Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency

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Endangered and Threatened Species Effects Determinations

Office of Prevention, Pesticides and Toxic Substances
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Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, Environmental Protection Agency

I. Purpose and Organization of This Document

The purpose of this document is to provide an overview of the Environmental Protection Agency's (EPA) ecological risk assessment process for the evaluation of potential risk to endangered and threatened (listed) species from exposure to pesticides. The assessments described in this document are conducted by the Office of Pesticide Programs (OPP).

Organized into eight sections and two appendices, this document begins with a description of the purpose and organization of the document (Section I). It continues with a brief overview of the statutory framework under which OPP operates (Section II), followed by a discussion of OPP's mission and organizational structure, and basic information about OPP's regulatory processes (Section III). Section III also acknowledges the importance of evaluating regulatory actions for their potential impact to listed species and briefly describes the steps being taken to ensure that listed species concerns are addressed.

Section IV provides an overview of the Environmental Fate and Effects Division (EFED), which conducts most of the initial screening-level assessments to evaluate the potential impact of pesticides on non-target species, including listed species. This section addresses EFED's procedures, data requirements, and processes to support the development of ecological assessments based on sound science.

Section V provides a comprehensive review of EFED's screening-level assessment process, which is based on risk assessment procedures outlined in guidance documents and standard evaluation procedures. If a pesticide is determined to potentially impact listed species, a species-specific assessment, which is described in Section VI, is conducted by another OPP division, the Field and External Affairs Division (FEAD).

Sections V and VI summarize the screening-level and species-specific assessments that are generally conducted in OPP. It should be noted, however, that the ecological risk assessment process within OPP may, on a case-by-case basis, incorporate additional methodologies, models, and lines of evidence that are technically appropriate for risk management objectives. Examples of additional information and methodologies include monitoring and incident data and evaluation of routes of exposure not routinely considered, but suggested by other lines of evidence.

Finally, the document concludes with a list of support documents (Section VII), references (Section VIII), and appendices.

II. Statutory Framework

A. Statutory Authority

EPA regulates pesticides under two major federal statutes: the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA), both amended by the Food Quality Protection Act (FQPA) of 1996. Under FIFRA, pesticides intended for use in the United States must be registered (licensed) by EPA before they may be sold or distributed in commerce. EPA will register a pesticide if scientific data provided by the applicant show that, when used according to labeling directions, it will not cause "unreasonable adverse effects on the environment". (FIFRA defines "unreasonable adverse effects on the environment" as "any unreasonable risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide .....") Under FFDCA, the Agency is responsible for setting tolerances (maximum permissible residue levels) for any pesticide used on human food or animal feed.

With the passage of the Food Quality Protection Act (FQPA) in 1996, both major pesticide statutes were amended to establish a more consistent, protective regulatory scheme grounded in sound science. FQPA mandated a single, health-based standard for setting tolerances for pesticides in foods; provided special protections for infants and children; expedited approval of safer pesticides; created incentives for the development and maintenance of effective crop protection tools; and required periodic re-evaluation of pesticide registrations and tolerances to ensure that the scientific data supporting pesticide registrations would remain up-to-date in the future. It should be noted that FQPA also limited the consideration of benefits when setting tolerances. FQPA did not address the consideration of ecological risk.

For this document, the focus will be on environmental risks, which are regulated under FIFRA.

B. Authority to Require Data

By law, the Agency has the authority to obtain data under three provisions of FIFRA:

- FIFRA 3(c)(1)(F) - Authorizes the Agency to require data to support an application for registration of a pesticide. OPP's data requirements are set forth in 40 *CFR* Part 158, but EPA has broad authority to ask for additional data or waive requirements, as appropriate. These data requirements are discussed under Section IV of this document.

- FIFRA 3(c)(2)(B) - Provides the authority to require additional data on currently registered products. These data must be "required to maintain in effect an existing registration of a pesticide." If EPA imposes a data requirement under this authority, EPA must allow enough time to design the study and generate data. In addition, EPA must comply with the Paperwork Reduction Act.

· FIFRA Section 6(a)(2) - Requires that pesticide registrants inform the Agency of any relevant adverse effects information relating to their products, even though it was not formally requested by EPA. Information reportable under this provision includes new information derived from scientific studies, such as efficacy failures of antimicrobial products and pest resistance. Incidents of adverse effects resulting from the use of pesticide products are also reported. The information collected under 6(a)(2) is tracked and regularly distributed to the various divisions in OPP, as appropriate. [See 40 *CFR* 15 and http://www.epa.gov/pesticides/fifra6a2/ for more information concerning EPA's published guidelines and regulations for Section 6(a)(2).]

C. Definitions and Types of Pesticides

Based on the Code of Federal Regulations (*CFR*), a pesticide is defined as:

> "Any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, or intended for use as a plant regulator, defoliant, or dessicant...." (40 *CFR* 152.3).

Substances that are not covered in this definition include, but are not limited to, deodorizers, non-toxic physical barriers against pests, fertilizers or other plant nutrient substances which do not target pest species. Some products meeting the definition of a pesticide are exempt from requirements of FIFRA, such as those for human drug use only, pesticide treated articles (clothing, paints, etc.), pheromones used in traps, food preservatives, or natural repellants such as cedar wood (40 *CFR* 152).

Based on 40 *CFR* 152.3, an active ingredient and an inert ingredient, respectively, are defined as follows:

> "Any substance (or group of structurally similar substances if specified by the Agency) that will prevent, destroy, repel or mitigate any pest, or that functions as a plant regulator, dessicant, or defoliant within the meaning of FIFRA section 2(a), except as provided in §174.3 of this chapter."

> "Any substance (or group of structurally similar substances if specified by the Agency), other than an active ingredient, which is intentionally included in a pesticide product, except as provided in §174.3 of this chapter."

Many different types of pesticides are available. They may be grouped according to the pests they control, their use pattern, or their chemical class. The following list provides some examples of the categories of pesticides that are grouped according to the pests they control:

· Insecticides - act pesticidally against the growth or survival of insects. Also includes specific types such as miticides, mosquito larvicides or adulticides;
· Herbicides - act pesticidally against plants, weeds, or grasses;

- Rodenticides - act pesticidally against rats or other rodents;
- Avicides - act pesticidally against damaging bird populations;
- Fungicides - act pesticidally against fungi on food or grain crops;
- Nematicides - act pesticidally against nematodes;
- Fumigants - gaseous pesticides used for invertebrate and fungal control;
- Antimicrobials - act pesticidally against microscopic organisms on a variety of sites;
- Plant Growth Regulators - accelerate or retard plant growth rates;
- Insect Growth Regulators - retard insect growth;
- Biopesticides - naturally occurring substances with pesticidal properties, including microbial pesticides, biochemical pesticides and plant incorporated protectants;
- Piscicides - act pesticidally against unwanted or invasive fish populations; and
- Molluscides - act pesticidally against slugs, snails, or bivalves.

Pesticides may also be categorized into the following general use patterns in order to determine registration data requirements: terrestrial, aquatic, greenhouse, forestry, domestic outdoor, and indoor (40 *CFR* 158). The terrestrial, aquatic, and greenhouse patterns are further divided into food crop and nonfood applications.

Pesticides that have similar chemical structures often have similar modes of action, as well as comparable fate and transport properties. Such chemicals may be grouped in the same chemical class. Some examples of chemical classes include the following:

- Insecticides: chloronicotinyl compounds (e.g., imidacloprid, nicotine), N-methyl carbamates (e.g., carbaryl, aldicarb), organophosphorus compounds (e.g., chlorpyrifos, diazinon), and pyrethroids (e.g., cyfluthrin, cypermethrin), and others.
- Herbicides: benzoic acids (e.g., dicamba), chloroacetanilides (e.g., alachlor, metolachlor), chlorophenoxy acids/esters (e.g., 2,4-D, MCPA), imidazolinones (e.g., imazamox, imazapyr), sulfonylureas (e.g., bensulfuron-methyl, rimsulfuron), thiocarbamates (e.g., butylate, molinate), and triazines (e.g., atrazine, simazine), and others.
- Fungicides: benzimidazoles (e.g., benomyl, thiabendazole), carboxamides (e.g., carboxin, flutolanil), and dithiocarbamates (e.g., maneb, ziram), and others.

III. Overview of the Office of Pesticide Programs

A. Mission of the Office of Pesticide Programs

EPA's overarching mission is to protect human health and to safeguard the environment – air, water, and land – upon which life depends. An important component of this goal is the protection of human health and the environment from unreasonable adverse effects resulting from the use of pesticides and to assure that pesticide residues that may occur in food are safe.

OPP's mission is both challenging and complex. OPP regulates the use of all pesticides in the United States and establishes maximum levels for pesticide residues in food, thereby safeguarding the nation's food supply. Pesticides play a role in many aspects of everyday life, from agriculture and greenhouses to lawns, swimming pools, hospitals, and food service establishments. There are about 20,000 registered pesticide product formulations, containing approximately 675 active ingredients and 1,835 other ingredients. About 470 pesticide active ingredients are used in agriculture, and EPA has established more than 9,000 tolerances (maximum allowable residue limits) for pesticides that may be present in food.

EPA's regulation of pesticides directly or indirectly affects approximately 30 major pesticide producers, another 100 smaller producers, 2,500 formulators, 29,000 distributors and other retail establishments, 40,000 commercial pest control firms, one million farms, three and a half million farm workers, several million industry and government users, and virtually all households.

B. Organizational Structure of the Office of Pesticide Programs

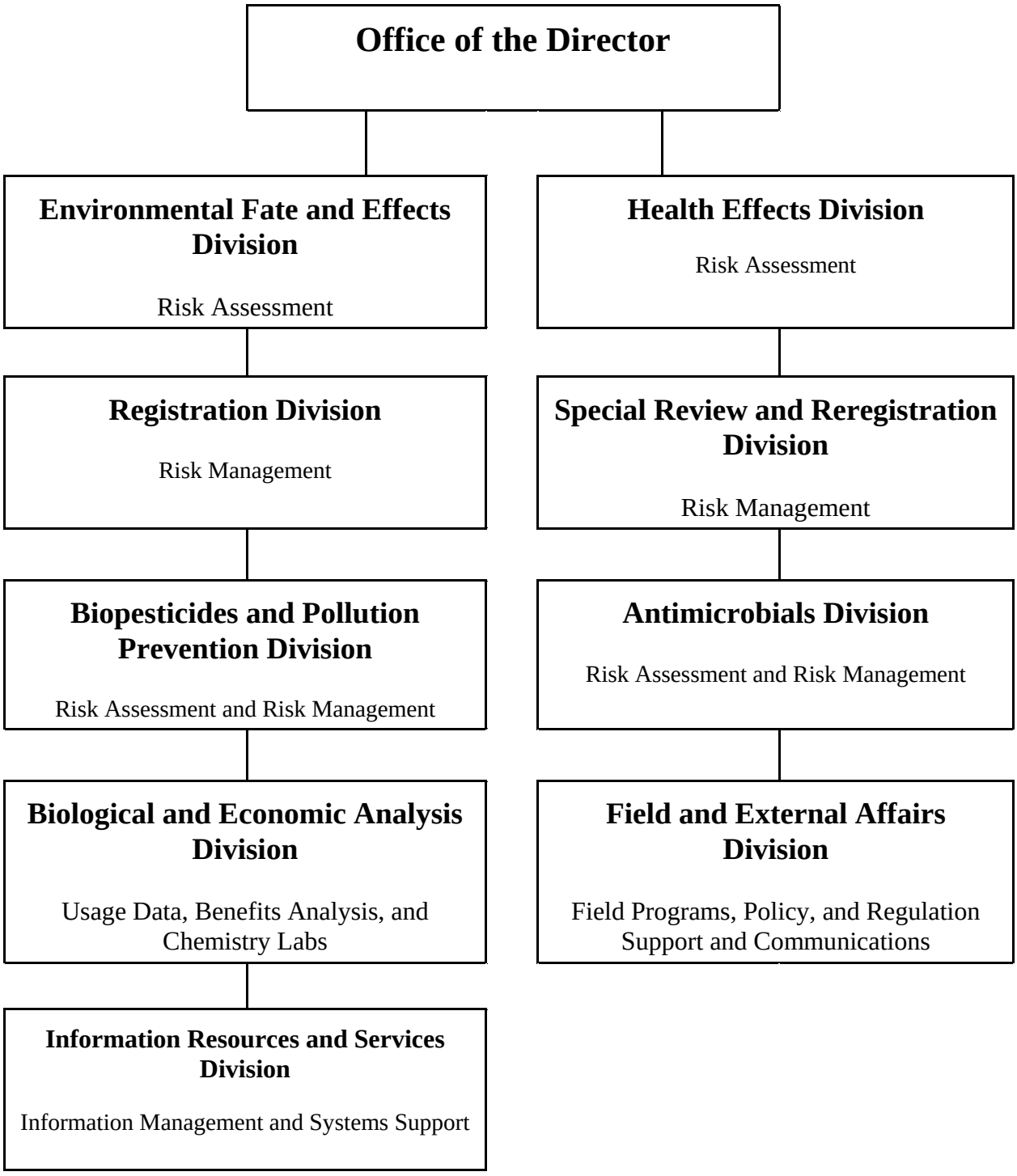
To fulfill its mission, OPP has nine divisions and the immediate office of OPP's Office Director. Approximately 800 people carry out a wide range of activities related to pesticide regulation and risk management. In addition, a large number of people in other EPA offices, including EPA's regional offices, provide administrative, legal, enforcement, and research support. Figure 1 provides a graphical representation of the organizational structure, which is described later in this section.

It should be noted that in OPP, a distinction is made between the role of the risk assessor and risk manager. Risk assessors use information and data concerning pesticide exposure and human and ecological effects to estimate the likelihood of adverse outcomes with varying pesticide use scenarios. Risk managers determine how the pesticide will be regulated. In regulating ecological effects, the regulatory decision is based on the results of the risk assessment and potential mitigation options, but may also include the integration of social considerations and economic factors (benefits information), and legal requirements. Trade-offs between different regulatory actions are evaluated, and value judgments applied to reach a decision.

Risk management addresses a variety of considerations that range from scientific to socio-economic considerations. The risk analysis focuses on providing an unbiased evaluation of risk, with assumptions and uncertainties clearly articulated. By separating the functions of the pesticide risk assessment and risk management processes, within the broader risk management framework, the integrity and transparency of the scientific analyses are maintained.

The policy regarding the interface between risk assessment and risk management grew out of a National Research Council report in 1983, referred to as the "Red Book", which emphasized the distinction between the two functions (National Research Council, 1983.) The Red Book proposed a strong separation of risk assessment and risk management, but also recognized the need and importance of continual interaction between the functions. Although the Red Book focused on human health, the policy was expanded to address ecological risk as well.

Figure 1: OPP Organizational Structure



1. Science-based Divisions

The following divisions focus primarily on conducting the risk and benefit assessments for conventional pesticides; they do not perform risk management functions. The results of the science assessments, including the ecological risk assessment for listed species, are forwarded to the risk management divisions discussed in the next section.

- Environmental Fate and Effects Division (EFED) - Conducts screening-level risk assessments to assess the ecological risk to non-target species, including the potential impact on listed species, and conducts refined ecological risk assessments. (See Section V for an overview of OPP's screening-level assessment process.) In addition, EFED evaluates drinking water exposure and sends its evaluations to the Health Effects Division to be considered in their human health risk assessments.

- Health Effects Division (HED) - Reviews data on pesticide human health effects and characterizes and assesses risks to humans and domestic animals, which are considered in risk management decisions. As part of the assessment process, HED's Metabolism Assessment Review Committee (MARC) considers whether pesticide metabolites and/or breakdown products are of toxicological concern and should be included in the dietary exposure/risk assessment and/or tolerance expression for foods and livestock feeds. In addition, a screening methodology has been developed to evaluate lower toxicity inert and active ingredients to determine that there is a reasonable certainty that no harm will result from the aggregate exposure to the pesticide residues before granting a tolerance or exemption from the requirement of a tolerance.

  HED does not participate directly in the development of an ecological risk assessment. However, HED does review acute mammalian toxicity data conducted on the active ingredient and formulations as well as two-generation reproductive toxicity tests, which are used by EFED to characterize mammalian wildlife toxicity. HED also reviews pesticide residue dissipation in food crops and animal feed items, which are used to estimate foliar dissipation half-lives for multiple application exposure modeling for wildlife. In addition, the information from the MARC (see Section V. B.2) and from the evaluation of lower toxicity inert and active ingredients (see Section V.A.2) may be useful for evaluating pesticide impacts to ecological resources.

- Biological and Economic Analysis Division (BEAD) - Assesses pesticide use and benefits information and operates analytical chemistry and antimicrobial testing laboratories.

2. Risk Management Divisions

The Registration Division and Special Review and Reregistration Division are responsible for making the final risk management decision on conventional pesticides, primarily

through the registration and reregistration processes. These divisions do not conduct risk assessments.

Both divisions consult with HED and EFED on questions related to the human and environmental risk assessments, respectively, and potential mitigation options once they have received the risk assessments and have begun to develop the regulatory decision. If necessary, a risk assessment may be conducted again at the request of the risk management division. This may be necessary because of changes made to the registration related to mitigation options, which could alter the results of the assessment.

- Registration Division (RD) - Coordinates and manages the regulatory actions involving the entry into the market place of new conventional pesticide products. These actions include the registration of new pesticide products, new uses of existing pesticide products, product and label amendments, experimental use permits, tolerances, and emergency exemptions based upon scientific evaluation of data and other considerations.

- Special Review and Reregistration Division (SRRD) - Coordinates and manages the reregistration of existing pesticides and reassessment of tolerances based upon a scientific evaluation of data and other considerations.

3. Science-based and Risk Management Divisions

In OPP, two divisions perform both risk assessment and risk management functions. It should be noted, however, that the role of risk assessor and risk manager in these divisions are never assumed by the same person.

- Antimicrobials Division (AD) - Provides full regulatory service for antimicrobial pesticides. This includes the registration and reregistration processes; conducting assessments for human health/dietary risk; residential and industrial worker exposure, environmental fate and ecological effects, drinking water exposure, product and residue chemistry, and the efficacy of public health pesticides.

- Biopesticides and Pollution Prevention Division (BPPD) - Focuses on biologically-based pesticides and measures that will reduce pesticide risks. BPPD's functions include risk and benefit assessments, risk management, tolerance reassessment, and the Pesticide Environmental Stewardship Program (PESP). PESP is a voluntary partnership between EPA and the pesticide user community to reduce risk from pesticide use in agricultural and non-agricultural settings.

4. Other Divisions

The remaining two divisions provide unique support functions for OPP.

- FEAD - Coordinates OPP's policies and regulatory development, international and field programs, such as Certification and Training, Agricultural Worker Protection Program, and others. FEAD also administers and coordinates the field implementation of the Endangered Species Protection Program and conducts species-specific risk assessments for listed species and their designated critical habitat. (See Section VI for further detail on the refined assessment process.) In addition, FEAD provides region/state/tribal coordination and assistance, legislation and Congressional interaction, and communication and outreach activities.

- Information Resources and Services Division (IRSD) - Provides information and computer support for OPP, maintains OPP's Web site and OPP databases, handles the Public Docket, and processes FIFRA section 6(a)(2) submissions.

C. Regulatory Processes

The two main regulatory processes in OPP are registration and reregistration. Registration focuses on decisions that allow new pesticide products to enter the market place or that allow registrants to make changes to the way existing pesticide products are sold, distributed, or used. While many registration decisions involve minor changes or applications for new products that are identical to currently registered pesticides, EPA devotes considerable resources to the review of applications involving new active ingredients and applications involving new uses of currently registered pesticides.

Reregistration is the review of older pesticides to ensure that they meet current health, safety, and environmental standards. The goal is to update labeling and use requirements and reduce risks associated with older pesticides, which were registered when the standards for government approval were less stringent than they are today.

1. Section 3 Registrations

Section 3 of FIFRA authorizes EPA to register new pesticide products and new uses of existing pesticide products for use in the United States. In registering pesticide products, EPA may place restrictions on the site or crop on which it is used; the method, amount, frequency, and timing of its use; and the storage and disposal practices. Some pesticides may be registered for more limited use in certain states. In addition, States, Tribes and Territories can place further restrictions on EPA-registered pesticide products used or sold within their own jurisdictions.

For a Section 3 registration action, the pesticide manufacturer submits to EPA a registration application, which includes the following information:

- Required test data;
- Information concerning the manufacturing process;
- Product chemistry;
- Human and environmental risk data packages;
- Tolerance information, consisting of information about pesticide residues on food; and
- Labeling information.

RD processes the application and tracks it. A project manager is assigned who:

- Completes a detailed review of the application;
- Assigns and coordinates the appropriate scientific review;
- Sets priorities and a timetable;
- Coordinates administrative action; and
- Communicates with the pesticide applicant or registrant concerning the review of its application.

RD assigns the scientific review to HED for an evaluation of human health risks and to EFED for evaluating environmental risks, including potential risks to listed species. HED integrates all the human health effects and exposure data into a comprehensive health risk assessment to assess the potential impact that the pesticide product or active ingredient will have on the human population. At the same time, EFED integrates scientific ecological effects and exposure information into an environmental risk assessment to assess potential impacts on the environment. Both the health and environmental risk assessments undergo a process of internal peer review by scientific experts.

RD's policy is to send forward all new chemicals submitted for a Section 3 registration to EFED and HED for a complete scientific review. For ecological risk, EFED provides an initial review and risk assessment for non-target species, including listed species. This assessment is conducted using data, which are required based on the uses of the pesticide.

Some pesticide uses, such as indoor application, are screened in RD to determine if there is a potential exposure to non-target organisms. If there is no exposure, these uses may not require environmental fate and ecotoxicity data or a full scientific review. For example, some specialized uses, such as indoor greenhouse applications, are screened to determine if there is a potential to effect non-target organisms through pesticide disposal. If not, data are not required and an ecological assessment is not conducted.

Section 3 amendment actions are screened in Registration Division to determine if there is an obvious change from the present labeled use. Those actions which indicate a change in the use are sent to the science divisions for review.

In cases where EFED's screening-level ecological risk assessment raises potential concerns related to listed species, FEAD conducts a species-specific evaluation to refine the assessment. EPA is implementing internal procedures to ensure that FEAD is routinely notified and has an opportunity to conduct its analysis if potential concerns related to listed species are identified.

After EFED and HED submit their risk assessments to the Registration Division, RD reviews the risk assessments and develops potential risk mitigation measures. RD makes a registration determination based on the statutory standards of FIFRA and FFDCA. If the application fails to meet these standards, RD notes the need for more or better data, labeling modifications, and/or use restrictions, and communicates the deficiencies to the applicant. If the application is approved, EPA will establish a tolerance if the pesticide is intended for use on food or feed and publishes a notice in the Federal Register.

2. Experimental Use Permits

Under FIFRA section 5 and the regulations (40 *CFR* 172), EPA may authorize field testing of unregistered pesticides through an experimental use permit (EUP). Generally the Agency issues EUPs for field experimentation involving 10 acres or more of land or 1 acre or more of surface water. The EUP establishes conditions for limiting the transportation,

application, and disposal of unregistered test products. The granting of an EUP also limits the sale and distribution of the test product only between approved participants in the test program, and use of the test product under conditions specified in the EUP. Pesticide companies typically request EUPs for efficacy testing and/or crop-specific residue chemistry data. Use-specific data are required to support an EUP, but are more limited in scope than for a Section 3. These data requirements (Section 112-1 in Support Document #34) along with the application procedures are described in Support Document #34. RD's policy is to send forward the core ecological and environmental fate data set if the EUP is for an outdoor use . This EFED review includes consideration of listed species.

3. Emergency Exemptions

Section 18 of FIFRA authorizes EPA to allow States and Federal agencies to apply a pesticide for an unregistered use for a limited time if EPA determines that emergency conditions exist. Most requests for emergency exemptions are made by state lead agricultural agencies, although the United States Department of Agriculture (USDA), United States Department of the Interior, and other Federal agencies also have requested exemptions. The process generally takes place as follows:

- Growers in particular regions identify a potential pest control problem situation that registered pesticides will not alleviate. The growers contact their state lead agency (usually the state department of agriculture) and request that the agency apply to EPA for a Section 18 emergency exemption for a particular use. The state agency evaluates the requests and submits its request to EPA for an emergency exemption if it believes the request is warranted. The uses are requested for a limited period of time, no longer than one year (except in the case of quarantine exemptions, which may be authorized for three years), to address the emergency situation only. To be responsive to the states and growers, EPA attempts to make decisions on the requests within 50 days of receipt of the application.

- During this 50-day time period, EPA performs a multi-disciplinary risk assessment of the requested use, relying largely on data that have already been reviewed for the pesticide. A dietary risk assessment, an occupational risk assessment, and an assessment of the emergency are conducted prior to making a decision. In addition, an ecological risk assessment, which includes listed species and non-target organisms, is also conducted. Within EFED, these assessments are given a high priority and thus conducted in an expedited basis. The procedures for these risk assessments are the same as for Section 3 registrations, but are limited to the scope of the Section 18 request. The Agency's evaluation also includes an assessment of the progress toward registration for the use in question.

Section 18 actions are screened in RD to determine if there is potential outdoor impact prior to referral to EFED for a screening-level risk assessment. For any action requiring a screening-level assessment, EFED conducts an assessment, which includes the evaluation of potential impacts to listed species. Because of statutory time restraints, these reviews require rapid turnaround and often consist of EFED simple refinements of previous assessments for similar uses and rates in the same geographic area. If preliminary concerns are determined, refined assessments are requested from FEAD

Actions that are repeated for a second year for the same use and geographic area are not referred for review. However, should they return for a third year they are again sent to EFED for review to determine if there have been any changes.

If the emergency appears valid and the risks are acceptable, EPA approves the emergency exemption request. EPA will deny an exemption request if the pesticide use may cause unreasonable adverse effects on health or the environment, or if emergency criteria are not met. As a matter of course, a state may withdraw an exemption request at any point in the process.

If a need is immediate, a state agency may issue a “crisis exemption” under which the State may use the unregistered pesticide product for up to 15 days or longer if a specific exemption is pending. The state notifies EPA of this action prior to issuing the crisis exemption, and EPA performs a cursory review of the use to ensure there are no obvious concerns. If concerns are noted, EPA confers with the state, and under extreme cases may not allow a crisis to be declared. If the state follows up the crisis with, or has already submitted, an emergency exemption request, the use may continue under the crisis exemption until EPA has made a decision on the request.

The nature of crisis exemptions precludes pre-use review of potential ecological effects, including the assessment for potential impacts to listed species. However, if the use is to continue beyond the 15-day limit that is allowed, the actions are referred to EFED for a screening-level assessment. If EFED determines there are concerns regarding listed species, the action follows the process previously outlined and FEAD conducts a species-specific assessment..

4. Special Local Need Registrations

Under Section 24(c) of FIFRA, states may register for use only in that state an additional use of a federally registered pesticide product or a new end use product to meet special local needs (SLN) as long as there is both a demonstrated "special local need," and a tolerance, exemption from a tolerance, or other clearance under FFDCA. “Special local need” means an existing or imminent pest problem within a state for which the state lead agency, based upon satisfactory supporting information, has determined that an appropriate federally registered pesticide product is not sufficiently available. EPA reviews these 24(c) requests and may approve or disapprove the state action. If the action is not disapproved, it becomes a permanent

registration under Section 3. States may not register pesticide products with new active ingredients under Section 24(c).

5. Reregistration Process

Under Section 4 of FIFRA as amended in 1988, EPA is reviewing older pesticides (those initially registered before November 1, 1984) to ensure that they meet current scientific and regulatory standards. This process, called reregistration, considers the human health and ecological effects of pesticides and results in decisions to reduce risks that are of concern. EPA also is reassessing tolerances (pesticide residue limits in food) to ensure that they meet the safety standard established by FQPA. EPA has integrated reregistration and tolerance reassessment to most effectively accomplish the goals of both programs.

Through the reregistration program, EPA is reviewing the human health and environmental effects of groups of related pesticide active ingredients. When EPA completes the reregistration review and risk management decision for a pesticide, the Agency generally issues a Reregistration Eligibility Decision (RED) document. The RED summarizes the risk assessment conclusions and outlines any risk reduction measures necessary for the continued registration of the pesticide in the U.S.

EPA may also issue an Interim Reregistration Eligibility Decision (IRED) for a pesticide that is undergoing reregistration, requires a reregistration eligibility decision, and also needs a cumulative assessment under FQPA. The IRED, issued after EPA completes the individual pesticide's aggregate risk assessment, presents an interim decision for the pesticide undergoing reregistration. It may include risk reduction measures -- for example, reducing risks to workers or eliminating uses that the registrant no longer wishes to maintain -- to gain the benefits of these changes before the final RED can be issued following the Agency's consideration of cumulative risks.

To be declared “eligible” for reregistration, pesticides must meet current scientific and regulatory standards. The pesticide must have a substantially complete database and must not cause unreasonable adverse effects to human health and the environment when used according to Agency approved labeling directions and precautions.

In addition, all pesticides with food uses must meet the safety standard of Section 408 of the FFDCA, as amended by FQPA. FFDCA as amended by FQPA also requires the reassessment of all existing tolerances and tolerance exemptions within 10 years, to ensure that they meet the safety standard of the new law.

Reducing risks is an important aspect of the reregistration program. EPA works with stakeholders including pesticide registrants, growers and other pesticide users, environmental and public health interest groups, the States, USDA and other Federal agencies, and others to develop voluntary measures or regulatory controls needed to effectively reduce risks of concern. Almost every RED includes some measures to reduce human health and/or ecological risks.

The possible ways of achieving risk reduction are extensive and include measures such as canceling pesticide products or deleting uses; declaring certain uses ineligible or not yet eligible (and then proceeding with follow-up action to cancel the uses or require additional supporting data); phasing out uses; restricting use of products to certified applicators; limiting the amount or frequency of use; improving use directions and precautions; adding more protective clothing and equipment requirements; requiring special packaging or engineering controls; requiring no-treatment buffer zones; requiring spray drift labeling; employing ground water, surface water, or other environmental and ecological safeguards; and other measures.

While assessing and mitigating human health risks is a significant aspect of the reregistration program, assessing and mitigating ecological risks also is an important part of the reregistration review process. In developing REDs and IREDs, the Agency's internal risk management process includes an evaluation of each ecological effects assessment by the ECOR Committee (Ecological Review Group) to ensure that ecological risks are fully considered and ecological risk mitigation options are fully vetted. The group consists of staff level personnel from FEAD, BEAD, RD, EFED, and SRRD. Issues related to listed species are discussed by this group and are addressed in the regulatory document that is prepared.

Specifically, SRRD has developed the following procedures to ensure high quality and consistent management of issues related to listed species during pesticide reregistration.

- History of the Chemical Relative to Listed Species - When a chemical is scheduled for reregistration, the Chemical Review Manager (CRM) conducts an analysis of the chemical file to determine if the following information is available: incidents involving listed species, earlier risk assessments indicating potential risks of concern, consultations with the Services, a Biological Opinion or other indications of concern for risks to listed species. A summary of this analysis is shared with the risk assessors and program managers in EFED and FEAD respectively and is included in the regulatory history section of the RED for the chemical.

- Summary of the Ecological Risk Assessment - When the ecological risk assessment is delivered to SRRD, the CRM carefully reviews the assessment, noting discussion of potential risks to listed species. The CRM summarizes the risk conclusions in the risk summary section of the RED. Additionally, review managers meet with risk assessors to ensure they have an accurate understanding of the risk conclusions and have appropriately summarized them in the RED.

- ECOR Review and Recommendations - For any chemical with potential risks to non-targets, including listed species, the CRM schedules a meeting with ECOR to ensure key experts in FEAD, EFED, RD, and BEAD are aware of the risk picture. Working together they develop a strategy to appropriately address risks to listed species and can initiate communications with other stakeholders as needed.

- Develop the Risk Management Decision - Through ECOR, the CRM works with experts in FEAD and EFED to develop the risk management decision and language that reflects the regulatory decision and rationale sections of the RED.

- Ensure Any Post-RED Changes Still Meet the Risk Management Goals - If, during a public comment period following publication of the RED, comments are submitted relating to risks to listed species, the CRM consults with FEAD and OGC if necessary to determine whether the comment affects listed species' risks.

  Also, if changes in the regulatory decision are indicated from comments submitted on any issue, the CRM discusses the comment(s) and alternative risk management options with FEAD and EFED to ensure that any new decision still meets the goals of the decision reflected in the RED.

6. Registration Review

FIFRA 3(g) specifies that EPA establish procedural regulations for conducting registration review and that the goal of the regulations shall be the Agency review of pesticide registrations on a 15-year cycle. An Advance Notice of Proposed Rulemaking was issued in 2000, which alerted stakeholders that EPA was beginning to develop the required procedural regulations. It explained EPA's preliminary interpretation of the authorizing legislation, presented EPA's goals in implementing the statutory provisions, presented the Agency's initial concept of how the registration review program might operate, identified several issues that needed to be addressed, and invited public comment. Since that time, OPP has continued to work on designing the program and is working on the proposed rule-making.

D. Addressing Potential Concerns Related to Listed Species

EPA acknowledges the importance of evaluating the regulatory actions described earlier for their potential to impact listed species. This evaluation may include conducting a screening-level assessment to determine if there is a potential concern. If a potential concern is identified, a species-specific assessment by FEAD may be warranted.

The assessments conducted, either at the screening or the more refined species-specific level, need to be based on a sound scientific process. This process entails using sound scientific methods, developing adequate supporting tools such as databases, and conducing adequate peer review to further strengthen the process. OPP continually works on incremental improvements to aspects of the scientific process, which are consistent with internal Agency policy and evolving Federal requirements.

For example, EFED has developed guidance to ensure consistent consideration and use of information in the open literature for ecological risk assessments of pesticide effects (Support Document #71). This guidance is for use by EFED scientists and steps to implement the

guidance have been initiated. The database that will be used to search the open literature will be EPA'S ECOTOX, a comprehensive tool for locating chemical toxicity data for aquatic life, terrestrial plants and wildlife. Relevant literature for ECOTOX is retrieved using a comprehensive search strategy designed to locate worldwide aquatic and terrestrial ecological effects literature. This database is also user-friendly, publicly-available, quality-assured and economical. (See Section V.B.2.b of this document for further information on the use of open literature data.)

EPA also recognizes that effective communication and administrative processes are needed between risk assessment and risk management divisions if a potential concern related to listed species is identified. To help EPA meets its obligations under the ESA, EPA is enhancing and will continue to improve documentation and communication of assessment results as they relate to listed species in OPP-related risk assessment and management decisions. This will be accomplished by implementing processes to ensure consistency, timeliness, and efficiency. Such documentation will extend beyond the initial screening level risk assessment efforts and will incorporate a transparent discussion of any changes to the assessment assumptions, data used for risk analyses, and the scientific, risk-based, rationale for any mitigation measures in risk management decisions related to listed and non-listed species.

IV. Overview and Organization of the Environmental Fate and Effects Division

EFED performs the following specific functions:

- Designs and reviews protocols for environmental data collection. Works cooperatively with other government or private entities to gather environmental measurement data;
- Reviews, evaluates, and validates data submitted under FIFRA or provided from other sources on the properties and effects of pesticides. Although EFED primarily reviews information on the active ingredient, data on formulations and degradates are also considered when available to the Agency;
- Assesses and characterizes ecological risk from varying pesticide scenarios in a screening-level assessment, which includes the consideration of listed species. The assessment addresses (1) fate and transport of pesticides in water, soil, and other environmental media; (2) toxicity to wildlife and vegetation; (3) exposure to non-target vegetation, aquatic life, birds, and other wildlife; and (4) effects on listed species. EFED also conducts a more refined assessment on a case-by-case basis.
- Assesses and characterizes pesticide residues in drinking water used for human consumption;
- Develops and maintains specific types of databases, such as the Ecological Incident Information System, and others; and
- Develops and advances methods and tools for environmental fate, ecological risk and drinking water assessments.

In conjunction with HED, EFED supports OPP's risk management divisions, RD and SRRD, in the overall risk assessment of pesticides. EFED also provides scientific expertise to other Agency programs and Federal agencies on the environmental fate and effects of pesticides and their exposure in various environmental media. In addition, EFED provides the underlying basis for the FEAD risk assessment (Biological Evaluation), which evaluates the potential impact on particular listed species as well as identifies where the risk criteria for listed species have been exceeded at the screening level.

EFED is composed of five Environmental Risk Branches (ERB I - V), the Immediate Office (IO), and the EFED Information Support Branch (EISB). The IO includes the Division Director and the Associate Division Director who manage the division. Staff in the IO consists of administrative support personnel, two senior scientists, and a communications officer who provide guidance and oversight on key division projects, implement the communication strategy for the division, and handle key administrative functions.

EISB supports the division in the areas of additional administrative services, filing and document storage, database development and management, contract management, and tracking chemical actions. The EISB consists of administrative support staff, contract specialists, computer experts, and scientists.

ERB-I through V are responsible for risk assessment functions described earlier. These branches are composed of biologists, statisticians, chemists, environmental engineers and scientists, agronomists, and hydrologists, predominately with Masters of Science and Doctorate degrees.

To introduce new employees to the risk assessment processes and to keep current scientists up-to-date, EFED holds training sessions and workshops. New employees are trained by providing them with documents related to the risk assessment processes, including the Support Documents provided to the Services. Formal presentations may also be held, which include topics such as an overview of OPP and the division and the ecological risk assessment process. Presentations on the assessment process may include providing an overview of the assessment process, the derivation of risk quotients, and risk assessment methodology refinements; fate and transport; spray drift; and water resources.

For longer tenured employees, workshops and training sessions are held to keep scientists up-to-date. For example, EFED held a workshop recently on aquatic exposure models used in the European Union to estimate pesticide concentrations in ground and surface water for use in risk assessments supporting pesticide registration decisions. The purpose of the workshop was to provide new information, examine a new tool that could be used to meet EFED's modeling needs, and think about how these models or a similar approach might be applied to meet modeling needs. Similar training sessions have included the use of statistics, computer software training, and other topics.

A. The Environmental Fate and Effects Division's Procedures

EFED scientists review and evaluate studies submitted in support of registration/reregistration of pesticides to determine if they are acceptable under FIFRA guidelines. This determination is based on the design and conduct of the experiment from which the data were derived, and an evaluation of whether the data submitted fulfill Agency requirements. In evaluating experimental design, the scientists consider methods generally recognized by the scientific community, the numbers of measurements made, and the use of controls in all phases of the experiment. They evaluate the conduct of each experiment in terms of whether the study was conducted in conformance with the design, good laboratory practices were observed, and results were reproducible. The scientists' review of a study is documented in a Data Evaluation Record (DER), which provides a summary review of the scientific study.

A template provides guidance for EPA scientists on how to complete a DER. Working with the Pest Management Regulatory Agency (PMRA) of Canada, EPA has developed 18 individual DER templates for the review of ecological effects and fate studies. Scientists use these templates to review and determine, on a case-by-case basis, whether each study is scientifically sound and provides sufficient information to satisfy applicable data requirements

In the DER, a study is categorized as to its usefulness in a risk assessment. While different terms have been used over the years to describe the quality and value of environmental

fate and ecological effects studies, there is consistency in the general meaning of the classifications and their application. The three general categories used for classifying scientific studies are (1) Core or Acceptable, (2) Supplemental, Upgradable, or Ancillary, and (3) Invalid or Unacceptable. (For a more detailed discussion, see Support Document #1.)

Studies are generally evaluated by contractors, who generate DERs under formats specified by EFED. The contractor DERs are reviewed by EFED staff scientists assigned to the pesticide assessment in order to finalize the data review. The branch Work Assignment Manager (WAM) oversees the contractor's performance, and QA/QC procedures are included in the contractor's statement of work. The branch WAM contacts the contractor if there are any problems with the review or if the review process needs to be changed.

After DERs for individual studies are developed, EFED scientists develop the exposure and effects characterizations and the risk characterization. These assessments are produced by an interdisciplinary team of scientists and are combined into an integrated science chapter which describes the potential impact of a pesticide on non-target organisms and the environment. Science chapters are sent to either SRRD or RD. Drinking water exposure assessments are sent to HED for incorporation into the human health risk assessments.

B. Data Requirements and Other Data Sources

As discussed previously, OPP has the authority, under FIFRA, to require data in support of the registration of a pesticide product. Accordingly, OPP has developed regulations (40 *CFR* Part 158) which specify the types and amount of information that pesticide companies must routinely submit to EPA to support the registration of pesticide products. Section 158.290 describes the environmental fate data requirements, Section 158.490 describes the wildlife and aquatic organisms data requirements, Section 158.540 describes the plant protection data requirements, and Section 158.590 describes the nontarget insect data requirements.

The data requirements are grouped according to general use pattern(s) and are listed as either required (R) or conditionally required (CR). In most cases, the data listed in Part 158 are sufficient to allow EPA to evaluate a pesticide application. In those cases where the data are not sufficient, EPA can impose additional data requirements. These data requirements may be revised from time to time to reflect statutory changes, policy changes and new technology. The current data requirements are identified in Support Document #29.

Over the course of conducting a risk assessment, the assessors may note data gaps or identify studies which do not completely satisfy the core elements for a particular requirement. In such cases, the risk assessor will evaluate whether requiring the study (or the repetition of the study when existing data are not completely satisfactory) would be likely to materially alter the conclusions of the risk assessment. This evaluation considers the nature of the use site for the pesticide, the types of effects already observed from available acceptable data, and the present conclusions of the risk assessment.

In the case of registration, risk managers are informed early on of major data gaps to provide them the opportunity to contact the applicant and obtain the data. For reregistration, risk managers hold a meeting with pesticide registrants early in the process to provide them the opportunity to identify the uses they will support. This meeting provides the risk assessor the opportunity to identify any major data gaps based on an overview of the available data.

If some data are available, then the assessment can be conducted and uncertainties and assumptions can be identified. If the assessor concludes that an additional study will not likely alter the present conclusions of the risk assessment, they would indicate the data deficiency to the risk manager and recommend that the study be held in reserve for reconsideration of its necessity, should future registrations be considered for the pesticide. The term "reserve" is used in its literal sense as meaning something set aside for a special purpose. Should a new use scenario in the future be considered for registration that would likely render the missing information critical to completion of a new risk assessment, then the data requirement could be reconsidered by the risk managers.

If a risk assessor concludes that a particular study has the potential to alter the conclusions of the risk assessment, and the risk manager believes that such potential creates an uncertainty regarding the confidence in making a regulatory decision, an interim decision may be made by the risk manager to grant a registration on the condition of the completion of an acceptable study.

Other data sources, such as open literature, can also be used in developing the risk assessment. Since this information is typically not collected using the EPA's test guidelines, it is normally considered supplemental information.

C. Processes to Support Sound Science

Sound scientific assessments are essential and serve as the foundation for regulatory decision-making in OPP. In order to advance the quality and consistency of EPA's ecological risk assessments, the Agency developed guidance for improving the ecological assessment process, risk characterization, and peer review process. EFED follows the Agency guidance and has also developed associated and complementary processes for promoting sound scientific assessments specific to pesticide regulatory decision-making.

1. Agency Guidance

a. Guidelines for Ecological Risk Assessments

The Agency's Guidelines for Ecological Risk Assessments (Agency Guidelines, Support Document #7) were issued to advance the quality and consistency of EPA's ecological risk assessments. As a next step in a continuing process of ecological risk guidance development, the guidelines draw from a wide range of source documents including peer-reviewed issue papers and case studies previously developed by EPA's Risk Assessment Forum. EFED has been and

will be continuing to advance its assessment processes, using the Agency Guidelines. This includes advancements to all three phases of the assessment process, including problem formulation, analysis, and risk characterization.

b. Risk Characterization Handbook

The Risk Characterization Handbook (Support Document #28) states the Agency's risk characterization policy. It provides a single, centralized body of risk characterization implementation guidance for Agency risk assessors and risk managers and calls for a transparent process and products that are clear, consistent, and reasonable.

The Handbook includes two parts. The first is the risk characterization guide, which describes the goals and principles of risk characterization, the importance of planning and scoping for a risk assessment, the essential elements to address in a risk characterization, the factors considered in decision-making by risk managers, and the forms the risk characterization takes for different audiences. The second part consists of appendices which contain the Agency's Risk Characterization Policy and case studies.

c. Peer Review Handbook

The Agency's Peer Review Handbook (Support Document #30) was issued in 1998 as a single, centralized form of implementation guidance for Agency staff and manager. This Handbook builds on an active tradition of peer review at EPA and reflects the Agency's long-standing commitment to peer review.

EFED has actively participated in the peer review process, which is discussed in more detail later in this Section (IV.C.3). The Handbook has served as an important guide and has helped to ensure that OPP decisions regarding ecological risk are fully supported by sound and credible science.

2. Tools to Promote Sound Science

EFED uses a variety of tools to ensure that the work performed meets the necessary level of quality and includes, but is not limited to, the following elements: Pesticide Assessment Guidelines, Standard Evaluation Procedures, the development and expansion of scientific databases, and Technology Teams.

a. Pesticide Assessment Guidelines

EFED has developed Pesticide Assessment Guidelines which provide the performance requirements and testing and reporting procedures for data required (Support Document #29) in support of registration/reregistration of a pesticide. The guidelines describe what data are required, test standards that should be considered in conducting the studies, specific reporting guidance for the tests, and examples of acceptable protocols, references and other aides to help

with planning and conducting the tests. They include Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms; Subdivision J, Hazard Evaluation: Non-target Plants; Subdivision L, Hazard Evaluation: Nontarget Insects; and Subdivision N, Chemistry: Environmental Fate (Support Documents #2, #3, #4, #5, respectively.)

b. Standard Evaluation Procedures

EFED has developed Standard Evaluation Procedures (SEPs) or guidance documents (Support Documents #8, #34 - #63) for each type of environmental test that is generally required to support the registration/reregistration of pesticides. EFED has also developed SEPs which describe the Agency's pesticide ecological risk assessment methods. These documents, which have been designed to ensure comprehensive and consistent scientific review of data, explain the scientific procedures used by EFED to evaluate environmental fate and effects data submitted to OPP. Revisions to the SEPs or proposals for new SEPs are discussed and developed within the six EFED Technology Teams, followed by review and approval by the Science Policy Panel. After internal approval by the Science Policy Panel and division management, the SEPs are reviewed by an external science peer review group, such as the Scientific Advisory Panel. (The Technology Teams, Science Policy Panel and Scientific Advisory Panel are discussed in more detail later in this Section [IV.C.2.d, IV.C.3.c, and IV.C.4, respectively)

c. Databases

EFED continues to develop, advance, and expand its databases and information systems to support a sound scientific process. These include the Ecotoxicity Database, Ecological Incident Information System, and Environmental Fate Database along with databases that address ground and surface water. In addition, EFED also uses EPA'S ECOTOX, a comprehensive tool for locating chemical toxicity data for aquatic life, terrestrial plants and wildlife. (See Section V.B.2.b. for further discussion.)

· OPP's Ecotoxicity Database - Over the last 30 years, pesticide manufacturers have submitted thousands of ecotoxicity studies to support the registration or reregistration of their pesticide products. Ecotoxicity studies measure the effects of chemicals on fish, wildlife, plants, and other wild organisms. EFED reviewed these studies according to criteria outlined in the Standard Evaluation Procedure Manuals and testing methods accepted by the scientific community. After reviewing these studies, EFED scientists determined if they were acceptable for use in the regulatory process. These data are used, along with consideration of other publically available effects data, in establishing the effects endpoints for screening-level risk assessments. (See Section V.B.2.b.)

  In 1991, EFED began electronically summarizing acceptable studies and has now entered over 15,000 summary records for about 680 pesticide active ingredients into a computerized database called the Pesticide Ecotoxicity Database. These summary records include endpoint measurements such as the LD50 (the amount or dose of a chemical which kills 50% of the exposed animals) and the NOEL or No Observed Effect

Level (the highest concentration of a chemical in a toxicity test that has no significant adverse effect on the exposed population of test animals). Although most of the toxicity information in this database was compiled from studies conducted by commercial laboratories, the database also contains acceptable studies, which meet the Agency's testing requirements, conducted by EPA; U.S. Department of Agriculture; and the U.S. Geological Survey (the former U.S. Fish and Wildlife Service). Further information is also available in Support Document #32.

· Ecological Incident Information System - In 1992, the Agency created a database called The Ecological Incident Information System (EIIS) to store information extracted from incident reports. (Documentation is provided in Support Document #22.) The two primary sources of incident reports are pesticide registrants and government agencies. Under Section 6(a)(2) of FIFRA, pesticide manufacturers are required to report to EPA any information related to known adverse effects to the environment caused by their registered pesticides.

The second major source of information is investigative reports which are voluntarily submitted to the Agency from state and other federal agencies that oversee agriculture, wildlife, natural resources, and environmental quality. Diagnostic reports are also obtained from the National Wildlife Health Institute (U.S. Geological Survey), the Patuxent Wildlife Research Center (U.S. Geological Survey), the Southwest Wildlife Cooperative Disease Study, and state wildlife forensic laboratories. In addition, information is also extracted from accounts of ecological incidents reported in newspapers and reliable internet sources.

Information included in EIIS includes the date and location of the incident, the type of adverse effects observed, the number of animals affected by species, and the identity of the pesticide or pesticides to which the incident was attributed. When available, further details may be entered about the rate and method of pesticide applications, legality of the pesticide use, weather conditions, and results of any chemical residue and cholinesterase activity analyses conducted during the incident investigation. Often insufficient information is available to confirm the cause of incidents with certainty. For each pesticide identified in the incident report, an EPA employee assigns a certainty index value to reflect the level of certainty that the specific pesticide caused the observed effects. The certainty index is set to *highly probable*, *probable*, *possible*, *unlikely*, or *unrelated* based on results of residue analysis and other evidence of cause. The certainty index is always reported along with the other incident data and should be carefully considered when interpreting incidents.

· Environmental Fate Database - OPP collects and reviews a variety of environmental fate studies submitted by pesticide manufacturers in support of the registration and reregistration review of pesticide products. After reviewing the data in these studies, OPP scientists summarize the information in DERs, REDs, and other reports.

In 2000, OPP initiated the development of a pesticide environmental fate database which will allow the user to search and view the data, query the fate database, and print reports that are found in these summary reports. OPP plans to complete the initial version of this database by the end of 2004.

d. Technology Teams

EFED has six Technology Teams (Tech Teams), which are organized by scientific disciplines and meet on a regular basis to promote sound science and work on technical issues within the Division. They include the Fate and Transport Team, Aquatic Biology Team, Plant Biology Team, Terrestrial Exposure Assessment Team, and Water Quality and Exposure Assessment Team. The purpose of these teams is to:

- Facilitate scientific consistency within disciplines, which includes consistency in data review, use of data in assessments, application of statistics and modeling, and use of assessment processes and tools;
- Provide a forum to keep up with scientific advances and to facilitate interaction between scientists with similar background or common scientific interest;
- Resolution of technical issues, resulting in new scientific guidance and procedures; and
- Provide a resource of information and guidance for scientific issues and new ideas.

Once a technical issue has been resolved, a policy is in place which outlines the basic steps for reviewing and approving new science guidance and procedures (Support Document #64). The length of time for implementation will vary, depending on the issues raised and whether external peer review is needed. However, provisions have been made to implement guidance and procedures which need an expedited review and approval. It should be noted that special project teams are also required to use the same procedures.

3. Internal Peer Review Mechanisms

a. Data Evaluation Records

All DERs are peer reviewed internally at the branch level by another EFED scientist with the appropriate expertise. After the branch-level peer reviewer approves and finalizes the DER, copies are sent to the EFED Tracking Team who forwards it to the appropriate risk management division.

b. Risk Assessments and Risk Characterizations

All risk assessments and risk characterizations are reviewed within a task team consisting of scientists from different disciplines. After the team reviews these documents, they are peer reviewed within the branch or in another EFED branch by a scientist with appropriate expertise.

Following branch-level review, divisional peer review is conducted by the Risk Assessment and Risk Characterization Review Panel (Review Panel) which consists of interdisciplinary scientists who peer review all major risk assessments and risk characterizations for new chemicals and for reregistration actions. This Panel is an important internal peer review mechanism and is composed of senior scientists in the division. In addition, FEAD scientists participate and provide technical comments on the assessment process in general and as it relates to listed species. After panel members have reviewed a specific risk assessment, they meet with scientists, provide feedback, and ask questions concerning the assessment.

c. Science Policy Panel

The Science Policy Panel is comprised of five experienced, highly qualified experts in the environmental and ecological risk assessment of pesticides. They are responsible for providing assistance to Tech Teams in policy problem formulation, review of proposed science policies for consistency and quality, and in developing implementation and communication plans for new policies. They are also responsible for participating in the EFED budget process and making recommendations regarding new projects and establishing priorities.

4. External Peer Review and Scientific Advisory Panel

All significant new science guidance and procedures as well as tools and methodologies are reviewed by the FIFRA Scientific Advisory Panel (SAP), EPA's peer review body for current scientific issues related to pesticides. It is comprised of nationally and internationally recognized scientific experts in toxicology, pathology, environmental biology, and related sciences; and members are appointed by the Administrator.

For example, the FIFRA SAP has peer reviewed the new tools and methodologies OPP has been developing in its initiative to refine the ecological assessment process for pesticides. This initiative, which began in 1997, was in response to recommendations from a meeting with the SAP in 1996 and built upon previous efforts in the Division. Throughout the development of this initiative, OPP has returned to the SAP several times to seek comments and recommendations on the progress being made. In some cases, EFED has sought guidance from the SAP on problematic issues and questions before proceeding further. Input from the SAP early in the development of tools and methods is critical to their successful implementation in the risk assessment process.

V. Overview of OPP's Screening-Level Ecological Risk Assessment Process for Aquatic Life, Wildlife, and Plants

This section provides an overview of the screening-level assessment process to evaluate the potential impact of pesticides on non-target organisms. (Section VI provides an overview of the species-specific assessment.) As previously mentioned, this process is consistent with the Agency's Guidelines for Ecological Risk Assessment (Support Document #7). Although this section reviews the general assessment process for screening-level assessments, this assessment process may, on a case-by-case basis, incorporate additional methods, models and lines of evidence that EPA finds technically appropriate for specific risk management objectives.

The majority of screening-level assessments are conducted in EFED for conventional pesticides. However, some screening-level assessments are also conducted in AD and BPPD for non-conventional pesticides. The ecological assessments conducted by AD and the microbial assessments conducted by BPPD are largely based on the process described in this section. However, BPPD also conducts assessments for biochemicals, which, because of their unique nature, do not typically follow the same procedures and are more qualitative in nature. The assessment processes conducted by AD and BPPD are described in Appendices A and B, respectively.

A. Problem Formulation

Before the risk assessment process begins, risk assessors and risk managers discuss (1) the potential value of conducting a risk assessment, (2) goals for ecological resources, (3) range of management options, (4) objectives of the risk assessment, (5) the focus, scope and timing of the assessment, and (5) resource availability. The characteristics of an ecological risk assessment are directly determined by agreements reached by risk managers and risk assessors during early planning meetings. In addition to discussions between risk assessors and risk managers, information provided by the pesticide registrants is also taken into consideration when developing the problem formulation. It should be noted that the problem formulation will document, when necessary, any aspects of the analysis that extend beyond the initial screening level risk assessment efforts. The problem formulation will allow for an analysis of any changes in risk estimates based on different assessment assumptions, including those that may be related to proposed mitigation options, and data used for risk analyses.

1. Defining the Regulatory Action

Prior to initiation of the risk assessment process, risk managers communicate the nature of the regulatory action to the risk assessors. For risk assessment activities supporting REDs, these communications are initiated with personnel from SRRD. For regulatory actions involving new pesticide active ingredients or new uses of active ingredients with existing registrations (FIFRA Section 3 actions), emergency exemptions (FIFRA Section 18 actions), and special local needs uses (FIFRA Section 24c actions), the regulatory communications are initiated with personnel from RD.

During this problem formulation phase, risk assessors and risk managers consider the following questions:

- What is the regulatory basis for the requested action under FIFRA? How does this action affect the temporal and geographic scope of the impact area of the risk assessment?
- What are the management goals and regulatory issues? How will the risk assessment clarify decisions concerning risk management options?
- Are there any policy considerations that everyone should be aware of?
- What precedents are set by similar risk assessments and previous decisions?

2. The Nature of the Chemical Stressor Considered in the Risk Assessment

The Agency routinely incorporates measures of exposure and effects for the pesticide active ingredient in the risk assessment process for all regulatory decisions. Additionally, EPA examines available formulated product information, environmental fate data, and toxicological data to determine the need to expand beyond the focus on the active ingredient to consider pesticide formulations, inert ingredients, or degradates of the active ingredient in a particular risk assessment to support registration of a specific pesticide product. Available formulated product information, environmental fate data, and toxicological data may come from a number of sources. These include section 6(a)(2) data, open literature data retrieved through ECOTOX (see Section V.B.2.b), and direct submissions in support of registration. The methods for incorporating environmental fate and effects data for formulations and active ingredient degradates into the risk assessment processes are described in Section V.B. 1 and 2, in which exposure and effects are discussed.

The Agency is currently developing procedures for assessing toxicity and risks associated with inert ingredients and surfactants in formulations (See Support Document #24) and will perform either qualitative or quantitative assessments of potential risk associated with these chemicals. The decision to perform either type of assessment is based on available information on the chemical characteristics of the inert ingredient and any information on the inert ingredient's toxicological characteristics. Information on an inert ingredient's toxicological characteristics may include available ecological effects information from the literature, or information on closely related chemical analogues and quantitative structure-activity relationships. Use of structural analogy or structure activity models is consistent with techniques employed in other Agency programs (e.g., the approach used by OPPT in evaluating new chemicals in commerce through the Premanufacturing Notification process). This information is used to determine if inert ingredients can be classified as (1) generally recognized as safe, (2) available data are insufficient to confirm little or no toxicity and would require additional study, or (3) there is sufficient toxicological and exposure concern to warrant a quantitative risk assessment similar to those conducted for active ingredients.

It is important to note that existing and vetted quantitative structure-activity relationships have focused on industrial chemicals, the types of compounds commonly found as inert

ingredients and surfactants in pesticide formulations. Establishing these relationships has been facilitated by the non-specific modes of toxic action of these compounds and are typically based on simple correlations between their acute potency to aquatic organisms as measured by lethality (e.g., LC50 values) and basic physical/chemical properties of the compounds. Application of quantitative structure activity relationships developed for industrial chemicals to predict effects for pesticide active ingredients is not scientifically defensible due to their different, and highly specific, modes of toxic action for these active ingredients when compared to industrial, organic chemicals.

The Agency does not routinely include, in its screening risk assessments, an evaluation of mixtures of active ingredients, either those mixtures of multiple active ingredients in product formulations or those in the applicator's tank. In the case of the product formulations of active ingredients, each active ingredient is subject to an individual risk assessment for regulatory decision regarding the active ingredient on a particular use site. If effects data are available for a formulated product, it is documented in the risk assessment and the quantitative or qualitative use of such formulation information follows procedures outlined in the discussion on exposure and effects characterization.

In accordance with risk assessment guidance, the Agency documents the scope of the chemical stressors considered in the risk assessment, the rationale for their consideration, the methods used to evaluate the attendant risks, and their contribution to the overall conclusions of the risk assessment.

3. Pesticide Use Characterization

For each regulatory action, product labeling provides information on the proposed and/or existing uses of the pesticide product. The pesticide labeling is the legal document that provides the user with instructions for use, use restrictions, and hazard statements (see Support Documents #67 and #68). Risk assessors use the information on the product labeling to define the nature of the pesticide use in the field. Use factors on the labeling are important for determining input parameters for exposure models and the magnitude of exposure to non-target organisms, including geographic locations most likely to be exposed. Labeling information crucial to ecological assessments include:

- Type of formulation, such as bait, granule, wettable powder, emulsifiable concentrate, etc.;
- Product purity, which is the proportion of that product that is the pesticide active ingredient;
- Proposed and/or existing application rates;
- Treated crop(s) and, if specified, target pest(s);
- Geographic limitations of use, if any;
- Application methods, such as aerial, ground, foliar, soil surface, soil incorporated, etc.;
- Application timing, such as season and time of day;

- Frequency of application, application intervals, and maximum number of applications per season; and
- Hazard advisory statements: protective measure for wildlife/aquatic habitats, groundwater, etc.

In addition to the information on the label, scientists consult with BEAD and the registrant for information on the following topics:

- Nature of the target pests,
- Geographical distribution of the pests, crop, and market of the pesticide,
- Temporal pattern of the pesticide's use, and
- Any unique aspects of the use of the pesticide under field conditions.

The characterization of pesticide use allows the risk assessors and risk managers to focus the risk assessment on specific use patterns that are representative of a larger variety of use patterns. Such groupings may consider the types of agricultural scenarios, the methods for pesticide application, and commonality of applications rates and timing. In this way, modeling and assessment resources can be concentrated on scenarios that reasonably represent the highest exposures among a suite of use scenarios.

4. Identification of Assessment Endpoints

The Agency Guidelines define assessment endpoints as "explicit expressions of the actual environmental value that is to be protected" which are "operationally defined by an ecological entity and its attributes" (Support Document #7). The ecological entity can be a species, a functional group of species, a community, an ecosystem, or another entity of importance or concern. An attribute is the characteristic of the entity that is important to protect and is potentially at risk.

The selection of clearly defined assessment endpoints is important because they provide direction and boundaries in the risk assessment for addressing risk management issues of concern. Each assessment endpoint needs one or more "measures of effect," which are changes in the attributes of an assessment endpoint itself or changes in a surrogate entity or attribute in response to exposure to a pesticide.

a. Direct Effects

The typical assessment endpoints for screening-level pesticide ecological risk assessments are reduced survival and reproductive impairment for both aquatic and terrestrial animal species from both direct acute and direct chronic exposures. These assessment endpoints, while measured at the individual level, provide insight about risks at higher levels of biological organization (e.g., populations). Hallam and Lassiter (1994) assert that toxicants do not affect populations or communities except through the impact on the individuals comprising the population or community and the demographics of birth, growth, and death that govern population dynamics. Similarly, Tanner (1978) indicates that the number of individuals within a population change (intrinsic rate of increase) primarily because of births (fecundity) and deaths (survival) and secondarily from migration in and out of a specific area. Investigations by Hakoyama et al. (2000) concerning risk factors of wildlife population extinctions suggest that toxicant effects on individual survivorship have important implications for both population rates of increase and habitat carrying capacity. If effects on the survival and reproduction of individuals are limited, it is assumed that risks at the population level from such effects will be of minor consequence. However, as the risk of reductions in survival and/or reproduction rates increase, the greater the potential risk to populations.

For terrestrial plants, the screening assessments are concerned with perpetuation of populations of non-target species (crops and non-crop plant species). Existing testing requirements have the capacity to evaluate emergence of seedlings as well as vegetative vigor. Although it is recognized that the endpoints of seedling emergence and vegetative vigor may not address all terrestrial plant life cycle components, it is assumed that impacts at emergence and in the active growth stages have the potential to impact individual competitive ability and reproductive success.

For aquatic plants, the assessment is concerned with the maintenance and growth of standing crop or biomass. Measurement endpoints for this assessment focus on algal growth rates and biomass measurements as well as similar measurements for vascular plants.

b. Indirect Effects for Listed Species

Screening-level assessments of indirect effects for listed species are discussed in Sections B.2.c and C.4 of this chapter. Species-specific assessments for indirect effects on listed species are developed, when required, after the screening-level evaluation is completed. (See Section VI for further discussion.)

c. Effects on Listed Species Critical Habitat

Screening-level assessments of effects upon critical habitat for listed species are discussed in Sections B.2.d and C.5 of this chapter. Species-specific assessments for critical habitat of listed species are developed, when required, after the screening-level evaluation is completed. (See Chapter VI for further discussion.)

5. Measures of Effects and Exposure: The Use of Surrogate Organisms

Rarely are toxicity data available for the species identified in the risk assessment endpoints. In the majority of cases, the screening-level risk assessment process relies on a suite of toxicity studies performed on a limited number of organisms in the following broad groupings:

- Birds (mallard duck and bobwhite quail) used as surrogate for terrestrial-phase amphibians and reptiles,
- Mammals (laboratory rat),
- Freshwater fish (bluegill sunfish, rainbow trout, and fathead minnow) used as a surrogate for aquatic phase amphibians,
- Freshwater invertebrates (*Daphnia magna*),
- Estuarine/marine fish (sheepshead minnow),
- Estuarine/marine invertebrates (*Crassostrea virginica* and *Mysidopsis bahia*),
- Terrestrial plants (corn, soybean, carrot (radish or sugar beet), oat (wheat or ryegrass), tomato, onion, cabbage (cauliflower or brussels sprout), lettuce, cucumber), and
- Algae and aquatic plants (*Lemna gibba, Skeletonema costatum, Anabaena flos-aquae, Selenastrum capricornutum, Clorell vulgaris, Scenedesmus subspicatus*)

Within each of these very broad taxonomic groups, an acute and a chronic endpoint are selected from the available test data. The selection is made from the most sensitive species tested within that organism group. If additional toxicity data for more species of organisms in a particular group are available, the selection need not be limited to the species listed above, but may be expanded to include data for other species/studies that meet the data quality classification of "supplemental." (See Support Document #1 for discussion of the data classification scheme.) Available scientific information from alternate sources (e.g. searches conducted using the

ECOTOX database described in Section V.B.2.b.1) is also examined for species within a taxonomic group for which other taxa are typically used as surrogates. For example, fish data are commonly used to evaluate impacts to amphibians. But, if toxicity data are available in the open literature on amphibians, these data may be used instead of the data on the surrogate species. In situations where such additional data are available, decisions are made regarding the quality and utility of such information in the risk assessment (e.g., a review of the validity and reliability of study protocols), which is consistent with the Agency's risk assessment guidance. The extent to which such additional data are either employed or rejected is described through a transparent, concise discussion. Regardless of the extent of data beyond the regulation-required set of toxicity studies, the risk assessment relies on selection of endpoints from the most sensitive species tested in acceptable studies.

Exposures estimated in the screening-level risk assessment for non-target organisms are likewise not specific to a given species. Aquatic organism (plant and animals) exposures are based on a set of standardized water body assumptions (water body size, watershed size, proximity to field, etc.) that result in high-end estimates of exposure (see Section V.B.1.b). Estimates of exposure for terrestrial birds and mammals assume that animals are in the treatment area, and exposure estimates involve grouping taxa based on food preferences (e.g., obligate insectivores, herbivores, granivores) and generic weight classes. Exposure for terrestrial plants considers surface runoff from treated fields as well as direct application via pesticide spray drift.

6. Identification of Data Gaps

When a data package is received for a registration of a new active ingredient or a new use, the submissions are reviewed to ensure that the environmental fate and ecological effects data sets are complete for the proposed pesticide use. For actions in which a database for the active ingredient is already available (i.e., reregistration, new uses of existing active ingredients, Section 18s, etc.), the risk assessor reviews the adequacy of existing and new submissions and previous assessments. In either case, whenever possible, data gaps are noted early on in the risk assessment process and communicated to the risk manager as discussed in Section IV.B. Data gaps are addressed as a source of uncertainty in the risk assessment conclusions, and the risk assessment discusses the potential for additional data to affect the risk assessment conclusions. In the absence of data, adverse effects may be assumed to occur until a study is submitted to indicate otherwise.

Once data gaps in the ecological effects and environmental fate databases are identified, the risk assessment team must determine whether it is possible to perform the risk assessment. A screening-level ecological risk assessment is possible when the data submitted on ecological effects and environmental fate of the pesticide are scientifically valid and complete based on the Agency's review criteria in the Standard Evaluation Procedures (see Support Documents #35 - #63). Studies for effects are classified in one of three categories: core, supplemental, and invalid. Core data are from studies found to be scientifically valid and conducted consistent with Agency testing guidelines. Supplemental data are from studies found to be scientifically valid but do not follow all requirements set forth in Agency testing guidelines. Invalid data are

from scientifically unsound studies. Similar classifications of data are set forth for environmental fate studies.

In some instances, a core study may not be available for a particular data requirement listed in 40 *CFR* 158. In this case, the risk assessment team may consider other sources of information to address the data gap (e.g., submitted studies considered to be supplemental and data from other sources not submitted as part of fulfillment of 40 *CFR* 158). If supplemental or non-guideline study data are available to address the type of information described by the associated guideline, then it may be used in the risk assessment after its use is carefully considered. Professional judgment is used by the risk assessment team to determine the utility of the available supplemental data for the proposed risk assessment. This latter evaluation may include reference to data quality objectives for specific types of studies, the degree to which adequate documentation is available to evaluate the technical merit of the data, and whether the data are applicable to the assessment endpoints established for the risk assessment. The Agency's risk assessment guidelines instruct risk assessors to clearly and concisely document the evaluation of all data considered in the risk assessment. Even if supplemental or non-guideline data are used to address a data gap in the risk assessment, the risk assessment team will still note the gaps in the guideline study requirements and provide the risk manager with a determination of the potential impact of those gaps upon the confidence of the risk assessment.

There may be other instances where there is a lack of scientifically valid data (i.e., neither core or supplemental data are available). In this situation, certain aspects of the risk assessment may not be performed. In such situations, discussions with the risk manager ensue to determine whether these data gaps will seriously limit regulatory decision-making. In the absence of data needed to make the required findings under FIFRA, EPA cannot register or reregister a pesticide.

B. Analysis Phase

1. Exposure Characterization

In most cases, an exposure characterization conducted in support of a regulatory decision of a pesticide provides a quantitative analysis of the critical environmental fate and transport properties of the pesticide active ingredient. However, there are situations where formulations are of demonstrated higher toxicity than the active ingredient alone, or where degradates occur in significant amounts or are of significant toxicological concern. In such situations, exposure characterizations would include a quantitative or qualitative analysis of the risk implications of organism exposure to these degradates or formulations in addition to the active ingredient. The Agency's risk assessment guidance instructs risk assessors to clearly and concisely describe the nature of the stressors evaluated in the risk assessment. This includes documentation of the potential significance of degradates and formulations in the risk assessment of pesticides. Section V.B.1.a., which is found below, and materials in Support Document #78, relating to HED's Metabolism Assessment Review Committee (Section V.B.2.), describe the process for including degradates in the risk assessment. Sections V.B.1.b.(2) and V.B.1.c.(2) discuss

specific exposure methods for the quantitative consideration of pesticide formulations in the risk assessment.

The quantitative expressions of the fate and transport properties, along with the information related to the use of the pesticide active ingredient and the physical, chemical, and biological conditions of the use sites are used to estimate the potential exposure of plants, wildlife, and aquatic life to pesticide residues in environmental media. This characterization includes information on how often, how long, and the amount of pesticide active ingredient and its degradates of concern to which an organism may be exposed. The exposure characterization is based on environmental fate and transport data, modeling, and monitoring information.

In order to quantitatively predict the fate and transport of a pesticide once it is introduced into the environment, OPP scientists review laboratory and field studies that measure how pesticide active ingredients interact with soils, air, sunlight, surface water, and ground water. These studies provide information concerning:

- The degradation of the pesticide active ingredient (how fast and by what process it is degraded in the environment) and how persistent the pesticide active ingredient is in the environment;
- The breakdown products that result from the degradation processes;
- The mobility of a pesticide active ingredient or its degradates or metabolites and how it will move from the application site; these studies predict the potential of the pesticide to volatilize into the atmosphere, move into ground or surface waters, or bind to the soil; and
- How much of a pesticide active ingredient and its degradates or metabolites will accumulate in the environment.

a. Fate and Transport Data Requirements and Study Evaluation

The Agency regulations found in 40 *CFR* 158.290 (Support Document #29) describe the types and amount of data the Agency commonly uses for assessing the environmental fate of an active ingredient. These data are generated from controlled laboratory and field studies, which are conducted under approved Guidelines and Good Laboratory Practices. They are used to determine the persistence, mobility, and bioconcentration potential of a pesticide and its major degradates in the environment.

The types of data required may vary depending on where the pesticide is used. Some of these studies, such as hydrolysis, photolysis, aquatic and soil metabolism, and terrestrial dissipation, are routinely conducted for all outdoor use pesticides. Others are conditionally required and are triggered by use or application patterns and basic product chemistry data.

Controlled environmental fate and transport laboratory studies are used to determine the persistence, mobility, and bioconcentration potential of a pesticide active ingredient and its major degradates. Persistence studies assess what happens to a pesticide active when it interacts

with water, soil, air, and sunlight. Mobility studies attempt to predict the potential of the active ingredient to volatilize into the atmosphere, move into ground or surface waters, or bind to soil. Bioconcentration studies evaluate the potential of an active ingredient to partition to aquatic biota and the degree to which bioconcentration can be reversed should external exposure to the active ingredient or degradates be reduced or eliminated. These studies are designed to help characterize how a pesticide active ingredient dissipates once it is released into the environment and to identify the major degradates that may result from these processes.

Degradation studies include hydrolysis, photodegradation in water, photodegradation in air, and photodegradation on soil. The hydrolysis study determines the potential of the pesticide active ingredient to degrade from the influence of water alone. Photodegradation studies determine the potential of the active ingredient to degrade in water, soil, or air when exposed to sunlight. During these studies, data are also collected concerning the identity, formation and persistence of major degradates.

Metabolism studies include aerobic soil metabolism, anaerobic soil metabolism, anaerobic aquatic metabolism, and aerobic aquatic metabolism. The soil microbial metabolism studies determine the persistence of the pesticide active ingredient when it interacts with soil microorganisms under aerobic and anaerobic conditions. The aquatic metabolism studies produce similar data, but are generated by active ingredient interaction with microorganisms in a water/sediment system. These studies also identify the significant degradates that result from biological degradation.

Mobility studies, which include leaching, adsorption/desorption, and volatility, provide information on the mode of transport and eventual destination of the pesticide active ingredient in the environment. Scientists can predict the degree of pesticide mobility in soil from data generated from leaching and adsorption/desorption studies.

Bioconcentration studies in aquatic organisms are used to estimate the potential of a pesticide active ingredient, under controlled laboratory conditions, to partition to the organisms from respiratory and dermal exposures. These studies also provide information on the degree to which bioconcentration of a pesticide or degradate can be reversed should pesticide levels in the surrounding aquatic environment be reduced.

Field studies which identify the environmental dissipation processes, assess the transformation, transport, and fate of pesticide active ingredient under actual use conditions with typically applied pesticide product at representative field sites. These studies characterize the relative importance of each route of dissipation of the pesticide active ingredient and its major degradates. Data generated from field dissipation studies can provide more realistic estimates (albeit limited in time and space) of the persistence and transport of an active ingredient and its degradates when the pesticide product is applied under actual use conditions.

Guidance for reviewing environmental fate and transport studies is provided in Subdivision N Guidelines and the associated Standard Evaluation Procedures (Support

Documents #5, # 41 - #44, #60 - #62.). However, OPP may also review sources of data other than those conducted according to the Subdivision N Guidelines, such as non-guideline studies submitted by the pesticide registrant and data published in the scientific literature. It is important to note that the manner in which additional non-guideline data are incorporated into a risk assessment is established on a case-by-case basis. The risk assessment team uses professional judgment in evaluating such aspects as:

- The data quality objectives of the study,
- Availability of documentation sufficient for evaluating the technical merit of the methods and results analysis, and
- General applicability of the results as compared to the exposure scenarios that are considered important in the risk assessment.

The Agency recognizes the importance of using the best available science in characterizing environmental exposure. Non-guideline data may be used to address data gaps in the assessment, even to the extent of providing quantitative values for dissipation pathway inputs for exposure modeling. These data may even be useful for addressing fate issues that are not specifically identified in the existing guideline studies. The risk assessment team must clearly and concisely document the environmental fate information considered in the risk assessment. Though data from non-guideline studies may be considered supplemental information in a risk assessment, they cannot be used to satisfy guideline requirements to support registration.

In addition to assessing the environmental fate of active ingredients, the Agency requirements indicate that the formation of degradates be monitored in the fate studies. This is often accomplished through the use of radio-labeled compound to ensure that detection limits are sufficiently low to allow for detailed tracking of the production of degradates. Degradates formed at greater than or equal to 10% of the applied radioactivity in the environmental fate studies are considered significant (i.e., major degradates) and must be identified (see Support Document #5). The 10% criterion is a general guideline, meaning that degradates approaching concentrations of 10% of the applied radioactivity are usually identified as well. In addition, degradates of known toxicological or ecotoxicological concern must be quantified and identified even when present at less than 10% of the applied radioactivity.

In order to identify degradates of toxicological concern, environmental fate scientists engage in discussions with human health reviewers in HED and ecotoxicology reviewers in EFED. (Support Document #78 provides additional information on the process used by the Agency to identify degradates of concern.) In accordance with Agency risk assessment guidance, the risk assessment team must clearly and concisely document the rationale of including or excluding degradates from consideration in the risk assessment.

Once the individual studies are reviewed and determined to be appropriate for inclusion in the risk assessment, OPP relies on the results of these studies to provide the quantitative fate and transport inputs for ecological exposure modeling. Selection of these input values are specific to the exposure model being used. (Guidance for the selection process can be found in

Support Documents #9, #17, and #18.) The following sections (B.1.b,c,and d) discuss exposure modeling methods available to OPP for screening-level risk assessments.

b. Aquatic Organism Exposure Modeling

(1). General Approach

For aquatic organisms, such as plants, fish, aquatic-phase amphibians, and invertebrates, OPP generally uses computer simulation models to estimate exposure to a pesticide active ingredient. These models calculate estimated environmental concentrations (EECs) in surface water using laboratory data that describe how fast the pesticide breaks down to other chemicals and how it moves in the environment. Section V.B.1.b (2) describes the Agency's approach for exposure modeling in situations where available information suggests that ecological risks from formulated products should be considered.

In aquatic organism modeling, a tiered system of modeling is used to efficiently allocate resources to assessment efforts of varying complexities and potential risks. The intent of the lower tiers is to provide a screening approach to estimate the concentration of a pesticide in water from sites that are highly vulnerable to runoff or leaching. OPP is confident that when a pesticide is not predicted to cause adverse effects on the environment using EECs generated from screening- level tiers, that the possibility of harming the environment is low. The assessment moves to a more refined one that is based on conditions more reflective of actual use site conditions, when Levels of Concern (LOCs), discussed later in this section, are exceeded using EECs based on generic assumptions (non-use site specific).

The first screening model employed is a generic one that is not specific to the particular use-site. This model, GENEEC2 (GENeric Estimated Environmental Concentration), is used to screen chemicals to determine the ones which potentially pose sufficient risk to warrant more detailed or refined modeling. The GENEEC2 calculates high-end estimates of surface water concentrations of pesticides in a generic farm pond. The Agency considers this scenario a high-end estimate for the following reasons:

- The input value for the application rate and number of applications is the labeled maximum;
- The entire watershed is assumed to be cropped and treated with the pesticide, and the watershed area is high relative to the volume of the water body;
- No buffer is assumed between the pond and the treated field;
- Runoff is assumed to be from a 6-inch rainfall over a 24-hour period; and
- The geographic location of use is regarded as representative of high-end potential for pesticide runoff and is not necessarily representative of runoff conditions for the labeled use.

GENEEC2 provides a rapid screen to separate the low risk pesticides from those that need more refined assessments. The model estimates high level exposure values of pesticides in surface water using the following inputs:

- Basic chemical characteristics,
- Pesticide label use and application information,
- Adsorption of the pesticide to soil or sediment,
- Direct deposition of spray drift into the water body, and
- Degradation of the pesticide in soil before runoff and within the water body.

GENEEC2 is a single-event model, based on a single, large rainfall/runoff event occurring on a 10-hectare field that removes a large quantity of pesticide at one time from the field to a pond that has a 20,000-liter water volume and is 2-meter deep. (See the GENEEC2 User's Manual and GENEEC2 Model Description for more information, which may be obtained from the following url: www.epa.gov/oppefed1/models/water/index.htm.)

If the LOC for risk to non-target species is not exceeded using GENEEC2 EECs, OPP is confident that there is no risk of concern. If the LOC is exceeded using GENEEC2 EECs, a small possibility exists, albeit unlikely, that an extreme exposure could exceed toxicity thresholds established in the effects characterization. However, the risk assessment team cannot discount the possibility that GENEEC2 model assumptions leading to such high-end exposure predictions may not be realistic for the labeled use of the pesticide. In those instances where exposure levels exceed the levels associated with the toxic threshold, a more realistic exposure characterization is established using a more comprehensive model (PRZM-3 and EXAMS II) and runoff conditions more reflective of labeled use sites.

The PRZM-3 and EXAMS II model provides more realistic, use-site specific EEC values by refining the model inputs for pesticide transport and transformation down through the crop root and unsaturated zone, and runoff and spray drift loading in the farm pond.

PRZM-3 is a process or "simulation" model that calculates what happens to a pesticide in treated fields on a day-to-day basis. It considers factors such as rainfall and plant transpiration of water, as well as how and when the pesticide is applied. It has two major components: hydrology and chemical transport.

The hydrologic component for calculating runoff and erosion of soil is based on the USDA Natural Resource Conservation Service curve number technique and the Universal Soil Loss Equation. Evapotranspiration of water from the root zone of the soil profile is estimated either directly from pan evaporation data or is based on an empirical formula (Penman 1948). Total evapotranspiration of water includes evaporation from crop interception, evaporation from soil, and transpiration by the crop. Water movement is simulated by the use of generalized soil parameters, including field capacity, wilting point, and saturation water content. To reflect the high-end of the distribution of pesticide exposures across varying sites, OPP selects hydrologic scenarios based on the targeting of model outputs.

The chemical transport component of PRZM-3 simulates pesticide application on the soil or on the plant foliage. Dissolved, adsorbed, and vapor-phase concentrations in the soil are estimated by simultaneously considering the processes of pesticide uptake by plants, surface runoff, erosion, decay, volatilization, foliar wash-off, and sorption.

Each PRZM modeling scenario represents a unique combination of climatic conditions, crop-specific management practices, soil-specific properties, site-specific hydrology, and pesticide-specific application and dissipation processes. Each PRZM simulation is conducted using up to 36 years of rainfall data to cover year-to-year variability in runoff. PRZM-3 allows the user to consider pulse loads and predict peak events. Daily edge-of-field loadings of pesticides dissolved in runoff waters and sorbed to sediment, as predicted by PRZM, are discharged into a standard water body ("standard pond" for ecological assessments) simulated by the EXAMS model.

EXAMS II is also a process model that simulates the processes that occur in the water body rather than on the agricultural field. EXAMS II takes the runoff and spray drift loadings generated by PRZM and estimates the concentration in the pond on a day-to-day basis. It accounts for volatilization, sorption, hydrolysis, biodegradation, and photolysis of the pesticide in the aquatic environment. Since EXAMS is a steady-state model, the water bodies are modeled as having constant volume. Multiple-year pesticide concentrations in the water column are calculated from the simulations as the annual daily peak, maximum annual 96-hour average, maximum annual 21-day average, maximum annual 60-day average, and annual average. The 1 in 10 year maximum values for each averaging period are used to calculate risk quotients. An input parameters selection manual, which provides guidance in selecting input values for using these models, can be found in Support Document #9.

For surface water modeling, PRZM/EXAMS assumes 5% and 1% spray drift for aerially and ground applied pesticides, respectively. The 5% assumption is based on a linear interpolation of spray drift data presented in Akesson (1990). (See Section V.C.4.10 for a comparison of these assumed drift levels with other drift modeling outputs.) The risk characterization section of the risk assessment includes a discussion of the potential impact of alternative drift estimates on the overall confidence of the risk assessment conclusions.

For pesticides that are currently on the market, water monitoring data may be available from EPA databases, U.S. Geological Survey, National Water-Quality Assessment Program, industry, states, and universities. These data are evaluated on a case-by-case basis to determine the likelihood, extent, and nature of pesticide concentration in water under current use practices and actual field conditions. The risk assessment team considers such study aspects as the points and frequency of sample collection, the analyte suite, and detection limits when determining how such data will be incorporated into the risk assessment. When reliable surface water monitoring data are available, EPA uses it to help characterize the levels of pesticide that are being detected in the environment. Monitoring, though, does not necessarily target pesticide use areas or the time of year when pesticide concentrations may be at their peak, and for this reason may not

provide a reliable estimate of acute exposure. If monitoring data shows higher confirmed detections than estimated by modeling, the higher monitoring values may be used in the risk assessment, and a re-evaluation of the model input parameters may be initiated to explore the impact of selected input values on the model output.

More detailed descriptions of these aquatic models can be found on EPA's Web site at the following url: www.epa.gov/oppefed1/models/water/index.htm

(2). Special Aquatic Exposure Methods for Pesticide Formulations

In situations where available toxicity data indicate that a pesticide formulation for registration in the United States may be more toxic to aquatic biota than indicated by active ingredient effects testing, it may be necessary to consider aquatic exposure to the formulation. Exposure modeling in these instances is limited to situations where direct instantaneous introduction of the formulation to surface waters occurs by direct application to those waters or by incidental application as a result of drift. The screening-level assessment model for such direct or incidental application is based on the standard farm pond scenario used for EXAMS modeling.

The limitation on the quantitative exposure modeling for formulations is based on the expectation that the varying physical-chemical properties of individual components of pesticide formulations will result in progressively different formulation constituents in environmental media over time. As the proportions of formulation components in environmental media differ from the proportions in the tested formulation, the assumption that environmental residues are toxicologically equivalent to tested formulations cannot be supported beyond the time period immediately following product application. This assumption is especially important in the case of runoff from treated areas to surface waters. In this case, partitioning and degradation properties for each formulation component suggest that the final proportion of the residues of these components in the receiving surface waters would not represent what was introduced and what was tested in an aquatic organism toxicity study using the formulated product.

While EPA does not require the same data on end-use products as the EU, the operation of the adverse effects reporting provisions in FIFRA section 6(a)(2) and implementing regulations assure that EPA has the same database for performing its ecological risk assessments as the EU. The Agency's methods for considering formulated product exposure in the screening-level aquatic organism risk assessment is functionally equivalent to the approaches developed by the European Union for evaluating pesticide formulation risks (see Support Document #80 - EU Council Directive 91/414/EEC).

c. Terrestrial Organism Exposure Modeling

(1). General Approach

Terrestrial wildlife exposure estimates are typically calculated for birds and mammals, emphasizing a dietary exposure route for uptake of pesticide active ingredients. These exposures are considered as surrogates for terrestrial-phase amphibians as well as reptiles. For exposure to terrestrial organisms, OPP primarily looks at the residues of pesticides on food items and assumes that organisms are exposed to a single pesticide residue in a given exposure scenario. Two approaches are used for estimating exposure to terrestrial wildlife, which are dependent on the application method: (1) spray applications and (2) granular, bait, and treated seed applications. Section V.B.1.c.2 describes the Agency's approach for exposure modeling in situations where available information suggests that formulation risks should be considered. It should be noted that, although the screening-level terrestrial wildlife risk assessment focuses, in large part on dietary exposure the Agency does consider the relative importance of other routes of exposure in situations where data indicate that pesticide exposures through routes other than dietary may be potentially significant contributors to wildlife risk. (Such data could be identified, for example, through the ECOTOX database. See Section VI.B.2.b.1.) OPP, in its risk characterization (see section VI.C), discusses the impact of consideration of other routes of exposure that have been identified as potentially important on the degree of certainty associated with screening-level risk assessment conclusions.

For spray applications, estimation of pesticide concentrations in wildlife food items focuses on quantifying possible dietary ingestion of residues on vegetative matter and insects. The residue estimates are based on a nomogram that relates food item residues to pesticide application rate. The nomogram is based on an EPA database called UTAB (Uptake, Translocation, Accumulation, and Biotransformation), a compilation of actual measured pesticide residue values on plants (Nellessen and Fletcher 1992), and work from Fletcher et al. (1994). (See Support Document #15).

In avian risk assessments, dietary residues are compared with toxicity endpoints based on dietary concentration (e.g., LC50 for acute effects). Conversely residues may be first converted to an ingested whole body dose. In the case of small mammals, for example, no dietary-based toxicity information is available so residues are converted to an ingested dose and compared to single oral-dose toxicity endpoints (i.e., LD50). The conversion of dietary residues to oral dose and then comparison with LD50 data is also performed for an avian risk assesment when the single oral dose route appears to provide a more suitable measure of effects than the dietary toxicity study. In either case, the first tier of the nomogram uses the maximum predicted residues. Subsequent refinements may consider mean residues. However, maximum residue values are used in the screening-level assessments for listed species. For mammals, the residue concentration is converted to daily oral dose based on fractions of body weight consumed daily as estimated from mammalian allometric relationships in EPA's Wildlife Exposure Factors Handbook (Support Document #33). In all screening-level assessments, the organisms are assumed to consume 100% of their diet as one food type, thereby eliminating the need at the screening level for evaluating mixtures of dietary items.

For granular, bait, and treated seed applications, estimation of loadings of pesticide per unit area are calculated. This approach, which is intended to represent exposure via multiple

routes and not just direct ingestion, considers observed effects in field studies and relates them to the pesticide applied to surface area. The label rate of application for the active ingredient is the basis for the exposure term. Using the following assumptions, the amount of pesticide per square foot is calculated:

- In-furrow applications assume a typical value of 1% granules, bait, or seed remain unincorporated;
- Incorporated banded treatments assume that 15% of granules, bait, seeds are unincorporated. This is an average of measurements ranging from 6 to 40 %; and
- Broadcast treatment without incorporation assumes 100% of granules, bait, seeds are unincorporated.

(2). Special Terrestrial Exposure Methods for Pesticide Formulations

In situations where available toxicity data indicate that a pesticide formulation for registration in the United States may be more toxic to terrestrial wildlife than indicated by active ingredient effects testing, it may be necessary to consider exposure to the formulation. Exposure modeling in these instances is limited to dietary exposure to residues for a time period immediately following pesticide product application.

The limitation on the quantitative exposure modeling for formulations is based on the expectation that the varying physical-chemical properties of individual components of pesticide formulations will result in progressively different formulation constituents in environmental media over time. Because the proportions of formulation components in environmental media differ from the proportions in the tested formulation, the assumption that environmental residues are toxicologically equivalent to tested formulations cannot be supported beyond the time period immediately following product application.

The Agency's methods for considering formulated product exposure in the screening-level terrestrial organism risk assessment follows approaches developed by the European Union for evaluating pesticide formulation risks (see Support Document #80 - EU Council Directive 91/414/EEC).

d. Non-Target Plant Exposure Modeling

As discussed previously in the aquatic organism exposure section, exposure for non-target aquatic plants is assessed in a manner consistent with exposure for other aquatic organisms.

Terrestrial and semi-aquatic plant exposure characterization employs runoff and spray drift scenarios contained in OPP's Terrplant model (Support Document #18). Exposure calculations are based on a pesticide's water solubility and the amount of pesticide present on the soil surface within the first inch of depth. For dry areas, the loading of pesticide active

ingredient from runoff to an adjacent non-target area is assumed to occur from one acre of treatment to one acre of non-target area; for semi-aquatic (wetland) areas, runoff is considered to occur from a larger source area with active ingredient loading originating from 10 acres of treated area to a single acre of non-target wetland. Default spray drift assumptions are 1% for ground applications and 5% for aerial, airblast, forced air, and chemigation applications. Drift is not considered for formulations of herbicides that are not spray-applied (e.g., granules); however, runoff is still considered and expressed on a percent of applied mass basis. A discussion of the uncertainties associated with the drift assumptions is included in section VI.C.6 .b.10 and are included in the risk characterizations for screening-level risk assessments.

2. Effects Characterization

In screening-level ecological risk assessments, effects characterization describes the types of effects a pesticide can produce in an organism and how those effects change with varying pesticide exposure levels. This characterization is based on an effects profile that describes the available effects (toxicity) information for various plants and animals and an interpretation of available incidents information and effects monitoring data. Environmental fate data, monitoring data, and computer models are used to estimate the exposure of non-target animals and plants to pesticide residues in the environment.

40 *CFR* Parts 158.490, 158.540, and 158.590 specify the types and amounts of data that the Agency needs to determine the risks of a pesticide to wildlife, aquatic organisms, and plants. The types of data needed can vary depending on how and where the pesticide is used. A list of the studies that the Agency may require in support of the registration or approval of certain pesticides is provided in Support Document #29.

In these tests, organisms are exposed to different amounts of pesticide active ingredient (and under certain conditions formulated product and degradates) and their responses to these varying concentrations are measured. Study endpoints are used to estimate the toxicity or hazard of a pesticide. (See Support Documents #45, #47-49, #52-53, #57, and #63 for toxicity categories.) The toxicity testing scheme is tiered, such that results from a lower level study are used to determine potential harmful effects to non-target organisms and whether further testing is required. Testing can progress from basic laboratory tests at the lowest level to applied field tests at the highest level.

For screening risk assessments, the following toxicity endpoints are used as inputs to the Risk Quotient (RQ) method for expressing risk (see Section V. C.1) :

<u>Aquatic Animals</u>

Acute assessment	Lowest tested EC_{50} or LC_{50} for freshwater fish and invertebrates and estuarine/marine fish and invertebrates acute toxicity tests.

Chronic assessment	Lowest NOEC for freshwater fish and invertebrates and estuarine/marine fish and invertebrates early life-stage or full life-cycle tests.
<u>Terrestrial Animals</u>	
Acute avian assessment	Lowest LD_{50} (single oral dose) and LC_{50} (subacute dietary).
Chronic avian assessment	Lowest NOEC for 21-week avian reproduction test.
Acute mammalian assessment	Lowest LD_{50} from single oral dose test.
Chronic mammalian assessment	Lowest NOEC for two-generation reproduction test.
<u>Plants</u>	
Terrestrial non-endangered	Lowest EC_{25} values from both seedling emergence and vegetative vigor for both monocots and dicots.
Aquatic vascular and algae	Lowest EC_{50} for both vascular and algae.
Terrestrial endangered	Lowest EC_5 or NOEC for both seedling emergence and vegetative vigor for both monocots and dicots**.**

While the above toxicity endpoints are routinely used to calculate screening-level risk assessment RQs, they do not represent a limitation on the types of toxicity endpoints that may be considered in the risk assessment. Over the course of evaluation of available toxicity data (see Section V.B.2 for a discussion of OPP's use of ECOTOX database for effects data searches), the risk assessment team may encounter other effects data that provide: (1) additional information on existing toxicity endpoints commonly used in the screening risk assessment, (2) insight on endpoints not routinely considered for RQ calculation, and/or (3) effects data on specific additional taxonomic groups (e.g., amphibian and freshwater mussel tests). Professional judgment is used and documented by the risk assessment team to determine whether and how available data on other toxicological endpoints are included in the risk assessment. This evaluation may include (1) reference to data quality objectives for specific types of studies, (2) the degree to which adequate documentation is available to evaluate the technical merit of the data, and (3) whether the data are applicable to the assessment endpoints established for the risk assessment. To decide if data are applicable to assessment endpoints, the risk assessment team uses professional judgment and available lines of evidence to determine if the toxicological endpoints can be linked to assessment endpoints in a reasonable and plausible manner.

As stated earlier in this section, the Agency routinely conducts screening-level risk assessments on an active ingredient basis. The only routine exception to this is for terrestrial plant effects analysis, where toxicity studies are conducted on the formulated product. Consequently, the majority of toxicity data received by the Agency relates to the active ingredient. However, Agency regulations have provisions for the request of additional data on formulated products. 40 *CFR* 158.75 allows the Agency to request additional data if routinely required data are not sufficient to evaluate the potential of a pesticide product to cause unreasonable adverse effects on man or the environment. In addition., 40 *CFR* 158.202 indicates

that acute aquatic animal toxicity testing may be required if any of the following conditions are met:

- The end-use product is applied directly to water when used as directed;
- Active ingredient LC_{50}/EC_{50} values are equal to or less than the maximum expected environmental concentration or the estimated environmental concentration in aquatic systems when the product is used as directed; or
- An ingredient in the end-use product is expected to enhance the toxicity of the active ingredient or is toxic itself to aquatic organisms.

Support Document #78 presents the Agency's process for the identification of degradates of potential toxicological concern. This information, in conjunction with any available toxicity data and data regarding the extent to which degradates are produced in laboratory and field environmental fate studies, will be considered by the Agency to determine the need for incorporating active ingredient degradates in a risk assessment. This evaluation, which is conducted by the Metabolism Assessment Review Committee, may be based upon information relating to (1) biologically reactive chemical moieties on both the active and degradates, (2) past experience with close chemical analogues, (3) consultation with Agency human health toxicologists, and (4) publically available literature. If degradates are considered by the Agency to be of toxicological significance as determined by the process outlined in Support Document # 78, the Agency evaluates the available information to determine if quantitative or qualitative consideration of degradate risks is warranted. The rationale supporting such decisions are documented in the risk assessment document. To be consistent with Agency risk assessment guidance, risk assessors must clearly and concisely describe this evaluation in the risk assessment.

Formulated product effects data are evaluated and included in the risk assessment when available. (See Section V.A.2 for sources of such information). Acute mammalian effects testing for formulated products is commonly submitted to the Agency. In addition, effects testing for formulations is required for registrations in other nations (EU Directive 91/414/EEC). The Agency provisions for submission of effects data under 40 *CFR* 159.165(b) suggest that formulation effects information conducted for other nations would be submitted to the Agency when it indicates that the formulation may be more toxic than the active ingredient. In addition, searches of the publicly available literature may identify additional effects data for formulations.

Before formulated product effects data can be considered quantitatively in the risk assessment, it must be evaluated for its applicability to formulations under consideration for registration. This evaluation includes a comparison of the confidential statement of formulation for the product proposed for registration with any available information on the constituents of the tested formulation. If the comparison suggests that the tested and proposed registration formulations are similar, the test data are used quantitatively in the risk assessment process. However, if a similarity is not supported by the available formulation information, the toxicity data on formulated products is documented, and the risk characterization qualitatively discusses

the potential implications the formulated toxicity may have on the confidence of the risk assessment conclusions.

a. Registrant-Submitted Studies for Direct Effects of Pesticides

Support Documents #45 - #57 and #63 list the universe of toxicity studies commonly submitted by pesticide registrants in support of registration proposals. 40 *CFR* Section 158 describes the criteria that serve as the basis for the requirements for each type of study. The Agency has determined, that under most situations, these effects data are sufficient for risk assessment purposes.

b. Open Literature Studies for Direct Effects of Pesticides

In addition to registrant-submitted data, the Agency also consults publicly available literature for additional toxicity information to be used in screening risk assessments, such as studies on additional taxa, toxicity endpoints, routes of exposure, or test materials. (See Section V.B.2.)

To ensure consistent consideration and use of information in the open literature for ecological risk assessments, OPP has developed guidance for its scientists (Support Document #71) and steps to implement the guidance have been initiated.

(1). ECOTOX

OPP uses the ECOTOX (ECOTOXicology) database as a search engine to identify open literature studies that may potentially be used in ecological risk assessments (http://www.epa.gov/ecotox). The ECOTOX database was selected because it is a user-friendly, publicly-available, quality-assured, comprehensive tool for locating open literature chemical toxicity data for aquatic life, terrestrial plants, and wildlife. Relevant literature for ECOTOX is retrieved using a comprehensive search strategy designed to locate worldwide aquatic and terrestrial ecological effects literature. This strategy is expected to capture the data from research that evaluates species and/or toxic effects, which fall outside the standard battery of required ecotoxicity tests.

The ECOTOX database is developed and maintained by EPA's National Health and Environmental Effects Research Laboratory, Mid-Continent Ecology Division (MED) in Duluth, Minnesota. ECOTOX includes unique toxicity data for aquatic life, terrestrial plants, and terrestrial wildlife and contains information on lethal, sublethal and residue effects. With regard to terrestrial animals, ECOTOX's primary focus is wildlife species, but the database does include some information on domestic species. Sources routinely used for ECOTOX searches are AGRICOLA, Cambridge Scientific Abstracts (CSA), BIOSIS and CAB Abstracts, Current Contents, ScienceDirect, and MED library journal holdings. Relevant sources are also identified from benchmark documents and review papers, and online ecotoxicology databases such as the U.S. Geological Survey's "Wildlife and Contaminants Online" website

http://www.pwrc.usgs.gov/contaminants-online/ and the Canadian Wildlife Service's "Reptile and Amphibian Toxicology Literature" website http://www.cws-scf.ec.gc.ca/nwrc-cnrf/ratl/index_e.cfm.

The ECOTOX database can issue two types of reports. The aquatic organism report includes toxic effects data on all aquatic species including plants and animals and freshwater and saltwater species, while the terrestrial organism report contains toxicity data for terrestrial animals and terrestrial plants.

The high level of quality assurance of the ECOTOX database makes it an important primary source for consistently searching open literature data. Extensive documentation for this database, ranging from Standard Operating Procedures, Coding Guidelines, Chemical Verification, and various procedures, are described in Support Documents #72 - #77.

Quality assurance procedures begin with literature acquisition and cataloging and continue through the chemical and species verification, the literature review process, data entry, and data retrieval. The ECOTOX literature is encoded by trained document abstractors. An intensive training period, a well-documented manual, and close interaction with the data coordinator help to ensure a high level of accuracy and consistency in the review process. Ten percent of the publications are independently reviewed by two different reviewers. These reviews are compared, and differences (if any) are documented, discussed, and resolved by the data coordinator.

This procedure provides a consistent attempt at finding data. Since there is a lag time of three months between literature acquisition and data availability in ECOTOX, OPP may request MED to search their reference files for any unreviewed studies on a chemical of concern. In addition, OPP will work with MED to identify citations and papers in their holdings that were not encoded in ECOTOX, including studies conducted on chemical mixtures, formulations, inert ingredients and surfactants, and survey and incident data.

(2). OPP Strategy for Conducting Literature Searches

OPP is refining a search strategy that it will follow for finding and filtering pesticide data in ECOTOX and is establishing guidance that describes how to evaluate the data output from ECOTOX. After identifying pesticide toxicity data in ECOTOX that may be useful in a pesticide risk assessment, copies of the journal articles and study reports will be retrieved so that the risk assessor may more closely critique the study. MED holds paper copies of all studies cited in the ECOTOX database and copies of applicable papers can be provided to OPP upon request.

This guidance, which will help maintain consistency concerning when and how data from open literature can be used, will help the risk assessor determine if an open literature study can be used in a pesticide risk assessment. Development of this guidance is being coordinated with other OPP quality assurance guidance. In addition, EPA science policy documents will be used

as a base in developing the guidance (http://www.epa.gov/osp/spc/2polprog.htm and http://www.epa.gov/oei/qualityguidelines), and the guidance will be similar to previous work by OPP (U.S. Environmental Protection Agency, 2003), Superfund (http://www.epa.gov/ecotox/ecossl/), Office of Water (U.S. Environmental Protection Agency, 2002a), and EVISTRA (U.S. Environmental Protection Agency, 2002b).

In accordance with established risk assessment guidance, the Agency will identify in the risk assessment (1) the effects data from the literature that were considered in the risk assessment, (2) the basis for decisions on the manner in which such data were incorporated in the risk assessment, and (3) the rationale for not including data obtained from the literature.

c. Open Literature Studies for Indirect Effects of Pesticides

To obtain best available information for interpreting the potential for indirect effects at the screening level, the Agency will utilize "species profiles", when available, prepared by the Services for other Federal action agencies (e.g., EPA's Office of Water). These summaries, or profiles, are considered current best available information concerning species' life history, ecology, population demographics, etc., and will be provided to the Agency by the Services. The Agency anticipates that the Services will provide the Agency with similar summary information for listed species not covered by existing "species profiles."

d. Open Literature Studies for Critical Habitat Evaluations

To obtain best available information for interpreting the potential for critical habitat evaluations at the screening level the Agency may utilize "critical habitat profiles", when available, prepared by the Services. These summaries, or profiles, are considered current best available information concerning principle constituent elements for specific species and will be provided to the Agency by the Services. Critical habitat profiles provide the Agency with an identification of the principle constituent elements or equivalent (e.g., lists of biological resource requirements for the listed species associated with the critical habitat).

C. Risk Characterization

Risk characterization is the integration of effects and exposure characterization to determine the ecological risk from the use of the pesticide and the likelihood of effects on aquatic life, wildlife, and plants based on varying pesticide-use scenarios. The Agency's policy and guidance (Support Document #28) requires that risk characterizations be prepared in a manner that is clear, transparent, reasonable, and consistent with other risk characterizations of similar scope.

1. Integration of Exposure and Effects Data - The Risk Quotient for Direct Effects

Risk characterization integrates the results of exposure and toxicity data to evaluate the likelihood of adverse ecological effects on non-target species. For most chemicals, the effects characterization is based on a deterministic approach using one point on a concentration-response curve (e.g., LC50). In this approach, OPP uses the risk quotient (RQ) method to compare exposure over toxicity. Estimated environmental concentrations (EECs) based on maximum application rates are divided by acute and chronic toxicity values. (Equations are provided in Support Document #8.)

2. Levels of Concern for Direct Effects - The Policy Tool for Interpreting Risk Quotients for Direct Effects

After risk quotients are calculated, they are compared to the Agency's LOCs. These LOCs are the Agency's interpretative policy and are used to analyze potential risk to non-target organisms and the need to consider regulatory action. These criteria are used to indicate when a pesticide use as directed on the label has the potential to cause adverse effects on non-target organisms. A discussion of the developmental history is provided in support document # 70. LOCs currently address the following risk presumption categories:

- Acute - Potential for acute risk to non-target organisms which may warrant regulatory action in addition to restricted use classification (acute RQ > 0.5 for aquatic animals, mammals, birds);

- Acute Restricted Use - Potential for acute risk to non-target organisms, but may be mitigated through restricted use classification (acute RQ > 0.1 for aquatic animals or 0.2 for mammals and birds);

- Acute Endangered Species - Endangered species may be potentially affected by use (acute RQ > 0.05 for aquatic animals or 0.1 for mammals and birds);

- Chronic Risk - Potential for chronic risk may warrant regulatory action, endangered species may potentially be affected through chronic exposure (chronic RQ > 1 for all animals);

- Non-endangered Plant Risk - RQ >1; and

- Endangered Plant Risk - Potential for effects in endangered plants (RQ>1).

It should be noted that both acute endangered species and chronic risk LOCs are considered in the screening-level risk assessment of pesticide risks to listed species. Endangered species acute LOCs are a fraction of the non-endangered species LOCs or, in the case of endangered plants, RQs are derived using lower toxicity endpoints than non-endangered plants. Therefore, concerns regarding listed species within a taxonomic group are triggered in exposure situations where restricted use or acute risk LOCs are triggered for the same taxonomic group. The Agency risk assessment also includes, both in the risk characterization and the endangered

species sections, an evaluation of the potential probability of individual effects for exposures that may occur at the established endangered species LOC. This probability is calculated using the established dose/response relationship and the median lethal dose estimate for the study used to establish the toxicity endpoint for the endangered taxa.

As discussed earlier in this document, the Agency is not limited to a base set of surrogate toxicity information in establishing risk assessment conclusions. The Agency also considers toxicity data on non-standard test species (e.g., amphibian data) when available. (See Section V.B.2.b.on searches for publically available effects information.) To the extent that such data meet data quality requirements, it is used to interpret the relevance of risk assessment LOCs in the context of other tested taxa.

3. Comparison of Field and Laboratory Data for Direct Effects

Given the general widespread nature of pesticide uses and the variability in the physical, chemical, and biological conditions associated with pesticide use sites, validation of the results of the existing screening risk assessment process would be impractical. However, OPP does consider data on exposure and effects collected under field conditions to make determinations on the predictive utility of the screening assessment.

After the 1992 Ecological, Fate, and Effects Task Force review of the testing requirements for environmental fate and ecological effects, the Agency decided to not require avian and aquatic guidelines field testing, except in unusual circumstances (Support Document #25). However, when field studies along with incident data reports and compliance monitoring studies are available, they are used to help elucidate the potential sources and magnitude of uncertainties when extrapolating from effects predictions based on laboratory toxicity data to effects occurrence in the field. As pointed out in the Agency's Guidelines for Ecological Risk Assessment (Support Document #7), developing solid relationships between cause and observed field effects adds to the certainty of the assessment. The criteria presented in these guidelines adopted from Fox (1991) and similar to other criteria reviewed by Fox (U.S. Department of Health, Education, and Welfare, 1964; Hill, 1965; and Susser, 1986a and 1986b) stressed the importance of the strength of association between the causative agent and the observed effect.

OPP routinely receives information on the field dissipation of pesticides under actual use conditions. These data provide the Agency with information on the persistence of the parent compound and the rate of production of degradates. Incorporation of the results of field dissipation data into the quantitative exposure modeling is problematic because of the nature of the model input requirements. However, overall rates and routes of pesticide decline as predicted by the fate models can be examined and compared with the results of the field dissipation models to determine the degree to which the risk assessment fate modeling may overstate exposure.

In addition to field dissipation measurements, scientists often consider available data on environmental media monitoring for pesticides. For example, the results of the screening

environmental models are compared with monitoring data for surface waters. As previously mentioned, though, there are practical limitations to surface water monitoring efforts. For example, non-targeted routine monitoring programs, such as the U.S. Geological Survey's National Water-Quality Assessment Program, are more useful for tracking trends than they are for establishing true peak concentrations. However, comparison of the Agency modeling results with such monitoring programs can provide some insight into the degree to which modeling results reflect realistic conditions in the field.

As discussed for surface water monitoring, field effects data are limited in the ability to account for the myriad combinations of physical, chemical, and biological variables that may affect organism response to pesticides in the environment. Consequently, field studies or incident reports cannot conclusively validate screening risk assessment predictions, but they can allow inferences on the reasonableness of the assessment predictions.

Incident information can add lines of evidence to provide context to the risk predictions from the screening level assessment. Sometimes this reporting provides limited information for an ecological assessment because most incidents are not reported, and those that are reported, often do not have enough information to assess cause and effect. Generally, it is assumed that the application was from normal use and was applied within the rates allowed on the labeling, unless otherwise indicated. On occasion, the use rates are reported in incident investigations, but actual documentation with scientific rigor is rare. Therefore, incident reports often provide limited information about the correlation between use rates and effect levels. However, consistent with components of the criteria described by Fox (1991), the greater the number of wildlife mortality incidents following application of a specific pesticide for a specific use, and the greater the number of individuals involved, the higher the confidence in the strength of the association. The more confidence in the association between incident and pesticide exposure, the more useful the information when evaluating risk conclusions derived from laboratory-based screening assessment methods. The Agency maintains a database, which is described in Section IV.C.2.c, of incident information to support risk assessment.

4. Indirect Effects Characterization for Listed Species

The Agency acknowledges that pesticides have the potential to exert indirect effects upon the listed organisms by, for example, perturbing forage or prey availability, altering the extent and nature of nesting habitat, etc.

In conducting a screen for indirect effects, the Agency uses the direct effects LOCs for each taxonomic group to make inferences concerning the potential for indirect effects upon listed species that rely upon non-endangered organisms in these taxonomic groups as resources critical to their life cycle. The Agency considers pesticide-use scenarios, resulting in RQs that are below all direct effect endangered species LOCs for all taxonomic groups assessed to be of no concern for risks to listed species either by direct or indirect effects.

a. Indirect Effect Analyses Where One or More Animal Taxonomic Group RQs Exceed the Endangered Species LOC

In cases where screening-level acute RQs for a given animal group equal or exceed the endangered species acute LOC, the Agency uses the dose response relationship from the toxicity study used for calculating the RQ to estimate the probability of acute effects associated with an exposure equivalent to the EEC. This information serves as a guide to establish the need for and extent of additional analysis that may be performed using Services-provided "species profiles" as well as evaluations of the geographical and temporal nature of the exposure to ascertain if a not likely to adversely affect determination can be made. The degree to which additional analyses are performed is commensurate with the predicted probability of adverse effects from the comparison of dose response information with the EECs. The greater the probability that exposures will produce effects on a taxa, the greater the concern for potential indirect effects for listed species dependant upon that taxa, and therefore, the more intensive the analysis on the potential listed species of concern, their locations relative to the use site, and information regarding the use scenario (e.g., timing, frequency, and geographical extent of pesticide application) Greatest concerns would exist when exposure is associated with a risk higher than the effects probability associated with the non-endangered LOC for a pesticide with an average slop of 4.5. When the Agency can, upon additional analysis at the screening level, support a not likely to adversely affect determination, the basis for the conclusion is documented in the endangered species section of the risk assessment. When the screening level assessment indicates a not likely to adversely affect can not be determined with this level of refinement, the findings and rationale are documented and additional analysis of the geographical and temporal nature of the exposure, as well as more in-depth evaluations of the biological and ecological requirements of potentially indirectly impacted species are addressed, as described in section VI, to ascertain whether a not likely to adversely affect determination can be made.

When screening-level chronic RQs for a given animal group equal or exceed the endangered LOC there may be a potential concern for indirect effects. The Agency then considers the nature of the chronic toxicological endpoint, Services-provided "species profiles", and further evaluation of the geographical and temporal nature of the exposure to determine if a rationale for a not likely to adversely effect determination is possible. When the Agency can, upon additional analysis at the screening step, support a not likely to adversely affect determination the basis for the conclusion is documented within the endangered species section of the risk assessment. When the screening level assessment or chronic effects indicates a not likely to adversely affect can not be determined with this level of refinement, the findings and rationale are documented and additional analysis of the geographical and temporal nature of the exposure, as well as more in-depth evaluations of the biological and ecological requirements of potentially indirectly impacted species are addressed, as described in section VI, to ascertain whether a not likely to adversely affect determination can be made.

In making decisions about the need and scope of additional indirect effects analysis for one or more listed species, the Agency considers the degree to which exposures exceed any acute or chronic levels of concern. The greater extent to which exposures produce effects or exceed

LOCs, the greater the concern for potential indirect effects and therefore the more intensive the analysis on the potential listed species of concern, their locations relative to the use site, and information regarding the use scenario (e.g., timing, frequency, and geographical extent of pesticide application).

b. Indirect Effects Where One or More Plant Taxonomic Group RQs Exceed the Endangered Species LOC

If plant RQs fall between the endangered species and non-endangered species LOCs, the Agency concludes a no effect determination for listed species that rely on multiple plants species to successfully complete their life cycle (termed plant dependent species). If plant RQs fall between the endangered species and non-endangered species LOCs, the Agency assumes a potential for adverse effects to those listed species that rely on a specific plant species in their life cycle (termed plant species obligates). In these situations the Agency may determine if listed organisms that are considered plant species obligates are within the pesticide use area. This is accomplished through a comparison of Services-provided "species profiles" and listed species location data. If no plant species obligates are within the pesticide use area, a no effect determination is made for indirect effects upon plant dependant listed species. The Agency may also consider temporal and geographical nature of exposure and the scope of available effects data to determine if any potential effects can be determined to be not likely to adversely effect a plant species obligate. The greater extent to which exposures produce effects or exceed LOCs, the greater the concern for potential indirect effects and therefore the more intensive the analysis on the potential listed species of concern, their locations relative to the use site, and information regarding the use scenario (e.g., timing, frequency, and geographical extent of pesticide application). If a no effect determination or, after additional analysis, a not likely to adversely affect determination cannot be supported at the screening level, the results of the assessment and any identified lists of plant species obligates documented and additional analysis of the geographical and temporal nature of the exposure, as well as more in-depth evaluations of the biological and ecological requirements of potentially indirectly impacted species are addressed, as described in section VI, to ascertain whether a not likely to adversely affect determination can be made.

If plant RQs are above non-endangered species LOCs, the Agency considers this to be indicative of a potential for adverse effects to those listed species that rely either on a specific plant species (plant species obligate) or multiple plant species (plant dependant) for some important aspect of their life cycle. The Agency may determine if listed organisms for which plants are a critical component of their resource needs are within the pesticide use area. This is accomplished through a comparison of Services-provided "species profiles" and listed species location data. If no listed organisms that are either plant species obligates or plant dependant reside within the pesticide use area, a no effect determination on listed species is made. If plant species obligate or dependent organisms may reside within the pesticide use area, the Agency may consider temporal and geographical nature of exposure, and the scope of the effects data, to determine if any potential effects can be determined to not likely adversely effect a plant species obligate or dependant listed organism. If a no effect determination or, after additional analysis a

not likely to adversely affect determination, cannot be supported at the screening level, the results of the assessment and any identified lists of plant species obligate and dependant listed organisms are documented and additional analysis of the geographical and temporal nature of the exposure, as well as more in-depth evaluations of the biological and ecological requirements of potentially indirectly impacted species are addressed, as described in section VI, to ascertain whether a not likely to adversely affect determination can be made.

In all cases, the analysis of indirect effects is presented in a transparent manner in the endangered species section of the screening-level risk assessment.

5. Critical Habitat for Listed Species

The Agency believes that the risk assessment analysis for listed species' indirect effects is relevant and provides a basis for an analysis of potential effects on a listed species' designated critical habitat, when such a designation has been prepared by the Services. Because pesticides directly impact living organisms, critical habitat analysis for pesticides is limited in a practical sense, to those principle constituent elements of critical habitat that are of a biological nature (e.g., the biological resource requirements for the listed species associated with the critical habitat). To the extent that principle constituent elements have been established by the Services in "critical habitat profiles", the available indirect effects screening approach can be applied directly to those elements. In situations where available "critical habitat profiles" do not directly identify principle constituent elements, screening-level LOCs used to evaluate indirect effects for the associated listed species (from the Services "species profiles"), are used in a manner similar to that described in V.C.4 above. A screening-level determination of potential modification upon designated critical habitat also incorporates spatial analysis, when such spatial coverage is readily available from the Services, to determine the overlay of designated habitat with the pesticide use area. The Agency discusses the critical habitat analysis, along with the information material to that analysis, in the endangered species section of the risk assessment.

6. Description of Assumptions, Uncertainties, Strengths, and Limitations of the Assessment

a. Assumptions and Limitations Related to Exposure for All Taxa

Screening-level risk assessments rely on labeled statements of the maximum rate of pesticide application, the maximum number of applications, and shortest interval between applications. Together, these assumptions constitute a maximum use scenario. The frequency at which actual uses approach these maximums is dependant on local pest pressure, resistance to the pesticide, timing of applications, and market forces. As discussed in the problem formulation section, the risk assessment team collaborates with BEAD to determine more typical use rates and application frequencies in order to provide risk managers with a more complete characterization of uses and their implications for ecological risk.

b. Assumptions and Limitations Related to Exposure for Aquatic Species

(1). Location of Species and Receiving Waters to Treated Field

As discussed earlier in the aquatic exposure section of this document, OPP's screening risk assessment assumes that the modeled water body is adjacent to the treated field. A possible case-specific modification to this assumption of adjacent location of the water body may be a downwind offset of the water body if spray drift buffers are included in the proposed product labeling.

For screening-level risk assessment purposes, the actual habitat requirements of any particular aquatic species are not considered. Instead an assumption is made that unspecified aquatic listed fish and invertebrate species occupy, **exclusively and permanently**, the water body being modeled.

With the possible exception of scenarios where pesticides are directly applied to water, it is assumed that no habitat use considerations specific for any species would place the organisms in closer proximity to pesticide use sites. An assumption of exclusive and permanent occupation of a modeled site represents the highest possible screening assumption of frequency within a treated or exposed area.

(2). Exposure for Aquatic Species Is Through the Dissolved Phase

For water column species, an assumption is made that the greatest bioavailable fraction of pesticide in surface waters is that which occurs as freely dissolved in the water column. Additional chemical exposure from materials associated with suspended solids or those associated with food items is not considered. In most currently registered pesticide cases, solids adsorption and bioconcentration occurs at lower levels than would be expected for such classically persistent bioaccumulative compounds as dioxins, halogenated biphenyls, some organochlorine pesticides, and some organometallics. The extent to which consideration of exposures to pesticide from suspended solids and diet is not quantified by the Agency and in situations where RQs fall close to the endangered species LOCs, the potential for additional exposure from these routes may be a limitation of the screening assessment.

(3). Dissipation in the Modeled Water Body

Mass transport losses of pesticide from the modeled water body, except for losses by volatilization, degradation and sediment partitioning, are not considered. Consequently, the current modeled water body is assumed to capture all mass of pesticide entering as runoff, drift, and erosion-associated material. It is also assumed that pesticide mass is never lost from the water body by overtopping or flow-through, nor is concentration reduced by dilution. In total, these assumptions lead to a near maximum possible aqueous concentration.

The current water body model does not account for any potential to concentrate pesticide through the evaporative loss of water. This limitation may have the greatest impact on the model's predictive ability for shallow water bodies, particularly vernal pools and potholes, where high surface-to-volume ratios of the water body accentuate the rate of evaporative loss and where the pesticide has low rates of degradation and volatilization. OPP is evaluating other models that will consider variations in water body volume and consider the effect of evaporative loss on concentrations of the pesticide and expects to present them to the SAP in 2004. As the Services research on the characteristics of vernal pools advances, the Agency and the Services will collaborate in developing future models for these exposure scenarios.

(4). Averaging Times for Aquatic Exposure

For an acute risk assessment there is no averaging time for exposure. An instantaneous peak concentration, with a 1 in 10 year return frequency, is assumed. The use of the instantaneous peak assumes that instantaneous exposure is of sufficient duration to elicit acute effects comparable to those observed over more protracted exposure periods tested in the laboratory, typically 48 to 96 hours. In the absence of data regarding time-to-toxic event analyses and latent responses to instantaneous exposure, the degree to which risk is overestimated cannot be quantified.

For chronic exposure risk assessments, the averaging times considered for exposure are commensurate with the duration of invertebrate life-cycle or fish-early life stage tests (21-28 days for invertebrates and 56-60 days for fish). Response profiles (time to effect and latency of effect) to pesticides likely vary widely with mode of action and with species and should be evaluated on a case-by-case basis as available data allow. Nevertheless, because the Agency relies on chronic exposure toxicity endpoints based on a finding of no observed effect, the potential for any latent toxicity effects or averaging time assumptions to alter the conclusions of an acceptable chronic risk assessment prediction is limited. The extent to which modeled durations of aqueous concentrations over- or underestimate actual exposure scenarios depends on such factors as localized meteorological conditions, runoff characteristics of the watershed (soils and topography), the hydrological characteristics of receiving waters, the fate characteristics of the pesticide active ingredient, and the method of pesticide application.

It should be noted that chronic effects studies are performed using a method that holds water concentrations in a steady state. This method is not likely to reflect conditions associated with pesticide runoff. Over the course of a typical run of the aquatic exposure models, pesticide estimated concentrations increase and decrease in surface water on a cycle influenced by rainfall events and degradation rates.

(5). A Well-Mixed Pond

Because the EXAMS model assumes instantaneous equilibrium and mixing, it does not consider the potential for higher short-term concentrations in the areas of the pond initially

receiving pesticide runoff (e.g., the shallow, near-shore areas of the pond) and drift (e.g., the near-surface layer of the pond). It is possible that concentrations immediately following introduction of runoff or drift will be higher in some areas of the pond than those modeled on the basis of instantaneous distribution of the chemical throughout the pond. However, the countering assumption of no averaging time for acute risks may lead to overestimation of exposures throughout the water body, as described previously.

The Agency is actively pursuing modeling techniques to possibly allow for greater or lesser dilution of surface runoff by receiving waters. These approaches, which are scheduled for SAP review in February 2004, may enhance the future understanding of water body residue levels near shore and near surface.

(6). Watershed to Pond Ratio

One parameter affecting estimates of aqueous concentrations within the PRZM/EXAMS model concerns the relationship of watershed area to pond volume. The assumption of a 10-hectare field running off to a 1-hectare pond of 2-meters depth is based on the USDA Natural Resource Conservation Service design criteria for farm pond construction.. Actual watershed to pond volume relationships, though, are driven by site characteristics (soil types, slopes, and meteorology).

It is possible that larger treated watershed areas will result in more mass of pesticide running off to the pond. However, this screening-level runoff may become insignificant when the watershed area becomes so large that it precludes a reasonable assumption of a closed pond with no outlets. The Agency believes, based on professional judgment, that the currently used screening watershed area to pond volume overestimates likely aqueous concentrations. As a result, it is evaluating other models that will consider variations in water body volume and expects to present them to the SAP in 2004.

(7). 100 Percent Pesticide Treatment of the Pond Watershed

The Agency assumes that 100 percent of the watershed is treated with the pesticide, which would result in a maximum possible exposure. This assumption may be realistic for small water bodies with associated small watershed areas, but for large watersheds, it would result in an overestimation of exposure.

(8). Frequency of Exposure During a Given Year - 1 in 10 Year Return Frequency

Screening assessments rely on events (either instantaneous or over an averaging period) that have a return frequency of 1 in 10 years. This is calculated using the peak value of each of the 36 years modeled. The 1 in 10 return frequency does not necessarily represent a 90^{th} percentile of all peaks over the years modeled. Existing surface water modeling outputs provide daily estimates of pesticide concentrations, which can be used to more completely characterize

exposure, when required. The Agency has reviewed a number of these model time series for both persistent and non-persistent compounds used as multiple applications per year and has determined that the 1 in 10 year return frequency peak commonly represents a value farther out on the upper bound of the distribution of daily concentrations than the 90th percentile, with some cases being greater than the 99.9 percentile.

(9). Dilution of Sediment

The EXAMS model estimates of water concentration are based on an equilibrium established between the compartments of the pond, principally water and sediments. In real world situations, sediments are constantly being added to water bodies from the erosion of the watershed. Over time, this has the effect of increasing the mass of the sediments compartment, though the actual exchange area with overlying water may remain relatively constant. In EXAMS, the mass of the sediment compartment remains constant and serves as the denominator for estimating sediment concentrations, and through equilibrium assumptions, influences estimates of surface water concentrations. In cases where chemicals have appreciable stability in the environment, the EXAMS pond model will tend to overestimate the concentration in pond sediments because it does not allow for renewed sediment mass following runoff events. This may lead to higher predicted concentrations in both sediments and surface water because equilibrium is assumed between the two compartments.

(10). Spray Drift

Surface water modeling using PRZM/EXAMS assumes 5% and 1% drift integrated across the surface of a pond adjacent to a treated field for aerially and ground applied pesticides, respectively. A comparison of these assumed values can be made with those from the first screening-level drift predictions from the AgDrift model. The following table presents AgDrift predictions for deposition of drift (fraction of applied pesticide amount) integrated across the surface of a standard pond which is immediately adjacent to a treated field and which has a 208.7-foot downwind width. In situations where the Agency's screening models suggest that spray drift is a significant source of exposure and therefore risk, the following information is considered in the risk characterization to evaluate the confidence of risk assessment conclusions.

Application Method	PRZM/EXAMS Drift	AgDrift Model Drift
Ground Low Boom Height	1%	0.17 % very fine to fine spray, 50th percentile of measured data 0.36 % very fine to fine spray, 90th percentile of measured data

		0.1 % fine to medium/coarse spray, 50th percentile of measured data 0.19 % fine to medium/coarse spray, 90th percentile of measured data
High Boom Height	1%	0.6 % very fine to fine spray, 50th percentile of measured data 0.78% very fine to fine spray, 90th percentile of measured data 0.16 % fine to medium/coarse spray, 50th percentile of measured data 0.28 % fine to medium/coarse spray, 90th percentile of measured data
Application Method	PRZM/EXAMS Drift	AgDrift Model Median Drift, 90th Percentile Application Conditions (Based on Best Professional Judgment)
Aerial	5%	0.7% coarse to very coarse spray 8.9% medium to coarse spray 12.7% fine to medium spray 24.3% very fine to fine spray

From this comparison, the baseline assumptions of drift currently used for PRZM/EXAMS modeling exceed the 90th percentile of drift predictions from AgDrift modeling for ground applications. The baseline drift assumption currently used for aerial application scenarios likely represents drift levels in excess of 90th percentile application conditions for coarse to very coarse sprays. However, aerial drift assumptions are below drift levels predicted by AgDrift for very fine to medium/coarse sprays using 90th percentile application conditions. The exact extent to which the currently used aerial drift assumption represents more frequently encountered application conditions is not presently quantified.

The extent to which a 5% versus another drift assumption alters estimated aqueous concentration estimates depends on specific use scenarios and can be influenced by the degree to which runoff contributes to the overall receiving water concentration. For example, if a persistent pesticide with low affinity for soils is used in a high runoff potential use area, drift may be only a minor route for pesticide loading to the receiving waters and the magnitude of assumed drift may have a limited effect on the concentration estimate. However, for non-persistent chemicals with high affinity for soils used in low runoff areas, drift may be the dominant route of pesticide entering receiving waters, and the assumptions of that drift may appreciably influence pesticide aqueous concentrations estimates.

It should be noted that the baseline drift assumptions for a water body located adjacent to a treated field are much higher than upper bound values for water bodies located at greater

distances from the treated area. The table below shows distances from the treated area where AgDrift assumptions for aerial drift to a water body would be approximated by the baseline drift assumption of 5%. Water bodies located closer to the treated field than shown below would be predicted to have drift loadings greater than the 5% assumption. The greater the distance from the treated field required to reach 5% drift, the greater the likelihood that actual water bodies could receive drift levels higher than the baseline 5% assumption.

Spray Category	Water Body Distance from Treated Field to Reach 5% Surface Integrated Drift in AgDrift Model (ft)
Coarse to very coarse spray	13.12
Medium to coarse spray	39.4
Fine to medium spray	105
Very fine to fine spray	643

This comparison suggests that the OPP assumption of 5% aerial drift would reasonably represent high-end estimates of drift for most water bodies when medium to very coarse sprays are used because a few water bodies are usually found within 40 feet of treatment areas. However, for very fine to medium spray uses, the confidence that the 5% drift assumption adequately characterizes drift to water bodies is diminished because a higher number of water bodies can be assumed to be located within 650 feet from treated fields. It should be noted that quantitative probabilities of water body locations from treated fields are likely to be crop and regionally specific.

The Agency includes a discussion of the impacts of chemical use specific estimates of drift as computed by AgDrift in the risk characterization and evaluates the extent to which alternative drift estimates may impact overall risk conclusions. Pesticide application conditions indicated by the product labels or agronomic practices associated with a specific crop or target pest are evaluated with respect to their associated droplet spectra. These expected spectra are compared with the AgDrift model predictions of drift to determine if default drift assumptions employed in EEC modeling are over- or underestimates. The degree to which drift is over or underestimated is considered when establishing bounds around EEC predictions and the extent to which these bounds lead to RQs that exceed listed species LOCs, or not, is presented.

c. Assumptions and Limitations Related to Exposure for Terrestrial Animals

(1). Location of Wildlife Species

For screening terrestrial risk assessments for listed species, a generic bird or mammal is assumed to occupy either the treated field, or adjacent areas receiving pesticide at a rate commensurate with the treatment rate on the field. Spray drift model predictions suggest that this assumption leads to an overestimation of exposure to species that do not occupy the treated field. AgDrift estimated drift to areas removed from the treated fields (below) indicates that off site drift is but a fraction of on-field treatment rate.

Spray Droplet Size Assumption	AgDrift Model Drift Point Estimates 0 to 990 ft from Field (Tier 1)
Very fine-fine	50% to 4%
Fine to medium	50% to 1%
Medium to coarse	50% to 0.5%
Coarse to very coarse	50% to 0.3%

For screening risk assessment purposes, the actual habitat requirements of any particular terrestrial species are not considered, and it is assumed that species occupy, **exclusively and permanently**, the treatment area being modeled. This assumption leads to a maximum level of exposure in the risk characterization. To the extent that a species does not reside exclusively and permanently in treated areas, exposure will be less, and presumably significantly less.

(2). Routes of Exposure

Screening-level assessments for spray applications of pesticides consider dietary exposure alone. Other routes of exposure, not considered in the assessment, are discussed below:

· Incidental Soil Ingestion Exposure

The screening-level risk assessment does not consider incidental soil ingestion. Available data suggests that up to 15% of the diet can consist of incidentally ingested soil depending upon species and feeding strategy (Beyer et al. 1994). A simple first approximation of soil concentration of pesticide from spray application shows the effect of not considering incidental soil ingestion:

Assuming an application of 1 pound /acre (1.12 kg/ha) of pesticide to a bare, very low density soil (1 g/cm3) incorporated to only 1-cm depth (actual incorporation depths may range from 5 to 20 cm), the following soil concentrations can be calculated for a depth of 1 cm:

soil concentration =
(((1.12 kg/ha)(1,000,000 mg/kg))/(100,000,000 cm^3/ha)))(1 cm^3/0.001 kg) = 11.2 mg/kg

Including this concentration into the standard screening-level method and assumptions for food item pesticide residues (e.g., 240 ppm residue assumption for short grass) shows that ingestion of soil at an incidental rate of up to 15% of the diet would not increase dietary exposure. In fact, for the majority of food items, inclusion of soil into the diet would effectively reduce the overall dietary concentration as compared to the present assumption of the entire diet consisting of the food source contaminated as per Fletcher et al. (1994) recommendations.

· Inhalation Exposure

The screening risk assessment does not consider inhalation exposure. Such exposure may occur through three potential sources: (1) spray material in droplet form at time of application, (2) vapor phase pesticide volatilizing from treated surfaces, and (3) airborne particulate (soil, vegetative material, and pesticide dusts).

Available data suggest that inhalation exposure at the time of application is not an appreciable route of exposure for birds. According to research on mallards and bobwhite quail, respirable particle size in birds (particles reaching the lung) is limited to a maximum diameter of 2 to 5 microns (U.S. Environmental Protection Agency, 1990). The spray droplet spectra covering the majority of pesticide application situations (AgDrift model scenarios for very-fine to coarse droplet applications) suggests that less than 1% of the applied material is within the respirable particle size.

Theoretically, inhalation of pesticide active ingredient in the vapor phase may be another source of exposure for some pesticides under some exposure situations. Under laboratory conditions established to mimic pesticide application to a field, Driver et al. (1991) demonstrated that organophosphate exposure via inhalation produced significant short-term acetylcholinesterase inhibition in exposed birds. The flux of pesticide from treated plant and soil surfaces can be appreciable for soil fumigants. However, the assessment of pesticide flux from treated surfaces and its subsequent distribution within the overlying atmosphere is complex and highly situation-specific, negating any confident generic assumptions regarding significance. Recognizing these limitations the Agency is evaluating options for modeling vapor phase exposures, including approaches for establishing near-field, near-ground air concentrations based upon equilibrium and kinetics-based air models. The Agency is also working on methods to account for potential differences in toxic potency of pesticide active ingredients when available toxicity data are limited. It is anticipated that these modeling approaches and toxicity extrapolation methods will be presented to the Agency's SAP in 2004 for avian risk assessment, and subsequent approaches for other taxa will be developed and incorporated into the risk assessment process based on the results of the avian peer review.

The impact from exposure to dusts contaminated with the pesticide cannot be assessed generically as partitioning issues related to application site soils and chemical properties render the exposure potential from this route highly situation specific.

· Dermal Exposure

The screening assessment does not consider dermal exposure, except as it is indirectly included in calculations of RQs based on lethal doses per unit of pesticide treated area. Dermal exposure may occur through three potential sources: (1) direct application of spray to terrestrial wildlife in the treated area or within the drift footprint, (2) incidental contact with contaminated vegetation, or (3) contact with contaminated water or soil.

Recent Agency refined risk assessment efforts for select mosquito adulticides and investigations into tools for quantifying dermal exposure suggest that interception of spray and incidental contact with treated substrates may pose risks to avian wildlife. In addition, research conducted by Driver et al. (1991) on northern bobwhite quail exposed to treated vegetation suggests that, for the organophosphate methyl parathion, dermal exposure may be a major contributor to avian dose under simulated field conditions. The available measured data related to wildlife dermal contact with pesticides are extremely limited. The Agency is actively pursuing modeling techniques to account for dermal exposure via direct application of spray and by incidental contact with vegetation. Presentation of these modeling approaches and toxicity extrapolation methods to the SAP is expected to occur in 2004 for avian risk assessment, and subsequent approaches for other taxa will be developed and incorporated into the risk assessment process based on the results of the avian peer review.

· Drinking Water Exposure

Drinking water exposure to a pesticide active ingredient may be the result of consumption of surface water or consumption of the pesticide in dew or other water on the surfaces of treated vegetation. For pesticide active ingredients with a potential to dissolve in runoff, puddles on the treated field may contain the chemical. Similarly, pesticides with lower organic carbon partitioning characteristics and higher solubility in water have a greater potential to dissolve in dew and other water associated with plant surfaces. Estimating the extent to which such pesticide loadings to drinking water occurs is complex and would depend upon the partitioning characteristics of the active ingredient, the types of soils of the treatment area, and the meteorology of the treatment area. In addition, the use of various water sources by wildlife is highly species-specific. As a result, the Agency is actively developing processes to quantify drinking water exposures from field puddles and dew. An initial screening approach for modeling drinking water exposure has been presented to the Agency's SAP and modifications to these modeling approaches are expected to undergo SAP review in 2004.

(3). Incidental Pesticide Releases Associated with Use

Agency risk assessments are based on the assumption that the entire treatment area is subject to pesticide application at the rates specified on the label. In reality, there is the potential for uneven application of the pesticide through such plausible incidents as changes in calibration of application equipment, spillage, and localized releases at specific areas of the treated field that

are associated with specifics of the type of application equipment used (e.g., increased application at turnabouts when using older ground application equipment). The Agency does not quantitatively account for such incidental releases of pesticides associated with labeled uses of the products, but it does indicate where such situations have resulted in wildlife mortality incidents and discusses this source of uncertainty in the risk characterizations.

(4). Residue Levels Selection

As discussed earlier in the exposure section of this document, the Agency relies on the work of Fletcher et al. (1994) for setting the assumed pesticide residues in wildlife dietary items. The Agency believes that these residue assumptions reflect a realistic upper-bound residue estimate, although the degree to which this assumption reflects a specific percentile estimate is difficult to quantify. Fletcher et al.(1994) maintains that the pesticide active ingredient residue assumptions employed by the Agency represent a 95th percentile estimate. In contrast to the Fletcher evaluation, field measurement efforts by Pfleeger et al. (1996) indicated that the Agency assumption of residues for short grass, broadleaf forage, and fruits were not exceeded. Agency predictions of residues were exceeded by 16% of long grass measurements, and 21% of seed/pod measurements. Finally, Baehr and Habig (2000) compared Agency residue assumptions with distributions of measured pesticide residues from the Agency's UTAB database. This comparison suggested that Agency residue assumptions (1) exceed the 99th percentile of the UTAB distribution for short grass and long grass, fall just below the 95th percentile for forage, and (2) fall between the 95th and 98th percentiles for fruits and seeds.

It is important to note that the field measurement efforts used to develop the Fletcher estimates of exposure involve highly varied sampling techniques. It is entirely possible that much of these data reflect residues averaged over entire above ground plants in the case of grass and forage sampling. Depending upon a specific wildlife species' foraging habits, whole above-ground plant samples may either underestimate or overestimate actual exposure. For example, wildlife, feeding on the tops of forage plants after application, may be exposed to higher concentrations of pesticide in plant tops than predicted by sampling efforts focusing on whole above-ground plant measurements

(5). Dietary Intake - The Differences Between Laboratory and Field Conditions

Acute and chronic risk assessments rely on comparisons of wildlife dietary residues with LC50 or NOEC values expressed in concentrations of pesticides in laboratory feed. These comparisons assume that ingestion of food items in the field occurs at rates commensurate with those in the laboratory. Although the screening assessment process adjusts dry-weight estimates of food intake to reflect the increased mass in fresh-weight wildlife food intake estimates, it does not allow for gross energy and assimilative efficiency differences between wildlife food items and laboratory feed. The significance of the gross energy content between laboratory feed and "field" diet can be seen in the following example:

- A typical laboratory avian feed, as used, contains approximately 2750 kcal/ kg.
- The Agency's Wildlife Exposure Factors Handbook (U.S. Environmental Protection Agency, 1993) presents the following dry-weight and fresh weight caloric contents for selected wildlife food items:

Food Item	Energy Dry (kcal/kg)	Energy Fresh (kcal/kg)
grasses	4200	1300
broadleaf forage	4200	2200
seeds	5100	4700
fruits	2000	1100
insects	5600	1600

On gross energy content alone, direct comparison of a laboratory dietary concentration-based effects threshold to a fresh-weight pesticide residue estimate would result in an underestimation of field exposure by food consumption by a factor of 1.25 - 2.5 for most food items. Only for seeds would the direct comparison of dietary threshold to residue estimate lead to an overestimate of exposure.

Differences in assimilative efficiency between laboratory and wild diets suggest that current screening assessment methods are not accounting for a potentially important aspect of food requirements. Depending upon species and dietary matrix, bird assimilation of wild diet energy ranges from 23 - 80%, and mammal's assimilation ranges from 41 - 85% (U.S. Environmental Protection Agency, 1993). If it is assumed that laboratory chow is formulated to maximize assimilative efficiency (e.g., a value of 85%), a potential for underestimation of exposure may exist by assuming that consumption of food in the wild is comparable with consumption during laboratory testing.

In the screening process, exposure may be underestimated because metabolic rates are not related to food consumption. For example, the Wildlife Exposure Factors Handbook (U.S. Environmental Protection Agency, 1993) includes allometric models for estimating both existing metabolic rate (EMR) and free living metabolic rate (FMR). EMR is the metabolic rate necessary for animal maintenance in captivity without body weight loss, a condition similar to caged test animals. FMR is the energy requirement for an organism in the wild. For passerine birds these relationships are as follows:

$$EMR\ (kcal/day) = 1.572\ (body\ weight\ g)^{0.6210}$$
$$FMR\ (kcal/day) = 2.123\ (body\ weight\ g)^{0.749}$$

Using a weight range for passerines of 10 - 150 g, the EMR predictions range from 6.6 to 35.3, and the FMR ranges from 11.9 to 90.5 kcal/day . Thus, it appears that not accounting for increased energy demands of organisms in the wild when comparing dietary residues to dietary toxicity thresholds represents about a two-fold underestimation in exposure potential.

Finally, the screening procedure does not account for situations where the feeding rate may be above or below requirements to meet free living metabolic requirements. Gorging behavior is a possibility under some specific wildlife scenarios (e.g., bird migration) where the food intake rate may be greatly increased. Kirkwood (1983) has suggested that an upper-bound limit to this behavior might be the typical intake rate multiplied by a factor of 5.

In contrast is the potential for avoidance, operationally defined as animals responding to the presence of noxious chemicals in their food by reducing consumption of treated dietary elements. This response is seen in nature where herbivores avoid plant secondary compounds. For agrochemicals, Dolbeer et al. (1994) reported that the use of methiocarb on fruit crops reduced depredation by birds. Of course, chemical treatment of food sources and any subsequent avoidance of those food sources by a species may, in itself, result in detrimental effects on the energetics of the species.

d. Assumptions and Limitations Related to Effects Assessment

(1). Sublethal Effects

For an acute risk assessment, the screening risk assessment relies on the acute mortality endpoint as well as a suite of sublethal responses to the pesticide, as determined by the testing of species response to chronic exposure conditions and subsequent chronic risk assessment. Examples of these sublethal endpoints include the following:

Aquatic Organisms	Test Type	Sublethal Measurement Endpoints
	Invertebrate Life-Cycle	Production of young by first generation
		Length of first generation
	Fish Early Life-Stage	Embryo hatch rate
		Time to hatch
		Time to swim-up
		Growth (length and weight)
		Pathological or histological effects
		Observations of other clinical signs
	Fish Life-Cycle	Embryo hatch rate
		Time to hatch
		Growth (length)
		Exposed adult egg production
		Second generation hatch rate
		Second generation growth
Birds	Reproduction	Maternal weight
		Eggs laid/hen
		Eggs cracked

		Eggshell thickness Viable embryos Hatchling number 14-day survivors Gross necropsy (organ lesions, fat and muscle deterioration) Observations of other clinical signs
Mammals	Two-Generation Reproduction	Total panel of reproduction parameters including: histopathology, parental and offspring growth, weight, mating, lactation, gonadal development milestones, sexual organ performance, and offspring production

Of course, a risk assessment team has the option of considering additional sublethal data in the assessment. This option is exercised on a case-by-case basis and only after careful consideration of the nature of the sublethal effect measured and the extent and quality of available data to support establishing a plausible relationship between the measure of effect (sublethal endpoint) and the assessment endpoints. This option includes a determination of whether there are clear, reasonable, and plausible links between the sublethal effect and survival or reproductive capacity of organisms in the field in accordance with the screening assessment endpoints of survival and reproduction capacity. The Agency documents the findings of such evaluations of additional sublethal effects in the effects assessment and includes a discussion of their potential effects upon the confidence of the overall risk assessment conclusions. The Agency anticipates that, through the SAP and related external peer-review processes in the scientific community, accepted risk assessment practices will continue to advance in this area. As with other risk assessment techniques, when new approaches are vetted through the peer-review process, the Agency will continue its practice of including state-of-the-science methodologies and anticipates collaborative efforts with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service in developing future sublethal endpoint analysis approaches for peer review.

(2). Age Class and Sensitivity of Effects Thresholds

It is generally recognized that test organism age may have a significant impact on the observed sensitivity to a toxicant. The screening risk assessment acute toxicity data for fish are collected on juvenile fish between 0.1 and 5 grams. Aquatic invertebrate acute testing is performed on recommended immature age classes (e.g., first instar for daphnids, second instar for amphipods, stoneflies and mayflies, and third instar for midges). Similarly, acute dietary testing with birds is also performed on juveniles, with mallards being 5 -10 days old and quail 10 - 14 days old.

Testing of juveniles may overestimate toxicity at older age classes for pesticidal active ingredients that act directly (without metabolic transformation) because younger age classes may not have the enzymatic systems associated with detoxifying xenobiotics. However, the influence of age may not be uniform for all compounds, and compounds requiring metabolic activation may be more toxic in older age classes. The screening risk assessment has no current provisions for a generally applied method that accounts for this uncertainty. In so far as the available toxicity data may provide ranges of sensitivity information with respect to age class, the risk assessment uses the most sensitive life-stage information as the conservative screening endpoint and includes an evaluation of all available age-class sensitivity information as it impacts the confidence of risk conclusions in the risk characterization section of the document.

(3). Use of the Most Sensitive Species Tested

Although the screening risk assessment relies on a selected toxicity endpoint from the most sensitive species tested, it does not necessarily mean that the selected toxicity endpoints reflect sensitivity of the most sensitive species existing in a given environment. The relative position of the most sensitive species tested in the distribution of all possible species is a function of the overall variability among species to a particular chemical. In the case of listed species, there is uncertainty regarding the relationship of the listed species' sensitivity and the most sensitive species tested.

Knowledge about the inherent interspecies variability is limited to information available from a small sampling of the overall universe of species (i.e., a relatively small number of species actually tested) and estimates statistically derived using classical sampling theory. Confidence in the use of the most sensitive species tested as a protective estimate of listed species sensitivity is a function of the size of the tested species pool, the representation of species tested across taxonomic groups of interest, and the variability across measured toxicity endpoints for the tested species.

It is likely that any given species can be arrayed throughout the distribution of sensitivities of given taxonomic groups to pesticides. In the case of species-specific assessments, there may be sufficient information on specific taxonomic groups to allow for more certain interspecies extrapolations for closely defined toxicological endpoints. The Agency is presently evaluating extrapolation methods to relate listed species or close taxonomic groups to tested species or taxonomic groups.

Without prior knowledge about relative position of individual tested species and a given species of concern (e.g., listed species) within the distribution of sensitivities for a given chemical, an evaluation of the ability of tested species to represent the most sensitive species (a lower limit to potential sensitivity to a toxicant) provides insight into the confidence of risk predictions to protect all species within a taxonomic group. This is achieved by a simple calculation:

probability of representing most sensitive species = number of tested species/total number of species

Given the small numbers of species tested and the comparatively large number of species for which these data are to represent, it is not likely that tested species represent the most sensitive species within the broad taxonomic groups used in the screening risk assessment. For example, if two bird species are randomly tested and there are 650 species of birds in the United States, the probability of capturing an endpoint representing the most sensitive species is 2/650 or roughly 0.3 percent.

Another method to evaluate assumptions concerning interspecies sensitivity is to estimate the probability of a measured value representing an nth percentile sensitive species (i.e., some reasonable or acceptable lower bound of potential sensitivity). Thus, the sampling of two

random bird species would have a probability of encompassing the 5th percentile species as follows:

probability of representing the 5th percentile or lower $=1-(1-p)^n =(1-(1-0.05)^2 = 0.0975$

Where: p is the target nth percentile (0.05 for this case) and
n equals the number of trials (2 for a random testing of two bird species)

It should be noted that such evaluations cannot provide information on the likely value of the toxicity endpoint when extrapolated from a tested species to the most sensitive or the nth percentile species. To do that, it is necessary to have information on the variability of the response among species. This can be accomplished by looking at the variance among tested species, provided it is accepted that the tested species are randomly sampled from the overall population. With only two species sampled within a taxonomic group, estimating the variability for the species sensitivity across that group is by nature uncertain. Indeed, sampling statistics would suggest that the confidence of predicting rare events from small sample sizes is not improved until the sample size approaches 30.

Departing from the usual sampling statistics for testing a single compound, toxicologists have turned to more robust data sets by looking at the available toxicity endpoints from a variety of tested compounds and predicting the level of sensitivity of species on the lower bounds of the distribution (often the convention is at the 5^{th} or 10^{th} percentile). For example, Luttik and Aldenberg (1997) evaluated 55 compounds with LD_{50} data on birds and 69 compounds with LD_{50} data for mammals. In each case, data were available for four or more species. Evaluation of the distribution characteristics of these data suggested that for small sample sizes of available LD_{50} data (N<4, a likely situation for many pesticide registrations), factors of 0.175 and 0.263 applied to the geometric mean of available data would approximate a 5^{th} percentile species sensitivity with 50% confidence. If greater confidence was desired in the prediction of the 5^{th} percentile species sensitivity from small data sets, the extrapolation factors would be even smaller. For example, Luttik and Aldenberg (1997) recommended extrapolation factors of 0.051 and 0.1, for situations where only two bird or mammal species are tested and the 5^{th} percentile and 95% confidence is required. The Agency is presently evaluating such extrapolation methods for aquatic species.

As discussed earlier in this document, the Agency is not limited to a base set of surrogate toxicity information in establishing risk assessment conclusions. The Agency also considers toxicity data on non-standard test species (e.g., amphibian data) when available. To the extent that such data meet data quality requirements, it is used to interpret the relevance of risk assessment LOCs in the context of other tested taxa.

e. Assumptions Associated with the Acute LOCs

Urban and Cook (Support Document #8) presented a mathematical analysis of the use of the 0.1 and 0.05 factor applied to the most sensitive LC_{50} or LD_{50} as the effects threshold for the

acute toxicity LOC for an endangered species. As summarized by Urban and Cook, 0.1 (LC_{50}) is equivalent to an individual risk of mortality of 1 in 30 million for a pesticide active ingredient with a probit slope of 4.5. Re-analysis suggests that this is in error. The calculation of dose (LC_k) associated with a defined response for a probit slope curve is as follows:

$$\log LC_k = \log LC_{50} + (\text{probit } k - \text{probit}5)/b$$

where: LC_{50} equals probit 5 and b equals slope
This can also be expressed as:

$$LC_k = (LC_{50})(10^{z/b})$$
$$\log LC_k = \log LC_{50} + (z/b)$$

where: z is the standard normal deviate and b equals the slope

Using a 10-fold difference between the LC_{50} of 100 and the LC_k (i.e., an LOC threshold of 0.1(LC_{50})) and a typical slope of 4.5, the solution for z would be -4.5. This standard normal deviate corresponds to a probability of mortality of approximately 1/300,000. Using a plausible range of slopes of 2 to 9 (e.g., the range of slopes with the insecticide carbofuran) the probabilities of individual mortality ranges from 1/50 to less than 10^{-16} at a LOC threshold of 0.1(LC_{50}).

The risk characterization section of the assessment document includes an evaluation of the potential for individual effects at an exposure level equivalent to the LOC. This evaluation is based on the median lethal dose estimate and dose/response relationship established for the effects study corresponding to each taxonomic group for which the LOCs are exceeded.

VI. Overview of OPP's Species-specific Ecological Risk Assessment Process for Aquatic Life, Wildlife, and Plants

A. Overview and Organization of FEAD

FEAD performs the following specific functions:

- Serves as domestic liaison with State and Tribal Governments and EPA Regional Offices as well as international liaison with individual countries and international organizations;
- Develops and coordinates the development of policies and regulations;
- Manages and responds to controlled correspondence and Congressional inquiries;
- Carries out routine and targeted communication activities for OPP; and
- Manages national regulatory and non-regulatory programs that rely on regional, state and tribal government offices for field implementation. This includes Certification of Pesticide Applicators, Worker Protection, Container Recycling and Design, Water Quality Protection, and Endangered Species Protection.

To carry out these functions, FEAD is organized into five branches: three branches that support OPP as a whole and two branches that carry out human health related or environmentally related field programs as follows:

- Government and International Services Branch (GISB) - Domestically, this branch serves as liaison with EPA's 10 regional offices and with the state agencies designated by the Governors and Tribal governments, to lead the pesticide regulatory program at the state and tribal levels. Additionally, GISB represents the Office on international issues and with international organizations.

- Policy and Regulatory Services Branch - Manages and coordinates the regulatory process for OPP and assists in the development of policies related to a variety of pesticide issues.

- Communication Services Branch - Coordinates communication activities for OPP, including the development of communication strategies on particular issues, general educational campaigns for the public on pesticide safety, and responses to controlled correspondence and Congressional inquiries.

- Certification and Worker Protection Branch - Develops and implements, through the Regional offices and State and Tribal agencies, nationwide programs for certifying that applicators of restricted use pesticides are competent to perform this function. This Branch also is responsible for the regulatory program to ensure agricultural workers are protected from pesticide exposures.

- Environmental Field Branch - Develops and implements, through the Regional offices and State and Tribal agencies, programs to help ensure pesticide use does not harm water quality, regulatory programs to ensure pesticide container integrity and containment of

pesticide storage areas, and OPP's program to assess the risks to and provide protection for listed species and critical habitat.

B. Purpose of the Species-Specific and Habitat-Specific Assessments

If the screening-level risk assessment indicates a pesticide may potentially impact, either directly or indirectly, listed species or critical habitat, OPP performs a more refined assessment. If that assessment does not support a "not likely to adversely affect" determination for all aspects of the action, FEAD on those aspects of the action for which the screening level assessment has not made such a determination. FEAD undertakes further refinement on those aspects of the action for which such a determination was not made. FEAD determines whether use of the pesticide "may affect" a particular listed species and if so, whether it is "likely to adversely affect" the species, or, in the case of critical habitat, whether use of the pesticide may destroy or adversely modify any principle constituent elements for the critical habitat, and if so, whether the expected impacts are "likely to adversely affect" the critical habitat. This section discusses the steps undertaken in a species-specific or habitat-specific assessment, which is based upon and is intended to supplement and refine the screening-level risk assessment.

OPP's goal for this process is to protect the listed species and critical habitat by potentially modifying a pesticide's use in a manner that is least disruptive to agriculture and other pesticide users. In order to accomplish this goal, refinements of the screening-level risk assessment, which makes assumptions that the species or habitat will be exposed at levels estimated in the environment, focuses on refining the exposure information for listed species or critical habitat. The result of these steps is an "effects determination" that the pesticide will have "no effect" on the listed species or critical habitat, "may affect but is not likely to adversely affect the species or critical habitat", or "may adversely affect the species or critical habitat."

Any changes to the assessment assumptions, data used for risk analysis, and risk mitigation measures that depart from the typical screening level approach are documented and their associated impacts upon the overall risk conclusions related to listed species is presented. Where appropriate, the quantitative estimation of risks will be recalculated..

The first step in the process is to improve the exposure estimates based on refining the geographic proximity of the pesticide's use and the listed species and/or critical habitat. If there is no geographic proximity, this information would support a determination that the pesticide use will have no effect on the species or critical habitat. If after conducting the first step of this analysis, FEAD determines that geographic proximity exists, FEAD examines both potential direct effects and any potential indirect effects of the pesticide use.

C. Effects Determinations

The "effects determination" is a determination of whether the pesticide will:

- Have “no effect” on the listed species or critical habitat,
- “May affect but is not likely to adversely affect” the listed species or critical habitat, or
- “May adversely affect the species or critical habitat”.

If during the screening-level assessment it is determined that there are no indirect effects and LOCs for listed species are not exceeded for direct effects, OPP declares there is “no effect” from that pesticide’s use on listed species and critical habitats. If, on the other hand, indirect effects are anticipated or exposure may exceed the LOCs for direct effects, FEAD usually declares that the pesticide’s use “may affect” the particular listed species or critical habitat.

If a determination is made that the pesticide’s use “may affect” the listed species or critical habitat, FEAD uses information to help characterize the potential for exposure at the predicted levels, and uses best professional judgment to distinguish those actions that “may affect but are not likely to adversely affect” a particular species or habitat from those actions that appear “likely to adversely affect” a listed species or critical habitat. The information used to characterize this degree of potential risk to a species is discussed later in this section.

D. Information and Data Sources Used in the Species-specific and Habitat-specific Assessments

A variety of information is used in the species-specific or habitat-specific assessment, which is intended to refine the screening-level risk assessment to more specifically determine exposure and characterize risk to a listed species or critical habitat. The information used and the purpose for which it is used is described below. Where personal communications provide information relevant to the assessment and characterization, this information is documented.

1. "DANGER" Program

The "DANGER" program is used to identify a list of species (and eventually critical habitats) that occur in counties where a particular commodity is produced. "DANGER" is a computerized database that has been populated with county-level occurrence information for listed species and with county-level information on agricultural crops and their acreage.

The county-level species locations were derived from the U.S. Fish and Wildlife Service's and U.S. National Marine Fisheries Service's (the Services) Federal Register Listing Notices and Recovery Plans, personal communications, and other documented sources. After compiled information from these sources, OPP_provided the compilation to the Services and requested verification. EPA incorporated the Services' corrections and has continued to update the information in the DANGER program with information extracted from the Services' Listing notices.

The information on county-level crop occurrence and acreage within counties of particular crops is extracted from the most recent U.S. Department of Agriculture's Agricultural Census (http://www.usda.gov/nass/). This Census is updated every five years . If it is known that a particular crop is either expanding or diminishing in acreage, information derived from personal communications with State agencies, commodity organizations, extension agents, etc. may be used to supplement the information derived from the computer database.

OPP anticipates updating or replacing DANGER with information being developed by the FIFRA Endangered Species Task Force (FESTF). Through FESTF, an industry task force, FEAD is anticipating access to element occurrence data for listed species and a computerized information management system that will consistently provide information on geographic co-occurrence of potential pesticide use areas and species location, at a finer scale than is currently available through the DANGER program. This system will be used by EPA to help refine geographic proximity of pesticide use to listed species and will be used by industry Task Force members to screen new pesticide registration applications for potential listed species implications.

2. Biological Requirements and Habits of Listed Species

The Agency's sources of best available and current information concerning species' life history, ecology, population demographics, etc., will include the Services' species' listing rules, species' recovery plans (when prepared), "status review" background documents, and "benchmark" or "foundational" studies identified by the Services since preparation of a listing rule or recovery plan. In addition, "species profiles" when prepared by the Services for other Federal action agencies (e.g., EPA's Office of Water) will be provided, upon request, to the Agency by the Services. Appropriate lead Service Field Offices or Lead Recovery Coordinators can also be contacted to provide any significant new information that may be available. In addition, information on the biological requirements and habits of a listed species are also obtained from other sources such as The Official World Wildlife Fund Guide to Endangered Species of North America (D.W. Lowe et al, 1990; C.J. Mosely, 1992; W. Beacham, 1994).

In the vast majority of situations, specific data within the above sources of information, together with the information used in screening level assessments, will be adequate to perform more refined analyses of direct and indirect effects on listed species and effects on critical habitat. Any literature searches performed by the Agency in an attempt to gather information beyond that which is held by the Services will be undertaken on a case-by-case basis for specific biological information and only when significant uncertainties remaining in a risk assessment prevent a reasonable effects analysis.

This information is assessed, together with data on commodity locations and geographic features (VI. D, 3 - 4) to determine whether spatial and temporal overlap in use and species activities and habits may result in exposure at a level and duration that produces the effect. This information may also assist EPA in evaluating the potential exposure levels and nature and magnitude of effects to listed species and critical habitat.

3. Sub-county Commodity Information

A variety of sources such as agricultural extension agents, commodity representatives, state departments of agriculture, etc. are considered for obtaining sub-county information, if available. This information is used to identify where a commodity is grown within a county, in order to determine whether use of a pesticide on that commodity may occur in proximity to a listed species.

4. Geographic Features That May Preclude Exposure

Further expert opinion may be considered, if available, about any geography within a county that would limit the production of a particular crop or would limit the movement of a listed species. This information is used to further refine the determination of whether pesticide use may occur in proximity to a listed species or its critical habitat.

5. Incident Information

The incident information (see Sections IV.C.2.c and V.B.2 for incident information sources) from the Ecological Incident Information System and also the ECOTOX database (though a database not specifically targeted to the collection of incident data) described previously is reviewed for incidents involving specific species or species that may be predictors of effects to listed species. This information is not used to make an explicit determination of whether a species may be affected by a pesticide's use, but rather to assist in characterizing the potential risk.

6. Sales and Use Information

Information on sales of a particular pesticide or the amount used is obtained, if available, from two sources. First, in states that require pesticide use reporting, information on the amount of a particular pesticide used within relevant geographic areas is obtained from the State government. (Currently the only state data used is California's Pesticide Use Report data at http://www.cdpr.ca.gov/docs/pur/purmain.htm.) Where these data are not available, information that may be voluntarily supplied by pesticide manufacturers is reviewed. This information is not used to make an explicit determination of whether a listed species may be affected by a pesticide's use, but rather to assist in characterizing the potential risk.

7. Local Use Practices

Information about local use practices, including but not limited to, numbers of applications, rates of pesticide applications, timing of applications, and methods of application may be obtained from a variety of sources such as regional or local commodity organizations, extension service specialists, and state government agencies. This information is not used to make an explicit determination of whether a species may be affected by a pesticide's use, but rather to assist in characterizing the potential risk.

8. Monitoring Data

Results of available monitoring or sampling data, including but not limited to data generated through the U.S. Geological Survey's National Water Quality Assessment Program are reviewed to determine whether a particular pesticide has been detected in relevant water bodies. Both the frequency of detection and the level detected are used to better characterize the potential risk to the listed species. Further details on the National Water Quality Assessment Program can be found at: http://water.usgs.gov/nawqa/

E. Exposure Characterization in the Species-Specific and Habitat-Specific Assessments

1. Geographic Proximity

a. A "DANGER" Query

OPP queries the “DANGER” program to determine in what counties a pesticide’s use and a listed species may co-occur. The comparison of counties in which listed species occur, with counties in which agricultural commodities are produced, is made to determine if there is overlap, and thus, potential for a listed species to be exposed to a pesticide registered on that commodity. The result of this query is a list of species that occur in a county and that have the potential for exposure to the pesticide. EPA is working with the Services to expand this tool to capture information regarding the location of critical habitat, as well. This list of co-occurrences is the first refinement and narrows the area of concern by excluding species and areas of critical habitat that do not occur in an area where exposure could occur. For example, a pesticide that is registered nationally for use on hops will only have potential to expose listed species that occur in geographic areas where hops are grown. The “DANGER” program will thus exclude from the list species and habitats that are not in geographic proximity to the pesticide’s use areas.

b. Sub-county Use of the Pesticide

For each use that potentially poses a risk of concern to listed species or critical habitats, the geographic areas in which those uses occur, on a sub-county basis are identified if possible. Continuing the example above, while hops are only grown in counties in the Pacific Northwest, they are not grown everywhere within those counties. Where information is available to determine sub-county geographic areas of a given commodity, that information is compared to species occurrence and a determination made whether the species may be exposed. This step may or may not refine further the list of pesticide/species or pesticide/habitat co-occurrences for which a potential concern exists.

If information is available about the specific geography of an area within a county that may limit the production of a particular crop or that would limit the range of a listed species, this information is compared to the list of co-occurrences to refine the list of where a potential concern exists. For example, if it is known that the county's elevation ranges from 1200 feet above sea level to 6500 feet above sea level, and it also is known that a particular crop cannot be grown above 4000 feet above sea level, parts of the county above that altitude may be discounted as of potential concern. Similarly, the Little Kern Golden Trout occurs at rather high elevations in Fresno County, CA, but these higher elevations are distant from the large expanse of agricultural crops in the San Joaquin Valley of that county. Many listed plants occur in forests or rangeland areas far removed from crops. If the use being evaluated is for a crop, such species likely will not be exposed. Some crops, such as cranberries, are grown only in very specific and small parts of a county and may not be near a listed species habitat. There is no "compendium" of such spacial distribution information, so when it is found in the course of a risk assessment, it is being documented and accumulated for future use. This refinement of geographic proximity may result in removal of some species or habitats from the list of those for which there is a concern.

2. Refine Exposure Estimates Using Specific Assessment Methodologies

A review of the assessment methodology used in the screening-level risk assessment is conducted to assess whether the methodology is the most appropriate method for the species-specific or habitat-specific assessment. For example, an older assessment for a cotton use may include only a Tier I exposure model using GENEEC, which is based upon a high default potential for runoff. But using a PRZM-EXAMS Tier 2 exposure model for a particular pesticide may indicate that the potential aquatic exposure is considerably lower. Even if a Tier 2 PRZM-EXAMS model was used in a cotton assessment, early assessments with this model included a scenario only for Mississippi cotton. But the results of a Mississippi cotton runoff model would not be appropriate for use in estimating environmental concentrations from cotton grown in California because of differences in geography, soils, and meteorological patterns. Alternative scenarios are selected from those developed by EFED and reflect upper bound exposure at the selected site following procedures described in internal EFED guidance (Support Document #81). To the extent that additional exposure scenarios are warranted, analyses are undertaken in concert with EFED scientists. Any changes to the assessment assumptions, data used for risk analysis, and risk mitigation measures that depart from the typical screening level approach are documented and their associated impacts upon the overall risk conclusions related to listed species is presented. Where appropriate, the quantitative estimate of risks will be recalculated.

OPP does not have scenarios developed for all crops, and for many crops the scenarios represent only one or possibly two locations. While additional scenarios are always under development, and OPP now has a suite of scenarios to address most major crops and several regions, it is seldom possible to have a model to exactly fit a particular site. A species-specific or habitat-specific risk assessment will make use of a scenario that, using best professional judgment, is the most appropriate for a particular situation. Assessing environmental concentrations using a more appropriate model for the particular area of the country where potential exposure may occur, could result in either higher or lower predicted environmental concentrations and thus, more or fewer species on the list of those for which there may be a concern.

3. Refine Exposure Based on Biological and Habitat Requirements

For each species still of concern for direct or indirect effects, FEAD determines whether there are any biological characteristics of the species or habits of the species that would preclude exposure at levels that may cause direct effects. This refinement is based on an evaluation of the sources listed in Section VI. D. 2. FEAD reviews the habitat requirements, biology and habits of each identified species to determine whether there is any factor that would preclude exposures of concern. For example, if the residues of concern occur only on short grasses, it is important to know whether the species of interest use short grass environments as cover or food.

For potential chronic effects identified in the screening-level risk assessment, FEAD focuses on whether there is temporal overlap in pesticide residues and species activities and habits that may result in exposure at a level and duration that produces the effect. For example, while a pesticide may be in the environment at levels that could cause an effect given a certain

duration of exposure, a species that migrates through the area may not experience exposure for a duration long enough to results in that effect. On the other hand, a species that occurs in the area and does not migrate, may have exposure durations that could result in the effect.

F. Risk Characterization

After the species-specific or habitat-specific assessment is completed, FEAD documents those situations that resulted in a determination that the pesticide had "no effect" on the listed species. FEAD will determine that an action "may affect" a listed species if the RQ exceeds the endangered species LOC, and a species-specific analysis indicates temporal and spatial overlap between pesticide use and the species presence, except when specific information (e.g., data on the mode of action) demonstrates that the listed species would not be affected. For "may affect" determinations, FEAD distinguishes between those that "may adversely affect" the species or habitat and those that "may affect but are not likely to adversely affect" the species or habitat. Where the species-specific assessment results in a conclusion that there are no indirect effects nor exposure at levels that may result in direct effects, the review is concluded with a determination of "no effect." All other determinations therefore, involve either indirect effects or some level of potential exposure that may result in direct effects.

The distinction between those situations in which FEAD makes a "likely to adverse effect" determination versus those in which it determines the pesticide "may affect but is not likely to adversely affect" the species, is made using best professional judgment about the significance and likelihood of the effects. In making this judgement, FEAD gives due consideration to the biological data collected during the species specific analysis, the additional information to help characterize the potential for exposure (see section VI.D) and other exposure and toxicity data and lines of evidence used in the screening level assessment.

Available information on incidents, sales and use of the pesticide, local use practices, and monitored levels in the environment are reviewed (see Sections VI. D. 5 - 8, above). These factors are used in combination, and in conjunction with the degree to which the LOCs were exceeded, to determine whether the predicted effect based on labeled use of the product, is likely to occur or not.

1. Incident Information

It is acknowledged that not every incident is documented and reported. However, a review of incident information for a particular species or for species of the same taxa that occur in proximity to the listed species can provide insight to whether the effect predicted is more or less likely to occur. For example, if a number of incidents were reported that the pesticide in question had drifted off site and damaged non-target non-listed plants, listed plants in the vicinity may also be at risk of harm.

2. Sales and Use of the Pesticide

Use of a particular pesticide may change and thus, a reliable distinction between a pesticide use that "may affect" and one that has no effect on a species cannot be made based on sales and use information. However, sales and use information over several past years can be used to weigh whether a predicted effect is more or less likely. For example, there may be 100,000 acres of a particular commodity grown in the vicinity of a listed species of concern. If the risk assessment, which resulted in a determination that the LOC was exceeded, was based on information that 100% of the crop was treated with the pesticide, but sales and use information combined with acres grown indicates that only 20% of the 100,000 acres is generally treated with the pesticide, concentrations in the environment may be less than modeled values.

3. Local Use Practices

Similarly, local use practices can be used to predict whether concentrations in the environment may be less than predicted through modeling. For example, if inputs to the model were based on highest legal application rates and maximum number of applications per season with the minimum legal interval between application, environmental concentrations could be predicted to be relatively lower than modeled if local practices were to treat only half as many times as permitted or at less than the maximum legal application rate.

4. Monitored Levels in the Environment

Most monitoring data available is from programs or studies designed for various purposes, often not for the purpose of determining the levels to which a species may be exposed. These data may underestimate exposure or overestimate exposure depending on a variety of factors, including the timing of sampling relative to pesticide use, the frequency of sampling and the analytical method used to determine the level of pesticide in the samples. For these reasons, monitoring data is not generally used to distinguish between a "no effect" determination and a "may affect" determination. However, it can be useful in weighing whether a predicted effect is more or less likely than would be indicated by modeling, when viewed in combination with the other factors mentioned in 1-3 above.

Considering this information, and the degree to which LOC's were exceeded in the screening-level risk assessment, FEAD determines that the pesticide is "may adversely affect" the listed species or that it "may affect but is not likely to adversely affect" the listed species.

G. Assumptions

Absent information to the contrary, FEAD makes some assumptions during its species-specific or habitat-specific assessment as indicated below:

- Where a pesticide is designed for a particular group of insects, others are not likely to be affected. Examples include specific strains of *Bacillus thuringensis* (BT) which are bred for certain pests.

- The nature of the use itself can preclude exposure in some situations. For example, baits will not affect flying insects; fumigants will not expose species that are not in treated burrows or fields.

- An herbicide that affects only broad-leafed plants will not have an effect on listed grasses, and an herbicide specific to grasses will not affect broad-leafed plants. In a few cases, this kind of distinction can be made for dicots and monocots, although often there is insufficient information to address monocots that are not grasses, which includes lilies, orchids, irises, onions, or sedges.

- Listed plants do not occur in cultivated fields. EPA acknowledges that they can get to such fields, and even germinate there. But the cultivation will not allow the plant to continue to exist there even in the absence of pesticide use. Therefore, the assumption is made that any effects to listed plants occur outside the treated field.

- A pond species or a species in first order streams is assumed to be represented for acute risk by the typical farm pond model. A species in a lake can be represented by a farm pond scenario as it may be adjusted for the larger size of the lake; but then it should also be adjusted, without quantitative models, for the mixing zone near the pesticide input to the lake.

- A species in 2nd or 3rd order streams is not represented by any current scenarios and thus, best professional judgment is applied to the result of models used for 1st order stream species.

- In examining food for listed fish, food will be aquatic arthropods, and the aquatic arthropod LC50 will be used for the most sensitive species unless (1) this appears to be far lower than the array of other aquatic invertebrate LC50s, and (2) the outlier species is not specifically important to the fish under consideration.

- For cover for fish, the EC50 for duckweed (*Lemna sp.)* is used and in the absence of any available data on duckweed, algae data are used. This assumption is based on the position that algae and duckweed are in different kingdoms, and as such duckweed is preferred over algae data to represent vascular plants. Should aquatic algae become listed, algae data rather than *Lemna* data would be used to represent the listed algae.

These assumptions would be used if information to the contrary was not available.

H. Environmental Baseline and Analysis of Cumulative Effects

For those actions that FEAD determines may affect listed species or may destroy or adversely modify critical habitat, (but for which FEAD cannot conclude the action is not likely to adversely affect such species or habitats), FEAD will contact the appropriate Service(s) and request information relating to the environmental baseline. Using the information the Services provide, FEAD will consider how the anticipated potential effects of the pesticide use are likely to impact the species or habitat and will include any additional relevant information from the Service's environmental baseline in its refined risk assessment. If EPA submits a request for formal consultation to the Service, the supporting materials will include the information on the environmental baseline provided by the Services.

In addition, if EPA submits a request for consultation to the Service for which it cannot conclude that the action is not likely to adversely affect listed species, FEAD will also include in its supporting materials an evaluation of the combined impacts of the use of the pesticide and other "cumulative effects." "Cumulative effects" are those effects of future State or private activities, not involving Federal activities, that are reasonably certain to occur within the action area of the Federal action subject to consultation." Because the "action area" for a pesticide may vary from relatively small to very large, FEAD will determine the scope and depth of the cumulative effects analysis on a case-by-case basis. Typically, the larger the action area, the more general the analysis will be. FEAD's initial and primary source of information on the identity of and potential for cumulative effects will be the listing notice and recovery plan that identify the major stressors for a species. As practicable, FEAD may also consult with local officials who are likely to be knowledgeable about future activities that could adversely affect the listed species.

VII. List of Support Documents

#1. Study Classifications Used by EFED in Data Evaluation Records (DER's) dated February 26, 2003. Draft.

#2. Pesticide Assessment Guidelines, Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms; EPA-540/9-82-024, October 1982

#3. Pesticide Assessment Guidelines, Subdivision J, Hazard Evaluation: Non-target Plants; EPA-540/09-82-020, October 1982

#4. Pesticide Assessment Guidelines, Subdivision L, Hazard Evaluation: Non-target Insects; EPA-540/9-82-019, October 1982

#5. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate; EPA-540/9-82-021, October 1982

#6. Deleted.

#7. Guidelines for Ecological Risk Assessment. Risk Assessment Forum. EPA/630/R-95/002F, April 1998.

#8. Hazard Evaluation Division. Standard Evaluation Procedure. Ecological Risk Assessment. EPA-540/9-85-001, June 1986.

#9. US EPA OPP EFED Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides. Version II. February 28, 2002.

#10. PRZM Standard Crop/Location Scenarios, Procedure to Develop and Approve New Scenarios, and PRZM Turf Modeling Scenarios to Date. Memorandum from EFED's acting Director, February 27, 2002.

#11. Pesticide Root Zone Model (PRZM) Field and Orchard Crop Scenarios: Standard Procedures for Conducting Quality Control and Quality Assurance.

#12. Policy for Estimating Aqueous Concentrations from Pesticides Labeled for Use on Rice. Memorandum from EFED's Acting Director, October 29, 2002.

#13. Mammalian Risk Assessments. February 23, 1995 Draft.

#14 Hoerger, F. and E.E. Kenaga. "Pesticide Residues on Plants: Correlation of Representative Data as a Basis for Estimation of Their Magnitude in the Environment".

#15. J.S. Fletcher, J.E. Nellessen and T.G. Pfleeger. 1994. Literature Review and Evaluation of the EPA Food-Chain (Kenaga) Nomogram, an Instrument for Estimating Pesticide Residues on Plants. Environ. Tox. Chem. 13(9): 1383-1391.

#16. Calculation of Terrestrial EECs. EFED Policy Memorandum from EFED Acting Director, August 26, 1999.

#17. Documentation for ELL-Fate Version 1.2, July 19, 2001.

#18. Automation of Environmental Exposure Concentrations (EECs) and Determinations of Risk Quotients (RQs) for Terrestrial Plants Using TerrPlant Model, Version 1.0. EFED Policy Memorandum from EFED Acting Director, October 16, 2002.

#19. Closure on Nontarget Plant Phytotoxicity Policy Issues. Memorandum from EEB/EFED Chief, October 21, 1994.

#20. Comparative Analysis of Acute Avian Risk from Granular Pesticides. US EPA OPP, March 1992.

#21. Guidance for Conducting Screening Level Avian Risk Assessment for Spray Applications of Pesticides. US EPA OPP, July 7, 2000.

#22. EIIS. Documentation for the Ecological Incident Information System. EFED Information and Support Branch, EFED, OPP. August 15, 2002.

#23. Guidance Document for Conducting Terrestrial Field Studies. EPA 540/09-88-109, September 1988.

#24. The Office of Pesticide Programs' Guidance Document on Methodology for Determining the Data needed and the Types of Assessments Necessary to Make FFDCA Section 408 Safety Determinations for Lower Toxicity Pesticide Chemicals. OPP US EPA, May 9, 2002.

#25. Decisions on the Ecological, Fate, and Effects Task Force. Memorandum from US EPA Assistant Administrator to Director of US EPA OPP, October 29, 1992.

#26. What the LOC is, and How it Should Be Used. Memorandum from EEB Chief, June 8, 1994.

#27a. Format and Risk Characterization. Additional Guidance for EFED Risk Assessment Documents. EFED Standard Operating Procedure. January 13, 2004.

#28. Science Policy Council Handbook. Risk Characterization. EPA 100-B-00-002, December 2000.

#29. US EPA 40 CFR Part 158 Data Requirement Tables.

#30. Science Policy Council Handbook. Peer Review. EPA 100-B-00-001, December 2000.

#31. Implementation Paper for the New Paradigm. Memorandum from OPP Office Director, August 25, 1993.

#32. Pesticide EcoToxicity Database.

#33. Wildlife Exposure Factors Handbook. Table of Contents and Introduction.

#34. Pesticide Assessment Guidelines, Subdivision I. Experimental Use Permits.

#35. Standard Evaluation Procedure. Non-target Plants: Vegetative Vigor - Tiers 1 and 2.

#36. Standard Evaluation Procedure. Non-target Plants: Aquatic Field Testing - Tier 3.

#37. Standard Evaluation Procedure. Non-target Plants: Growth and Reproduction of Aquatic Plants - Tiers 1 and 2.

#38. Standard Evaluation Procedure. Non-target Plants: Seed Germination/Seedling Emergence - Tiers 1 and 2.

#39. Standard Evaluation Procedure. Non-target Plants: Terrestrial Field Testing - Tier 3.

#40. Standard Evaluation Procedure. Non-target Plants: Target Area Testing.

#41. Standard Evaluation Procedure. Terrestrial Field Dissipation.

#42. Standard Evaluation Procedure. Soil Photolysis.

#43. Standard Evaluation Procedure. Aerobic Soil Metabolism Studies.

#44. Standard Evaluation Procedure. Soil Column Leaching Studies.

#45. Standard Evaluation Procedure. Acute Toxicity Test for Freshwater Fish.

#46. Standard Evaluation Procedure. Daphnia Magna Life-Cycle (21-Day Renewal)Chronic Toxicity Test.

#47. Standard Evaluation Procedure. Acute Toxicity Test for Estuarine and Marine Organisms (Shrimp 96-Hour Acute Toxicity Test).

#48. Standard Evaluation Procedure. Estuarine Fish 96-Hour Acute Toxicity.

#49. Standard Evaluation Procedure. Acute Toxicity T4est for Estuarine and Marine Organisms (Mollusc 96-Hour Flow-Through Shell Deposition Study).

#50. Standard Evaluation Procedure. Fish Early Life-Stage.

#51. Technical Guidance Document. Aquatic Mesocosm Tests to Support Pesticide Registrations.

#52. Standard Evaluation Procedure. Avian Single-Dose Oral LD50.

#53. Standard Evaluation Procedure. Avian Dietary LC50 Test.

#54. Standard Evaluation Procedure. Avian Reproduction Test.

#55. Guidance Document for Conducting Terrestrial Field Studies.

#56. Standard Evaluation Procedure. Honey Bee – Toxicity of Residues on Foliage.

#57. Standard Evaluation Procedure. Honey Bee - Acute Contact LD50.

#58. Standard Evaluation Procedure. Field Testing for Pollinators.

#59. Standard Evaluation Procedure. Pesticide Spray Drift Evaluation: Droplet Size Spectrum Test and Drift Field Evaluation Test.

#60. Standard Evaluation Procedure. Anaerobic Soil Metabolism Studies.

#61. Standard Evaluation Procedure. Hydrolysis Studies.

#62. Standard Evaluation Procedure. Aqueous Photolysis Studies.

#63. Standard Evaluation Procedure. Acute Toxicity Test for Freshwater Invertebrates.

#64. Policy Establishing Procedures for Reviewing and Approving New Science Policy.

#65. EFED’s Revised Policy Guidance for Section 18's.

#66. Information on Exposure Modeling Work Group.

#67. Atrazine 4L Herbicide Pesticide Label.

#68. Lorsban - 4E Pesticide Label.

#69. Use the NOAEC from Aquatic Chronic in Risk Assessment.

#70 Background on the Development of LOCs.

#71b. Procedure for the Inclusion of Open Literature Searches in Pesticide Screening Level Risk Assessments for Ecological Effects. January 21, 2004.

#72. Section 1. Database and Documentation Overview. MED ECOTOXICOLOGY DATABASE SOP's. September 1997.

#73. ECOTOX. ECOTOXicology Database System. Literature Search and Citation Identification. MED ECOTOXICOLOGY DATABASE SOP's. April 2001.

#74. ECOTOX. ECOTOXicology Database System. AQUIRE Coding Guidelines. August 2003.

#75. ECOTOX Data Entry Procedures (AQUIRE). MED ECOTOXICOLOGY DATABASE. June 2000.

#76. ECOTOX. ECOTOXicology Database System. Chemical Verification and Database Entry Procedures (EcoChem). April 2001.

#77. ECOTOX. ECOTOXicology Database System. Taxonomic Name Verification Procedures (CRITTERS). September 2001.

#78. Draft. SOP for Metabolism Assessment Review Committee. July 5, 2002.

#79. Microbial Sample Case Studies.

#80 European Union Directive 91/414/EEC.

#81. Memorandum and Attached Procedure - "Pesticide Root Zone Model (PRZM) Field and Orchard Crop Scenarios: Standard Procedures for Conducting Quality Control and Quality Assurance. January 21, 2004.

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Appendix A. Overview of OPP's Screening-Level Ecological Risk Assessment Process for Antimicrobial Pesticides

I. Background

The Antimicrobials Division (AD) in OPP is responsible for the registration and reregistration of antimicrobial pesticides. Antimicrobial pesticides include those that claim mitigation or control of bacteria, viruses, fungi, protozoa, algae, slime, and most recently prions. Antimicrobial products used in or on humans or animals are considered drugs and are approved and regulated by the Food and Drug Administration (FDA). The AD regulates antimicrobial pesticides used on or in inanimate objects, such as wood, floors, and walls; industrial processes or systems; on surfaces, in water or other liquids to prevent or reduce contamination, fouling, or deterioration.

AD reviews data submitted by registrants and conducts screening-level risk assessments using the basic process outlined for EFED. These assessments are conducted for individual pesticide active ingredients, formulations, and degradates to evaluate the ecological risk of antimicrobial pesticides to non-target species, including the potential impact on listed species. Formulated product and/or degradate tests are conditionally required for terrestrial and aquatic animal species, and aquatic plants using the same approach used by EFED. Formulated product tests are always required for terrestrial plant studies, and special leaching studies.

In addition to the data required under FIFRA, AD uses open literature data routinely. A great deal of literature is available for both the pesticide and non-pesticidal uses of these chemicals and is considered during the assessment process. Searches are conducted by a contractor.

AD also reviews human health data that can be useful for predictions of adverse effects to mammalian wildlife, information on pesticide residue dissipation in food crops and animal feed items, and leach rate data from treated objects. These data can be used to estimate dissipation half-lives for long term exposure scenarios.

II. Ecological Effects Testing

AD's current practice is similar to EFED's assessment process described in Section V and uses a tiered system of ecological effects testing to assess the potential risks of proposed pesticide uses to non-target plants (§158.540 of the current regulatory text), aquatic and terrestrial vertebrates and invertebrates (§158.490), and nontarget insects (§158.590). These tests include short-term acute, subacute, reproduction, and field studies, which progress from the basic laboratory tests to the applied field tests. The results of each set of tests must be evaluated to determine the potential of the pesticide to cause adverse effects and to determine whether further testing is required. These data requirements provide the Agency with ecological effects information and allow the Agency to determine if registration is appropriate and if precautionary

label statements concerning toxicity or potential adverse effects to nontarget organisms are necessary.

A. Antimicrobial Pesticide Categories

Antimicrobial pesticides currently fall within one of the following 12 categories:

- Agricultural premises and equipment, such as animal houses/pens/milk houses;
- Food handling/storage establishments premises and equipment, such as food storage areas, processing plants, restaurants, transport vehicles;
- Commercial, institutional and industrial premises and equipment, such as hotels, theaters;
- Residential and public access premises, such as homes, shelters, public buildings;
- Medical premises and equipment, such as medical related facilities - clinics, hospitals;
- Human drinking water systems, such as public/private/emergency water systems;
- Materials preservatives, indoor food/feed, indoor non-food/feed, indoor/outdoor non-food/feed;
- Industrial processes and water systems, such as cooling towers, pulp/paper mills;
- Antifoulants, such as boat bottoms, crab/lobster pots, underwater structures;
- Wood preservatives, such as freshly cut logs, utility poles, fence posts, railroad ties;
- Swimming pools, such as swimming pools, jacuzzis, hot tubs; and
- Aquatic areas, such as lakes, streams, drainage ditches, ponds.

B. Use Categories with Minimal Expected Environmental Exposure

Of the 12 antimicrobial use categories, eight are indoor and related uses: agricultural premises and equipment; food handling and storage establishments, premises and equipment; commercial, institutional and industrial premises and equipment; residential and public access premises; medical premises and equipment; human drinking water systems; materials preservatives; and swimming pools.

Movement of antimicrobials from these indoor uses into the general environment is most likely to occur through water and moves from rinsates and flushes to effluent water to the aquatic environment. The Agency believes that environmental exposures from these uses are likely to be small for one or more of the following reasons:

- These uses are not rapidly or directly connected to aquatic environments.
- Antimicrobials tend to be degraded or bound in the presence of biological matter.
- In some cases effluents are processed in water treatment plants.

Therefore, AD believes these uses pose little prospect of significant environmental exposure to non-target terrestrial and aquatic organisms

Given the low prospect of significant environmental exposure from this group of uses, AD requests only a small set of ecological effects and environmental fate data for these use

scenarios. The data requirements are avian acute oral LD_{50} (Guideline 850.2100), an acute freshwater fish LC_{50} (Guideline 850.1750), an acute freshwater invertebrates EC_{50} (Guideline 850.1010), and a hydrolysis study (Guideline 832.2120). These studies characterize hazard to target species for label hazard statements and if an unexpected spill were to occur. AD may request the testing of additional species or higher tier testing based on the results of this basic set of studies or reports of adverse effects in the literature or via FIFRA 6(a)(2).

C. Use Categories with Significant Expected Environmental Exposure

The remaining four use categories are industrial processes and water systems (once-through and all others), antifoulants, aquatic areas, and wood preservatives. (Only once-through systems directly introduce the antimicrobial into the environment in effluent. Recirculating industrial processes and water systems, in which the antimicrobial is re-circulated in the treated system or is disposed of as a hazardous waste, do not result in direct discharge of antimicrobial pesticide into the environment.) These uses either occur outdoors, discharge effluent directly to the outdoors or result in materials treated with antimicrobials (i.e. wood preservatives and antifoulants) being placed in the environment, thereby leading to potentially significant environmental exposure. AD utilizes the same battery of ecotoxicity and environmental fate studies requested by the EFED for agricultural sites. In addition, AD requests product leach rate tests (antifoulant paints, wood preservatives), when appropriate.

III. Ecological Effects Assessment

A. Exposure Assessment

Field residue monitoring studies, when available, are used to estimate EEC's. These additional, higher-tiered studies (e.g., avian, fish, and invertebrate reproduction studies, sediment toxicity studies, aquatic field studies) may be required when basic data and environmental conditions suggest possible adverse effects, in order to determine whether the pesticide meets the requirements for registration and to determine the need for mitigation. Data from these studies are used to estimate the potential for chronic effects, taking into account the measured or estimated residues in the environment.

In some cases, the results of field studies may give rise to the need for further testing and/or field residue monitoring. Field residue monitoring may be requested of the registrant in lieu of higher tier biological field studies (Support Document # 7 and #25). The Agency makes this determination on a case-by-case basis, considering such information as the pesticide's intended use, use rates, toxicity, physical and chemical properties; the parent compound's environmental fate characteristics and transformation products (such as metabolites and degradation products); nontarget organisms likely to be exposed; and the likelihood of exposure.

When field residue monitoring data are not available, models are used to estimate EEC's. The models account for dosage per unit area, half-lives of the chemical in soil and water, soil adsorption/desorption, leaching rate, and other factors. AD generally uses the fate models used

by the EFED and occasionally uses Luttik-Johnson for antifoulant paints. In addition, AD is assessing additional models for antifouling and for large scale runoff scenarios. AD is currently participating on workgroups formed by the Organization for Economic Cooperation and Development that are evaluating the various models available for antifouling paints, wood preservatives, and cooling towers.

B. Toxicity Assessment

AD generally only requires toxicity data for antimicrobial pesticides expected to have high exposure. For pesticides with low exposure based on labeled uses or other information, AD has adopted an approach that should allow registrants to generate fewer toxicity studies in total than those required for high exposure uses. Under this approach, registrants of low exposure antimicrobials may perform tests in a tiered fashion. After initially required tests are conducted, additional testing may be required for low-exposure uses if the result of the initial tests trigger the need for additional data.

High exposure uses include human or animal drinking water, fruit and vegetable rinses, egg washes, metal cutting (metalworking) fluids, swimming pools, outdoor aquatic uses in lakes, rivers or streams which have the potential to contaminate potable water, indirect food uses with residues >200 parts per billion (ppb), and any other uses not already specified which require a tolerance or exemption from the requirement for a tolerance. Low exposure uses consist of all other uses, which are expected to pose little or no exposure.

An antimicrobial use is considered an indirect food use when it is not applied directly to food, but is used in such a way that food may reasonably be expected to bear inadvertent residues through contact with treated surfaces and articles. Examples of antimicrobial uses which may result in inadvertent residues in food through normal use are sanitizers and disinfectants, which may be used in food handling areas.

C. Risk Assessment Methods and LOCs

The risk assessment methods used to evaluate potential risk are similar to those used by the EFED and are based on the RQ, which is compared to AD's LOCs. The LOCs currently address the following risk presumption categories:

(1) **Acute high** - Potential for acute risk is high, and regulatory action may be warranted in addition to restricted use classification;
(2) **Acute Restricted Use** - Potential for acute risk is high, but this may be mitigated through restricted use classification;
(3) **Acute Listed Species** - Potential for acute risk to listed species is high, and regulatory action may be warranted, and
(4) **Chronic Risk** - Potential for chronic risk is high, and regulatory action may be warranted.

AD does not perform assessments for chronic risk to plants, acute or chronic risks to nontarget insects, or chronic risk from granular/bait formulations to mammalian or avian species.

The ecotoxicity test values (i.e., measurement endpoints) used in the acute and chronic risk quotients are derived from the results of required studies. Examples of ecotoxicity values derived from the results of short-term laboratory studies that assess acute effects are:

- LC_{50} - fish and birds,
- LD_{50} - birds and mammals,
- EC_{50} - aquatic plants and aquatic invertebrates, and
- EC_{25} - terrestrial plants.

Examples of toxicity test effect levels derived from the results of long-term laboratory studies that assess chronic effects are:

- LOEC - birds, fish, and aquatic invertebrates,
- NOEC - birds, fish and aquatic invertebrates, and
- MATC - fish and aquatic invertebrates.

For birds and mammals, the NOEC value is used as the ecotoxicity test value in assessing chronic effects. Other values may be used when justified. Generally, the MATC (defined as the geometric mean of the NOEC and LOEC) is used as the ecotoxicity test value in assessing chronic effects to fish and aquatic invertebrates. However, the NOEC is used if the measurement endpoint is production of offspring or survival.

Risk presumptions, along with the corresponding RQs and LOCs are summarized in Table 1.

Table 1. Risk Presumptions for Terrestrial Species

Risk Presumption	RQ	LOC
Birds and Wild Mammals		
Acute High Risk	EEC[1]/LC50 or LD50/sqft[2] or LD50/day[3]	0.5
Acute Restricted Use	EEC/LC50 or LD50/sqft or LD50/day (or LD50 < 50 mg/kg)	0.2
Acute Listed Species	EEC/LC50 or LD50/sqft or LD50/day	0.1
Chronic Risk	EEC/NOEC	1

[1] abbreviation for Estimated Environmental Concentration (ppm) on avian/mammalian food items

[2] $\frac{\text{mg/ft}^2}{\text{LD50 * wt. of bird}}$ [3] $\frac{\text{mg of toxicant consumed/day}}{\text{LD50 * wt. of bird}}$

Risk Presumptions for Aquatic Animals

Risk Presumption	RQ	LOC
Acute High Risk	EEC[1]/LC50 or EC50	0.5
Acute Restricted Use	EEC/LC50 or EC50	0.1
Acute Listed Species	EEC/LC50 or EC50	0.05
Chronic Risk	EEC/MATC or NOEC	1

[1] EEC = (ppm or ppb) in water

Risk Presumptions for Plants

Risk Presumption	RQ	LOC
Terrestrial and Semi-Aquatic Plants		
Acute High Risk	EEC[1]/EC25	1
Acute Listed Species	EEC/EC05 or NOEC	1
Aquatic Plants		
Acute High Risk	EEC[2]/EC50	1

Acute Listed Species	EEC/EC05 or NOEC	1

[1] EEC = lbs ai/A
[2] EEC = (ppb/ppm) in water

IV. Assessments for Listed Species

AD's registration and reregistration documents contain a section on listed species. When LOCs for listed species are exceeded, AD will note in the document that LOC's are exceeded. Listed species exceeding LOC' s are tabulated by state/county and assessed for their proximity to the pesticide. FEAD is then consulted for further analysis of the species at risk. FEAD provides appropriate recommendations for mitigation/restrictions on use if necessary.

Appendix B. Overview of OPP's Screening-Level Ecological Assessment Process for Biological Pesticides

I. Background

The Biopesticides and Pollution Prevention Division (BPPD) was created for the purpose of bringing safer pesticide products into the marketplace and to encourage the adoption of these safer, reduced risk products and related integrated pest management (IPM) practices. The safer, reduced risk products that are scientifically reviewed and registered are known as biological pesticides or biopesticides. Biopesticides are distinguished from conventional chemical pesticides by their unique modes of action, low use volumes, natural occurrence, generally low to no persistence in the environment, and, for many biopesticide active ingredients, target species specificity.

There are three categories of biopesticides: biochemicals, microbials, and plant-incorporated protectants (PIPs). As defined in 40 CFR §158.65 (a) and (b), Biochemical Pesticides include, but are not limited to compounds such as semiochemicals, natural plant and insect hormones and synthetic growth regulators, and enzymes. Microbial Pesticides include microorganisms and their toxic metabolites such as bacteria, fungi, viruses, and protozoans, as well as novel microbes (i. e. genetically-modified or nonindigenous species). In 40 CFR §152.3, a Plant Incorporated Protectant (PIP) is defined as a "pesticidal substance that is intended to be produced and used in a living plant, or in the produce thereof, and the genetic material necessary for the production of such a pesticidal substance. It also includes any inert ingredient contained in the plant, or produce thereof."

The Biochemical Pesticide Branch (BPB) is responsible for the registration of biochemical pesticides. Microbial pesticides and PIPs are the responsibility of the Microbial Pesticides Branch (MPB). Prior to registration, the potential for any biological pesticide to cause adverse effects to non-target organisms, including listed species, and

the environment must be thoroughly investigated. Due to the unique nature of these pesticides, slightly different, but generally complimentary and overlapping approaches, are used by BPB and MPB to assess the potential risks involved with the use of biochemical and microbial pesticides and PIPs.

Section II of this appendix describes the assessment process for biochemical pesticides, and Section III addresses microbial pesticides and PIPs.

II. Non-Target Organism Risk Assessment for Biochemical Pesticides

Before beginning a description of the biochemical pesticide risk assessment process, it is important to first describe the nature of biochemical pesticides, how they are distinguished from conventional chemical pesticides, and their pesticidal mode of action.

A. What are Biochemical Pesticides

A biochemical pesticide is defined by the following two criteria:

- It is a generally naturally-occurring substance (or is structurally similar and functionally identical to a naturally-occurring substance), and
- It has a non-toxic mode of action.

It is important to note that not all biochemicals are naturally-occurring. An example of synthetic substances that meet the criteria for classification as a biochemical are synthetic Lepidopteran pheromones, which are structurally and functionally identical to the naturally occurring pheromones produced by moths and butterflies.

Additionally, the "natural occurrence" of a substance does not immediately lead to the presumption that it has a non-toxic mode of action. An example of a substance in this category would be pyrethrum, a natural insecticide obtained from certain chrysanthemum flowers that is known to be a very potent neurotoxin. This toxic mode of action would preclude pyrethrum from being classified as a biochemical.

B. Non-Toxic Modes of Action:

There are several non-toxic modes of action whereby biochemicals accomplish their pesticidal activity. These are grouped according to the following categories:

- Plant and insect growth regulators (PGRs and IGRs)
- Semiochemicals
  - Pheromones
  - Attractants/repellents (including irritants)
- Suffocating agents

- Desiccants
- Coatings
- Systemic Acquired Response (SAR)-inducers

Biochemical PGRs and IGRs include those substances that mimic or block the activity of naturally-occurring growth substances. Pheromones are be used as either mating disruptants or as attractants to lure target pests (usually insects) into traps. Attractants and repellents encompass all those substances generally considered to be non-pheromone semiochemicals. Suffocating agents (typically oils) act by physically preventing respiration of the target pest, resulting in death by asphyxiation. Desiccants accomplish their activity by solubilizing or physically perturbing waxy cuticles of plants or insects such that the organisms succumb to rapid evaporative water loss. Coatings are substances commonly found in the environment (e.g. clay particles), and have a passive mode of action (i.e. there is no biochemical interaction against the target pest). When applied to plant foliage, coatings function as physical barriers to infections by plant pathogens, cause unpalatable abrasiveness to phytophagous insects, or act as physical irritants. Substances that induce the SAR response have no direct activity against the target pest, but function to enhance the inherent capacity of plants to resist infection by plant pathogens, or produce secondary plant metabolites that cause the plant to be unpalatable, or possibly toxic to a pest (e. g. increase phenolic content).

Although biochemical pesticides, by definition, act via a non-toxic mode of action, they can still be lethal to the target pest. Due to the broad-spectrum, non-species-specific activity of many biochemical pesticides, all unintentional exposure pathways and potential lethality to non-targets must be assessed. Furthermore, a non-toxic mode of action against the target pest does not presume a lack of toxicity to non-target organisms. The following discussion will focus on the detailed information that are required by reviewers to conduct an risk assessment.

C. Characterization of the Risk

Risks to non-target organisms are characterized via a preliminary assessment of toxicity (or lethality) and of all conceivable exposure pathways to non-targets by application of the biochemical pesticide. The risk characterization is summarized in the following equation:

Toxicity (or Lethality) x Exposure = Risk

Due to non-toxic modes of action and/or lack of exposure to non-targets by most biochemical pesticides, **a Risk Quotient (RQ) is not typically calculated** since the point estimates of either toxicity and/or exposure will usually be at or near zero. A qualitative assessment is conducted, which is discussed in the next section.

D. Components of the Risk Assessment

The preliminary assessment of toxicity is facilitated by a complete understanding of the product chemistry of the biochemical active ingredient and by the use pattern of the end-use product. These data/information include (but are not limited to):

- Mode of action;
- Persistence/degradation rate;
- Environmental fate (what are the degradation products and where do they go);
- Product formulation (is it a liquid, granular, or dust);
- Application method (e.g. foliar, soil, or fog applications; seed treatments);
- Application rate and timing (amount per unit area;, applications/growing season; early, mid-, and/or late season applications);
- Use sites (terrestrial or aquatic; agricultural, natural area, or urban/homeowner); and
- Target pest(s).

Other data/information may be required on a case-by-case basis, depending on the nature of the active ingredient and the use sites proposed for the product. The risk assessor also must have an in-depth understanding of the chemistry of the formulated product, particularly of the "other" (formerly known as inert) ingredients (buffers, diluents, stabilizers, surfactants, etc.) that are applied with the end-use product. These intentionally added ingredients may have unanticipated adverse effects to non-targets and the environment.

E. Risk Assessment for Listed Species

Potential risks to all non-target organisms are considered when evaluating a biochemical pesticide and, therefore, specific risk assessments for listed species are usually not conducted. As it will be discussed in more detail below, registrants are

required to present studies, data, and/or information demonstrating a lack of toxicity and/or exposure to any non-target species (avian, fish, aquatic invertebrate, insect, and plant) via the use of a biochemical pesticide end-use product according to its proposed label directions. The unique characteristics of biochemical pesticides, which generally have non-toxic modes of action, low use volumes, and ready biodegradability (low to no persistence), usually minimize the risks to all non-targets, including listed species.

If the BPB risk assessor, upon review of the product label use directions and use sites, determines that there is a potential for exposure to non-target organisms, the registrant will be required to revise the product label language to ensure that the potential exposure to non-targets will be mitigated. These revisions may include, but are not limited to, changes in application timing and/or deletion of selected use sites. When the biochemical has a broad spectrum (non-specific) and lethal (but non-toxic) mode of action, revisions to product label use directions, use sites, and environmental hazards statements may also be required._An example of a lethal, but non-toxic model of action is a suffocating oil, such as soybean oil.

Most biochemicals are registered for use in agriculture and horticultural/ornamental sites, and to a lesser extent in public recreation areas (e.g., golf courses, city/county parks, etc), railroad/highway/electrical rights-of-way, and homeowner settings. If a listed species is expected to be exposed from a pesticide on a labeled use site, the risk assessor will consult with FEAD to determine whether the proposed use of a biochemical pesticide will result in exposure to listed species. If it is determined that exposure will occur and that such exposure has the potential for adverse effects, BPPD and FEAD will arrange for a consultation with the appropriate agency (U.S. Fish and Wildlife Service and/or U.S. National Marine Fisheries Service). Potential exposure will be minimized as previously described by evaluating the product label and requiring revisions to the label language and, if necessary, restricting and/or deleting certain use sites.

Similarly, if biochemical pesticides are intended for use in natural areas (nature preserves, state parks, national forests, etc.) or if there is a potential for off-site movement to such areas, the products will be evaluated on a case-by-case basis, as described above, to determine exposure to listed species and other non-target organisms. Exposure is not considered to be a problem if the registrant can unequivocally demonstrate (via EPA-guideline studies or publically available technical data) that the biochemical pesticide is non-toxic to all potentially exposed non-target organisms, including listed species, or that it will not significantly and permanently disrupt the normal biological activities of potentially exposed non-targets.

It is important to note that most biochemical pesticide active ingredients are already present in the environment and that non-target organisms are already regularly exposed to these substances. Furthermore, the amount of biochemical active ingredient applied is often less than what is present in the environment. It should also be noted that other governmental agencies (state, local, and/or federal) that have land

management responsibilities may provide additional site-based assessments to determine whether they will use a particular biochemical pesticide to control pests and protect listed species.

F. The Biochemical Risk Assessment

Once the components of the risk assessment have been assembled, the risk assessor uses this information to assess the full range of potential and actual exposure pathways of a biochemical pesticide to non-target organisms and the environment. Toxicity (or lethality) data for the toxicity component of the risk equation are typically obtained from the tiered guideline studies conducted and submitted by the registrant to support a registration. A list of non-target organism study requirements for biochemicals, arranged as Tiers I, II, and III, is presented in a table in 40 CFR §158.690 (d). The tiered study guidelines are summarized below:

Tier I	Tier II	Tier III
Avian Acute Oral Toxicity	Volatility	Terrestrial Wildlife Testing
Avian Dietary Toxicity	Leaching	Aquatic Animal Testing
Freshwater Fish LC50	Adsorption/Desorption	Non-Target Plant Studies
Freshwater Invertebrate LC50	Octanol/Water Part. Coeff.	Non-Target Insect Studies
Non-Target Plant Studies	UV Absorption	
Non-Target Insect Studies	Aerobic Soil Metabolism	
	Aerobic Aquatic Metabolism	
	Soil Photolysis	
	Aquatic Photolysis	

Tier I guideline studies are basically acute toxicity studies designed to determine acute, short-term effects of pesticide exposure to non-target organisms. The need for Tier II and Tier III studies are triggered only when one or more Tier I studies demonstrate significant adverse effects to non-targets. Tier II studies are environmental fate studies that provide additional information on the degradation and persistence of biochemical pesticides and the potential for subchronic/chronic exposure. Tier III studies are longer term and more rigorous non-target studies on terrestrial and aquatic organisms and will be needed especially if the active ingredient is shown to persist in the environment.

It is important to note that no biochemical active ingredient or product has yet triggered a requirement for Tier II or Tier III non-target organism and ecological fate/effects studies.

Once the exposure pathways to non-target organisms have been determined and the potential for toxicity (or lethality) to non-target organisms is understood, a risk assessment is conducted that incorporates all exposure, toxicity, target pest, and use pattern information.

Upon completion of the risk assessment, the biochemical pesticide is subjected to a risk management analysis. This is generally conducted by the Regulatory Action Leader (or RAL) for the product, in close consultation with the science reviewer(s). The RAL is the principal point of contact with the registrant of a particular product and is responsible for administratively guiding the product through the registration process.

G. Risk Assessments for Straight-Chain Lepidopteran Pheromones (SCLPs)

Non-target organism risk assessments are not typically conducted for products containing straight-chain lepidopteran pheromones (SCLPs). SCLPs are a group of pheromones consisting of unbranched aliphatics having a chain of nine to eighteen carbons, containing up to three double bonds, ending in an alcohol, acetate or aldehyde functional group (40 *CFR* ???). This structural definition encompasses the majority of known pheromones produced by insects in the order Lepidoptera, which includes butterflies and moths. Based on the data available to the Agency **(Federal Register Notice 1/26/94 & OECD, 2000)**, adverse effects on nontarget organisms are not expected from the use of SCLPs because these pheromones are released in very small quantities in the environment and act on a select group of insects (i.e., species-specific). SCLPs are biodegradable by enzyme systems present in most living organisms, and should present no problems with their normal physiology. For example, the known metabolism of long-chain fatty acids predicts that SCLPs would be metabolized either by _-oxidation yielding a series of paired carbon losses or by complexing with glucuronide and excretion by the kidneys (Federal Register v.60, Aug.30/95).

H. Waiver Requests

Submission of guideline studies is the most unambiguous approach to satisfy the data requirements for registration. The guideline studies are designed to provide the BPB risk assessor with the necessary information to assess the risks posed by a biochemical pesticide when it is used according to its proposed label directions. However, there may be circumstances where the registrant believes that conducting a study to support a particular data requirement is unnecessary, or may be too costly to conduct. The registrant may then request a waiver from the requirement for conducting one or more guideline studies.

Study waiver requests must be addressed on a guideline-by-guideline basis for all Tier I data requirements. Each waiver request must be accompanied by a scientific rationale, including technical information/data, that credibly supports the waiver request and will assure the BPB risk assessor that a guideline study will not be needed to complete the risk assessment.

Data from non-guideline studies are acceptable on a case-by-case basis only if they provide information/data that is equivalent to information/data that would have been generated by guideline studies, *and* they are conducted according to generally accepted scientific principles. Non-guideline studies obtained from the open technical literature, which is routinely searched, must have a reasonably complete description of the materials and methods to assure the BPB risk assessor that the submitted data will be useful in completing the risk assessment. Journal abstracts and reports from technical meeting proceedings generally do not contain sufficient information and, therefore, are typically classified as unacceptable for use in risk assessments. Similarly, testimonials found in advertising literature and anecdotal information unsupported by credible data are also unacceptable.

Another approach to supporting waiver requests is to demonstrate that there will be no exposure of non-target organisms (either directly or indirectly) to the biochemical pesticide following application to the proposed use site(s) and target pest(s) listed on the product label. For example, if the registrant request waivers from the study data requirements for fish toxicity and aquatic invertebrate toxicity, it must be demonstrated that the product is intended solely for terrestrial uses *and* that it is highly unlikely that fish or aquatic invertebrates would be exposed to the biochemical pesticide directly or indirectly (via runoff or spray drift). The product label would also be required to contain specific language warning the product user to avoid applying the product on or near aquatic sites and environmental hazards statements indicating that the product is toxic to fish and aquatic invertebrates. Alternatively, the registrant could present data demonstrating that the active ingredient rapidly degraded to non-toxic compounds following application, thereby minimizing exposure. The "other" (inert) ingredients in an end-use product must also be considered when developing a scientific rationale to support a waiver request.

I. Risk Management

After the risk assessment is completed, the biochemical pesticide is subjected to a risk management analysis by the RAL for the product, in close consultation with the science

reviewer(s). If minor risks regarding toxicity/lethality of the biochemical pesticide are identified in the risk assessment, the risks may be mitigated by addition of precautionary statements and environmental hazards statements (see discussion above under Waiver Requests) on the product label.

Conversely, if it is determined that risks cannot be mitigated with restrictive label language, and that severe adverse effects may result if the product is used as intended, BPPD may recommend that the product be transferred to the Registration Division where it would be treated as a conventional chemical pesticide and would receive a higher level of scrutiny and the reduced data requirements would not apply. Usually, if adverse non-target organism and environmental effects are indicated in the risk assessment it is also likely that there may be analogous adverse effects to human health.

J. Guidance for Non-Target Organism, Fate, and Expression Data Requirements

For biochemical pesticides, guidance for all non-target organism, fate, and expression data requirements may be found in the following Subpart D, Data Requirement Tables: 40 CFR §158.202 and in 40 CFR §158.690 (d). Specific information on individual non-target organism, fate, and expression testing guidelines is located in the OPPTS Harmonized Guidelines Series 850 and Series 835, and may be accessed in downloadable format at the U.S. EPA website at:

www.epa.gov/docs/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Series

and

www.epa.gov/OPPTS_Harmonized/835_Fate_Transport_and_Transformation_Test_Guidelines/Series/

Ideally, biochemical pesticides will have little or no effects on non-target organisms, degrade rapidly in the environment, have low application rates and are applied when non-targets are least likely to be present.

BPPD has registered many products that have broad spectrum effects on targets and non-targets, that persist in the environment, and/or are applied at relatively high rates. These issues are typically managed by the use of restrictive language (i.e. explicit use directions and precautionary statements) on the product label. For example, if a product has been determined to be a hazard to honey bees or other pollinators, the registrant will be instructed to have a label statement that restricts application of the biochemical pesticide at times when these beneficial non-target insects are present at the use site.

II. Endangered Species Risk Assessment for Microbial Pesticides

A. Characterization of the Listed Species Risk

BPPD must identify all biological pesticides whose use may cause potential adverse impacts on listed species and their habitats by determining which flora and fauna may be affected by the proposed product. This determination is made by examining the information on non-target species and host range data of the proposed pesticide. Available information on the biology and toxicity of the microbial pest control agent (MPCA), non-target effects data submitted for registration, and the pre-registration host-range studies are used to identify the non-target plants and wildlife that may be adversely affected. The data examined include avian, wild mammal, freshwater, estuarine and marine plants and wildlife, terrestrial plants and several orders of insects. Because of the relative specificity and limited host range of MPCAs, the listed species most likely to be affected are usually related to the target pests. (Five sample case studies are provided in Support Document #79.)

1. Exposure Assessment

The listed species related to the non-target organisms that may be affected are identified to see if the use patterns of the pesticidal product will encroach on their habitat. The U.S. Fish and Wildlife Service web site (http://endangered.fws.gov/) is consulted for the identification of listed species and their location by state(s) and their habitat within the state(s). Internal EPA documents or search programs, such as DANGER which identify overlap of the habitat of listed species with agricultural crops, may also be used. If overlap of the habitat of listed species and pesticide use sites does not exist, a "no effect' finding is made. (Refer to case study #1, An ES Assessment for *Bacillus thuringiensis* Cry 3bb1 Delta Endotoxin in Corn by Habitat Overlap Evaluation, and case study #2, *M.anisopliae* for an example of a case where habitat overlap cannot be determined).

2. Integration of Exposure and Effects Data Using the RQ

When the use pattern of a pesticidal MPCA may overlap with the habitat of any listed species related to a species susceptible to the pesticide, a risk characterization is performed. Risk characterization integrates the results of exposure and toxicity data to evaluate the likelihood of adverse effects on non-target species. In this approach, BPPD uses the RQ method to compare exposure over toxicity.

For most pesticides, the effects characterization is based on a deterministic approach using the LC_{50}. Estimated Environmental Concentrations (EECs) based on maximum application rates are divided by acute toxicity (LD_{50}) values. The methods are based on the procedures described in Section V and include risk assessment criteria for listed species. These species risk endpoints have also been accepted by the Office of Endangered Species (1980).

A typical risk assessment starts with a determination of the EEC based on maximum application rates and the LD_{50} value for a given species. The ratio of the EEC and LD_{50} can then be compared to some relative quotient ranking to indicate possible acute adverse effects to non-target organisms. The criteria for a "may effect" determination for listed species include the following:

Acute Risk: Species may be potentially affected by use when the acute RQ is >0.05 (20-fold safety factor) for aquatic or when the RQ is >0.1 (10-fold safety factor) for terrestrial species.

Chronic Risk: Species may potentially be affected through chronic exposure when the chronic RQ > 1 (for all animals).

Plant risk: Potential for effects in plants (RQ > 1).

In OPP a safety factor of 5x is applied to the acute RQ for terrestrial non-endangered organisms. The more stringent safety margin criteria for listed species were developed to accommodate uncertainty of a no-effect level *based on the toxicity data available for*

related non-endangered species. It is impossible to obtain LC_{50} or LD_{50} data for listed species, and thus it must be assumed that the sensitivity of these species is similar to that of closely related indicator organisms.

A potential "may effect" risk to listed species can be evaluated by comparing the toxicity value from the most sensitive species tested to a conservative estimate of exposure. The most conservative approach is to apply the safety factor (10-fold for terrestrial and 20-fold for aquatic) to the LC_{50} or LD_{50} from the most sensitive species tested to accommodate uncertainty in the risk assessment process. A safety factor is desirable to ensure protection of species in which even a single death is of special concern.

When the RQ meets or is higher than the safety margins given above, a "no effect" finding is made in cases where there may be an overlap of species habitat and pesticide use. (Refer to case studies #3 and #4 as examples for an actual application of the RQ method in BPPD).

If, however, the calculated RQ is less than the level set by the above criteria, then BPPD presumes that there will be a "may effect" risk to the species and BPPD, in cooperation with FEAD, will initiate consultation with the FWS. (Refer to case study #5 for an example of restrictions placed on *B.thuringiensis* uses by a FWS consultation.)