEP) for Soil Column Leaching Studies. (June 1985), pages 8-17.

The analysis and identification of the parent and degradates should be carried out by well established analytical techniques.

Industry Comment

If one can draw conclusions on mobility, then the use of validated bioassay techniques should be allowed. Precision of the analytical method should be sufficient to allow measurement of a soil partition coefficient.

Industry Recommendation: By whatever analytical method, the precision of the analytical method should be sufficient to allow measurement of a soil partition coefficient.

EPA Response

With nearly all chemicals, conventional analytical techniques (e.g., TLC, HPLC, etc.) are preferred, although detection of decreasingly smaller concentrations of compounds may pose a significant analytical challenge.

The Agency recognizes that a variety of immunoassay techniques have been developed over the years, with new ones appearing with increasing frequency. We agree that some of these emerging techniques may be the only ones with sufficient sensitivity or specificity to detect parent compounds and/or degradates of concern. However, their use should be discussed with the Agency early in the registration process, so that the merits of the method can be evaluated.

A joint EPA/Industry work group has been formed to discuss the development of acceptance criteria for bioassay methods used in association with mobility studies.

12. Rejection Factor: Soil used in the study was not prepared properly.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 65.
- Addendum 6 on data reporting for Leaching and Adsorption/Desorption Studies. page 6.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-312 & C-313.

It appears that the soils used in this study were not aged to allow for microbial degradation so that the mobility of the degradates could be monitored to determine their leaching potential in ground water.

Industry Comment

We are assuming that this rejection refers to "aged" soil column leaching studies. For these studies, the testing of degradates may be determined from either 1) aging the test substance under aerobic conditions for 30 days or one half-life (whichever shorter) in one soil type and performing soil column leaching or soil TLC studies, or 2) performing batch equilibrium studies on individual degradates.

Industry Recommendation: Prepare soils for the "aged" study by aging the test substance for 30 days or one half-life (whichever is shorter) for case 1 above. Otherwise, perform batch equilibrium studies on individual degradates. Further clarification of how to prepare soil leaching columns is needed. EPA should rewrite a separate guidance document for conducting aged soil column leaching studies to address the following issues: 1) the number of soils which must be tested, and 2) preparation of "aged" soil. Industry proposes that only one soil column study should be conducted with sandy loam soil to examine reasonable worst-case leaching potential.

EPA Response

Additional guidance on conducting aged soil column leaching studies is available in the Standard Evaluation Procedure (SEP) for Soil Column Leaching Studies (June 1985).

The current EPA policy requires that the test substance be aged under aerobic conditions for 30 days or one half-life

(whichever is shorter), followed by Soil Column Leaching studies of that aged soil; soil TLC studies are no longer recommended.

Alternately, the Batch Equilibrium study can be conducted with each pure degradate (synthesized or purified from the aged soil) which had previously been identified as a degradate of concern in the degradation (abiotic, biotic) studies. For further details, please see the response to Rejection Factor 1.

It is recommended that mobility studies for unaged parent use the Batch Equilibrium protocol as the testing method; however, the batch equilibrium study using characterized aged soil (instead of individual degradates) is inappropriate and may lead to invalid results. The Agency continues to accept aged mobility studies using soil columns.

The Agency does not agree with the recommendation that only one soil column study be conducted with sandy loam soil to examine the worst-case leaching potential. "Worst-case" leaching potential cannot be accurately predicted from the use of a single soil; a sandy loam soil may not present a "worst case" for many pesticides. The Agency requires information on the leaching potential of a chemical in scenarios other than the worst case in order to fully understand the leaching characteristics of the pesticide and its degradates. Ideally, the Agency prefers individual batch equilibrium studies for the parent and, where feasible, for major degradates. The registrant may however elect to perform column leaching studies. After aerobic aging of the parent in four soils, the treated and aged soils are then placed on the appropriate, respective soil columns, with proper care having been taken in the preparation/packing of the columns. The study will then proceed as described in the SEP for column leaching studies.

13. Rejection Factor: Test solution was not characterized.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 64.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-311.

The test solutions must be analyzed with an appropriate analytical methods, to positively identify the parent and its degradates and to monitor any impurities that might be present in the test solutions.

Industry Comment

By whatever analytical method, the precision of the analytical method should be sufficient to allow measurement of a soil partition coefficient.

Industry Recommendation: The analytical method should be precise enough to allow measurement of a soil partition coefficient of the parent compound and/or, degradates, as appropriate.

EPA Response

No comment.

14. Rejection Factor: The data were presented on a percentage basis with no actual concentrations.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. In some cases, studies rejected solely on these reporting deficiencies are likely to be upgraded by the registrant by the submission of the additional data.

Industry Comment

More clarification regarding this rejection factor is needed.

Industry Recommendation: Please provide further information so industry can comment on this rejection factor.

EPA Response

This factor relates to the reporting of raw data for the calculation of partition coefficients. It appears that, instead of reporting the actual data on the concentration of test substance in each stage of the adsorption/desorption phases, data were only presented as percentages; it was not possible to determine whether these percentages were "percentage of applied" or "percentage recovered." Since the reviewer was unable to ascertain how much test substance was used, it became extremely difficult to confirm the registrant's calculations.

Other Industry Comments/Other Concerns

The increasing use of computer models for assessing pesticide mobility requires the generation of a range of K_d

values. The batch equilibrium study is preferred. Soil column leaching studies and soil TLC studies are suitable for comparing the mobility of degradates to mobility of the parent. The Guidelines should be modified to show that the soil column leaching study provides supplemental data on degradates. If the Agency does not accept soil TLC data as the primary measure of mobility, this study should be removed from the guideline.

The triggering of leaching and adsorption/desorption studies needs to be addressed. If the K_{ow} is greater that 1000, then the compound will be strongly adsorbed and there is no need to conduct an adsorption/desorption experiment. Likewise, the continued reporting of Freundlich isotherms when other more appropriate adsorption models may apply, is unnecessary and should be deleted as a Guideline requirement in special cases. Also, alternative approaches for providing mobility information should be discussed and given latitude in meeting data requirements. For example, consideration should be given to the use of OECD Adsorption/Desorption Guideline 106.

In addition industry would like to see an entire rewrite of the guidance for conducting leaching/adsorption/desorption studies, with separate guidance from the Agency for both batch equilibrium and aged column leaching studies.

EPA Response

The Agency agrees that the soil TLC study should be eliminated from the guidelines. In the past, however, the Agency has allowed registrants to provide K_d values calculated from R_f values using the Hamaker's equation, provided that there was an adequate database (reference material of known K_d in the same test soils) so that the Hamaker's equation could be applied in a scientifically sound manner.

The Agency welcomes the opportunity to discuss the larger issue of setting criteria for triggering degradate studies based on physical/chemical properties, etc. as part of a joint EPA/Industry work group. Such a dialogue would also prove helpful in laying the groundwork for future revision of the guidelines.

The reporting of Freundlich isotherms is required, in part, for computer-modeling purposes. However, the registrants are encouraged to also apply the data to other adsorption models when additional information may be gained.

With respect to the OECD 106 guideline, the Agency has been aware of on-going revisions of OECD guidelines and efforts to

define soil selection for these studies. The Agency is also aware of the current development of environmental fate guidelines for pesticides by the European Community.

GUIDELINE 163-2 LABORATORY VOLATILITY

1. Rejection Factor: Analytical methodology was insufficient.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 71-74.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-316 & C-319.

This rejection factor pertains to basic information required for the laboratory volatility study. Appropriate analytical methods are required to monitor the air samples and determine the actual rate of volatilization under controlled conditions.

Industry Comment

The analytical methodology should be appropriate to meet the intent of the study. The laboratory volatility study is an intermediate step in determining the environmental fate of the chemical, and the analytical method need not be overly precise if the purpose of the study is to confirm the need for field studies.

Industry Recommendation: The purpose for conducting the experiment and the significance of the results should be considered when evaluating the analytical method. If the study demonstrates that volatilization is unlikely to be a significant mechanism for environmental dissipation, then an analytical method which allows the determination of 5-10% of the amount applied may be adequate.

EPA Response

The Agency agrees that the analytical methodology should be appropriate to meet the intent of the guideline, which is to determine the actual rate or extent of pesticide volatilization from soil, and assumes that the reference to 5-10% of applied refers to the residue level above which identification is required. An analytical method of sufficient sensitivity is almost always required to determine the actual rate or extent of volatilization from soil.

As a trigger for the volatility requirement, the Agency has determined that where vapor pressure exceeds 10^{-4} mmHg, these studies are almost always required. Where vapor pressure is less

than about 10^{-6} mmHg, these studies are almost never required. Between these two limits, the Agency will continue to require the volatility studies on a very limited case-by-case basis, usually dependent on human and ecological toxicity concerns.

The Agency is considering other parameters that may be more appropriate for use in determining the need for the volatility studies. The use of the ratio of Henry's Constant to k_d as a trigger factor is a topic for further discussion.

2. **Rejection Factor:** **The study was not carried out over a long enough period of time to clearly define a volatility decline curve.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 73.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-316.

Monitoring of air samples should be conducted continuously or at intervals which increase with time until the nature of the residue decline curve has been clearly established.

Industry Comment

The laboratory volatility study has historically been used to assess volatilization only for chemicals which the EPA believed posed a significant inhalation hazard to workers. The changing use of this study, as indicated in the foreword to the rejection rate analysis, requires updated guidance on conduct of the study. Studies for assessing environmental fate may need to be longer than those for assessing the risk to workers.

The changing expectations for the study will require clarification of several requirements, including determination of the nature of the residue decline curve. Recent work by Jury, et al. (1983a, 1983b, 1983c) has shown that several volatilization patterns can be expected depending on the physical properties of the compound. Demonstrating that volatilization of the pesticide follows the expected behavior should be adequate characterization of the "residue decline curve".

References

Jury, W. A., W. F. Spencer, and W. J. Farmer. 1983a. Behavior Assessment Model for Trace Organics in Soil: I. Description of Model. J. Environ. Qual. 13:558-564.

Jury, W. A., W. F. Spencer, and W. J. Farmer. 1983b. Behavior Assessment Model for Trace Organics in Soil: I. Chemical Classification and Parameter Sensitivity. J. Environ. Qual. 13:567-572.

Jury, W. A., W. F. Spencer, and W. J. Farmer. 1983c. Behavior Assessment Model for Trace Organics in Soil: I. Application of Screening Model. J. Environ. Qual. 13:573-579.

Industry Recommendation: The laboratory volatility guideline should be revised to reflect its current use in assessing environmental fate. The study should be required only when the vapor pressure of the active ingredient is greater than 1 X 10^{-5} mm Hg at 25°C, and other physical properties of the active ingredient indicate that volatilization will be a significant mechanism for dissipation.

EPA Response

The Agency agrees that there may be insufficient guidance available for the Volatility data requirements, particularly as they apply to the determination of the environmental fate of pesticides. The Agency and Industry have agreed to form a joint workgroup to discuss and resolve issues regarding the appropriate criteria for triggering and conducting laboratory and field volatility (163-2 and 163-3) studies. These criteria will be incorporated into any future revisions of this guideline.

3. Rejection Factor: **The soil was not analyzed immediately after treatment. Therefore, the application rate was not confirmed.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-316 & C-319.

Application rate must be known, since the monitoring of the test substance (volatilization rate of the pesticide) is based on the initial concentration of the pesticide used on soil.

Industry Comment

The volatilization rate of the pesticide is calculated from the concentration of the pesticide in air and the surface area of the soil. If volatilization is determined by the difference in soil concentrations with time, the initial concentration must be known. It is not necessary to know the initial concentration in soil if the concentration in air is measured directly. Analysis of the soil merely provides confirmation that the pesticide was applied at the desired rate. While analysis of the soil may be desirable, it is not essential, if there is other evidence to validate the application rate. Known weights or volumes of chemical added to the soil and demonstrated stability in the test solution could be the minimum evidence supporting proper application rate.

Industry Recommendation: Confirmation of application rate must be provided by soil analyses or by other means such as known weights or volumes applied to the soil.

EPA Response

The Agency agrees that the analysis of soil provides confirmation that the pesticide was applied at the desired rate. This information is necessary because the application rate should approximate the highest recommended rate for a single application. However, according to current guidelines, volatilization cannot be determined by the difference in soil concentrations with time; decreases in the concentration of a pesticide in soil cannot distinguish between a decrease due to volatilization and that due to soil metabolism of the test material. Therefore, air samples must be collected and analyzed for the active ingredient and/or major degradates where any volatilization has occurred.

Due to the carefully controlled conditions under which laboratory volatility studies are conducted, the Agency agrees that known weights or volumes of pesticide applied to the soil can be used to confirm the rate of application, provided that the known weights or volumes of pesticide added to the soil at the desired application rate can be verified by the registrant.

4. Rejection Factor: **No material balance was reported or the data reported was insufficient.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-316.

This experiment is designed to measure the volatilization of a pesticide under controlled laboratory conditions. This is achieved by measuring the test substance applied at the beginning of the study and then accounting for it at the end of the experiment. A good material balance (90-110%) is a prerequisite for any valid laboratory study.

Industry Comment

The requirement for a material balance of 90-110% can best (frequently only) be met by use of radiolabeled test substances, and Industry agrees that radiolabeled formulations of many products can be simulated in laboratory tests. However, when it is not possible to use radiolabeled products, EPA should be flexible in its material balance requirement.

The FIFRA Accelerated Reregistration Phase 3 Technical Guidance, page C-316 and the Pesticide Assessment Guidelines 163-2 state that the study is conducted to determine the concentration of the active ingredient in air following application of a typical end use product to soil. The requirement for a good material balance expands the scope of the study to include soil analyses and degradation product analyses (see rejection factor 5) which complicate the study and duplicate the requirements of the aerobic soil metabolism study.

The laboratory volatility study complements an aerobic soil metabolism study and should be viewed in context. Laboratory volatility studies should not be required when the aerobic soil metabolism study has already demonstrated the significance of volatilization as a mechanism of dissipation.

Industry Recommendation: Laboratory volatility studies should be designed to determine volatilization of active ingredients when applied as a typical end use product. Registrants should not be required to conduct aerobic soil metabolism studies on each typical end use product. Registrants should concentrate on reporting accurate analyses of the active ingredient in air.

EPA Response

The Agency agrees that the volatility requirement should not be imposed if acceptable metabolism studies prove that volatilization is not a likely route of dissipation of the pesticide. However, the identification of volatile compounds produced during the metabolism studies remains a requirement; the need for further studies on volatile degradates would depend on toxicity concerns.

The Agency is considering other parameters that may be more appropriate than vapor pressure for use in determining the need for the volatility studies. The use of the ratio of Henry's Constant to k_d as a trigger factor is a topic for further discussion.

The use of radiolabeled test material continues to be the best technique for generating acceptable material balances, including trapping/identification of volatile degradates, and determination of whether or not any of the test material has sorbed to the sides of the test vessel. Identification of degradates in soil is usually not required if acceptable metabolism studies are available. However, the determination of the concentration(s) of active ingredient and/or major degradates in air is still needed.

5. Rejection Factor: Not all major formulation categories were tested.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), pages 71 & 72.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data.

Industry Comment

If the registrant can provide information to demonstrate that there is a worst-case formulation, then only one test should be required.

EPA Response

The Agency would agree to accepting results from one laboratory volatility study using a "worst-case" formulation of the chemical if the registrant is prepared to be regulated under

"worst-case" assumptions. As a point of interest, if the specific chemical involved is marketed in two or more formulations (e.g., an EC and a Dust), the formulated products may be sufficiently different to trigger additional testing in several other guideline areas, including Field Dissipation (164-1).

6. Rejection Factor: **The soil was autoclaved before the test.**

EPA Guidance on this Factor

EPA does not have any formal guidance on autoclaving of the test soils. However, autoclaving soils significantly changes their physical and chemical properties, which may affect the adsorption of pesticides by the soils. Also, sterile soil would not generate metabolites, some of which might be volatile.

Industry Comment

Studies which attempt to simulate actual conditions should be conducted on soil which has not been autoclaved unless there are compelling reasons to slow the rate of degradation by eliminating microorganisms.

The FIFRA Accelerated Reregistration Phase 3 Technical Guidance, page C-316 and the Pesticide Assessment Guidelines indicate that the study is conducted to determine the concentration of the active ingredient in air following application of a typical end use product to soil. Neither document requires the volatilization of metabolites to be determined.

Industry Recommendation: EPA should develop and publish guidance on use of sterilized soils. Volatilization studies of metabolites should not be a general requirement.

EPA Response

For those pesticides that degrade rapidly in soil (i.e., within hours of application), the Agency would consider requests for a waiver of the laboratory volatility requirement. However, the registrant would be required to demonstrate that the rate of degradation was such that equilibrium could not be established. If the parent compound degrades rapidly, information on the volatility of its degradates will be of primary importance.

If the registrant chooses to use sterilized soil to study the volatility of rapidly degraded compounds, the study must

include reference chemicals of known volatility. The sterilization technique used must avoid, to the maximum extent possible, any alteration of the soil matrix which could distort the mobility characteristics.

Although the guidelines do not specifically address the volatility of metabolites, significant volatile degradates must be identified unless it can be shown that they are not of toxicological or ecotoxicological concern.

7. **Rejection Factor:** **The rate of volatilization was incorrectly calculated and could not be determined with the information provided.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-319.

This issue is normally not a criterion for rejection of a study, and is usually repairable by the submission of additional data. However, if the intent of the study cannot be met by the submission of this additional data, then a new study would be required.

Industry Comment

Volatilization rates should be calculated correctly. Additional guidance from EPA on the correct calculation should be provided.

EPA Response

The Agency acknowledges the need for additional guidance for this guideline; this point will be considered when the Subdivision N guidelines are revised.

8. **Rejection Factor:** **The experiments were not replicated.**

Rejection factors 7 and 8 relate to basic information required by the EPA. The information pertains to important study parameters that must be reported so that a technical evaluation of the data can be made. In some cases, studies rejected solely on these reporting deficiencies are likely to be upgraded by the registrant by the submission of the additional data.

Industry Comment

In experiments which require analysis of samples taken over time, unusual results are readily apparent. Replication may not be necessary when a clear pattern of volatilization has been demonstrated.

Industry Recommendation: EPA should explain its expectations for replication and the level of statistical significance required.

EPA Response

The purpose of the study is to provide information on the actual rate or extent of pesticide volatilization from soil under controlled conditions; the "demonstration of a clear pattern" of volatilization from soil does not necessarily address the question of rate or extent. The intent is not to replicate the experiment, but, at a minimum, to perform duplicate analysis at each sampling interval. Guideline 160-5 of Subdivision N specifies that the registrant provide a summary of the data, an analysis of the data, sufficient data for the Agency to verify calculated statistical values, and a statement of conclusions to be drawn from the analysis. If only a single data point is provided at each sampling interval, its variability cannot be determined.

ADDITIONAL AGENCY COMMENTS

If a chemical has the potential to be highly volatile (the vapor pressure exceeds 10^{-4} mm Hg) and if volatile components are trapped in the volatile traps in the aerobic metabolism (162-1) study, then it is apparent that volatilization will be a significant mechanism for dissipation of the active ingredient. The Agency would then consider accepting a waiver request for the laboratory volatility data requirement. However, the field volatility data requirement (163-3) would then be imposed. A proposed trigger for the field study is 20% of the dose (either as parent or a degradation intermediate, excluding $^{14}CO_2$) being volatilized in the aerobic metabolism study.

GUIDELINE 163-3 FIELD VOLATILITY STUDIES

1. Rejection Factor: The soil data were inadequate to confirm the application rate.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 75.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-320 & C-321.

Application rate is required to accurately determine the volatility of the test substance and to ensure that the study conditions closely resemble actual use conditions.

Industry Comment

Confirmation of the application rate by some method is necessary to ensure that the study conduct meets the intent of the protocol. The EPA Guidance assumes that the registrant seeks to simulate actual use conditions and that the application method will give a homogeneous distribution in soil. The registrant may design the study to maximize the potential for volatilization or simulate actual use conditions such as by applying the chemical to a cropped field. In either case, soil analyses may not provide a satisfactory indication of the application rate due to inhomogeneity of the application. Direct application of some formulation types, such as granules, will not give a homogeneous distribution of product, and the determination of application rate by soil analysis may give unsatisfactory results.

In a volatility study, soil data are used to confirm the application rate and provide a measure of the amount of chemical remaining in the field. The volatilization rate of the chemical and its concentration in air are determined by air sampling, not by soil analyses.

Industry Recommendation: Generally, soil samples should be obtained immediately after application to confirm the application rate. When soil analyses are not adequate by virtue of factors inherent in the study design, alternatives such as known weights or volumes applied should be acceptable. Verified calibration of the application equipment and demonstrated performance of the equipment may be acceptable also.

EPA Response

The Agency agrees that the analysis of soil provides confirmation that the pesticide was applied at the desired rate. This information is necessary because the application rate should approximate the highest recommended rate for a single application under field conditions. However, the Agency also agrees that environmental factors at the time of application (such as wind speed and crop cover) can affect the amount of pesticide found in the soil. Therefore, soil analysis or other means such as known weights or volumes of pesticide applied to the soil may be used to confirm the rate of application, provided that the calibration and performance of the application equipment is verified.

2. **Rejection Factor: Data on soil characteristics was not provided.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 75.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-320 & C-321.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. Information on the soil class, texture, pH, and percent organic matter is necessary to verify that the soil is representative of agricultural soils. If foreign soils are used, such data on soil class, textural classification, and crop use are needed to indicate its similarity to U.S. soils.

Industry Comment

Data on soil characteristics should be provided by the registrant. The guidance on use of foreign soil conflicts with the FIFRA Accelerated Reregistration Phase 3 Technical Guidance, page C-320, which indicates that the study must be conducted in the United States.

Industry Recommendation: The following soil characteristics should be provided by the registrant: soil class, texture, pH, organic matter content and CEC. Studies conducted on foreign soils which are similar to U.S. soils should be acceptable.

EPA Response

The Agency has previously allowed field studies to be conducted outside of the United States; a recent example is a field dissipation study in an apple orchard in Canada. This rare event was permitted due to the high degree of similarity of climate and soil characteristics to those in apple-producing regions in the United States. The Agency will continue to consider the acceptability of non-domestic field studies on a case-by-case basis. Before initiating field studies outside the United States, the registrant should obtain approval from the Agency.

3. Rejection Factor: The description of experimental conditions were insufficient.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines (1982), page 74-77.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-320-C-322.

This issue does not normally result in the rejection of a study, and is usually repairable by the submission of additional data. This rejection factor relates to basic information required by the EPA. The information pertains to important study parameters that must be reported so that a technical evaluation of the data can be made.

Industry Comment

The experimental conditions should be described in sufficient detail to allow the determination of volatilization. Weather conditions such as wind speed and temperature should be provided. Estimates of evapotranspiration through measurement of water flux or solar flux should be provided as necessary. The following references provide experimental designs which can be used to determine volatility and indicate which experimental conditions are necessary.

Jury, W. A., W. F. Spencer, and W. J. Farmer. 1983. Behavior Assessment Model for Trace Organics in Soil: I. Model Description. J. Environ. Quality 12(4):558-564.

Glotflety, D. E., A. W. Taylor, B. C. Turner and W. H. Zoller. 1984. Volatilization of Surface-Applied Pesticides from Fallow Soils. J. Agric. Food Chem. 32:638-643.

Glotflety, D. E. , M. M. Leech, J. Jersey, and A. W. Taylor, 1989. Volatilization and Wind Erosion of Soil Surface Applied Atrazine, Simazine, Alachlor and Toxaphene. J. Agric. Food Chem. 37:546-551.

Majewski, M. S., M. M. McChesney and J. N. Seiber. 1991. A Field Comparison of Two Methods for Measuring DCPA Soil Evaporation Rates. Environ. Tox. Chem. 10:301-311.

Ross, L. J., S. Nicosia, M. M. McChesney, K. L. Hefner, D. A. Gonzalez, and J. N. Seiber. 1990. Volatilization, Off-Site

Deposition and Dissipation of DCPA in the Field. J. Environ. Qual. 19:715-722.

Industry Recommendation: EPA should develop guidance for specific experimental details which must be reported. The guidance should reflect several acceptable study designs which have been reported in the literature references.

EPA Response

There is an international interest in the loading of organic compounds into the atmosphere; in addition, the Office of Air within EPA is interested in the transport of pesticides off the site of application. An additional concern in the field is the dissipation of the pesticide from both the soil and the plant surfaces. The Agency is willing to discuss any sampling scheme for the field study which would also help us address international and Agency concerns.

The Agency agrees that there may be insufficient guidance available for the Field Volatility data requirement, particularly as it applies to the determination of the environmental fate of pesticides. The Agency and Industry have agreed to form a joint workgroup to discuss and resolve the issues regarding the appropriate criteria for triggering and conducting laboratory and field volatility (163-2 and 163-3) studies. These criteria will be incorporated into any future revisions of this guideline.

ADDITIONAL AGENCY COMMENTS

The registrant may request that the field volatility data requirement be waived if and only if volatiles are monitored during the terrestrial field dissipation study (164-1). If the

registrant chooses this approach, the registrant should design into the terrestrial field dissipation study a component capable of monitoring the volatiles seen in the lab, whether in the aerobic soil metabolism (162-1) or the laboratory volatility (163-2) study.

GUIDELINE 164-1 TERRESTRIAL FIELD DISSIPATION STUDIES

1. Rejection Factor: **The original concentration of the pesticide was not reported or the reported application rate was not confirmed in soil samples taken immediately posttreatment.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 9.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). p. 19.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-7.

Soil samples are taken immediately post-treatment to establish the concentration of the pesticide in the soil at the beginning of the study. In addition, the actual application rate of the pesticide must be known to confirm that the maximum label rate of the pesticide was used. Dissipation rates at different pesticide application rates can vary unpredictably because the soil microorganisms and plants responsible for the degradation process may respond differently at different concentrations of the pesticide.

Industry Comment

Industry concurs with the Agency that it is essential to measure the concentration of parent and metabolites immediately post-treatment.

It is also essential to specify the nominal application rate by detailed reporting of the preparation of the tank mixture components (by weight or volume) and by reporting details of the calibration of application equipment. Industry does NOT recommend the routine analysis of tank mixtures which can often produce misleading results (dependent on formulation type and sampling technique).

The EPA's guidance has been consistent on the use of the maximum label rate for a terrestrial field dissipation study. Industry concurs.

Industry agreed (May 8, 1991 letter on "Subpart N" revisions) with previous Agency advice that three replicate samples (either replicated by sub-plot or by composition from samples taken across the entire treated area) should be taken on all sampling occasions. Industry believes that the mean analyte concentration immediately post treatment should normally be expected to be below the nominal application rate. This is particularly true for applications where crop interception is significant, but it also applies to bare soil applications.

With certain active ingredients and/or application techniques (e.g. granular formulations or certain very labile or volatile active ingredients) it is difficult to account for most of the chemical applied. Experience has shown that the recovery immediately after application may often be expected to be between 60 and 80% of the nominal value. This does not give adequate cause for rejection of a field dissipation study provided the registrant submits adequate documentation to confirm the amount of chemical applied to the plot by the application equipment.

Industry is aware of very few, if any, compounds whose dissipation rates differ markedly within the normal use rate range of a pesticide. Industry believes soil types, etc. are more significant variables determining the dissipation rate of a chemical.

Industry Recommendation: EPA should stress the importance of the detailed reporting of proper application equipment calibration and application mixture preparation in order to confirm application at the normal rate.

EPA Response

The Agency agrees that slightly reduced or exaggerated applications would not be expected to markedly alter the apparent dissipation characteristics. However, in order to have as clear a picture as possible of the environmental fate of a pesticide under field conditions, the immediate post-application rate should be as close to nominal as possible. It may even be advisable to apply a slightly exaggerated (i.e., 1.1X) rate to assure that soil levels approximate the maximum label rate.

The Agency agrees that detailed reporting of the equipment calibration and mixture preparation are important, but notes that such information can not be used to confirm the application rate

and verify the amount of pesticide that actually reached the field. Other methods for confirming the application rate, besides actual soil sampling, is a topic for further discussion.

We agree that routine analysis of tank mixtures is not appropriate for this guideline; the analysis of tank mixtures is more pertinent to the Tank Mix (164-4) data requirement.

2. Rejection Factor: The pattern of formation and decline of the degradates was not addressed.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 11.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 4, 15, 20, 21.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-324-14.

A primary purpose of the field dissipation study is to identify and quantify the degradates of a pesticide when the pesticide is applied under typical field conditions. Although the aerobic soil metabolism study (162-1) provides information on the identity and amounts of degradates which occur when the pesticide is applied to soil in a laboratory situation, patterns of formation and decline of degradates under actual use conditions may be different from those observed in the laboratory.

Industry Comment

Industry disagrees that one purpose of a field dissipation study is to identify degradates formed under field conditions.

The field dissipation study should provide information on the formation/decline of parent and/or degradates for which satisfactory analytical methods have been developed.

Industry does not believe there is adequate guidance on which degradates merit analysis in the field dissipation study (see Rejection Factor 4).

Industry Recommendation: Improved guidance on the selection of potential degradates for analysis in field dissipation studies should be agreed between the Agency and Industry (see Rejection factor 4).

EPA Response

The Agency does not agree with Industry's first comment. While the purpose of the laboratory studies is to provide guidance on what degradates to look for in the field, the purpose of the field studies is to provide a comprehensive environmental fate profile of the chemical and its degradates under actual use conditions. Those degradates identified under laboratory conditions must also be analyzed for in the field.

In response to Industry's second comment, the Agency remains concerned that the degradates of ultra-low (<50g ai/Ha) application rate pesticides may be difficult to detect in the laboratory, and may be even more difficult to detect under field conditions, and that the development of newer, more sensitive methods of analysis may be required.

The Agency agrees with the Industry recommendation. All residues of concern identified in the laboratory studies (microbial degradation, hydrolysis, and photodegradation) and present in those studies at levels greater than or equal to 10% of the applied dose rate, should be analyzed for.

The Agency recognizes that analysis of samples from field studies (which use non-radiolabeled typical end use products) for all residues of concern identified in the laboratory studies (which use radiolabeled material) may not always be feasible. The Agency will take this into consideration when reviewing the study.

3. **Rejection factor:** **The sampling was not done to depths sufficient to define the extent of leaching.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 11.

- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). p. 4, 21.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-12.

Results from the field dissipation study along with data from other environmental fate studies are used to determine the leaching potential of a pesticide and whether ground water monitoring studies are needed. If it can not be determined how far through the soil a pesticide or its degradates have moved by leaching, the potential for contamination of ground water cannot be assessed.

Industry Comment

Industry previously proposed (May 8, 1991 comments on Subdivision N revision, page 59) a new guideline requirement involving studies similar to field dissipation studies, but requiring soil coring and analysis to 90-120 cm on sites that favored mobility. This approach concentrates detailed investigation of potential pesticide/degradate mobility on the situations where it is most probable.

Industry fully agrees that potential soil mobility is a vital objective of the field dissipation study.

Industry Recommendation: Industry recommends that detailed investigation of potential parent/degradate mobility should be concentrated on no more than two vulnerable sites from which deep cores will be taken.

EPA Response

The field dissipation data requirement was designed to define dissipation characteristics of a pesticide when used according to label directions, which include typical use sites. The selection of particularly vulnerable sites as the initial testing sites would therefore only be appropriate where such sites were typical of the proposed use pattern. As an example, a proposed fungicide to be used on citrus could be tested at a vulnerable site in Florida.

With reference to this rejection factor, sampling must still be done to a depth sufficient to define leaching at the typical use site. "Sufficient" depth means that cores must be taken to 90 cm divided into, at most, 15 cm segments (smaller increments may be required depending upon the limit of quantification), and

analyzed until one residue-free core is found. Thus, a maximum of two segments would need to be analyzed for relative immobile compounds, while as many as six segments may have to be analyzed (usually later in the study) for more mobile compounds (or compounds with mobile major degradates). The remaining (unanalyzed) cores should be retained, frozen, at least until the study is found acceptable by the Agency, provided there are adequate storage stability data to support the maximum duration of storage.

4. Rejection Factor: Characterization of residues was not provided for all sites or the soil was not analyzed for the correct residues or for all residues.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 11.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 4, 15, 20, 25.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-324-23.

Ideally, the parent and major degradates as identified from the laboratory studies (the soil metabolism studies and possibly the hydrolysis and photolysis studies) which may be present at 0.01 ppm or 10% of the applied should be monitored in the field dissipation study. However, because the field studies generally use unlabeled material, the analytical methods used in the laboratory studies may not be appropriate for analyzing field samples. The analytical methods used for the analysis of soil samples must be capable of identifying and quantifying residues in field samples in order to determine the dissipation of the pesticide and its degradates.

Industry Comment

Industry believes the term "characterization of residues" is potentially misleading; it is frequently confused with "identification". In the case of a field dissipation study (unless radio-labelled material is used) neither term is correct.

Industry believes that a field dissipation study should only be expected to confirm the formation/decline of potentially significant metabolites. Therefore the term "not analyzed for..all residues" is misleading.

Analysis of very labile parent or metabolites may be discontinued after 2 sampling points have shown no detectable residues.

In situations where a complex mixture of degradates can occur via microbial and/or physical processes in or on the soil, discussion between the Agency and the registrant must consider

relevant factors to agree on a list of degradates for analysis. Important factors include:

1) Longevity of degradate in laboratory studies.

2) Potential mobility of degradate (aged leaching study).

3) Is the compound a "terminal residue"?

4) Can the metabolite be analyzed as part of a "catch-all" generic analytical method?

5) Likely concentration in the soil vs. analytical LOD.

6) Application rate of the active ingredient (and hence potential maximum metabolite concentration).

7) Potential human effects and ecotoxicology of degradate.

8) Similarity of the metabolite to other compounds which can serve as "marker" analytes.

Industry Recommendation: Industry recommends that a joint EFGWB/Industry work group determine suitable analytes for investigation in field dissipation studies. Analysis for more than two or three "marker" analytes should rarely, if ever, be necessary.

Industry recommends that only metabolites present at levels greater than 10% of applied should be identified and that normally only these significant metabolites should be considered for analysis in field soil studies. An exception might be other, less abundant, metabolites demonstrated to have the potential to leach.

EPA Response

In order to determine the persistence, run off potential and leachability of a pesticide and its degradates under typical field use conditions, one must be able to both identify and quantify the pesticide and its degradates.

For further guidance on which degradates must be considered, see the EPA response in Rejection Factor 2 above.

The Agency would concur with the discontinuation of analyses after two sampling points have shown no detectable residues, if and only if the analytical method used had an acceptable Limit of Detection and acceptable recoveries.

A joint EPA/Industry work group has been formed to discuss and resolve the issues surrounding terrestrial field dissipation studies. As part of this work group, the criteria used to determine the selection of degradates for analysis that may be found in the field dissipation studies will be addressed. These criteria will be incorporated into any future revisions of this guideline.

5. Rejection Factor: Complete soil characteristics and field test data were not provided.

EPA Guidance on this Factor

- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 8.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 3, 4, 14, 16.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-9.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data.

This information must be accurate to evaluate the conditions under which the field study was conducted. This is a critical element in determining the rate of dissipation of the test substance. For instance, dissipation data are affected by the type of soil, the amount of rainfall, the slope of the test site, etc. In addition, this information is needed to determine

whether the study was conducted under suitable conditions, representative of the intended use pattern.

Industry Comment

Industry agrees that proper field data reporting is essential to understanding field soil dissipation data.

EPA Response

No comment.

6. Rejection Factor: **The analytical methodology was insufficient to identify the residues (in one case, the analytical method could not distinguish between the parent and its degradates).**

EPA Guidance on this Factor

- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 10.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 4, 20, 24.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-324-23.

A primary purpose of the field dissipation study is to identify and quantify the degradates of a pesticide when the pesticide is applied under typical field conditions. Because the field studies most commonly use unlabeled material, the analytical methods used in the laboratory studies may not be appropriate for analyzing field samples. The analytical methods used for the analysis of soil samples must be capable of identifying and quantifying residues in field samples in order to determine the dissipation of the pesticide. Unless the method of analysis used is sufficiently specific, evaluation of the dissipation of the pesticide under field conditions becomes meaningless.

Industry Comment

The analytical method is not expected to identify residues, merely to quantify them. However, Industry agrees that a method

must be sufficiently specific so that assignment of a detector response to a specific analyte is unambiguous.

Industry agrees that it is ideal to have specific methods for all analytes. However, in certain circumstances (e.g. a class of related metabolites) it is appropriate to have a "catch-all" common-moiety method.

Because common moiety approaches sum the total of various metabolites they may be considered as improving the sensitivity of the overall analyses.

Industry agrees that if a company cannot avoid using a "common moiety" analytical method, EFGWB may reasonably assume that a majority of detected chemical is present as the most toxic or mobile representative of the compounds quantified by the technique. Given this assumption, meaningful (but "worst case") evaluation of the results is possible.

Industry Recommendation: EPA should accept "common moiety" methods where they are cost effective and where the registrant is prepared to be regulated under "worst-case" assumptions.

EPA Response

A "common moiety" method of analysis, which expresses pesticide residue concentration in the sample as the sum total of all the various residues with that particular moiety, with no regard to the identity of the individual components, may be acceptable in some cases. For those pesticides and their degradates that have been shown in the laboratory to be of little or no toxicological/ecotoxicological concern, relatively immobile, and not persistent, a "common moiety" method may be appropriate. However, if there is a concern about the parent or any of its degradates, then the analytical method must be able to distinguish between the residues. The Agency wishes to refrain from basing its exposure assessment on the assumption that the greatest exposure is to the most toxic residue, particularly when analytical methods are available to define, with certainty, the identity of the residues of concern in the field.

Before initiating field studies using a "common moiety" analytical method, registrants should request approval from the Agency.

For those chemicals that meet the criteria described above, registrants may resubmit any studies that were rejected solely on the basis of the "common moiety" analytical technique. These studies will then be reevaluated to determine if they contribute

to the understanding of the dissipation of the pesticide and its degradates in the environment.

7. Rejection Factor: **The data were too variable to accurately assess the dissipation of the test substance.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 80.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 11.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 15, 27.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-324-14, 19.

Variability in data from a field dissipation study can arise from non-uniform application of the test substance to the test plots, inadequate or improper soil sampling, or an unreliable analytical method. The dissipation rate and half-life estimates of the test substance are usually estimated using regression analysis performed on the data in order to indicate how well the dissipation rate is described by a first-order kinetics model. If the data are highly variable, the estimates of the half-life provided by the regression analysis are unreliable.

Industry Comment

Industry acknowledges that data from field dissipation studies are frequently variable. Many of the potential sources of variation are inherent in the field use pattern (e.g., granular banded applications, seasonal soil temperature variations, weather, plough back of residues etc.). Care must be taken in field studies to reduce and/or understand variability as far as possible (e.g. Industry's agreement to analyze replicate samples at each sampling interval). Efforts to reduce/explain variability should be clearly reported.

Despite this inherent variability, Industry accepts that it is responsible for controlling variability as far as possible in field soil dissipation studies

Industry believes that the inability to calculate a dissipation half life with a high degree of confidence from field soil dissipation study data should not be a reason for the rejection of a study. Industry strongly disagrees with the assumption that all field dissipation rates should fit a first-order model. (Reasons for multi phasic dissipation behavior have been presented in the literature See References 1-4).

Industry recommends that registrants seek the best interpretation of parent/degradate dissipation kinetics possible. This should be based on their expert knowledge of the chemical's properties and related field factors (e.g., seasonal variations in temperature and/or soil saturation level). The basis for calculating half lives should be clearly explained by the registrant in reports; risk managers should ensure that half lives used for computer modelling have been calculated from the most appropriate subset of the field data.

Industry strongly discourages the use of a rejection factor such as "too variable". The important objectives of the field dissipation are to investigate the potential persistence and mobility of parent/degradates. Normally, sampling/analytical variability only influences half-life measurement when the half life is relatively long. In this circumstance, it is preferable to quote a range for the half life for each site since that is what will be found in practical agricultural use of the chemical. It will frequently provide useful model sensitivity information to use half life ranges in mathematical modelling of run off or leaching. Registrants accept that EPA will initially use the "worst case" half life indicated by a study; to negate such a value, Industry will either have to present well-justified arguments or conduct further studies.

Field dissipation studies are normally conducted on two or more sites. The Agency should consider the agreement between half life ranges measured at the various sites before rejecting a study on the basis of data variability.

Industry Recommendation: EPA should consider the half lives/mobilities measured in field soil dissipation studies as indicative of a tendency of the active ingredient/degradate to dissipate/move. Neither criterion is a "hard" number. A range of potential half lives should always be considered when modelling, etc. is needed.

Industry recommends that registrants seek the best interpretation of parent/degradate dissipation kinetics possible rather than assuming that first order kinetics are applicable.

EPA Response

The Agency recognizes that some amount of variability is inherent in any field study. However, excessive variability brings into question the validity of the data. In essence, the data needs to describe a clear pattern of dissipation.

Although the Agency stated that the dissipation rate and half-life are usually estimated by a first-order model, we agree that the use of other models to estimate field dissipation rates may sometimes be more appropriate. We also agree that the basis for calculating half-lives should be clearly explained. If the registrant has chosen to use a subset of the field data to calculate those half-lives, they must provide a justification for doing so.

Field factors such as seasonal variations in temperature and or soil moisture may affect dissipation kinetics. Field dissipation studies are normally conducted on two or more sites representative of the areas where the pesticide is expected to be used. These areas often differ markedly in climate and soil characteristics; therefore, it would not be unexpected to find that half-lives will also differ markedly. However, the Agency does not see how a comparison of half-life ranges between dissimilar sites might be useful in explaining data variability within a single site. Each study should stand on its own.

8. Rejection Factor: The freezer storage stability data were inadequate.

EPA Guidance on this Factor

- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 10.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). p. 21.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-324-20.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data.

Freezer storage stability of soil samples is not usually a problem in the laboratory studies because the samples can be frozen immediately after collection and are not stored for long periods of time. However, in field studies, soil samples usually cannot be refrigerated or frozen immediately after collection. In addition, over the many weeks (or months) of the study, samples can accumulate in a freezer prior to analysis. Therefore, a contemporaneous "spiking" study must be conducted, in which a known amount of active ingredient is added to portions of soil from an untreated area of soil at the test site at the same time that soil samples from the treated areas are collected. The "spiked" samples are then stored under the same conditions as samples from the test plot, and all samples are analyzed at the same time. This should indicate whether the pesticide in the samples from the test plots is degrading in the soil during handling and storage, and if so, whether it is possible to normalize the results to account for the amount of change during storage. If the data cannot be corrected in this way, it is not possible to distinguish between the amount of the dissipation occurring during storage and the dissipation occurring under field conditions, and the study must be repeated.

Industry Comment

Industry agrees that adequate freezer storage stability information on one soil is critical to ensure that a field soil dissipation program is valid.

Most registrants and contractors currently routinely cool samples immediately after sampling and freeze cores within a few hours.

Criteria for "acceptable" storage stability need to be harmonized with the Residue Chemistry branch requirements.

Industry Recommendation: Industry does not agree that the use of field spiking procedures is essential to validate field dissipation studies; nevertheless, it can be a valid approach. Freezer storage stability may also be measured in a carefully controlled laboratory study designed for that purpose. Data from field-spiked samples or from laboratory samples may be used at the registrant's discretion.

EPA Response

Note: The following discussion is consistent with the position of the Chemistry Branches in HED on the requirements for storage stability data (Health Effects Division memo dated January 14, 1993). The registrants

are referred to that document for additional guidance. Industry may, at its option, propose an alternative guidance document for Agency consideration.

Chemicals may degrade during storage, even under ideal storage conditions. Therefore, storage stability data are essential in order to be confident that any degradation measured in the test system was due solely to the environment of that test system, and not due to handling and storage. Storage stability in soil is chemical specific; in addition, a chemical's stability when stored in different soils can vary unpredictably.

The stability of the parent compound and its suspected degradates (as best can be determined prior to conducting the study) under storage conditions should be determined before the initiation of the field study to assure proper sample handling. In any case, evidence must be provided confirming that the levels of residues and their relative proportions did not change during the period between collection and final analysis.

At this time the Agency believes field spiking is important for those studies conducted under field conditions to ensure proper handling of samples in the field and their timely refrigerated storage; however the Agency has agreed to let industry develop a draft storage stability guidance document to address this and other storage stability issues. Final Agency judgement on this issue will be reserved for the Storage Stability follow-up guidance.

9. Rejection Factor: **The maximum label rates were not used, and the soil incorporation procedure recommended on the label was not followed.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 7.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 15-16.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-7.

The field dissipation study is done to evaluate the dissipation of the pesticide under typical use conditions. Because dissipation rates at different rates of application of a pesticide can vary unpredictably, application at the maximum label rate is needed to estimate dissipation when the largest amount of pesticide permitted by the product label is added to the soil. Incorporation techniques (how the pesticide is mixed with the soil after application) can also affect the rate of dissipation. If a pesticide is sprayed on the surface of the soil (where it can be photodegraded), the rate of degradation and the degradates formed may be completely different than if the pesticide is incorporated or injected into the soil.

Industry Comment

Industry fully agrees that a field soil dissipation study should employ the maximum label rate and that application methodology should mimic the "worst case" field approach required on the label (in terms of maximizing mobility).

If a number of application methods/incorporation approaches are permitted on the label, the registrant should explain why the selected method is believed to represent the worst case with respect to chemical mobility.

Industry recommends that if a new use is proposed for a compound at a higher rate than those used in the initial soil dissipation studies, the EPA should carefully consider the weight of the evidence on half lives before requesting another soil dissipation study on the basis of the higher field rate.

Industry Recommendation: Where the compound label requires multiple applications, Industry continues to recommend (See May 8, 1991 letter regarding Subpart N revisions) that a single application to a bare plot totalling the annual loading of the pesticide will be satisfactory.

Where a number of application methods or incorporation approaches are permitted, the registrant should perform a soil dissipation study for the use pattern that represents the worst case with respect to chemical mobility.

EPA Response

The Agency continues to prefer that a pesticide be applied according to label directions, including acceptable and common agricultural practices. For example, if the label calls for weekly applications all summer, then this is how it should be applied when tested. We do not believe that combining all

applications into a single application would accurately represent the projected dissipation under field conditions. Nevertheless, the Agency will consider variations on this approach, on a case-by-case basis.

Requests to amend the label to increase the application rate may result in the need for additional field monitoring based on the specific use patterns and the magnitude of the increase. Therefore, the need for additional testing is usually determined on a case-by-case basis.

We agree that some latitude should be allowed in the selection of application/incorporation methods where more than one method appears on the label. However, the registrant must assure the Agency that the method selected represents the worst case with respect to chemical mobility and/or persistence.

10. Rejection Factor: The formulation and method of application were not specified.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 78-79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 9.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 3-4.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-6, 7.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data.

Rates of dissipation of the active ingredient in a pesticide may be affected by formulation of the product. For example, a product formulated as a dust will be affected by degradation processes differently than a product formulated as a granule, an emulsifiable concentrate, an ultra low volume, or a microencapsulated. Therefore, separate field dissipation studies may be needed if the major formulation categories are significantly different. The means of application (e.g., surface spray, incorporation, soil injection) can affect the dissipation

rate as well; in addition, the means of application must be known in order to determine whether a procedure is used that is not recommended on that particular product.

Industry Comment

Industry agrees that the product formulation and application methodology need to be fully specified in the study report.

Industry believes that soil dissipation studies should not be needed to differentiate among liquid formulations (e.g., EC or ULV); however, a change in formulation between granules, microencapsulated formulations (or equivalent slow release formulation) and/or liquid formulations may require a study at one location to confirm that the half-life/mobility has not varied significantly.

EPA Response

No comment.

11. Rejection factor: **The plants were harvested after application and the time of harvest was not given.**

EPA Guidance on this Factor

- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 9.

- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 16.

If plants on the treated plots were harvested shortly after application, the majority of the test substance, intercepted by plant surfaces, may have been removed from the test site, resulting in an insufficient amount of pesticide reaching the soil. In situations where a dense crop cover exists, a study using a bare soil plot will be necessary to determine the half-life of the parent compound and the patterns of formation and decline of degradates. A study where the pesticide is applied to a vegetated plot would provide supplemental information only.

Industry Comment

Industry agrees that if crops are present on the test field, harvest dates should be reported; however, the EPA comments are contradictory. The first point suggests that conducting a study in the presence of plants may be OK if the plants are not harvested shortly after application. The second point states that use of a vegetated plot is of supplemental value only. This discrepancy requires clarification.

Industry agrees (May 8, 1991 letter page 60) that a bare soil plot is more likely to give consistent half-life/degradate behavior information. If no mobility is demonstrated in a bare soil plot study, no further work is needed. However, if mobility is observed, the registrant may elect to conduct an additional study using a cropped plot. The presence of a dense cover of a transpiring crop will totally alter the plot hydrology and thus the behavior of a relatively mobile compound, in addition to reducing the amount of chemical reaching the soil surface.

Turf studies are a special case of this rejection factor. Because chemical application across the plot is essentially even, NO BARE SOIL plots should be needed.

Industry Recommendation: Industry recommends that a bare soil plot be used to determine half-lives/degradation rates of a compound normally used on a dense or variable crop canopy (e.g. cotton or vines). However, a cropped plot study may be necessary later if compound/degradate mobility becomes a significant issue.

Industry recommends that no bare soil plots be required for turf dissipation studies.

EPA Response

With reference to Industry's first comment, application to a cropped field, with immediate post-application removal of the treated crop, would be expected to severely distort the results of the study. Levels of pesticide in the soil might be extremely low, even on the day of application, due to interception of the material by plant foliage.

With reference to dissipation from turf, the Agency has evaluated the dissipation of many chemicals. Dissipation characteristics have varied widely between turfed and bare ground plots. Chemicals which were found to be immobile in soil nevertheless demonstrated significant run off potential when applied to turf. Others which were highly mobile on bare ground demonstrated virtually no potential to leach to ground water on turfed plots. Therefore, both studies are needed to gain a clear understanding of the dissipation of the pesticide under field conditions.

The Agency recognizes that current guidance does not adequately address the complications associated with determining the dissipation of a pesticide from a cropped field with a dense canopy. However, bare ground dissipation studies alone can not satisfactorily describe the dissipation of a pesticide applied to, for example, the foliage in an orchard. Therefore, in those cases where a dense canopy exists, both a bare ground study and a cropped study are required. Where a significant amount of pesticide is not intercepted, either bare ground studies or cropped studies may be conducted.

The Agency acknowledges the need for additional guidance for this guideline; this point will be considered when the Subdivision N guidelines are revised.

12. Rejection factor: **Pretreatment samples were contaminated.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 79.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 9.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). pp. 15, 18, 20.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-2.

Pretreatment samples are needed to determine the presence or absence of background residues in the soil. If background residues are detected, it may be due to prior pesticide application or a deficiency in the analytical method. If background residues were present, it would not be possible to distinguish between the dissipation of residues already present and the dissipation of those added during the study. In addition, repeated exposures of soil microorganisms to a pesticide can often enhance the dissipation rate of the pesticide over what would be expected from a single application to an untreated soil.

Industry Comment

Industry agrees that only in a very rare circumstance should it be necessary to perform a field soil study on a plot containing significant background residues of the analyte(s).

Industry Recommendation: As long as the objectives of the study can be met, even the presence of relatively small amounts of residue should not be considered a reason for rejecting a study.

EPA Response

Field dissipation studies in which the soil in the field plot contains background residues are difficult to review; it may not be possible to distinguish between the dissipation of residues already present and the dissipation of those added during the study. Also, previous treatment with the same chemical may result in alteration of the soil microbial populations, which could distort the rate or nature of the

dissipation. In either case, previous history of treatment with the subject pesticide (or one with similar degradates) would strongly suggest the need for a replacement study.

13. Rejection factor: More than one pesticide was applied to the crop.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 78.
- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 9.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). p. 15.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-4.

The presence of additional pesticide(s) may interfere with the dissipation rate of the pesticide under study, or may affect the dissipation rate of the active ingredient in unpredictable ways, either by increasing or decreasing the dissipation rate.

Industry Comment

Industry disagrees that this is a realistic reason for rejection. A field soil dissipation study should be conducted on a plot maintained using typical agrochemical practices in the region. If a herbicide would typically be applied during the season to remove weed competition or an insecticide be used to kill insect pests then such practices should be performed in the study, provided:

- The records detailing additional pesticide application are fully comprehensive and explain why the compound was applied.
- The additional pesticide is not of the same chemical class as the test chemical.
- There is no analytical interference.

- Industry is aware of few, if any, instances where the use of a second pesticide (in the same season) will affect the behavior of a test chemical.

EPA Response

The dissipation of the pesticide under field conditions is usually sufficiently complex that the presence of additional chemicals with similar physicochemical characteristics raises the question of interference, either with the observed rate/ dissipation pattern, or with the subsequent chemical analysis. If the registrant applies multiple products, they must provide evidence for noninterference between components. Where several active ingredients are customarily applied together, the Agency may require data to support the Tank Mix data requirement (guideline 164-4).

14. **Rejection factor: The experiment was conducted at only one site instead of the two recommended in the Guidelines.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 78-89.

- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). p. 15-16.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-5.

This factor does not constitute a rejection factor. Data from an acceptable study can partially fulfill the terrestrial field dissipation data requirement; acceptable data are still required from one or more additional sites, as well as data from bare-ground studies.

Industry Comment

Industry agrees that this is not a rejection criterion.

Industry is concerned about the EPA comment that "data are still required from one or more additional sites, as well as data from bare ground studies". Bare ground data is only required where dense crop canopies would confuse the picture of dissipation behavior.

Industry agrees that data from two sites with deep coring are required to define field dissipation behavior.

If needed, additional information on dissipation half life ranges may be obtained from laboratory study data, historical soil studies and/or additional field soil studies conducted with soil coring to only 45 cm.

EPA Response

For the Agency's response to the question of the need for bare ground studies, please see Rejection Factor 11 above.

15. Rejection Factor: The Limit of Detection and recovery efficiencies were not reported.

EPA Guidance on this Factor

- Environmental Fate - Addendum 2 - Series 164-1 (1986). p. 10.
- Environmental Fate and Effects Division Standard Evaluation Procedure for the Terrestrial Field Dissipation Study (1989). p. 3, 4, 15, 24.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-324-22.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data.

The limits of detection (LOD) for the parent and degradates under field conditions may be higher than those observed in the laboratory studies, but must be reported to allow evaluation of the study. If during the field study an analytical method was used which had a relatively high LOD, observations of "no residues" or "not detected" may be the result of poor methodology rather than an absence of residues in the soil.

Industry Comment

Industry agrees with the EPA on this comment.

EPA Response

No comment.

Additional Rejection Factor: **Study rejected because deep strata contained residues immediately post application.**

Industry Comment

Studies have been rejected when immediate post-application samples have contained residues in deep strata when pre application samples were residue free. Normally, these detects occurred before the site received irrigation or rainfall.

Registrants have been unable to convince EPA that these detects have been artifacts caused by taking cores through recently deposited residues. Soil science and logic dictate that significant pesticide movement cannot take place without irrigation or rainfall.

Normally, samples taken at the next sampling interval show no contamination since the sprayed application mix has had an opportunity to dry and are thus less prone to spurious transfer through the soil profile during coring.

Industry Recommendation: Industry recommends that immediately post application, samples be taken only to a 6" depth (one faction) in order to avoid misleading contaminated samples.

EPA Response

The Agency is aware of several techniques which are in use which minimize contamination of deep soil strata. We continue to prefer that immediate post-application samples be taken to a depth of 6 inches **below the maximum depth of incorporation.** As an example, if it were necessary to take samples from depths deeper than 6 inches, excavation of the surface soil before sampling the greater depths would prevent contamination. In addition, the use of zero-contamination soil sampling tubes should minimize the amount of contamination.

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3. Scow, K.M. and J.Huston. 1992. Effect of diffusion and sorption on the kinetics of biodegradation: theoretical considerations. J. Soil Sci. Soc. Am. 56:119.

4. Timme, G., H. Frehse, and W. Laska. 1986. Statistical interpretation and graphic representation of the degradational behaviour of pesticide residues. II. Pflanzenschutz-Nachrichten 39:187.

ADDITIONAL AGENCY COMMENTS

The Agency and Industry are currently discussing the issues surrounding and arising from the fairly common observation that levels at time 0 do not confirm the field application rates.

GUIDELINE 164-2 AQUATIC (SEDIMENT) FIELD DISSIPATION STUDIES

1. Rejection Factor: Complete field test data were not provided.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 84.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-327-5, 7.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data.

The reviewer must have this information in order to evaluate the conditions under which the field study was conducted, a critical element in determining the rate of dissipation of the test substance. For instance, dissipation data are affected by the type of soil or sediment at the site, the characteristics of the water being treated, the flow rate of the water through the treated site, the time of year, the topography of the test site, etc. In addition, this information is needed to determine whether the study was conducted under suitable conditions, representative of the intended use pattern.

Industry Comment

Industry agrees that a complete description of the test site, weather data, application details, etc., should be provided to the reviewer to assure him that the study was conducted under a representative use pattern.

Industry Recommendation: Agency guidance specifically for aquatic dissipation studies is needed. Industry would like to participate in this process.

EPA Response

The Agency acknowledges the need for additional guidance for this guideline, and would welcome Industry's participation in the development of additional SEPs for the remaining guidelines for which no SEPs currently exist.

2. Rejection factor: **The analytical methodology was insufficient to determine the residue.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 84.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-328-17.

A primary purpose of the aquatic field dissipation study is to identify and quantify the degradates of a pesticide when the pesticide is applied under typical use conditions. Because the field studies most commonly use unlabeled material, the analytical methods used in the laboratory studies may not appropriate for analyzing field samples. The analytical methods used for the analysis of sediment and water samples must be capable of identifying and quantifying residues in field samples in order to determine the dissipation of the pesticide. Unless the method of analysis used is sufficiently specific, evaluation of the dissipation of the pesticide under field conditions may be unclear or unreliable.

Industry Comment

Industry agrees that the analytical methods for sediment and water should be able to read metabolites found in the laboratory degradation studies. Industry disagrees with the need to turn field dissipation studies into outdoor metabolism studies. Industry also disagrees with the routine requirement to quantitate individual metabolites in field studies. Only in cases where the laboratory studies show the formation of a compound which is suspected of being especially toxic or mobile should metabolite quantitation be required in the field. The use of total "common moiety" methods should be the option of the registrant.

Dissipation rates of metabolites are often not possible due to the limited number of data points on both the incline and decline end of the curve. Some metabolites never reach concentrations much above the detection levels or exist as erratic hits due to their transient nature.

Industry Recommendation: The Agency should not require individual metabolite quantitation in this study on a routine base. This requirement should be based on a review of the results of the laboratory degradation studies and should be triggered by the formation of toxic, persistent or mobile

degradates. The use of "common moiety" methods should be the option of the registrant.

EPA Response

The Agency does not agree with Industry's first comment. While the purpose of the laboratory studies is to provide guidance on what degradates to look for in the field, the purpose of the field studies is to provide a comprehensive environmental fate profile of the chemical and its degradates under actual use conditions. All residues of concern identified in the laboratory studies (microbial degradation, hydrolysis, and photodegradation) and present at levels greater than or equal to 10% of the applied dose rate, should be identified in the field.

A "common moiety" method of analysis, which expresses pesticide residue concentration in the sample as the sum total of all the various residues with that particular moiety, with no regard to the identity of the individual components, may be acceptable in some cases. For those pesticides and their degradates that have been shown in the laboratory to be of little or no toxicological/ecotoxicological concern, relatively immobile, and not persistent, a "common moiety" method may be appropriate. However, if there is a concern about the parent or any of its degradates, then the analytical method must be able to distinguish between the residues. The Agency wishes to refrain from basing its exposure assessment on the assumption that the greatest exposure is to the most toxic residue, particularly when analytical methods are available to define, with certainty, the identity of the residues of concern in the field.

Before initiating field studies using a "common moiety" analytical method, registrants should request approval from the Agency.

For those chemicals that meet the criteria described above, registrants may resubmit any studies that were rejected <u>solely</u> on the basis of the "common moiety" analytical technique. These studies will then be reevaluated to determine if they contribute to the understanding of the dissipation of the pesticide and its degradates in the environment.

3. **Rejection factor: The material balance was insufficient.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 81.

Although an adequate material balances for this guideline is extremely difficult to obtain, the study must define the rate of degradation of parent as well as the rate of formation and decline of all major degradates. The specified rejection criterion is probably related to a specific failure on the part of the experimenter to account for the modes and extent of dissipation in the submitted study.

Industry Comment

Industry agrees that both water and sediment residues must be quantitated at each sampling time interval to account for the distribution of residues between these phases. However, a true material balance in a field study is not possible and the agency should not reject a study on this basis.

The Agency needs to define more clearly what they mean by an adequate material balance.

Industry Recommendation: EPA needs to better define what is meant by material balance in an aquatic field study. A SEP or guidance document is needed for this study. Industry would like to participate in the development of a guidance document.

EPA Response

The Agency agrees that a true material balance is not possible for a field study; the study was probably rejected because of a failure on the part of the experimenter to account for the modes and extent of dissipation in the submitted study. The Agency acknowledges the need for additional guidance for this guideline, and would welcome Industry's participation in the development of additional SEPs for the remaining guidelines for which no SEPs currently exist.

4. Rejection factor: Data were too variable to assess dissipation.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 41.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-328-20.

Variability in data from an aquatic dissipation study can arise from non-uniform application of the test substance to the test plots, inadequate or improper sediment or water sampling, or an unreliable analytical method. The dissipation rate and half-life estimates of the test substance are usually estimated using regression analysis performed on the data in order to indicate how well the dissipation rate is described by a first-order kinetics model. If the data are highly variable, the estimates of the half-life provided by the regression analysis are unreliable.

Industry Comment

Due to the way they are conducted, field studies produce variable data. Since the EPA guidance (164-1) is to preferentially use the label use pattern, some products produce highly variable data unavoidably, i.e., banded granular formulations, air blast sprayer applications, applications to rice paddies. Further, dissipation rates do not follow 1st order kinetics over the entire range of dissipation. Force fitting 1st order kinetics produces low correlations coefficients.

In an aquatic dissipation study, variability is introduced by the flooding of the field following application or by applying the chemical into a flooded field. In both cases, residues partition between soil and water in an inconsistent way depending on the soil type and water depth in the immediate sampling area. In addition, as the residues fall to levels near the limit of detection, the analysis results become even more variable.

Consequently, the agency should not reject studies solely on the basis of a low correlation coefficient.

Industry Recommendation: EPA needs to define what variability is acceptable in various use patterns.

EPA Response

The Agency recognizes that some amount of variability is inherent in any field study and agrees that studies should not be rejected provided the variability is suitably explained. Variability frequently can be estimated by the analyses of the application samples or the interception techniques (cards, plates, etc.), which permit a check of the homogeneity of application.

The Agency stated that the dissipation rate and half-life estimates are usually estimated by a first-order model. We agree that the use of other models to estimate field dissipation rates may be more appropriate at times. We also agree that the basis for calculating half-lives should be clearly explained by the registrant.

The Agency agrees that variability of data from the aquatic dissipation study can be affected by the timing of the application(s) and the partitioning between the water and soil phases. The Agency acknowledges the need for additional guidance for this guideline; this point will be considered when the Subdivision N guidelines are revised.

GUIDELINE 164-3 FORESTRY FIELD DISSIPATION STUDIES

1. Rejection factor: **The data provided were either insufficient or too variable to accurately establish a pattern of dissipation of a chemical and its primary degradate in a forest environment.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 41.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-331,332-9,-10,-11,-12,-13.

Variability in data from a forestry dissipation study can arise from non-uniform application of the test substance to the test plots, inadequate or improper sampling of soil, sediment, water, or plant material due to a weak study protocol, or an unreliable analytical method. The dissipation rate and half-life estimates of the test substance are usually estimated using regression analysis performed on the data in order to indicate how well the dissipation rate is described by a first-order kinetics model. If the data are highly variable, the estimates of the half-life provided by the regression analysis may be unreliable.

Industry Comment

No comment.

EPA Response

No comment.

2. Rejection factor: **The sampling protocol was inadequate.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 86-87.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-331,332-9,-10,-11.

In forestry dissipation studies, required samples include soil, sediment, water, or plant material from the treated forest area, collected at the approximate recommended sampling intervals for the type of material sampled, and for the length of time necessary to establish the patterns of decline of parent, and the formation and decline of degradates, in each of the materials sampled. Deficiencies in any of these components could cause the study to be rejected.

Industry Comment

No comment.

EPA Response

No comment.

3. **Rejection factor: The application rate was not reported.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 86.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-331-3.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data. Other factors may have contributed to the EPA's decision to reject the study. The forestry dissipation study is done to evaluate the dissipation of the pesticide under typical use conditions. Dissipation rates at different rates of application of a pesticide can vary unpredictably because the soil microorganisms and plants responsible for the degradation process may respond differently at different concentrations of the pesticide. In addition, the actual application rate of the pesticide must be known to confirm that the maximum label rate of the pesticide was used.

Industry Comment

No comment.

EPA Response

No comment.

4. Rejection Factor: **No storage stability data were provided to confirm that samples did not degrade prior to analysis.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-332-17.

This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data. Freezer storage stability of samples is not usually a problem in the laboratory studies because the samples can be frozen immediately after collection and are not stored for long periods of time. However, in forestry studies, soil, sediment, water, and plant tissue samples usually cannot be refrigerated or frozen immediately after collection. In addition, over the many weeks (or months) of the study, samples can accumulate in a freezer prior to analysis. Therefore, a contemporaneous "spiking" study must be conducted, in which a known amount of active ingredient is added to portions of soil, sediment, water, or plant material from an untreated area near the test site at the same time that samples from the treated areas are collected. The "spiked" samples are then stored under the same conditions as samples from the test plot, and all samples are analyzed at the same time. This should indicate whether the pesticide in the samples from the test plots is degrading during handling and storage, and if so, whether it is possible to normalize the results to account for the amount of change during storage. If the data cannot be corrected in this way, it is not possible to distinguish between the amount of the dissipation occurring during storage and the dissipation occurring under field conditions, and the study must be repeated.

Industry Comment

No comment.

EPA Response

No comment.

5. Rejection Factor: **Field test data were incomplete.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 87-88.

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-332-14.

This information is needed to determine if the study was conducted under conditions representative of the intended use pattern. This issue does not normally result in the rejection of a study, and the study is usually repairable by the submission of additional data. EPA requires this information to evaluate the conditions under which the field study was conducted to determine the dissipation rate of the test substance. For instance, dissipation data have different effects depending on the time of year it is applied, the amount of rainfall, the slope of the test site, etc.

Industry Comment

No comment.

EPA Response

No comment.

GUIDELINE 164-4 COMBINATION TANK MIXES FIELD DISSIPATION STUDIES

There were no studies screened for this guideline. However, guidance on this topic appears in Subdivision N - Environmental Fate Guidelines (pages 89-91). There is no SEP for this guideline. This guideline is essentially the same as specified in the SEP for 164-1 (Terrestrial Field Dissipation), with the only difference being that, in addition to separate field studies for each active ingredient in a product, two or more active ingredients are also tested for their own interactions under field conditions.

GUIDELINE 164-5 LONG-TERM TERRESTRIAL FIELD DISSIPATION STUDIES

There were no studies screened for this guideline. However, guidance on this topic appears in Subdivision N - Environmental Fate Guidelines (pages 91-94) and in the Acceptance Criteria and the Guidance for Summarizing Studies [see pages C-335-338 of the Phase 3 Guidance]. This guideline is essentially the same as specified in the SEP for 164-1 (Terrestrial Field Dissipation), with the only difference being the increased duration of the study.

GUIDELINE 165-1 CONFINED ACCUMULATION IN ROTATIONAL CROPS STUDIES

NOTE: The Confined Accumulation in Rotational Crops and Field Accumulation in Rotational Crops data requirements have been transferred to the Chemistry Branches (Health Effects Division). RSCB has accepted responsibility for reviewing these studies and for setting rotational crop intervals or tolerances, as necessary.

1. Rejection factor: The residues in soil were not characterized.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 96.
- Environmental Fate - Addendum 7 - Series 165-1 (1988). p. 13.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-339-14.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93). See Appendix C: "Pesticide Reregistration Rejection Rate Analysis Residue Chemistry/Environmental Fate Follow Up Guidance for Conducting Rotational Crop Studies".

The purpose of the confined accumulation study is to determine the nature and amount of residue uptake in rotational crops. This process is assessed by analyzing the level and, if necessary, the nature of the residues in rotational crops in the confined accumulation study.

Industry Comment

Industry agrees that, as indicated in the above EPA Guidance, the purpose of the confined rotational crop study is "to determine the nature and amount of residue uptake in rotational crops." As indicated in the Pesticide Assessment Guidelines "such data are used to establish realistic crop rotation restrictions ... or to provide information for determining if tolerances are needed in rotational crops." Industry further agrees that quantification of total radioactive residues in soil during the study will aid in interpretation of the results of the study. However, the character of the residues

in the soil has already been determined in the aerobic soil metabolism, and as a result, characterization of residues in the confined rotational crop study is not necessary.

Industry Recommendation: Industry agrees that quantification of total radioactive soil residues during the study will aid in interpretation of the results. However, the requirement for characterization of the soil residues should be eliminated provided that a suitable aerobic soil metabolism study has been conducted.

EPA Response

Since the chief consideration for requiring confined rotational crop studies is dietary in nature, the Agency agrees with Industry that soil analysis is not required and need only be performed at the Registrant's discretion. Interested parties are directed to the guidance paper on conducting rotational crop studies referenced above.

2. Rejection factor: The length of freezer storage of the crops was not reported and no freezer storage stability data were provided.

EPA Guidance on this Factor

- Environmental Fate - Addendum 7 - Series 165-1 (1988). p. 12.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-341-6.
- Additional Guidance for Conducting Plant and Livestock Metabolism Studies (7/16/92).
- Guidance on Generating Storage Stability Data in Support of Pesticide Residue Chemistry Studies (1/14/93).
- Guidance on Submission of Raw Data (1/14/93).

This issue is important in accepting a confined study. The information needed to upgrade the experiment may be available.

Industry Comment

Industry agrees that storage stability data needs to be provided (if the samples are stored for an extended period of

time) for the parent and metabolites in tissue samples. Sine the nature of the residue is unknown at the start of the study, flexibility is required on how this data is obtained.

Industry Recommendation: Industry recommends that EPA accept a 4- to 6-month grace period for sample storage during which no storage stability information would be required, provided that samples have been stored properly. If samples are stored more than 6 months, the registrant should:

a) Reference storage stability data already obtained from relevant sample types and storage conditions in other studies; or

b) Analyze a representative substrate as soon as practicable (i.e., within 4 to 6 months of collecting the samples), and then repeat the analysis at the end of the study. The chromatographic profiles may be compared to insure that no gross changes have occurred during storage.

This is consistent with the policy on plant metabolism studies currently in force in the Chemistry Branches of the Health Effects Division (P. Paul conversation with R. Loranger, 6/23/92).

EPA Response

Chemicals may degrade during storage, even under ideal storage conditions. Therefore, storage stability data are essential in order to be confident that any degradation measured in the test system was due solely to the environment of that test system, and not due to handling and storage. Storage stability is chemical specific and a chemical's stability under storage can vary depending upon the matrix in which it is stored (e.g., soil, water, organic extract, plant tissue, fish tissue, etc.). In light of the difficulty of spiking samples before the identity of the residue is known and the length of time needed for metabolism studies, the present Agency position is that storage stability data should not normally be required for samples analyzed within 4-6 months of collection, provided evidence is given that attempts were made to limit degradation of residues by appropriate storage of matrices and extracts during the analytical portion of the study. In other words, as stated in the SEP on animal metabolism, "The reviewer should be convinced that storage conditions have not invalidated the Registrant's results..."

Interested parties are directed to three guidance papers cited above regarding storage stability, metabolism and raw data for information on how the Agency will handle this question in confined rotational crop studies.

3. Rejection factor: The study application rate does not reflect normal or maximum use rates and the application rate was not confirmed.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 95.
- Environmental Fate - Addendum 7 - Series 165-1 (1988). p. 10.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-339-1.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).

Confined accumulation studies determine the amount of biomagnification of an active ingredient by crops grown in treated soil. The amount of biomagnification observed at different pesticide application rates can vary unpredictably because the plants grown in the treated soil may respond differently to different concentrations of the pesticide. Therefore, it is not possible to extrapolate the amount of uptake conducted at rates other than when the maximum label rate is applied.

Industry Comment

Industry agrees that the application rate of the pesticide does need to be confirmed and should approximate the maximum use rate. If/since the identity and purity of the applied test material has been established prior to application, it is necessary only to determine total radioactivity in the soil immediately after application.

Industry Recommendation: Industry recommends that EPA place strong weight in the proper reporting of application methods, preparation of doses, etc., in order to confirm the application rate and not reject studies based on the time zero soil analysis.

EPA Response

The Agency believes that the maximum application rate must be used when confined rotational crop studies are performed. However, time zero soil analysis is not required to confirm the

application rate. The industry recommendation concerning reporting of application methods and dose preparation is reasonable. Again, interested parties are directed to the guidance paper on conducting rotational crop studies referenced above.

4. Rejection factor: Material balances were not provided.

EPA Guidance on this Factor

- Environmental Fate - Addendum 7 - Series 165-1 (1988). pp. 5, 13.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-339-13.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).

The Acceptance Criteria of the Phase 3 Technical Guidance states that this criterion is considered supplemental for this guideline and may not be required for every study.

Industry Comment

Industry agrees that attempts should be made to identify as much of the radioactive residues in the plant tissues as possible. However, the confined rotational crop study is an open study subject to loss of volatile compound and $^{14}CO_2$ (generated by degradation), as well as movement of the materials in the soil. Therefore, obtaining a "material balance" or "recovery of applied material" is not a reasonable objective.

Industry Recommendation: Eliminate the need for complete "recovery of applied material" in the confined rotational crop study. Require only analysis of plant residues.

EPA Response

The Agency concurs with elimination of the need for complete "recovery of applied material" for all times in the confined rotational crop study. In fact, since soil analysis is no longer required, this factor becomes moot.

5. **Rejection factor:** **The test substance was less than analytical grade.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 95.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-339-2.
- Additional Guidance for Conducting Plant and Livestock Metabolism Studies (7/16/92).
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).

The purpose of the confined accumulation in rotational crops study is to determine the nature and amount of pesticide residue uptake in rotational crops. If the test substance is less than analytical grade (usually <95% active ingredient), the contaminants in the test substance as well as residues arising from the parent may accumulate in the test crops and confuse the evaluation of the study.

Industry Comment

Industry agrees that the radiolabeled material used in the study needs to have a purity of at least 95%. See also Industry comments and recommendation under Guideline 162-3, Rejection Factor 6.

EPA Response

For laboratory studies conducted with radiolabeled chemicals, the use of a test substance with low radiopurity may unnecessarily complicate the identification of degradation products since the fate of the parent and its degradates is followed by monitoring the radioactivity.

Industry should strive for a radiopurity of ≥97%. A lower radiopurity may be acceptable with adequate justification. The Agency understands that achieving a high level of radiopurity may depend on the chemical characteristics of the specific compound and on the type of radioisotope used. The Agency further acknowledges that some chemicals may require extensive preparation in order to achieve this high level of radiopurity, and has previously concurred with time extensions for submission of data to allow for such preparation. The Agency has also

previously accepted the use of lower purity radiochemicals with adequate justification as to why higher radiochemical purity could not be achieved.

6. Rejection factor: **The supporting raw data were not provided.**

EPA Guidance on this Factor

- Environmental Fate - Addendum 7 - Series 165-1 (1988). p. 9, 14.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-323-7.
- Guidance on Submission of Raw Data (1/14/93).

This factor alone is not sufficient to reject a study, as the registrant has the option to provide reprints of methods, other studies, raw data, relevant letters/memos and material which will help support the registrant's conclusions. However, if the raw data were necessary to confirm some conclusion or calculation proposed by the registrant, this information must be provided.

Industry Comment

Industry agrees that "data ... necessary to confirm some conclusion or calculation proposed by the registrant ... must be provided. However, representative data should be sufficient instead of all of the raw data. In addition, Industry requests that the EPA define "raw data".

Industry Recommendation: Industry agrees that representative data must be provided to support conclusions and calculations. However, Industry requests that EPA define "raw data".

EPA Response

The Agency has provided additional information about raw data in the 1/14/93 document cited above.

Additional Rejection Factor No. 1: Characterization/identification of residues.

Industry Comment

It is noteworthy that a primary objective of the study, i.e., to determine the nature of the residues in rotational crops was not cited as a key reason for rejection of this study type. This issue is of concern to registrants. Since Residue Chemistry Branch have committed to producing a guidance document on characterization/identification of residues in plant metabolism studies, Industry requests that the requirements for the confined rotational crop studies be harmonized with this document, wherever possible. Requirements for rotational crops should not exceed those for plant metabolism and indeed cross-referencing to the plant metabolism should eliminate the need for detailed structural confirmation in many cases.

Industry Recommendation: Harmonize guidelines for characterization/identification of rotational crop residues with those for plant metabolism.

EPA Response

As noted in the 2/23/93 document on rotational crops, the Agency will be applying the same criteria to plant metabolism and confined rotational crop studies. The Registrant is referred to the document entitled "Additional Guidance for Conducting Plant and Livestock Metabolism Studies" (7/16/92).

Additional Rejection Factor No. 2: Tiered Approach to Confined Accumulation in Rotational Crops.

Industry Comment

The confined rotational crop study is an extremely difficult and time consuming study to perform. It is the equivalent of performing several plant metabolism studies with additional complicating factors such as: extremely low residue levels; uptake of more than one moiety from the soil; exposure to residues over the whole plant growth cycle. These factors yield complex metabolic profiles. To add to this complexity the present guideline also requires duplication of work being performed in the areas of soil metabolism, terrestrial field soil dissipation, etc. In its May 8, 1991 comments on the

reevaluation/update of PAG, Subdivision N, Industry proposed a tiered approach to rotational crop issues which would concentrate on the primary aims of the study, i.e., defining the nature and amount of residues in rotational crop.

Industry Recommendation: Industry requests that EPA urgently review their proposal and adopt a tiered approach to rotational crop issues.

EPA Response

The Confined Accumulation in Rotational Crops data requirement has been extensively "refined" over the past few years. The Agency has reviewed Industry's comments in its 5/8/91 submission and acknowledges the need to consider revision of the Confined Accumulation in Rotational Crops data requirement. The Agency believes that the approach discussed in the document entitled "Guidance on How to Conduct Studies on Rotational Crops" (2/23/93) reflects a tiered approach.

Additional Rejection Factor No. 3: Time Line of Two Years Too Short.

Industry Comment

A time line of two years for this study is unreasonably short. The study generally requires a new preparation of radiochemical because of the large amounts required, has an in-life phase of at least eighteen months (often with a seasonally dependent start date) followed by the identification of complex metabolic pathways.

Industry Recommendation: Amend the time line for this study type to four years. Alternatively, under the proposed tiered approach allocate 2.5 years for Tier 1.

EPA Response

The Agency is amenable to reevaluating the time lines to be certain that adequate time is given to the registrant to conduct the study. However, due to the time restraints of reregistration, a time line in excess of 2.5 years would not be acceptable for the confined study.

GUIDELINE 165-2 FIELD ACCUMULATION IN ROTATIONAL CROPS STUDIES

1. **Rejection factor:** **The source of pesticide residues in control samples of both crops and soils were not verified.**

EPA Guidance on this Factor

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-342-10.

- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).

As some control (untreated) crops and soils contain pesticide residues, it should be verified that the same (or similar) pesticide(s) were not previously applied to the test area. If background residues are detected, it may be due to prior pesticide application or a deficiency in the analytical method. If background residues of the test pesticide were present, it would not be possible to distinguish between the bioaccumulation of residues already present and the bioaccumulation of those added during the study.

Industry Comment

Industry agrees that pesticide residues in the control samples may create confusion in interpreting the results. Some explanation should be given, when possible. Analysis of the control soil before application will indicate whether there are any residues present in the soil at the time of application.

Industry Recommendation: Provided it does not compromise the results of the study, contamination of the control samples should not be considered a reason for rejection of a study.

EPA Response

The methods employed to analyze the rotational crops should be specific for all pesticide residues of concern in the subject commodities. If the analytical procedure determines interfering compounds it would be considered to be deficient and this would be a cause for rejection of the studies. It would also be desirable to employ sites on which the test pesticide had not been previously applied. If residues are found in control crop samples, the Agency will not automatically reject the field studies. The total study will be examined and consideration given to factors such as the relative levels of residues in treated and control samples. Again, analysis of the soil is not required.

2. Rejection factor: **There was a large degree of variability in the data with no explanation provided.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 100.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-343-19.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).
- Subdivision O - Residue Chemistry Guidelines (1982).

Variability in data from a field accumulation study can arise from non-uniform application of the test substance to the test plots, inadequate or improper plant sampling, or an unreliable analytical method. If the data are highly variable, the extent of uptake of residues of concern under field conditions cannot be clearly demonstrated.

Industry Comment

Industry agrees that some explanation should be given when there is a large degree of variability.

Industry Recommendation: Since this study type is likely to produce considerable variation in results this should not result in rejection providing adequate explanation is given.

EPA Response

The Agency agrees that this study can produce considerable variation in results (e.g., field factors such as seasonal variations in temperature and soil saturation level may affect dissipation/accumulation kinetics), and should not be rejected provided the variability is suitably explained.

The Chemistry Branches of HED have taken over responsibility for the review of these studies and, under the tiered approach discussed in the 2/23/93 document cited above, variability is not an important problem. If detectable residues of concern are observed at the maximum practical plant back interval (12 months) or a shorter desired plant back interval, then tolerances for rotational crops are required and a complete battery of field trials are required as discussed in Subdivision O also cited above. The larger number of trials needed for establishment of tolerances would cover any variation of the levels of residues in rotational crops.

3. Rejection factor: Residues in soil were not analyzed.

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 100.
- Environmental Fate - Addendum 1 - Series 165-2 (1986). p. 4.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-343-16.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).

The Chemistry Branches of HED have taken over responsibility for the review of these studies and, as discussed in the 2/23/93 document cited above, soil analysis is no longer required. Therefore this will no longer be a rejection factor.

Industry Comment

Industry agrees that soil residues analysis is necessary in this study.

Industry Recommendation: Residues in soil should be analyzed at times of treatment, at time of planting of the rotational crops to define root zone concentration, and at the time of rotational crop harvest for the crop with the longest maturation period. Soil samples from at least the 0- to 15-cm and 15- to 30-cm depths should be analyzed to determine root-zone concentrations. However, if the study is carried out at the same time as the terrestrial field soil dissipation study (164-1), then soil analysis from those samples will suffice.

EPA Response

See discussion above.

4. **Rejection Factor: Planting to harvest intervals were not provided.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 100.
- Environmental Fate - Addendum 1 - Series 165-2 (1986). p. 1.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-345-2.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).
- Subdivision O - Residue Chemistry Guidelines (1982).

This issue does not normally result in the rejection of a study, and the study is usually upgradable by the submission of additional information. The extent of uptake of pesticide residues must be determined at the growth stages appropriate for the various rotational crops, since rotational crops can be harvested either at maturity (food crops) or when immature (forage for domestic animals; some vegetable crops). The planting to harvest intervals provide the age of crop (and an estimate of its growth stage) at time of sampling. In addition, this information is needed to determine whether the crops were harvested under suitable conditions representative of the intended use pattern.

Industry Comment

Industry agrees that information on the planting to harvest intervals should be provided.

EPA Response

See discussion above.

5. **Rejection Factor: The field test data were incomplete.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 99-100.
- Environmental Fate - Addendum 1 - Series 165-2 (1986). pp. 2-3.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-342-11.
- Guidance on Submission of Raw Data (1/14/93).

This issue does not normally result in the rejection of a study, and the study is usually upgradable by the submission of additional information. The Agency must have this information to accurately evaluate the conditions under which the field study was conducted, which is a critical element in determining the extent of accumulation of the test substance. Field test data include: the identity of the crop planted on the treated soil; a description of how and when the crop was planted; how and when the subject pesticide was applied; the weather (temperature, rainfall, wind speed and direction) and condition of the field at time of application; the formulation of the pesticide applied; the application rate and the application technique; and irrigation (when applied and how much). This information is also required to determine whether the study was conducted under suitable, representative, and appropriate conditions, representative of the intended use pattern. Also, see the 1/14/93 document on raw data cited above.

Industry Comment

Industry agrees that field test data should be provided.

EPA Response

See comments above.

6. **Rejection Factor: The test substance was not characterized.**

EPA Guidance on this Factor

- Subdivision N - Environmental Fate Guidelines (1982). p. 98.
- Environmental Fate - Addendum 1 - Series 165-2 (1986). p. 2.
- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (1989). p. C-342-2.
- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).
- Subdivision O - Residue Chemistry Guidelines (1982).

This issue does not normally result in the rejection of a study, and the study is usually upgradeable by the submission of additional information. In the field accumulation study, the test substance can be applied as a typical end-use product; if so, the composition of the product to be used must be given to determine if it reflects the actual formulations to be registered and applied in the real world (Also, see Subdivision O - Residue Chemistry Guidelines).

Industry Comment

Industry agrees that the test material should be characterized.

EPA Response

See comments above.

GUIDELINE 165-3 ACCUMULATION IN IRRIGATED CROPS STUDIES

There were no studies screened for this guideline. However, guidance on this topic appears in Subdivision N - Environmental Fate Guidelines (pages 101-103) and in the Acceptance Criteria and the Guidance for Summarizing Studies [see pages C-346-349 of the Phase 3 Guidance].

Industry Comment

Many of the comments made on the field rotational crop studies apply to this type of study. Notably, these studies are very complex to run in the field and large variability is to be expected.

GUIDELINE 165-4 ACCUMULATION IN FISH

1. Rejection Factor: **The analytical methodology was insufficient to detect the residue.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 105.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-350

The identification of those extractable residues present at levels greater than or equal to 0.05 ppm is a critical element of the fish accumulation study. One of the primary reasons this study is conducted is to identify the residues that accumulate in fish after exposure to a constant level of a pesticide. Therefore, the analytical method used to analyze for residues in the fish tissue and surrounding water must be sensitive enough to the detect and distinguish between those residues.

Industry Comment

No argument if comments in factor #2 below are considered.

EPA Response

See comments in factor #2.

2. Rejection Factor: **Some degradates present in small concentrations in edible and non-edible fish tissues were not identified and/or quantified.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 105.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-350.

The identification of those extractable residues present at levels greater than or equal to 0.05 ppm is a critical element of the fish accumulation study. A primary reasons this study is

conducted is to identify the residues that are accumulated in fish after constant exposure to a pesticide.

Industry Comment

Industry agrees that identification of residues in the fish is an important part of the study. According to the Pesticide Assessment Guidelines, Subdivision N, the purpose of the fish accumulation study is "to determine if pesticide residues accumulate in fish used as human food sources and to determine the extent of pesticide residues in edible portions of such fish." Identification of individual analytes that account for 10% of the residues or 0.05 ppm (whichever is greater) in the various fish fractions is sufficient for characterization of residues.

Industry Recommendation: Require identification of individual analytes in the fish that account for a minimum of 10% the total residues or 0.05 ppm (whichever is greater), along with the determination of BCFs for the fish.

EPA Response

The Agency has agreed to further discussion with industry on this topic and will finalize its position at that time.

3. **Rejection Factor:** **The study on the effects of storage on the analytical results of samples was not completed.**

EPA Guidance on this Factor

- Addendum 8 on Data Reporting to Pesticide Assessment Guidelines: Laboratory Studies of Pesticide Accumulation in Fish. (March 1988), page 9.

- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), page C-352.

Even under ideal conditions, chemicals may degrade during storage. Therefore, if samples are taken and stored before analysis, a storage stability study is required in order to assess the effects, if any, of storage on those samples. In many cases, studies rejected due to storage stability data problems may be upgraded by the registrant by the submission of additional data/information.

Industry Comment

Industry agrees that storage stability data need (if the samples are, in fact, stored) to be provided for the parent and metabolites in tissues samples. This data may be obtained from sources other than the present test samples as long as the data are relevant (i.e., similar type samples and similar storage conditions and lengths.

Industry Recommendation: Industry recommends that EPA accept a 4- to 6-month grace period for sample storage during which no storage stability information would be required, provided that samples have been stored properly. If samples are stored more than 6 months, the registrant should:

a) Reference storage stability data already obtained from relevant sample types and storage conditions in other studies; or

b) Analyze a representative substrate as soon as practicable (i.e., within 4 to 6 months of collecting the samples), and then repeat the analysis at the end of the study. The chromatographic profiles may be compared to insure that no gross changes have occurred during storage.

This is consistent with the policy on plant metabolism studies currently in force in the Chemistry Branches of the Health Effects Division (P. Paul conversation with R. Loranger, 6/23/92).

EPA Response

Chemicals may degrade during storage, even under ideal storage conditions. Therefore, storage stability data are essential in order to be confident that any degradation measured in the test system was due solely to the environment of that test system, and not due to handling and storage. Storage stability is chemical specific and a chemical's stability under storage can vary depending upon the matrix stored (e.g., soil, water, organic extract, plant tissue, fish tissue, etc.). Therefore, the Agency is concerned that a blanket 4- to 6-month grace period for sample storage, during which no storage stability information would be required, may not be appropriate for environmental fate testing. The Agency does however agree that unless a pesticide/residue of concern is otherwise known to be volatile or labile, storage stability data will not be needed for samples stored frozen for ≤30 days.

For frozen storage intervals >30 days, it is recommended that evidence be provided confirming that the identity of

residues did not change during the period between collection and final analysis. The Agency has agreed to let industry develop a draft storage stability guidance document to address this and other storage stability issues. Final Agency judgement on this issue will be reserved for the Storage Stability follow-up guidance.

Ideally, storage stability data should be obtained concurrently with the particular environmental fate guideline study, not independent from it. However, concurrent storage stability studies will not be required in many cases. Provided that the pesticide residues are found to be stable in the matrices of interest, a storage stability study run in a separate freezer at a different time period will be acceptable if the storage conditions (particularly temperature) are the same as those in the corresponding environmental fate guideline study. However, for pesticides whose residues are known or suspected to be unstable or volatile, concurrent studies may be needed. In fact, for such pesticides, it is advisable to run a storage stability study in advance to determine proper storage conditions and maximum storage times before treated samples are placed into storage.

4. Rejection Factor: Data on the concentration of the parent and its degradates in the exposure water were not submitted.

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), pages 105, 106.
- Addendum 8 on Data Reporting to Pesticide Assessment Guidelines: Laboratory Studies of Pesticide Accumulation in Fish. (March 1988), page 9.
- FIFRA Accelerated Reregistration Phase 3 Technical Guidance. (December 1989), pages C-350, C-352.

The concentration of the test substance must be high enough to facilitate chemical identification of residues in fish. However, it must not exceed 1/10 the 96 hr LC_{50} of the test species in order to avoid any toxic effects which could stress the fish and affect their bioaccumulation of the pesticide. The exposure water must also be free of degradates which could stress the fish. Finally, in order to calculate a bioconcentration factor (BCF), which gives an indication of the potential for the pesticide to be accumulated in fish tissues, the concentration of

the pesticide in the test water must be known and must remain constant.

Industry Comment

Industry agrees that data on the total concentration of pesticide and key degradates in the test exposure water should be provided. In the case or rapidly metabolized compounds it is not possible to maintain a constant nominal concentration of the

parent pesticide. This is not a problem, since similar degradation will occur in natural water.

Industry Recommendation: EPA should flexibly interpret the need to maintain a constant concentration in low-solubility, lipophilic, readily degradable compounds.

EPA Response

The Agency agrees that some degree of flexibility in the experimental design is warranted, however significant deviations from the guidance of Subdivision N must be adequately justified. Studies should be designed and conducted to meet the objectives of 165-4. A relatively stable steady state concentration of the parent can be achieved using a flow-through system. For rapidly metabolized compounds, the number of turnovers may need to be increased.

5. Rejection Factor: **Mortality and growth/weight patterns of fish throughout the study were not provided.**

EPA Guidance on this Factor

- Subdivision N: Environmental Fate Guidelines. (1982), page 105.
- Addendum 8 on Data Reporting to Pesticide Assessment Guidelines: Laboratory Studies of Pesticide Accumulation in Fish. (March 1988), pages 7, 8, 9.

As discussed above, it is imperative that the fish are not stressed during this study which determines the accumulation potential of a pesticide and the nature of the accumulated residues. Two ways in which this can be confirmed include tracking fish mortality and growth. Unacceptably high mortality or unusual growth patterns may signify a problem that could invalidate the study. This rejection factor relates to basic

information that must be reported so that a technical evaluation of the data can be made. In most cases, studies rejected solely on this reporting deficiency are likely to be upgraded by the registrant by the submission of the additional data/information.

Industry Comment

Industry agrees that gross observation of the mortality and growth patterns of fish throughout the study should be provided. However, detailed weights of the fish should not be necessary since there are generally an insufficient number taken to allow statistical analysis of biological development.

Industry Recommendation: Require only gross observations and not measurement of actual weights of the fish.

EPA Response

As supplementary information, we agree that only gross observations should be required. The study should also report the 96-hr LC_{50}.

GUIDELINE 165-5 FIELD ACCUMULATION STUDIES OF AQUATIC NON-TARGET ORGANISMS

There were no studies screened for this guideline. However, guidance on this topic appears in Subdivision N - Environmental Fate Guidelines (pages 107-108) and in the Acceptance Criteria and the Guidance for Summarizing Studies [see pages C-354-357 of the Phase 3 Guidance]. There is no SEP for this guideline.

GUIDELINES 166-1, -2, -3 - GROUND WATER MONITORING STUDIES

There were no studies screened for these guidelines. Guidance on this topic is currently being developed by the Ground Water Section of EFGWB. There are no SEPs for these guidelines.

GUIDELINES 167-1, -2 - SURFACE WATER/RUN OFF STUDIES

There were no studies screened for these guidelines. Guidance on this topic is currently being developed by the Surface Water Section of EFGWB. There are no SEPs for these guidelines.

GUIDELINE 201-1 DROPLET SIZE SPECTRUM

There were no studies screened for this guideline. However, guidance on this topic appears in Subdivision R - Pesticide Spray Drift Evaluation, the Standard Evaluation Procedure- Pesticide Spray Drift Evaluation: Droplet Size Spectrum Test and Drift Field Evaluation Test, and in the Acceptance Criteria and the Guidance for Summarizing Studies [see pages C-402-403 of the Phase 3 Guidance].

GUIDELINE 202-1 DRIFT FIELD EVALUATION

There were no studies screened for this guideline. However, guidance on this topic appears in Subdivision R - Pesticide Spray Drift Evaluation, the Standard Evaluation Procedure- Pesticide Spray Drift Evaluation: Droplet Size Spectrum Test and Drift Field Evaluation Test, and in the Acceptance Criteria and the Guidance for Summarizing Studies [see pages C-404-406 of the Phase 3 Guidance].

IX. SUMMARY TABLE OF REJECTION FACTORS

161-1 HYDROLYSIS STUDY

1) A material balance was not provided
2) The study was not conducted in the dark.
3) The study duration and number of sampling intervals were insufficient to establish the decline and half-life.
4) It was not specified that the buffer solutions were sterile; before, it could not be determined if degradation was due to hydrolysis or biotic processes.
5) The test substance was not characterized.
6) The incubation temperature was not maintained.
7) Insufficient data were presented to support the reported conclusion.
8) Degradation curves and regression analysis were not provided.

161-2 PHOTODEGRADATION STUDIES IN WATER

1) The light source was not adequately characterized and was not compared to sunlight.
2) Degradates were not identified.
3) The material balances were incomplete.
4) The test solutions were not buffered and the pH of the water was not reported.
5) The analytical methodology was incomplete and no raw data was provided to support the conclusions.
6) The sampling protocol was inadequate.
7) The temperatures of the test solutions were not reported.
8) Volatilization was neither measured nor controlled.
9) A photosensitizer was used as the co-solvent.
10) It was not specified that the test solutions were sterile.
11) The study was terminated before the half-life of the test substance was established or before 30 days.
12) The coefficients of determination for the data used to determine the half-lives were very poor.
13) The stability of the pesticide under refrigeration was not addressed.

161-3 PHOTODEGRADATION ON SOIL

1) The material balance was incomplete.
2) Volatilization was neither measured nor controlled.
3) Artificial light source was not similar to natural sunlight.
4) The test substance was not technical grade or pure.
5) Raw data were not provided.
6) The incubation temperature was not provided.
7) Degradates were not identified.
8) The test was not performed on soil.
9) The treatment rate was not reported.

161-4 PHOTODEGRADATION IN AIR

1) The pesticide degradation in the vapor phase could not be distinguished from degradation that occurred in material adsorbed to the sides of the glass container.
2) Air samples were never analyzed separately from nonvaporized pesticide.
3) The material balance was low.
4) High percentages of unidentified material were reported.
5) The registrant did not measure the vapor pressure at the temperature the study was conducted.
6) The analytical method was inadequate.
7) The spectrum of the artificial light source was not similar to that of natural sunlight.
8) A photosensitizer was present in the primary stock solution.
9) No raw data was submitted.

162-1 AEROBIC SOIL METABOLISM

1) Residue identification was incomplete.
2) The material balance was inadequate.
3) The study was conducted for an inadequate length of time to establish the patterns of formation and decline.
4) Purity of the test substance was not specified.
5) The experimental design was inadequate to assess the metabolism in soil.
6) The incubation temperature was not reported.

7) The soil textures could not be confirmed because the soils were not classified using the USDA Soil Textural Classification System.
8) The analytical methodology was incomplete and no raw data were provided to support conclusions.
9) The raw data examined did not support the half-life reported by the registrant.
10) Degradate characterization data were presented as percent of recovered rather than percent of applied.

162-2 ANAEROBIC SOIL METABOLISM

1) Residue identification was incomplete.
2) The material balance was inadequate.
3) The purity of the test substance was not specified.
4) The storage stability data were not provided, although the raw data indicate that both soil samples and extracts were stored prior to analysis.
5) Degradates present in small concentrations were not identified.
6) The experimental design was inadequate to accurately assess the degradation under anaerobic conditions.
7) The length of frozen storage was not specified. Frozen storage stability data are required to confirm that the residues were stable.
8) Method detection limits were not provided.
9) Large discrepancies existed in the data for duplicate samples collected after anaerobic conditions were established. The data, therefore, cannot be used reliably to calculate the rate of degradation in soil under anaerobic conditions.
10) The study was conducted for an inadequate length of time to establish the patterns of formation and decline of the pesticide under anaerobic conditions. The study should have been conducted for 60 days.
11) No raw data were provided to support the conclusions.
12) A complete description of the test water, including the pH and dissolved oxygen content, was not provided.
13) The soil was not classified according to the USDA Soil Textural Classification System.

162-3 ANAEROBIC AQUATIC METABOLISM

1) The sampling protocol was inappropriate because it contained too few sampling intervals and was inadequate to establish the half-life for the pesticide.
2) The pesticide residues were quantified using a chemically nonspecific analytical method. No attempt was made to characterize the pesticide residues in soil and water matrices.
3) Material balances were incomplete.
4) Degradates were not identified.
5) The test substance was not technical grade or purer.
6) The test water was not characterized. Foreign soils were not completely characterized and may not have been typical of those in the United States. The soil must be representative of that found at an intended use site.

162-4 AEROBIC AQUATIC METABOLISM

1) The sampling schedule was inadequate.
2) Material balances were incomplete.
3) Residues were incompletely characterized.
4) The test water was not characterized.

163-1 LEACHING/ADSORPTION/DESORPTION

1) Degradates were not identified.
2) The test soils were autoclaved prior to conducting the study.
3) The material balance was incomplete.
4) Soils and sediments were incompletely characterized.
5) Desorption of a major degradate was not addressed.
6) Foreign soils were used which may not be typical of soils in the United States.
7) Kd values (values of soil/water relationships) were not reported.
8) The desorption phase was done serially, with incomplete removal of the supernatant at each step.
9) The soil texture could not be confirmed because the soil was not classified using the USDA Soil Textural Classification System.
10) It was not established that the equilibrium time used was sufficient for the soil:solution slurries to reach equilibrium.
11) The bioassay methods used in the study were not acceptable analytical techniques.
12) Soil used in the study was not prepared properly.
13) Test solution was not characterized.
14) The data were presented on a percentage basis with no actual concentrations.

163-2 LABORATORY VOLATILITY

1) Analytical methodology was insufficient.
2) The study was not carried out over a long enough period of time to clearly define a volatility decline curve.
3) The soil was not analyzed immediately after treatment. Therefore, the application rate was not confirmed.

4) No material balance was reported or the data reported was insufficient.
5) Not all major formulation categories were tested.
6) The soil was autoclaved before the test.
7) The rate of volatilization was incorrectly calculated and could not be determined with the information provided.
8) The experiments were not replicated.

163-3 FIELD VOLATILITY

1) The soil data were inadequate to confirm the application rate.
2) Data on soil samples was not provided.
3) The description of experimental conditions were insufficient.

164-1 TERRESTRIAL FIELD DISSIPATION

1) The original concentration of the pesticide was not reported or the reported application rate was not confirmed in soil samples taken immediately post-treatment.
2) The pattern of formation and decline of the degradates was not addressed.
3) The sampling was not done to depths sufficient to define the extent of leaching.
4) Characterization of residues was not provided for all sites or the soil was not analyzed for the correct residues or for all residues.
5) Complete soil characteristics and field test data were not provided.
6) The analytical methodology was insufficient to identify the residues (in one case, the analytical method could not distinguish between the parent and its degradates).
7) The data were too variable to accurately assess the dissipation of the test substance.
8) The freezer storage stability data were inadequate.
9) The maximum label rates were not used, and the soil incorporation procedure recommended on the label was not followed.
10) The formulation and method of application were not specified.
11) The plants were harvested after application and the time of harvest was not given.
12) Pretreatment samples were contaminated.
13) More than one pesticide was applied to the crop.
14) The experiment was conducted at only one site instead of the two recommended in the Guidelines.
15) The method of detection limit and recovery efficiencies were not reported.

164-2 AQUATIC FIELD DISSIPATION

1) Complete field test data were not provided.
2) The analytical methodology was insufficient to determine the residue.
3) The material balance was insufficient.
4) Data were too variable to assess dissipation.

164-3 FORESTRY FIELD DISSIPATION

1) The data provided were either insufficient or too variable to accurately establish a pattern of dissipation of a chemical and its primary degradate in a forest environment.
2) The sampling protocol was inadequate.
3) The application rate was not reported.
4) No storage stability data were provided to confirm that samples did not degrade prior to analysis.
5) Field test data were incomplete.

165-1 CONFINED ACCUMULATION IN ROTATIONAL CROPS

1) The residues in soil were not characterized.
2) The length of freezer storage of the crops was not reported and no freezer storage stability data were provided.
3) The study application rate does not reflect normal or maximum use rates and the application rate was not confirmed.
4) The test substance was less than analytical grade.
5) The supporting raw data were not provided.

165-2 FIELD ACCUMULATION IN ROTATIONAL CROPS

1) The source of pesticide residues in control samples of both crops and soils were not verified.
2) There was a large degree of variability in the data with no explanation provided.
3) Residues in soil were not analyzed.
4) Planting to harvest intervals were not provided.
5) The field test data were incomplete.
6) The test substance was not characterized.

165-4 ACCUMULATION IN FISH

1) The analytical methodology was insufficient to detect the residue.
2) Some degradates present in small concentrations in edible and non-edible fish tissues were not identified and/or quantified.
3) The study on the effects of storage on the analytical results of samples was not completed.
4) Data on the concentration of the parent and its degradates in the exposure water were not submitted.
5) Mortality and growth/weight patterns of fish throughout the study were not provided.

X. CONCLUSIONS

Overall, the rejection rates for environmental fate have shown improvement. The pre-1986 aggregate rejection rate for environmental fate was 54 percent, and the post-1988 rejection rate is 28 percent. The photodegradation - water (161-2), photodegradation - soil (161-3), leaching ((163-1), terrestrial field dissipation (164-1) and aquatic field dissipation (164-2) guidelines have shown a continuous and substantial downward trend in their rejection rates. The rejection rate for photodegradation - water has dropped from 53 percent to 19 percent; for photodegradation - soil from 53 percent to 18 percent; for leaching from 57 percent to 19 percent, for terrestrial field dissipation from 52 percent to 27 percent, and for aquatic field dissipation from 95 percent to 21 percent. While the improvement has been substantial, their current rejection rates are still high, in light of OPP's goal of 10%.

Four guidelines have not shown improvement. The pre-1986 rejection rate for aerobic soil metabolism (162-1) was 25 percent and the post-1988 rate is 32 percent; for anaerobic soil metabolism (162-2), the pre-1986 rejection rate was 33 percent and the post-1988 is 53 percent; for confined crop rotation (165-1), the average rejection rate is 55 percent; and for bioaccumulation in fish (165-4), the average rejection rate is 39 percent.

The rejection rates associated with those studies that are part of the sequencing and triggering of the ground water monitoring studies appear to pose the greatest risk to delaying REDs. This is based on the amount of time it takes (12 years) to complete the two sequences that could in turn result in two more levels of higher tier studies being triggered. High rejection rates at the first level are likely to cascade into the second level (see Chart 1) contributing to high rejection rates there as well. This will result in substantial delays in satisfying the data requirements for guidelines in these two levels as well as postpone the determination of whether a ground water monitoring study should be required. The terrestrial field dissipation study is a critical study, given its role of characterizing dissipation under actual field conditions as well as triggering the higher tier ground water monitoring requirements.

The three most frequently cited factors that have led to the rejection of studies include: (1) inadequate materials balance; (2) degradates/residues not adequately identified; and (3) failure to adequately establish half-life.

Industry provided substantial insight into: (1) where further Agency guidance would be most useful; and (2) why certain rejection factors occur. Some of the rejection factors reflect very difficult technical problems. For example, revaporization

from the walls of test containers make an accurate derivation of the formation and decline of the parent and degradates in the photodegradation in air (161-4) study extremely problematic.

The tight time frames imposed by FIFRA '88 force industry to start studies before results from other pertinent studies have been reviewed and approved by the Agency. Consequently, rejection factors in the earlier studies can cascade down into the subsequent sequence of studies causing them to be rejected as well. Industry also pointed out that the time lines for certain studies were too short.

Industry asserted that the single most important factor that has contributed to the high rejection rates in environmental fate is the many changes the Agency has made in guideline requirements, which have been retroactively imposed on studies that had already been initiated.

The Chemistry Branches of Health Effects Division (HED) have taken over the responsibility for review of studies which determine whether pesticide residues of concern are observed in rotational crops as a result of uptake from soil of previously treated fields (Guideline Nos. 165-1 and 165-2). This transfer was performed because the concern over residues in these situations is chiefly dietary. While the Branches were not in attendance at the meeting held with the industry, the 2/23/93 document entitled "Guidance on How to Conduct Studies on Rotational Crops" has altered some of the data requirements for rotational crop studies making certain of the previous rejection factors moot, especially those dealing with analyses of residues in soil. This paper along with the metabolism, storage stability and raw data documents prepared earlier in response to the Residue Chemistry section of the rejection rate project have provided additional guidance which addresses the remainder of the industry's concerns over rejection factors for rotational crop studies.

XI. RECOMMENDATIONS

As a result of the rejection rate analysis and the ensuing discussions with Industry, both EPA and Industry realize the need for additional guidance on various environmental fate requirements. EPA and industry intend to develop and issue the following documents:

Storage Stability Guidance proposal	Delivered draft 7/27/93
Raw Data Guidance Proposal	Delivered draft 7/27/93
Interim Protocol Proposal for 161-4	Delivered draft 7/27/93
SEP Proposal for 162-4	Delivered draft 7/23/93
Guidance on Conducting Studies on Rotational Crops	Delivered on 2/23/93 (EPA)

Industry has also agreed to provide position papers regarding cut off points for 161-1 and 161-2. The development of these documents should further reduce rejection rates for environmental fate.

Consistent with EPA's Definition of Reregistration, the Agency shall review and evaluate all studies according to criteria that (1) were in place at the time of the Phase III Guidance or (2) were agreed to by EPA and the registrant in specific protocols prior to the initiation of the study, whichever comes later. The use of new criteria is not a valid reason for rejecting a study submitted to satisfy reregistration data requirements.

The Agency intends to distribute all relevant environmental fate policy notes to NACA, CSMA and CMA for distribution to their members.

The Agency and Industry have also agreed to discuss and resolve the issues regarding the appropriate criteria for triggering and conducting:

a) the photodegradation in air (161-4) study;
b) mobility - adsorption/desorption (163-1) studies;
c) laboratory volatility (163-2) and field volatility (163-3) studies;
d) conducting field dissipation (164 series) studies.

Given the technical problems identified in the analysis with the photodegradation in air (161-4) study, in the interim the Agency will reevaluate the need for this study where it has already been required.

Finally, SRRD intends to continue tracking rejection rates for environmental fate guideline studies. If significant reductions in the rejection rates for these studies are not realized, further regulatory action may be required.

XII. APPENDIX A - EPA GUIDANCE DOCUMENTS

EPA distributed the following guidance documents to guide registrants on the correct procedures for conducting environmental fate studies. Specific references to these materials are made under each of the rejection factors listed.

- Subdivision N, Chemistry: Environmental Fate Guidelines - Series 160 through 165-5 (EPA Number 540/09-82-021, October 1982).

- Subdivision R, Pesticide Spray Drift Evaluation (EPA Number 540/9-84-002, April 1984).

- Subdivision O - Residue Chemistry Guidelines (1982).

- FIFRA Accelerated Reregistration - Phase 3 Technical Guidance (EPA Number 540/09-90-078, December 1989).

- Data Reporting Guidelines:

  Environmental Fate - Addendum 1 - Series 165-2 (EPA Number 540/09-86-149), June 1986.

  Environmental Fate - Addendum 2 - Series 164-1 (EPA Number 540/09-87-200), December 1986.

  Environmental Fate - Addendum 5 - Series 162-1 (EPA Number 540/9-82-021), January 1988.

  Environmental Fate - Addendum 6 - Series 163-1 (EPA Number 540/09-88-026), January 1988

  Environmental Fate - Addendum 7 - Series 165-1 (EPA Number 540/09-88-050), 1988.

  Environmental Fate - Addendum 8 - Series 165-4 (EPA Number 540/09-88-051), March 1988.

- Standard Evaluation Procedures:

  Hydrolysis Studies (EPA Number 540/9-85-013), June 1985.

  Aqueous Photolysis Studies (EPA Number 540/9-85-014), June 1985.

  Soil Photolysis Studies (EPA Number 540/9-85-016), June 1985.

Aerobic Soil Metabolism Studies (EPA Number 540/9-85-015), June 1985.

Anaerobic Soil Metabolism Studies (EPA Number 540/09-88-104), August 1988.

Soil Column Leaching Studies (EPA Number 540/9-85-017), June 1985.

Terrestrial Field Dissipation Studies (EPA Number 540/09-90-073), December 1989.

Pesticide Spray Drift Evaluation: Droplet Size Spectrum Test and Drift Field Evaluation Test (EPA Number 540/9-86-131), June 1986.

- Other Guidance Prepared By Health Effects Division

- Additional Guidance for Conducting Plant and Livestock Metabolism Studies (7/16/92).

- Guidance on Generating Storage Stability Data in Support of Pesticide Residue Chemistry Studies (1/14/93).

- Guidance on Submission of Raw Data (1/14/93).

- Guidance on How to Conduct Studies on Rotational Crops (2/23/93).

APPENDIX B - Environmental Fate Guidelines

161-1: Hydrolysis
161-2: Photodegradation - water
161-3: Photodegradation - soil
161-4: Photodegradation - air
162-1: Aerobic soil metabolism
162-2: Anaerobic soil metabolism
162-3: Anaerobic aquatic metabolism
162-4: Aerobic aquatic metabolism
163-1: Leach/adsorption/desorption
163-2: Volatility - lab
163-3: Volatility - field
164-1: Terrestrial field dissipation
164-2: Aquatic field dissipation
164-3: Forest field dissipation
164-5: Long term soil dissipation
165-1: Confined rotational crop (Now Responsibility of Chemistry Branches/HED)
165-2: Field rotational crop (Now responsibility of Chemistry Branches/HED)
165-3: Accumulation - irrigation crop
165-4: Bioaccumulation in fish
165-5: Bioaccumulation - aquatic non-target
166-1: Ground water - small prospective
166-2: Ground water - small retrospective
201-1: Droplet size spectrum
202-1: Drift field evaluation

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

FEB 23 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Guidance on How to Conduct Studies on Rotational Crops.

FROM: Ed Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

and

Debra Edwards, Ph.D., Chief
Chemistry Branch I: Tolerance Support
Health Effects Division (H7509C)

TO: Peter Caulkins, Acting Director
Special Review and Reregistration Division (H7508W)

and

Lawrence Culleen, Acting Director
Registration Division (H7505C)

THRU: Penelope A. Fenner-Crisp, Ph.D., Director
Health Effects Division (H7509C) 2/23/93

Earlier this year the Chemistry Branches of HED took over responsibility for the review of data generated on rotational crops (Guideline No.'s 165-1 and 165-2). The attached paper was prepared by a team consisting of Dr. R. Perfetti, Dr. R. Loranger, Dr. W. Hazel, F. Suhre, M. Rodriquez and R. Quick in order to provide guidance to Registrants and Chemistry Branch personnel on how to conduct and review these studies. This document will be utilized by the Chemistry Branches in future reviews of rotational crop studies.

We recommend that this paper be provided to all interested parties.

cc (With Attachment): L. Rossi, S. Irene, RBP, RF, Petition Review Aids File and Rotational Crops File

GUIDANCE ON HOW TO CONDUCT STUDIES ON ROTATIONAL CROPS

INTRODUCTION

The Chemistry Branches of Health Effects Division (HED) have taken over the responsibility for review of studies which determine whether pesticide residues of concern result in rotational crops as a result of uptake from soil of previously treated fields (Guideline Nos. 165-1 and 165-2). This transfer was performed because the concern over residues in these situations is chiefly dietary. The following paper is intended to provide additional guidance to HED personnel and other interested parties as to the requirements and procedure for review of submitted studies.

HISTORICAL

Studies on "Confined Rotational Crops" (Guideline Number 165-1) and "Field Rotational Crops" (165-2) are conditionally required under 40 CFR 158 for uses of pesticides on terrestrial food crops and aquatic food crops. As stated in Subdivision N, a rotational crop use is any field-vegetable crop use, aquatic crop use or any other site use on which it is reasonably foreseeable that any food or feed crop may be produced after application of a pesticide. The purpose of these studies is to determine the nature and amount of pesticide residue uptake into rotational crops. The confined study uses radioactive material applied to a small plot (often laboratory/greenhouse). Results of these "hot" studies are used to determine whether field studies (using non-radioactive pesticide) are needed to measure residues in rotational crops grown under actual field conditions. Based on these data appropriate crop rotation restrictions (time from application to planting of rotational crop) may be established and the need for tolerances on the rotated crops determined.

Review of these studies has been conducted by the Environmental Fate and Ground Water Branch (EFGWB) in the Environmental Fate and Effects Division (or its predecessors in earlier organizations of OPP). Presumably this assignment was based on the importance of soil residues as a factor in determining levels of residues in rotational crops.

Traditionally the confined study has served as a worst-case indicator of whether residues could occur in rotational crops. The study is often conducted indoors using potted plants, conditions which would tend to reduce the dissipation of the pesticide in the soil. Until recently, if detectable residues of concern were found in the crop during the confined study after the proposed rotational crop interval, the field trials would normally be required to assess whether residues occur in rotational crops under actual growing conditions. In some cases registrants have volunteered to perform field studies to refute results of the confined study, especially if the registrant did not want a rotational crop

interval on the label. If detectable residues were found in the field studies for crops having a 12 month plantback interval (or after a shorter interval the registrant desired on the label), the registrant would be directed to seek a tolerance under the FFD&CA. In this case, a tolerance petition was submitted and responsibility for review shifted to the Chemistry Branch in HED.

Recently, EFGWB has been using the results of the confined studies alone to determine whether tolerances are required for rotational crops. Under this revised process, EFGWB has deferred to Toxicology Branch when radioactive residues of the parent compound or closely related metabolites were found in the crops during the hot study. In other words, the field trials have been eliminated as an early step in determining the need for rotational crop tolerances. Under that procedure, if Toxicology Branch (TOX) concluded that the residues identified in the confined study were not toxicologically significant or, if they were toxicologically significant, but the levels present were not toxicologically significant, then no tolerance was required. However, if TOX concluded the opposite, the registrant was referred to the Chemistry Branches in HED.

Scientific Considerations

Confined Rotational Crop Studies: 165-1

The protocol for performing the three required confined rotational crop studies (small grain, leafy vegetable and root crop) is provided in Pesticide Assessment Guidelines Subdivision N. Acceptance Criteria were discussed in the Agency's Phase 3 Technical Guidance Document. Confined rotational crop studies are essentially metabolism studies; therefore, it is recommended that the publication entitled "Additional Guidance for Conducting Plant and Livestock Metabolism Studies" (7/16/92) be consulted before conducting a confined rotational crop study. (It should be noted that, in the case of confined rotational crop studies, the application rate is 1X, not an exaggerated rate.) . This paper will refer frequently to that document when discussing various phases of the subject experiments. A flow diagram describing the approach discussed in this paper is provided in Figure 1 at the end of this document.

The following should be considered when a confined rotational crop study is to be conducted. The test material should be the pure active ingredient radiolabeled (PAIRA) with ^{14}C in a non-labile position (e.g., in a ring). The parent compound only should be applied to the appropriate soil type (usually a sandy loam) at the maximum label rate (1X) and the required three rotated crops (small grain, leafy vegetable and root crop) should be planted at appropriate soil aging intervals (e.g, 1, 4, 7 or 9, and 12 months). Sampling of the soil is not required and need only be performed at the Registrant's discretion. The crops should be

harvested and the appropriate plant parts (see Pesticide Assessment Guidelines Subdivision O, Table II) should be sampled and combusted to determine the total radioactive residue (TRR). At this point, if each of the three crops demonstrate a TRR of <0.01 ppm in edible portions at one of the plantback or soil aging intervals then the Chemistry Branches will conclude that no further work and no tolerances are needed. An appropriate rotational crop restriction can be set at the shortest interval where no TRR is ≥0.01 ppm, provided that the Registrant is willing to place this interval on the label. If the TRR is <0.01 ppm in all three crops at the one month interval, then no plantback restriction will be needed on the label. If, however, in the three confined studies, the minimum intervals at which the TRR is <0.01 ppm differ, then the rotational crop restrictions will be set at the interval appropriate to each tested crop group with the longest interval being applied to all other (untested) rotated crops. The following example should be considered:

> The TRR for leafy vegetables is <0.01 ppm at the 1 month plantback interval, the root crop TRR is <0.01 ppm at the 4 month interval and the grain crop TRR is <0.01 ppm at the 9 month interval. The rotational crop restrictions would be 1 month for leafy vegetables, 4 months for root crops and 9 months for small grains and all other rotated crops.

It is the Registrant's prerogative to perform additional confined rotational crop studies on other crops to establish less restrictive intervals based on levels of radioactivity.

In rare cases, TOX may have concerns regarding the presence of a pesticide or metabolite at levels <0.01 ppm. Determination of the presence (or absence) of specific metabolites of concern at levels <0.01 ppm may be required in these cases.

If <u>any</u> of the plants in the confined studies exceed the trigger value (0.01 ppm) at the 12 month interval, then the nature of the residue in those test crops having a TRR >0.01 ppm must be determined. The Registrant is referred to the 7/16/92 guidance document discussed above (see also the comment regarding the application rate for confined rotational crop studies) for a description of the procedures which need to be followed to accomplish this determination. If any one of the three crops shows <0.01 ppm at a given interval but the Registrant desires a shorter interval on the label for that crop where the TRR is >0.01 ppm, then the composition of the TRR in that rotated crop (at the desired interval) should be determined as described above for the crop parts where the trigger value (i.e., 0.01 ppm) was exceeded. If several samples of the crop are available at the desired interval, the sample having the highest TRR should be utilized. In either of the above cases, this information is needed in order that

the Agency can make a conclusion as to whether the residue is an inadvertent residue of no concern or whether cold field trials are needed to make that determination.

If the metabolism in rotated crops appears to be different than that in the primary crop, that is, if different metabolites are observed in rotated crops than in primary crops, the Agency will make a determination as to whether the different rotational crop metabolites are of concern at the levels observed. If necessary, the HED Metabolism Committee will be consulted to expedite this decision.

The following are examples of the situations described above;

The primary (target) crop metabolism studies indicate that the parent and metabolites A, B, C, D and E are present in the plant. The Agency decides that only the parent and metabolite B need to be regulated in the tolerance expression. The following three scenarios might be encountered regarding rotational crops:

1) The confined rotational crop studies indicate that the TRR is >0.01 ppm and that parent and metabolites A, B, C and D are present. Limited rotational crop field trials will normally be required with analysis for parent and metabolite B if it is determined that these residues could be present at detectable levels. If, however, metabolites A, C and D are present at much higher levels in the rotational crops than in the primary crop, the HED Metabolism Committee may be consulted as to whether the other metabolites need to be quantitated.

2) The confined rotational crop studies show that the TRR is >0.01 ppm and that the radioactive residue consists of no parent and metabolites D and E. In this case the Agency would normally conclude that this is an inadvertent residue of no concern situation and no field trials would be required. A rotational crop restriction may be necessary. As above however, if metabolites D and E are present at much higher levels in the rotational crops than in the primary crop, the HED Metabolism Committee may be consulted as to whether these metabolites need to be quantitated.

3) The confined rotational crop studies indicate that the TRR is >0.01 ppm and that there is no parent present but that the major portion of the TRR consists of a new metabolite F. This will require a decision, as to whether there is toxicological concern over the new metabolite. At this point the HED Metabolism Committee may be consulted for an expedited decision. If it is concluded that the metabolite is of concern at the levels likely to be present, then F should be analyzed for in the limited rotational crop field trials. If it is decided that F is of no concern then, as in 2 above, this is an inadvertent residue of no concern situation and no field trials are necessary. However, a rotational crop restriction may be necessary.

It is recommended that the confined studies be submitted to the Agency as soon after completion as possible, so that the Agency can make a conclusion as to whether there is a potential inadvertent residue of concern (i.e., will limited field trials be needed ?) as expediently as possible. This will allow the Registrant to design the field trials in a more efficient manner (i.e., what compounds require analysis in the field trials).

Field Rotational Crop Studies (Limited and/or Extensive): 165-2

If the level of the total radioactive residue in the confined rotational crops exceeds 0.01 ppm at the desired rotational interval or at 12 months, and once the nature of the residue in the rotational crops is understood, then the Registrant should consider the Agency's position regarding the residue to be regulated in the primary crop (see discussion above) to decide whether the first tier of field trials should be initiated. That is, if the composition of the TRR in the rotational crops is such that residues which are regulated in the primary crop are observed at levels ≥0.01 ppm in the rotational crop (following the criteria set forth in the 7/16/92 document with the exception of exaggerated application rates), then field trials should be performed. For further guidance on the protocols for carrying out these trials see Pesticide Assessment Guidelines Subdivisions N and O as well as the following comments.

The limited field trials should be conducted on a representative crop (as defined in 40 CFR 180.34 (f)) at two sites per crop for the following 3 crop groups: root and tuber vegetables , leafy vegetables and cereal grains for a total of 6 trials. The 6 trials should be conducted on a specific crop in each of the three crop groups which the Registrant intends to have as a rotational crop on the label. The soil should be treated at the maximum label rate and the maximum number of applications and the appropriate crops should be planted after the minimum aging interval. The crops should be harvested and all of the plant parts prescribed in Subdivision O, Table II should be analyzed for the residues of concern observed in primary crops as well as any other residues of concern specific to rotational crops which fulfill the criteria set forth in the Confined Rotational Crop section of this paper. Detection limits for rotational crops should be comparable to those for primary crops.

If no detectable residue are observed in raw agricultural commodities in the limited field trials, then no tolerances will be needed. However plantback restrictions will normally be needed unless confined or field studies show no detectable residues of concern at a 30 day plantback interval.

If the limited field studies above indicate that detectable residues will occur, then rotational crop tolerances will be required. The requirement for number of trials would be the same as

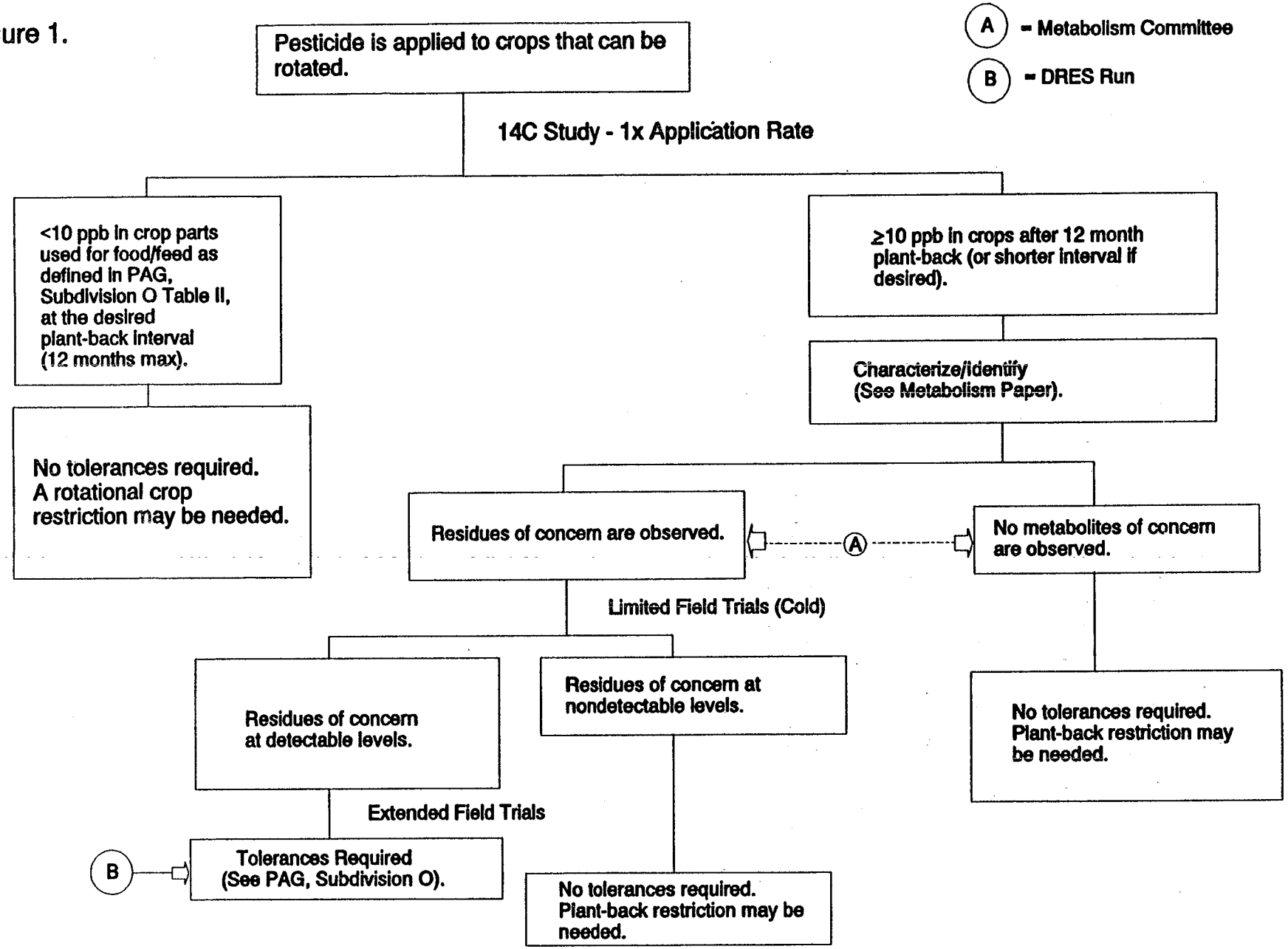
that to establish primary tolerances on all crops (or crop groups) which the Registrant intends to have as rotational crops on the label. If the Registrant desires to allow the "universe" of crops to be rotated, then magnitude of the residue data is required on representative crops (see 40 CFR 180.34 (f)) for all crop groups which could be planted in a typical crop rotation sequence. With respect to treatment, these trials should be conducted in the same manner as discussed above for the limited trials. If the Registrant believes that a lesser number of crops would be rotated because of the nature of the pesticide or due to the way it is used, then guidance should be obtained from the Agency regarding specific data requirements in that case. If tolerances exist on the crops to be rotated as a result of a primary use, then rotational data on these crops would be required only if residues in rotated crops are significant in comparison to those in the primary crop.

Regulatory Considerations

It is the Agency's position that data waivers or agreements concerning rotational crop requirements granted previously by EFGWB/EFED should continue to be effective under this new guidance and therefore HED will not reactivate rotational crop data requirements in these cases.

In the future, under revised Guidelines, the limited field rotational crop requirement may be altered so that an increased number of limited field trials will be required. This requirement will not be applied retroactively.

Figure 1.


A = Metabolism Committee
B = DRES Run
Pesticide is applied to crops that can be rotated.
14C Study - 1x Application Rate
<10 ppb in crop parts used for food/feed as defined in PAG, Subdivision O Table II, at the desired plant-back interval (12 months max).
No tolerances required. A rotational crop restriction may be needed.
≥10 ppb in crops after 12 month plant-back (or shorter interval if desired).
Characterize/identify (See Metabolism Paper).
Residues of concern are observed.
A
No metabolites of concern are observed.
Limited Field Trials (Cold)
Residues of concern at detectable levels.
Residues of concern at nondetectable levels.
No tolerances required. Plant-back restriction may be needed.
Extended Field Trials
B
Tolerances Required (See PAG, Subdivision O).
No tolerances required. Plant-back restriction may be needed.

Physical/Chemical Properties
(submitted with product chemistry data)

Solubility
171-2

Degradation Studies
(Defines abiotic and bic
rates of breakdown)

Lab Studies

Hydrolysis
161-1
R
1 YR

Photodegradation - water
161-2
R
1 YR

Photodegradation - soil
161-3
R
1 YR

Aerobic soil metabolism
162-1
2

Data generated:
1. Material balance
2. 1/2 life - parent & degradates
3. Graph of formation & decline of parent & degradates

Preliminary environmental fate assessment

(based on lab studies; gives potential routes of breakdown, routes of off-site movement, uptake in non-target organisms, and bioaccumulation; data used in screening models)

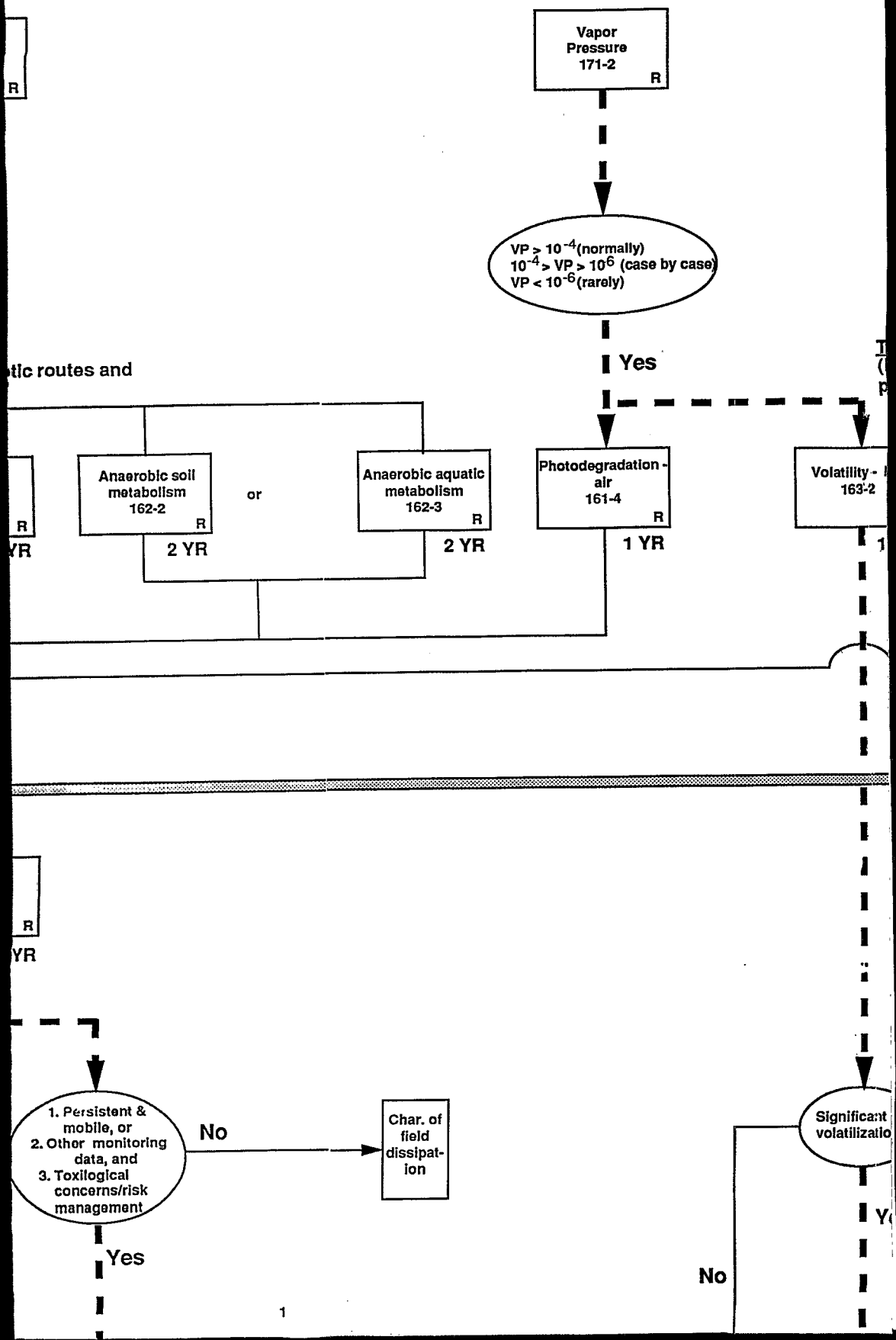
Terrestrial field dissipation
164-1
2

Data generated:
1. 1/2 life-parent & degradates
2. Decline-parent & degradates
3. Vertical leaching movement - parent & degradates

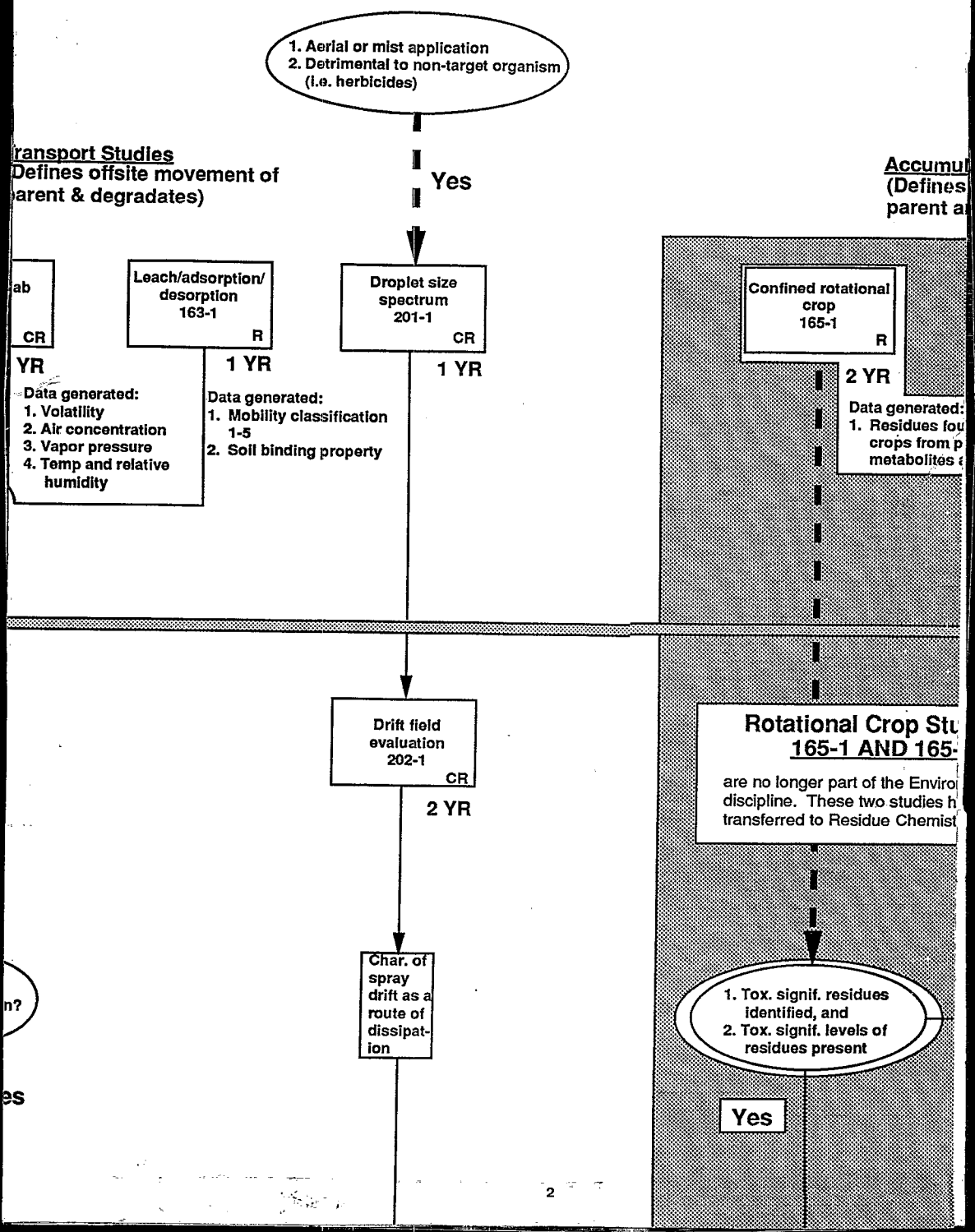
Half-life determined?

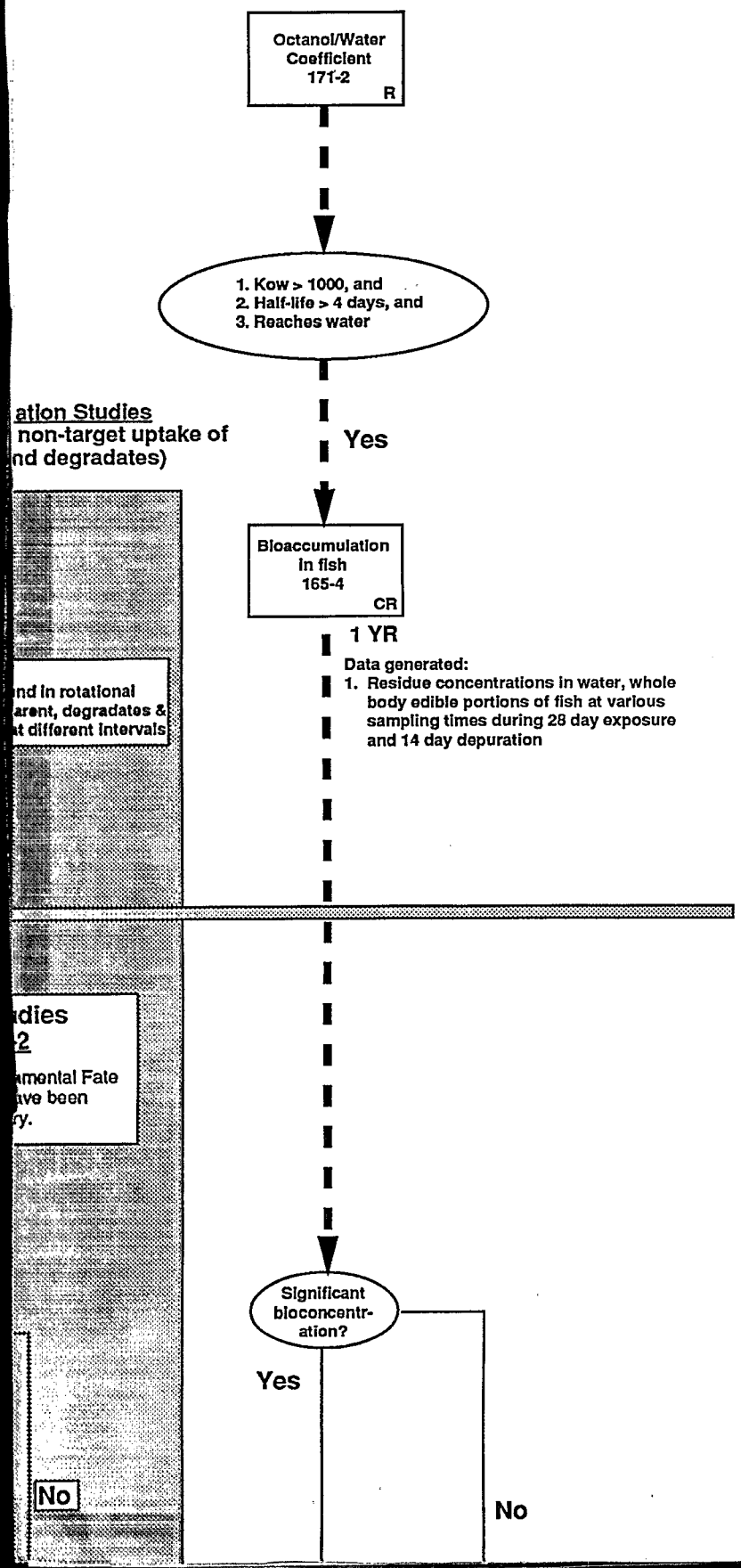
No

ENVIRONMENTAL FAT
Ch
Terrestrial Field An

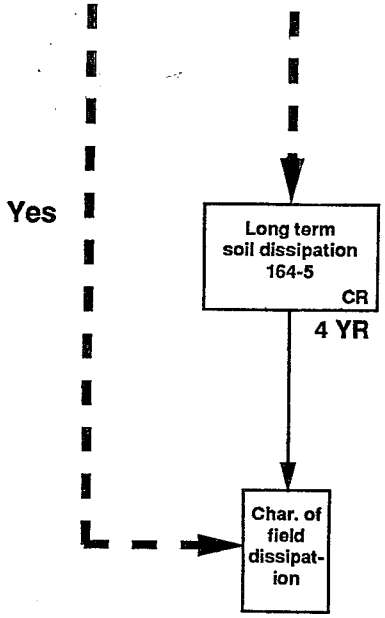


'E AND GROUND WATER
ıart 1
d Vegetable Crop Use



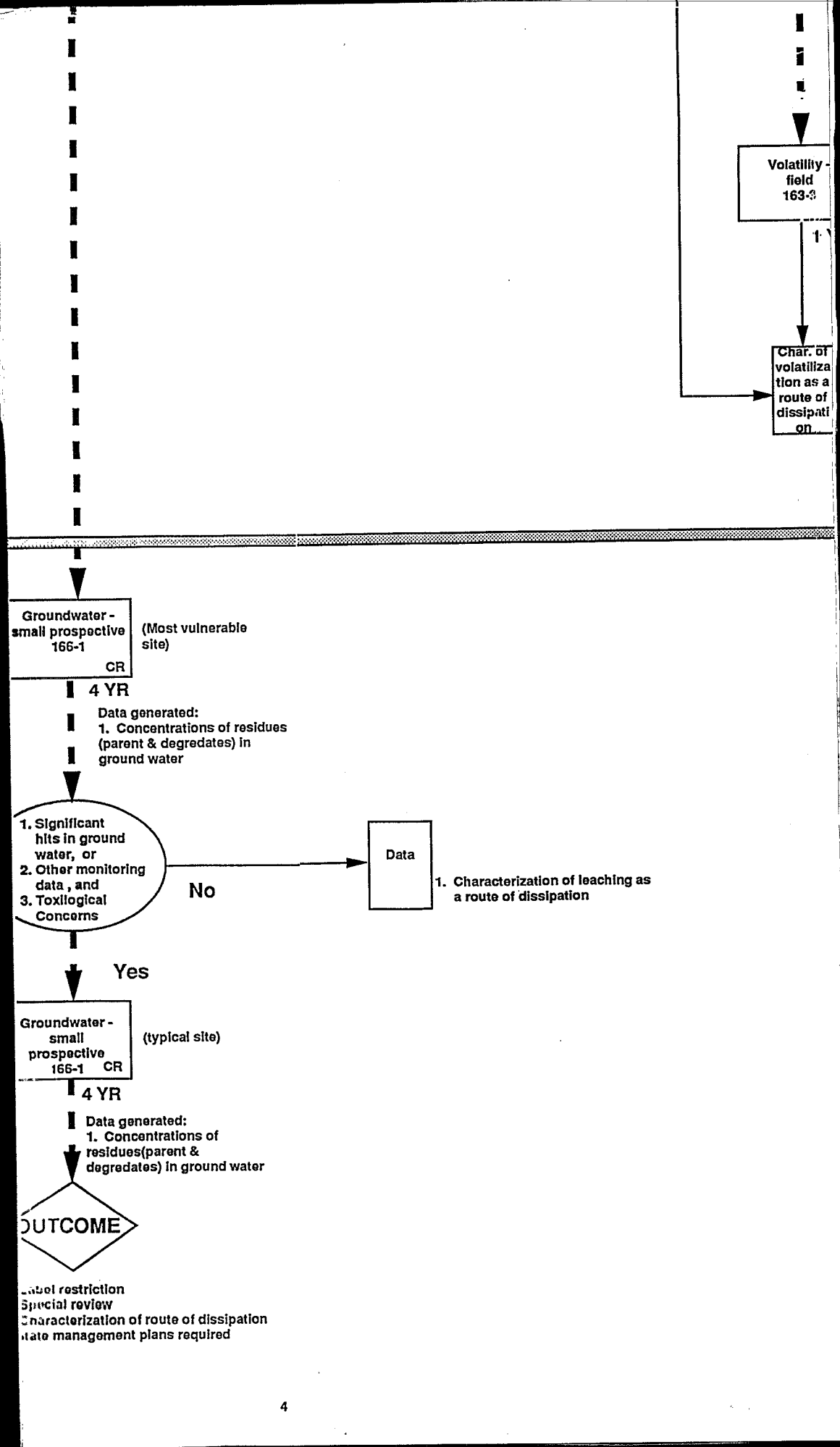

Octanol/Water
Coefficient
171-2
R
1. Kow > 1000, and
2. Half-life > 4 days, and
3. Reaches water
ation Studies
non-target uptake of
nd degradates)
Yes
Bioaccumulation
in fish
165-4
CR
1 YR
Data generated:
1. Residue concentrations in water, whole body edible portions of fish at various sampling times during 28 day exposure and 14 day depuration
nd in rotational
arent, degradates &
t different intervals
dies
2
mental Fate
ve been
y.
Significant
bioconcentr-
ation?
Yes
No
No

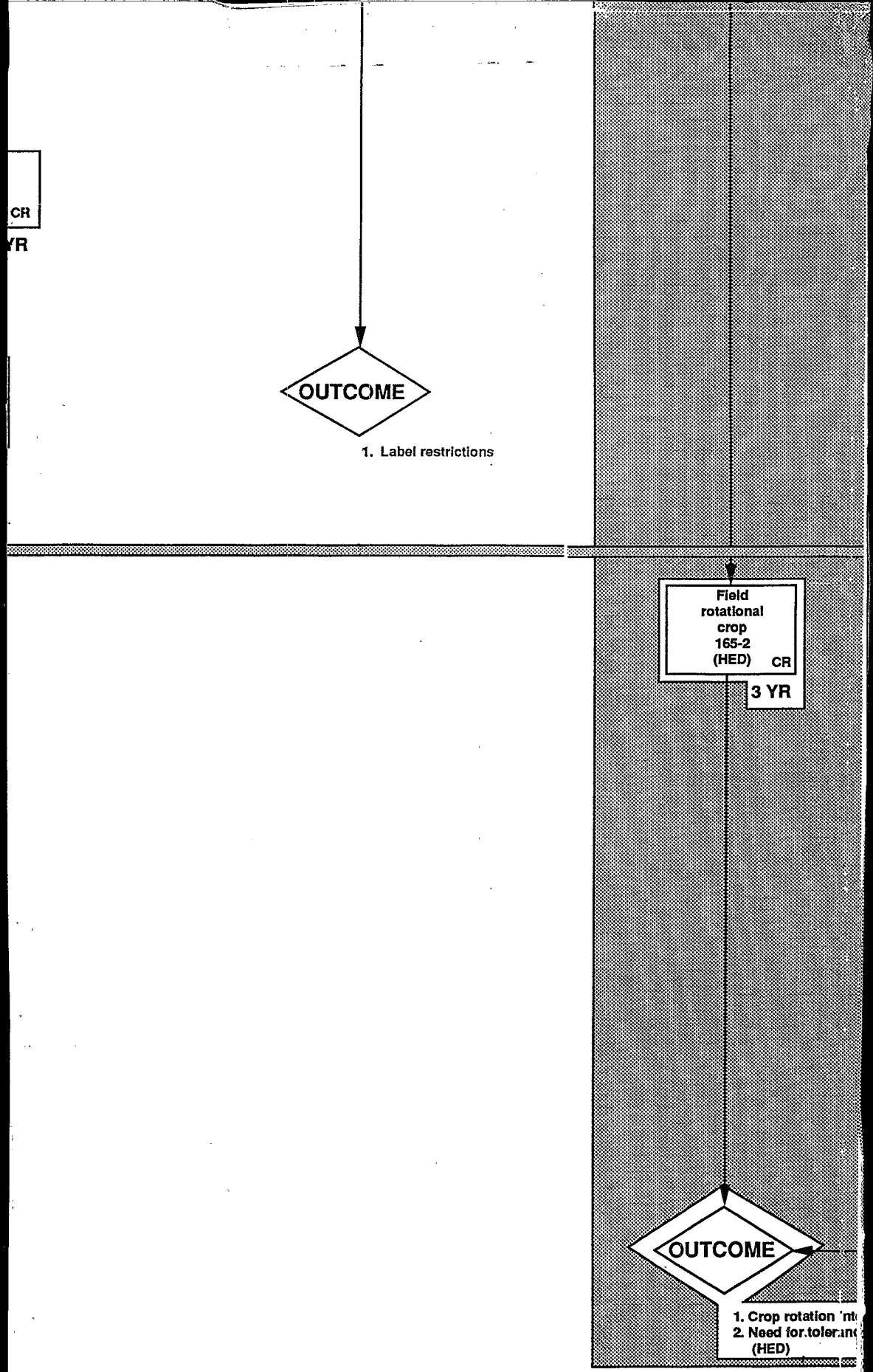
Field Studies

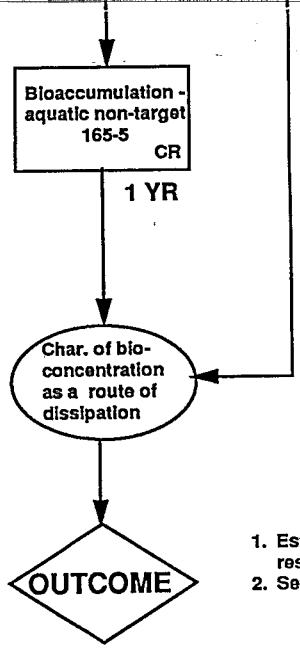


Environmental fate assessment

(based on lab and field data; gives field dissipation rates, potential to leach, runoff, volatilize, or bioaccumulate under typical field conditions for pesticide and breakdown products. The environmental fate assessment may include modeling estimates)


Volatility - field 163-3
Char. of volatiliza tion as a route of dissipati on
Groundwater - small prospective 166-1 CR
(Most vulnerable site)
4 YR
Data generated:
1. Concentrations of residues (parent & degredates) in ground water
1. Significant hits in ground water, or
2. Other monitoring data , and
3. Toxilogical Concerns
No
Data
1. Characterization of leaching as a route of dissipation
Yes
Groundwater - small prospective 166-1 CR
(typical site)
4 YR
Data generated:
1. Concentrations of residues(parent & degredates) in ground water
OUTCOME
Label restriction
Special review
Characterization of route of dissipation
State management plans required


CR
YR
OUTCOME
1. Label restrictions
Field rotational crop 165-2 (HED) CR
3 YR
OUTCOME
1. Crop rotation 'nt
2. Need for.toler.anc
(HED)



1. Establish label restrictions
2. Set action levels

rval restrictions
e on rotational crop

= Guideline study

= Information sent to Environmental Effects Branch for risk assessment

= Regulatory outcome

= Condition statement

= Sequence

= Trigger