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PURDUE PESTICIDE PROGRAMS

Purdue University Cooperative Extension Service

PESTICIDES AND ECOLOGICAL RISK ASSESSMENT

History, Science, and Process

Fred Whitford, Coordinator, Purdue Pesticide Programs

Douglas Urban, Senior Scientist, EPA Environmental Fate and Effects Division

Monte Mayes, Environmental Toxicologist, DowElanco

Jeff Wolt, Risk Assessment Leader, DowElanco

Edited by

Arlene Blessing, Purdue Pesticide Programs

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Introduction

Scientists and the public often are at odds with respect to potential risk and the perception of risk. Are "risks" from pesticides in our environment real or perceived? What is their nature, and what is "reasonable risk"? These questions are at the heart of public debate concerning pesticide use. The public wants absolute, clear, definitive answers; there is little tolerance for equivocal scientific terminology. Society has been impatient with scientists and regulators over unresolved questions concerning potential health and environmental risk; but today's risk assessment methodologies facilitate the process of addressing risk and risk perception.

The risk assessment process is a critical component of pesticide product development and regulatory review. The principles of risk assessment applied to pesticides are fundamentally the same as those applied to bridge and highway design, pharmaceuticals, and innumerable consumer products. The process is directed toward establishing an objective basis on which to assess risk potential relative to the likelihood of injury. This publication provides background information on the process of risk assessment and the role it plays in pesticide registration. It is intended to foster a better understanding of ecological risk assessment procedures, thus equipping the reader to make informed personal decisions on health and environmental risks associated with pesticide use.

The Evolution of Federal Pesticide Regulations

The United States Congress legislates pesticide laws to manage health and environmental risk. Pesticides are currently regulated under two major federal laws: the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA); and the Federal Food, Drug, and Cosmetic Act (FFDCA). FIFRA gives the U.S. Environmental Protection Agency (EPA) the authority to register pesticides; to require appropriate chemical, toxicological, and environmental studies; and to prescribe labeling use restrictions aimed to prevent unreasonable adverse effects on human health and the environment. Pesticides that come into contact with food and animal feed are regulated under FFDCA, which gives EPA the authority to establish tolerances (maximum pesticide residues allowed) in food and feed. The FQPA of 1996 modified FFDCA and FIFRA to broadly extend the authority to conduct risk assessments.

Regulations for pesticide registration specify data requirements, methods for conducting studies, procedures for risk assessment, and labeling content. EPA uses these as tools to determine whether a pesticide can be used without unreasonable effects on human and environmental health. EPA's assessment also addresses specific risks to humans and the environment and appraises potential economic, social, and environmental impact associated with use of the pesticide. In effect, the decision-making process balances potential risk to humans and the environment against projected economic, social, and environmental benefits.

There have been many changes in pesticide products and registration requirements

during the last decade. What was acceptable risk, yesterday, may not be, today. Policies and decisions on acceptable risk change, over time; and as public awareness and concerns over pesticide risk increase, so do registration requirements.

Early Federal Laws Focused Primarily on Benefits

The Insecticide Act (1910) prevented the manufacture, sale, or transport of impure or improperly labeled insecticides and fungicides. Its primary focus was to ensure that products were labeled adequately and that container contents were stated precisely

on the label. The Insecticide Act contained no registration requirements and did not set safety standards.

The Insecticide Act was replaced in 1947 by a more comprehensive law: the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA was the first law to require pesticide manufacturers to register their products with the United States Department of Agriculture (USDA), which was responsible for registering all pesticides prior to sale or movement via interstate or foreign commerce.

Pesticide regulations were expanded again in 1954 with an amendment to the Federal Food, Drug, and Cosmetic Act. The amendment required tolerance limits for pesticide residues on agricultural commodities; and it limited the amount of residue that could remain in or on a food crop after application, according to "good agricultural practices." A 1958 amendment, the Delaney Clause, prohibited establishment of tolerances for carcinogenic food additives. However, it applied only to pesticides for which residues were greater in the actual food item than in the raw agricultural commodity. The registration process was changed in 1964 when FIFRA was modified to give USDA the authority to deny or cancel product registration.

Environmental Movement Changed Public Perception of Pesticides

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Increases in environmental awareness in the 1960s, exemplified by Rachel Carson's *Silent Spring*, changed forever how pesticides would be viewed by the American public. The most commonly used insecticides at that time were part of a chemical class of compounds called chlorinated hydrocarbons which includes the well-known insecticide

DDT. Emerging environmental groups and the news media accurately portrayed these pesticides as chemicals that bioaccumulate in the environment, disrupt links in the food chain, and poison wildlife. *Silent Spring* captured the public's attention and rallied a cry for greater public awareness of environmental issues.

The environmental movement added balance to discussion on the benefits of pesticide use, providing awareness of the risks posed to people, wildlife, and ecosystems. FIFRA 1964 established procedures for suspending the registration of pesticides determined to be unsafe, and the growing environmental movement formed powerful lobbies that supported additional legislation. Politically astute individuals and organizations directed their attention to Congress, lobbying for legislation that would help protect the

economy, the environment, and public health. As a result, manufacturers and users were held more accountable for reducing both short- and long-term risks of pesticide use. The public looked to Congress to pass enforceable legislation requiring pesticides to be scientifically evaluated prior to release for agricultural, commercial, or consumer use. While the debate has shifted over the years as issues have emerged and changed, it remains a primary obligation of manufacturers, through government oversight, to understand and minimize risks posed by pesticides.

Government Policies Shift Toward Risk Reduction Strategies

In 1970, Congress created the United Sta Environmental Protection Agency (EPA) and, in 1972, strengthened FIFRA dramatically to give EPA more regulatory authority.

Changes in FIFRA, since 1970, have resulted in a major philosophical shift in pesticide regulation. Originally, FIFRA required regulators to review and register pesticide products. But in 1972, in the interest of risk reduction and pollution prevention, Congress changed FIFRA fro a labeling law to a comprehensive statute designed to regulate the manufacture, distribution, and use of pesticides. Pesticic manufacturers were then required to supp all registrations by providing prescribed scientific studies showing that use of the product would not cause "unreasonable adverse effects on human health or the

environment."

In addition to requiring scientific data in support of pesticide registration, FIFRA v modified to prohibit any use of a pesticide inconsistent with its labeling. In other words, the label became the law; and violations for not following the label coul result in label enforcement via license revocation and fines. Recognition that not all pesticides pose the same risk led to the FIFRA statute (1972) whereby pesticides deemed safe for application by the genera public are commonly referred to as *general-use pesticides*, while those posing greater risk are classified as *restricted-use pesticides*. The purchase and application o restricted-use pesticides are limited to certified applicators *or* persons supervised by certified individuals.

To ensure that adverse effects on human health and the environment can be prevented, pesticide registration, product labeling, government enforcement, and applicator education form the foundation a comprehensive framework to regulate th manufacture, use, and disposal of pesticid

Because Congress did not intend FIFRA t be solely an environmental bill, an industry bill, or a farm bill, sincere efforts were ma to balance the needs of all stakeholders. Since benefits play an important role in decision-making under the act, Congress amended FIFRA to

allow USDA and interested parties to explain how cancellation of pesticides might impact the public adversely by denying potential benefits along with potential risks. Regulatory decisions are based on the balance of risk versus benefit (risk-benefit analysis).

EPA Issued Scientific Testing Guidelines

As required under the revised FIFRA, EPA publishes scientific testing guidelines and regulations to ensure that studies in support of pesticide registration employ the best scientific tests and methods. The regulations stipulate what testing is required and how the studies are to be performed. Prior to the inclusion of testing guidelines, pesticide manufacturers conducted many studies on the impact of their products on mammals, birds, fish, and the environment. EPA guidelines stipulated for the first time certain toxicological, ecological, residual, and environmental fate studies.

Risk assessments require data on toxicological end points and exposure. FIFRA guidelines and regulations place a formaland increasedresponsibility for testing requirements on pesticide manufacturers. The data developed as the result of the guidelines, combined with the available tools to estimate exposure levels, formed the beginning of EPA's risk assessment process.

The generation of new data has allowed the registration process to improve and mature. Advances in science, new experimental tools, and new thinking (driven by desire on the part of EPA and manufacturers to improve the science of risk assessment) yield more complex data for review; thus, EPA is obligated to review growing numbers of massive and intricate data sets supporting pesticide registration and to upgrade its work force with scientists schooled in such specific disciplines as environmental chemistry and toxicology.

Pesticide Manufacturers to Follow Good Laboratory Practices

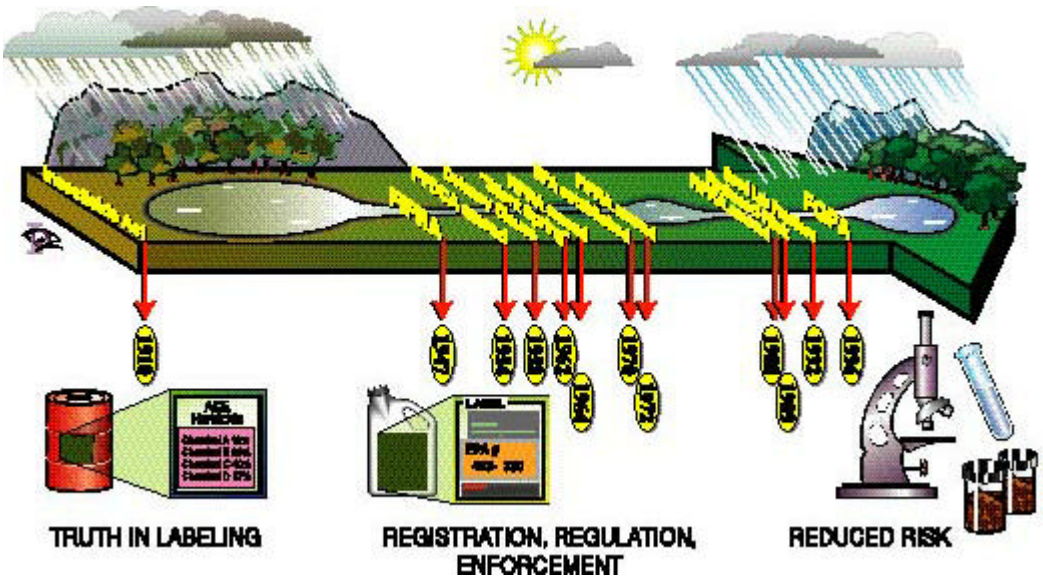
Defensible scientific data from standardized procedures (protocols) are required if regulators are to credibly assess product registration. In the mid 1970s, fraudulent practices surfaced in one large-contract

toxicology laboratory, triggering questions within EPA as to the quality of data used as a basis for registration decisions. EPA's concern led to *Good Laboratory Practice Standards* describing how studies must be conducted. These standards are commonly called Good Laboratory Practices (GLPs).

The registration of a pesticide requires well-designed studies conducted by trained scientists and reported accurately, with documentation. GLPs ensure quality, integrity, credibility, and consistency of data used in assessing risk. GLPs describe how laboratory and field studies must be planned, performed, monitored, recorded, and reported. They require pesticide manufacturers to comply with a set of standard quality assurance procedures for generating experimental data. This documentation provides an audit trail which facilitates verification that studies were properly performed and reported; and it affords EPA reviewers confidence in their conclusions.

EPA Moves Toward Risk Characterization

In the early years of pesticide regulation, comprehensive risk assessments were uncommon because the technology and scientific knowledge necessary to accurately interpret the data were unavailable. But in the late 1980s, risk assessors began to develop a new philosophy. They recognized that the emphasis



should shift from toxicity assessment, alone, to include exposure studies, uncertainty, and professional judgment. The implementation of these additional considerations, coupled with improved scientific applications, has greatly enhanced EPA's decision-making process.

EPA Policy Shifts to Reduced-Risk Pesticides

In the late 1980s and 1990s, EPA developed a policy focused on reduced-risk pesticides, offering manufacturers the incentive of quicker registration decisions for development of "safer" products. The policy favors pesticides that have less potential to cause adverse health and environmental effects than those currently registered. Registration applications documenting reduced, low-risk characteristics are granted priority consideration in the review process, reducing the usual two- to four-year registration process to as little as six months. Expedient reviews allow "reduced-risk" pesticides to move more quickly to the marketplace; and the use of this incentive to encourage the development of "safer" pesticides places EPA

in a better position to manage pesticide risk in the marketplace of tomorrow.

The Food Quality Protection Act

Congress passed the Food Quality Protection Act of 1996 (FQPA), amending both FIFRA and FFDCA to provide a more comprehensive system for regulating pesticides. Under previous pesticide laws, EPA was required to balance potential risks against potential benefits of a pesticide during the registration review process; but FQPA established a single, health-based safety standard for all pesticide residues in all foods and greatly reduced consideration of pesticidal benefits. FQPA requires that tolerances must be determined to be explicitly "safe"; that is, there must be "reasonable certainty" that tolerance levels will result in "no harm." FQPA also requires EPA to consider all nonoccupational sources of pesticide exposure, both dietary and nondietary, when establishing tolerances; and exposure to other chemicals that may have a common mechanism of toxicity must be considered, as well.

FQPA further requires that EPA specifically address potential risks to infants and children. It mandates that special attention be paid to the possibility that chemicals may disrupt the endocrine system, and that periodic reevaluation of all pesticide registrations and tolerances is essential to ensure ongoing validity.

One of the consequences of FQPA is the need to further refine the risk assessment process, particularly in regard to assessing potential risks

from multiple sources and routes of exposure. It is clear that risk assessment plays an increasingly critical role in the process of pesticide registration and reregistration.

EPA Uses Risk Assessment to Set Safety Standards

In FIFRA, the United States Congress set the standard for making pesticide registration decisions: "...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." Thus, both human health and ecological risk assessments are essential to the decision-making process behind pesticide registration. Environment is defined to include "water, air, land, and all plants and man and other animals living therein, and the interrelationships which exist among these." The environmental protection component weighs heavily in risk assessment decisions.

Use of Risk Assessments: Registration, Reregistration, and Special Review

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The primary decisions that EPA must make concerning pesticides are to

- register a new product,
- reregister an existing product,
- cancel a current registration, and
- determine if labeling protects human health and the environment.

Risk assessments are performed by EPA during registration and reregistration processes. They are

also conducted whenever new findings suggest that adverse effects might result from use of a previously registered product. There are four end points to which assessments are directed: Experimental Use Permit; Registration; Reregistration; and Special Review.

Experimental Use Permit

Prior to completing all studies required for full registration, registrants often submit a smaller data package along with a request for an Experimental Use Permit (EUP); an EUP allows a registrant to apply the product to as many as 5,000 acres to evaluate performance. EPA reviews the abbreviated package and judges whether there is a potential for risk to humans or the environment under limited use conditions; if there is no such indication, an EUP is issued.

Registration

During the registration process, EPA evaluates all data in support of active ingredients not previously registered, as well as new uses (for a registered product) that would require label changes. When requesting product registration, the pesticide manufacturer (registrant) must submit to EPA all data required by FIFRA. When all individual studies have been reviewed, the results are factored into human and ecological risk assessments to evaluate whether requested uses for the product present unacceptable risk to human health or the environment. Review and assessment are conducted by representatives of all disciplines within EPA: product, residue, and environmental chemistry; human health; and ecological effects.

Reregistration

From the very beginning, FIFRA intended that all registered pesticides be reregistered every five years; but economics nullified that intent. FIFRA Amended 1988 required additional fees*re*registration feesto be paid by manufacturers submitting a product for reregistration, thus helping to provide the necessary funding. All data used to support pesticides registered before 1984 became subject to reevaluation and upgrading, if necessary, to comply with current guidelines and standards. The refined data enhances the ability of EPA and the registrant to judge whether risk conclusions and registration decisions made during the initial product registration process meet today's

made during the initial product registration process meet today's standards.

Policy changes alter the emphasis of regulatory actions in reregistration programs. Instead of moving riskier pesticides into the lengthy special review process, the focus is to reduce risk by negotiation, e.g., by changing application rates, increasing application intervals, or using alternative application methods. These measures often take the form of label changes designed to mitigate the amount and duration of exposure.

Special Review

FIFRA gives EPA the statutory responsibility not only to register pesticides but also to take regulatory actionsincluding cancellationunder certain unusual conditions: for instance, when new information on a currently registered pesticide indicates that normal use of the product may result in unreasonable adverse effects. Special reviews are initiated when concern is heightened by specific circumstances, such as

- when new evidence from laboratory studies suggests that the pesticide may pose higher or different risks than were predicted;
- when a pesticide is linked to fish or bird incidents; or
- when workers become ill.

Benefits to EPA and the Public

The risk assessment process and the resources expended to conduct intensive special reviews provide benefits to EPA and the public:

- EPA's mission to protect public health and the environment from unreasonable adverse effects can be more readily fulfilled.
- The well-defined risk assessment process for both human health and ecological effects helps EPA make consistent, well-informed registration decisions.
- Effective communication of the process to pesticide manufacturers fosters timely registration decisions.
- The risk assessment process encourages in-depth review similar to peer review of basic research.
- The process provides a forum where EPA scientists can reach consensus on conclusions drawn from risk assessment. In fact, scientists in academia and those from the private sector canand doshare the consensus.
- The process helps guide EPA's decision on whether additional data are needed to clarify a potential risk.

Risk Assessment as a Market-Oriented Process for Manufacturers

Corporate decisions on whether or not to develop potential pesticide products are based on risk assessment, marketability, and projected cost of production. Risk assessments must be conducted periodically throughout the development and commercial life of a pesticide, oftentimes beginning with limited, preliminary data acquired very early in the development process. As more data become available, risk assessments are refined by virtue of an enhanced understanding of the toxicological properties and chemical fate of the pesticide, as well as better exposure estimates. Scientists who develop data often serve as experts who present and interpret it for risk managers. The development team assesses data at various intervals to decide whether to cancel or continue research and plans for commercialization of the product.

A thorough, well-organized risk assessment process

- defines guidelines for required tests and identifies risk standards that will be used to quantify the data;

- stipulates full reevaluation of studies that supported initial (or former) registration of a product to verify sufficiency according to current standards and to identify any need for additional testing prior to reregistration;

- enables manufacturers to identify and eliminate high risk products early in the development process, thus minimizing expenditures in support of a product that most likely would not be granted registration; and

- requires sound, factual documentation of the registration process as a basis on which customers, company management, and stockholders can calculate their commitment to advancement of the product.

Registrants often use similar or more stringent criteria than those used by EPA and

conduct a preliminary review of their own data; this assists registrants in gauging their products' prospects for registration. Preliminary reviews also may serve as indicators of the amount of time EPA might spend evaluating the data, that is, how quickly products might be registered. If potential adverse effects are identified during any risk assessment, scientists must decide if and how the potential risk can be reduced; for example, by changes in formulation, methods of application, use rates, and marketing, or by use of personal protective equipment. Strategies for reducing risk involve what is known as *risk refinement.*

For example, suppose a pesticide applied at a rate of one pound of active ingredient per acre has the potential to cause unreasonable risk to foraging bobwhite quail in treated fields. A risk assessment may indicate that rates at or below 0.75 pound per acre would negate that potential. So, to mitigate risk, product development teams may be asked to reduce the proposed use rate.

Lowering the application rate of a product requires reassessment of its efficacy. For this example, an application rate of 0.75 pound per acre would control most broadleaf weeds in corn, but two resistant perennial weeds would not be controlled at that rate. Based on this information as well as data indicating risk potential at higher rates, the product development team might conclude that the product would not compete successfully in the marketplace; if so, commercial development would cease.

The Science of Risk

Assessment

As practiced by EPA, risk assessment provides the regulated pesticide industry with straightforward methods and criteria to estimate risk. It is a well defined formal decision-making process which, ideally, incorporates scientific knowledge about a pesticide into the risk assessment along with inherent uncertainties. The result takes form as a set of science-based estimates that describe the likelihood of the pesticide to adversely impact human health, wildlife survival and fitness, and environmental quality, and which are sufficiently conservative to account for uncertainties in the process.

Risk Assessment as a Multistep Analysis

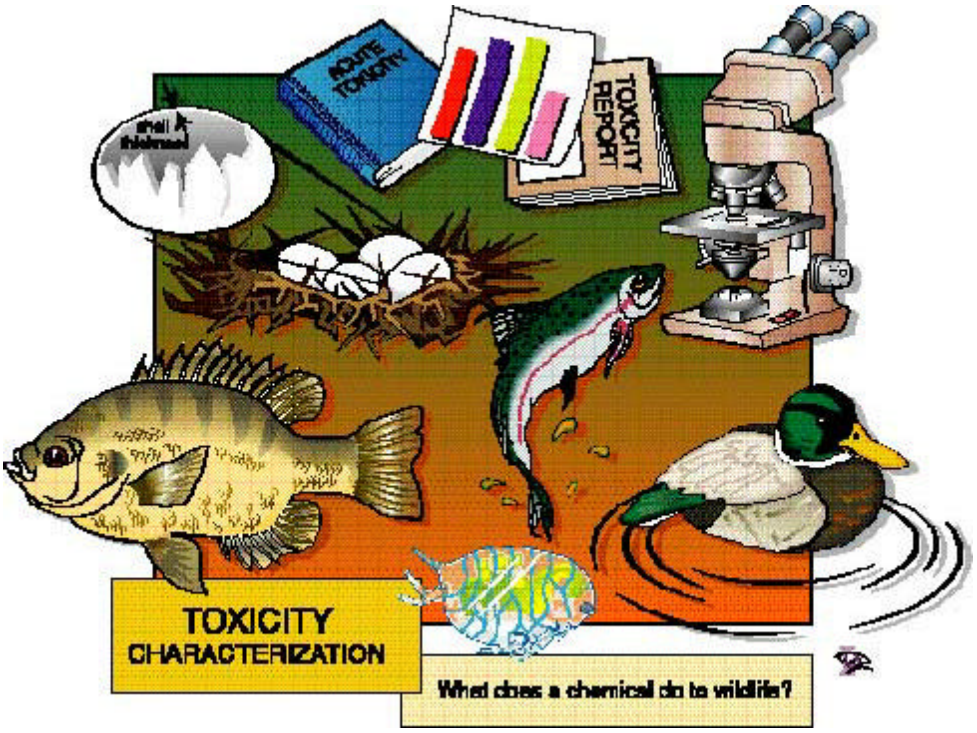
Human health and ecological risk assessments often are preliminary in nature and may be based on limited data and/or very conservative assumptions. As more research data are compiled and more accurate assumptions considered, the more precise and comprehensive the risk assessmentand the greater the confidence in conclusions drawn. However, if initial risk assessments indicate no cause for concern, a more refined risk assessment may not be necessary.

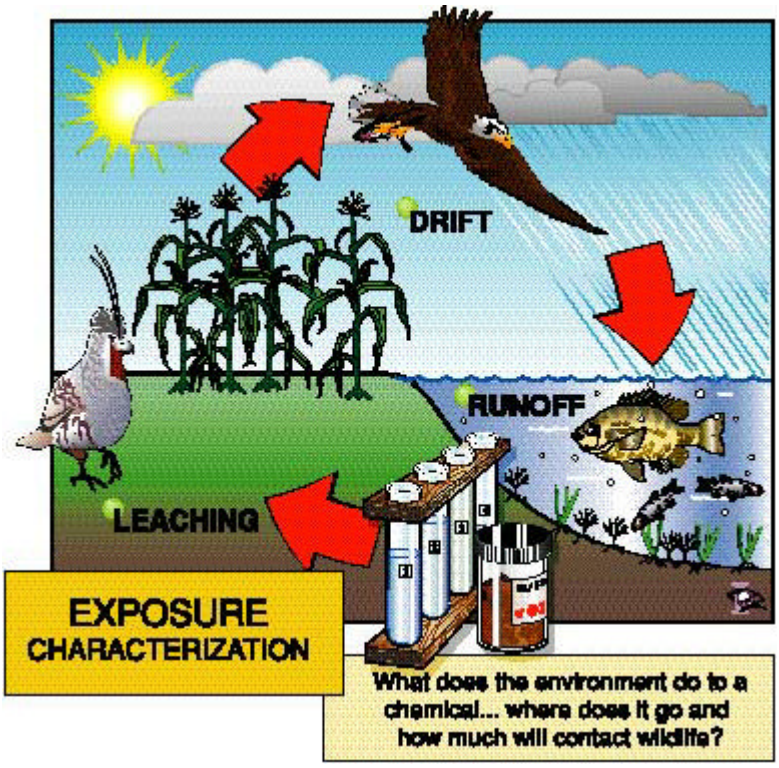
Quantitative risk assessment is a function of toxicity and exposure. The risk assessment process involves multiple steps, beginning with an appraisal of toxicity and exposure and concluding with a characterization of risk.

Toxicity Characterization

Toxicological characterization is commonly based on laboratory studies; that is, it reflects adverse effects observed when animals are intentionally administered a range of concentrations of the pesticide being studied. Toxicity can be characterized by mortality or by sublethal effects within the range of doses tested.

An important aspect of toxicological evaluation is determination of the relationship between magnitude of exposure and extent and severity of observed effectscommonly referred to as *dose-response*. The dose-response relationship identifies dose levels at which adverse effects occur, as well as the no observed effect concentration (NOEC). For risk assessment, the lowest NOEC, LD_{50}, etc., is used to estimate risk.





Exposure Characterization

Contact with a chemical in the environmentin the workplace, at home, or in air, food, water, or soilconstitutes exposure. Exposure concentrations may be either estimated or measured, based on the amounts and manner in which the chemical is used, the physical properties of the chemical, and data from laboratory and field experiments. Exposure assessments ascertain the exposure of people, wildlife, and plants to pesticides in the environment. The extent of exposure depends on the type of use (crop, lawn, and garden treatment; mosquito control; indoor pest control), application rate, method of application, and frequency of

application, along with the breakdown, partitioning, and movement of the chemical in the environment. An adverse effect is predicted only if exposure approaches or exceeds dose levels that have resulted in adverse effects in toxicology studies.

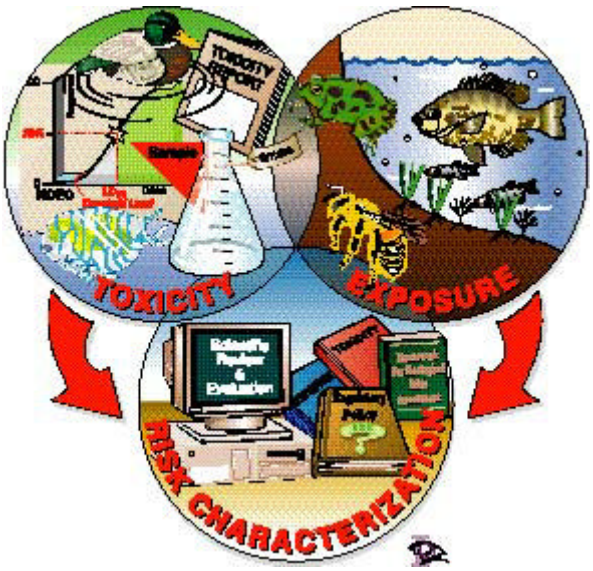
Risk Characterization

Risk characterization defines the likelihood that humans or wildlife will be exposed to hazardous concentrations. Thus, risk characterization describes the relationship between exposure and toxicity. Risk assessors identify species likely to be exposed, the probability of such exposure occurring, and effects that might be expected.

Suppose that a sampling for a given pesticide in the environment yields an estimated exposure level of 3 ppb (parts per billion) in water, and that a short-term laboratory study shows that an exposure level of 100 ppb produces an adverse effect in bluegill sunfish. How could this information be integrated to predict the outcome of fish exposed to the chemical?

In this particular example, it is understood that fish may be exposed to 3 ppb without

negative effects; but adverse effects do occur in bluegill exposed, short-term, to 100 ppb. A risk assessor might express no concern for fish at an exposure level of 3 ppb since it is significantly below the 100 ppb threshold for injury. But risk characterization often is not that simple.



For example, the risk assessor may need to consider whether prolonged exposure of the fish, at a level of 3 ppb, might trigger adverse effects; whether another life stage (e.g., embryo) might be more vulnerable than the adult; and whether another fish species might be more sensitive than bluegill. Another consideration is that organisms (predators) higher in the food chain might be at risk if the pesticide accumulates in fish on which they prey.

The Ecological Risk Assessment Process

Ecological risk assessment is a process whereby toxicity (effects data) and exposure estimates (environmental concentrations) are evaluated for the likelihood that the intended use of a pesticide will adversely affect terrestrial and aquatic wildlife, plants, and other organisms. Data required to conduct an ecological risk assessment include the following:

- Toxicity to wildlife, aquatic organisms, plants, and nontarget insects
- Environmental fate
- Environmental transport

- Estimated environmental concentrations
- Where and how the pesticide will be used
- What animals and plants will be exposed
- Climatologic, meterologic, and soil information

Assessment Requires an Understanding of Toxicology, Ecology, and Processes

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Assessing and characterizing risk to ecological systems, including a myriad of nontarget aquatic and terrestrial organisms as well as surface and ground water, is a much younger and more complex science than that of human health risk consideration. Ecological risk assessment considers a greater range of complex issues and covers more species than does human health risk assessment: fish, aquatic invertebrates, aquatic and terrestrial plants, nontarget insects, birds, wild mammals, reptiles, and amphibians.

Each species within an ecosystem fulfills specific ecological roles. Plants are the primary producers of chemical energy in any terrestrial or aquatic ecosystem. They capture sunlight and convert it to energize new plant growth, forming the bottom of the food chain. Energy flows through the food chain when organisms consume plant tissues and are, in turn, consumed. For instance, green algae are one-celled microscopic organisms that are a staple food item for invertebrates such as water fleas and mysid shrimp; these invertebrates, in turn, become food for young fish and small fish species. The fish are then consumed by predators such as larger fish, amphibians, birds, and aquatic mammals. Because of the dynamics

of the flow of energy, perturbations of the most seemingly minor species may lead to observable (measurable) impact on the entire ecosystem. However, because of the ability of organisms and populations to adapt to perturbationsthat is, because they are resilienteffects on one or more components of an ecosystem may result in minimal ecological change.

Adverse environmental effects at various levels may involve more than energy flow. For instance, adult mussels are nearly sedentary at the bottom of moderately flowing streams, but they filter algae and other small organisms from the water. Young mussels must attach to the gills or fins of certain fish, where they remain as harmless parasites (for weeks or months) until their internal organs develop; then they drop from their host into the stream bank substrate. Without the host species, some mussel populations cannot survive.

Toxicity Characterization

Toxicity testing identifies concentrations that, when administered to surrogate animals, result in a measurable adverse biological response. These measured concentrations and associated toxicity end points basically describe *what the chemical does to the environment*in this case, a single living organism.

Testing for Adverse Effects on Wildlife

Specific terrestrial and aquatic tests are mandated by federal law and described in the

Code of Federal Regulations, 40 CFR Part 158. Subpart E of Part 158, Terrestrial and Aquatic Nontarget Organisms Data Requirements, clearly describes the tests required for registration of a pesticide. Some tests are not required for every pesticide product, but are listed in the regulations as *conditionally required.* Conditionally required tests are not mandated unless the use pattern or information generated from required tests indicates a need for additional testing. For instance, early life stage fish tests or invertebrate life cycle tests are conditionally required for most pesticide products. These tests become mandatory when scientific data indicate that the pesticide is relatively stable in the aquatic environment and that concentrations at or below one part per million produce significant acute mortality.

The technical grade of an active ingredient normally is the substance used in pesticide screening tests. Federal regulations specify the conditions under which the end use product (the formulation) must be tested. In all cases, effects observed and measurements recorded for animals and plants exposed to pesticides must be compared to control species (fish, invertebrates, birds, plants, or animals) held under identical conditions but not exposed to the chemical.

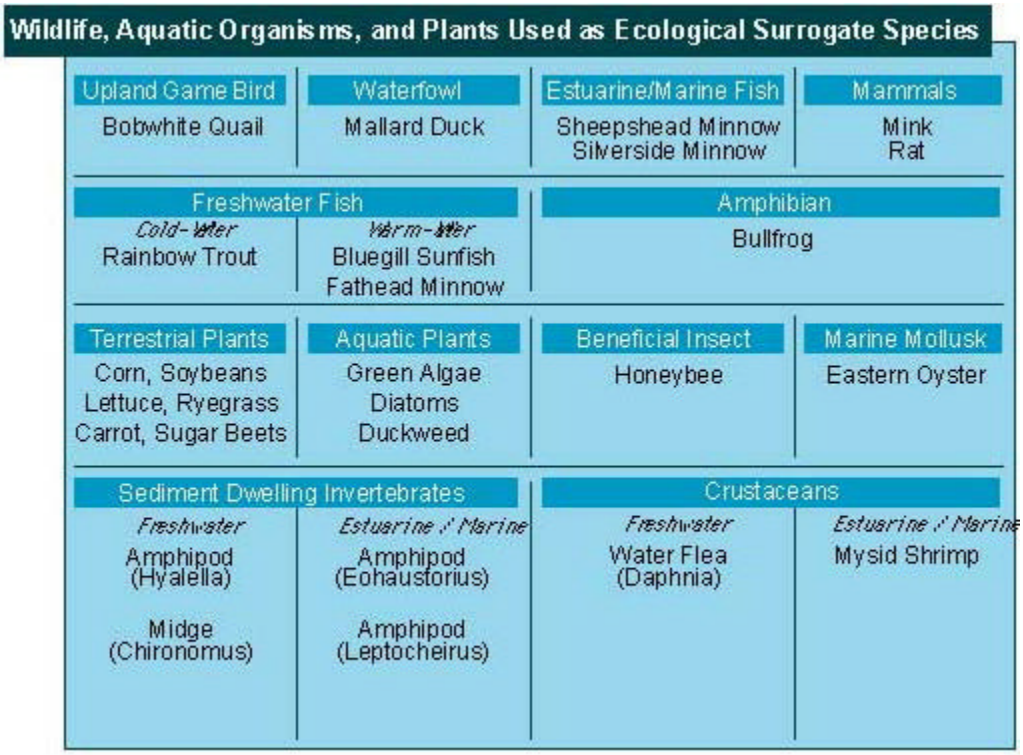
Testing surrogate species allows scientists to observe adverse effects that may result from short-term (acute) and long-term (chronic) exposure. Exposure for short periods at high concentrations is used to determine concentration levels necessary to produce mortalitylethal dosesas well as sublethal effects on one stage of an organism (e.g., juvenile or adult). These tests, for example, address immediate consequences to fish and wildlife exposed to concentrations of the pesticide.

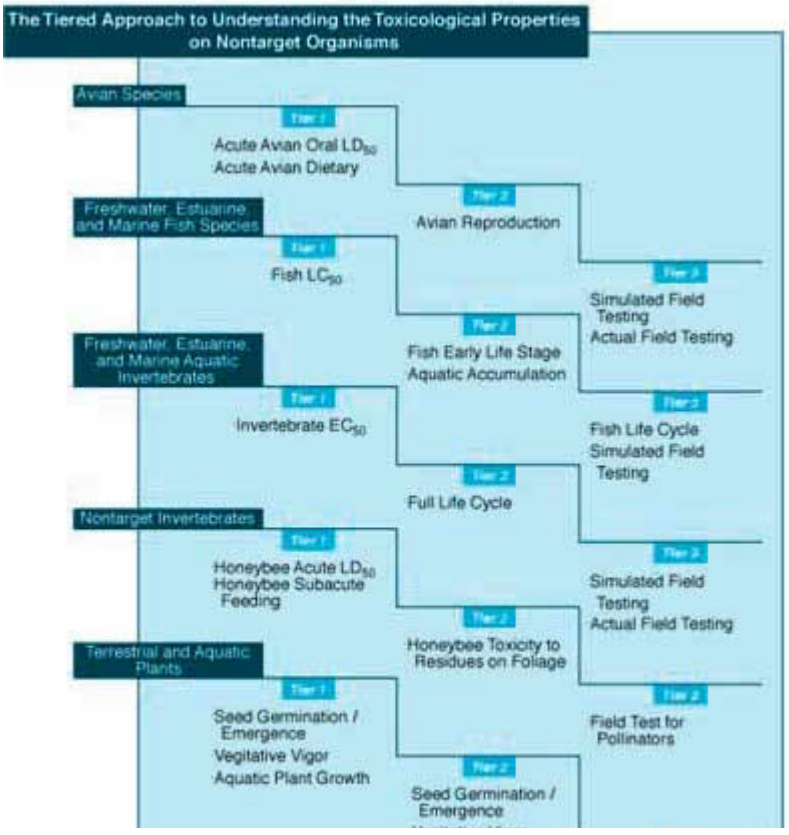
The more complex chronic tests are used to examine, in detail, how the pesticide will impact various stages of an animal's life cycle

(e.g., bird embryo development). As noted previously, chronic data are required when acute tests indicate that the toxicity of the pesticide exceeds a trigger limit and when the environmental fate or use of the pesticide indicates that nontarget organisms may be impacted. The data from chronic tests are essential to accurate prediction of long-term effects on fish and wildlife.

Potential Impacts Modeled by Indicator Species

Surrogate organisms used in toxicological testing are selected to represent various trophic levels within an ecosystem. For instance, adverse effect data on bobwhite quail exposed to a pesticide are used to generalize how that pesticide might adversely affect all upland game birds. *Daphnia* (the water flea) models freshwater crustaceans, and the Eastern oyster models freshwater and marine mollusks. An assumption key to ecological risk assessment is that data on surrogate species adequately describe how a pesticide will impact the broader spectrum of plants and animals.


Wildlife, Aquatic Organisms, and Plants Used as Ecological Surrogate Species
Upland Game Bird
Bobwhite Quail
Waterfowl
Mallard Duck
Estuarine/Marine Fish
Sheepshead Minnow
Silverside Minnow
Mammals
Mink
Rat
Freshwater Fish
Cold-Water
Rainbow Trout
Warm-Water
Bluegill Sunfish
Fathead Minnow
Amphibian
Bullfrog
Terrestrial Plants
Corn, Soybeans
Lettuce, Ryegrass
Carrot, Sugar Beets
Aquatic Plants
Green Algae
Diatoms
Duckweed
Beneficial Insect
Honeybee
Marine Mollusk
Eastern Oyster
Sediment Dwelling Invertebrates
Freshwater
Amphipod (Hyalella)
Midge (Chironomus)
Estuarine / Marine
Amphipod (Eohaustorius)
Amphipod (Leptocheirus)
Crustaceans
Freshwater
Water Flea (Daphnia)
Estuarine / Marine
Mysid Shrimp


The Tiered Approach to Understanding the Toxicological Properties on Nontarget Organisms
Avian Species
Acute Avian Oral LD50
Acute Avian Dietary
Avian Reproduction
Freshwater, Estuarine and Marine Fish Species
Fish LC50
Simulated Field Testing
Actual Field Testing
Fish Early Life Stage
Aquatic Accumulation
Freshwater, Estuarine, and Marine Aquatic Invertebrates
Invertebrate EC50
Fish Life Cycle
Simulated Field Testing
Full Life Cycle
Nontarget Invertebrates
Honeybee Acute LD50
Honeybee Subacute Feeding
Simulated Field Testing
Actual Field Testing
Honeybee Toxicity to Residues on Foliage
Terrestrial and Aquatic Plants
Seed Germination / Emergence
Vegitative Vigor
Aquatic Plant Growth
Field Test for Pollinators
Seed Germination / Emergence

A Tiered Approach to Testing

Toxic levels of a pesticide and descriptions of potential adverse effects are developed using a tiered (sequential) approach. Tier 1 studies, the most fundamental, are primarily acute laboratory studies that examine concentrations necessary to cause mortality or acute sublethal effects. Tier 2 involves longer-term, reproduction and life-cycle studies that provide more complex data on the pesticide's impact on the entire life cycle of the test animal. Tier 3 studies examine the impact of a pesticide on animals in simulated environmental or actual field conditions.

Testing for Adverse Effects on Avian Species

There are three major laboratory tests for avian effects:

- Acute oral LD_{50}
- Acute dietary LC_{50}
- Reproduction

In both acute oral and acute dietary studies, the primary route of exposure is through ingestion; either the pesticide is introduced directly into the subjects' crops (acute oral exposure), or it is incorporated into their diet (acute dietary exposure). Examples: *Acute oral exposure* occurs when a bird ingests a large single dose. *Acute dietary exposure* may result from ingestion of pesticide residues on food items.

The *acute avian oral* LD_{50} test assesses the effect of a single, oral dose of a pesticide administered to bobwhite quail or mallard ducks. Birds that survive a dose are observed for two weeks for subsequent mortality and sublethal effects such as wing droop, disorientation, abnormal behavior, and reduced food consumption. The test yields the LD_{50} level and the NOEC. The LD_{50} level represents the dose which can be expected to kill 50 percent of the test population; and the NOEC reflects the maximum

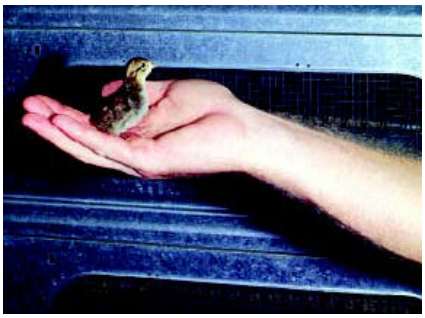
dose that produces no observed effect on the test population.

Deriving the *acute avian dietary* LC_{50} involves feeding bobwhite quail and mallard ducks a pesticide-treated diet for five days. A three-day observation period follows, during which the birds are fed a control diet; abnormal behavior and food consumption are recorded. In addition to the LC_{50} (lethal concentration of pesticide in the diet, in ppb), the process yields the NOEC values for the pesticide being tested.

Bobwhites from a one-generation reproduction study conducted to assess pesticidal effects on reproductive success.

Avian *reproduction* testing involves feeding birds a pesticide-treated diet for ten weeks prior to egg laying and throughout the laying season. Data generated from the reproduction study include the number of eggs laid, the number of normal hatchlings, the number of survivors at 14 days after hatch, and eggshell thickness. The NOEC for any of these end points can be used in risk assessment.

In addition to the three major tests, *simulated* and *actual field tests* are conditional, i.e., they may be required by EPA on a case-by-case basis.



Young bobwhite, approximately seven days old, from a reproduction study monitored for effects on survival and growth.

A *simulated field test* might include placing mallards, bobwhite quail, or geese in outdoor cages, under circumstances that mock exposure in the wild, and exposing them to the pesticide at a rate and frequency prescribed by the pesticide label.

Canada geese on turf plot. Studies are conducted to measure avoidance of treated turf. Birds are monitored to determine amount of time spent in the treated and untreated halves of the test plot.

An *actual field study* might involve a pesticide application to an orchard, after which various data are recorded. Besides the number of dead and dying birds observed, additional data might be gathered, including survival of dependent young, residues on wildlife food sources, and residues in animal tissues (as evidenced by autopsy and tissue sampling).

Testing for Adverse Effects on Freshwater and Estuarine/Marine Fish

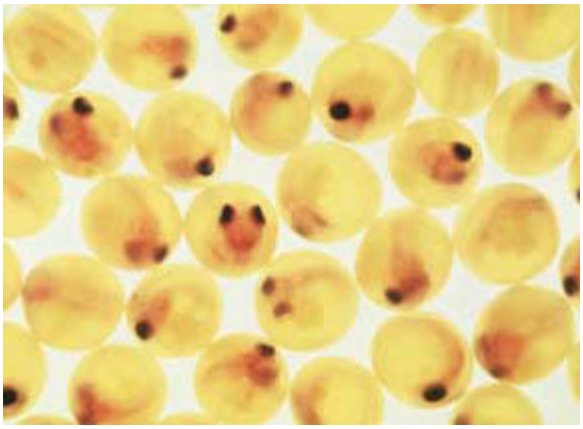
A single concentration of the test pesticide is added to the water in an aquarium, and soon thereafter the fish are placed in the water.

Acute LC50 tests most often employ rainbow trout and bluegill sunfish (tested separately) that are actively feeding but have yet to spawn. Fish are exposed to vari-ous concentrations of the pesticide to determine the dose-mortality response and, as well, the sublethal responses over 96 hours (4 days).

The results generated from acute LC50 tests include the 96-hour LC50 and the NOEC. A number of behavioral changes and pathological observations also are recorded, such as erratic movement and swimming at the surface. Gross pathological observations could include protrusion of the eyeball, sloughing of skin, and increased skin pigmentation.

The early life stage test examines how a pesticide will impact the embryonic and larval stages of fish. Data generated by early life stage tests include

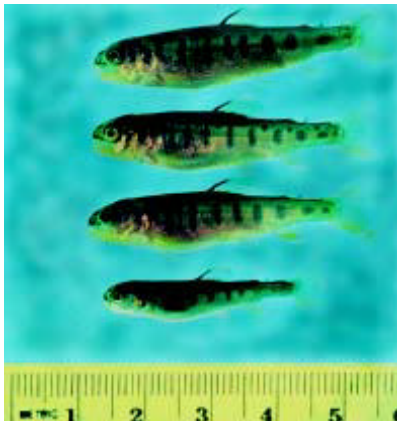
- number of embryos hatched,
- amount of time embryos require to hatch,
- embryo mortality,
- larval weight, and
- larval length.



The NOEC for these parameters is determined by comparing treatment groups with controls.

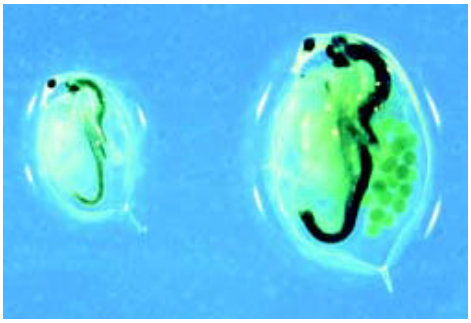
Fish life cycle studies use fathead minnows to represent freshwater fish species and sheepshead minnows as surrogates for estuarine fish species. The time needed to complete a fish life cycle study is 260 to 300 days. Fish are exposed to a pesticide from one stage of their life cycle to the same stage in the subsequent generation (egg to egg). Fish embryos are placed into water containing a known pesticide concentration, and

observations are made from the egg stage through spawning. The eggs laid by the first generation and the larvae that emerge are followed for an additional 28 days. NOEC determination is based on control response and treatment response.



Fish bioaccumulation studies begin with fish exposed to a known pesticide concentration in water. During specific time periods, fish are sacrificed to determine the pesticide concentration in their tissues. Fish are separated into filet samples (edible portion) and samples with all other parts combined [visceral (inedible) portion]. Bioconcentration studies are conducted until concentrations identified in fish tissues remain fairly level for at least 28 days. The fish are then placed in clean water and the time required for residues to be removed from their tissues determined. This provides information regarding potential food chain effects.

Testing for Adverse Effects on Freshwater Aquatic Invertebrates



Two primary tests are included in assessment of pesticidal effects on invertebrate species: *acute* $EC_{50,}$ and *aquatic invertebrate life cycle. Daphnia* (fresh-water crustaceans in which females can self-fertilize) are typically used in both studies.

Invertebrate acute EC_{50} tests provide information on how newly hatched daphnids respond to a pesticide over a 48- or 96-hour exposure period. The objective is to estimate the concentration of pesticide that will immobilize the daphnid. Immobilization is measured by gently shaking a

vessel containing daphnids lying on the bottom. Those that swim for less than 15 seconds are considered immobile. The concentration calculated to immobilize 50 percent of the daphnids is considered the EC_{50}.

Testing for Adverse Effects on Estuarine and Marine Organisms

The *acute toxicity test* is the primary study used to address the toxicity of pesticides to estuarine organisms. A crustacean (mysid shrimp), an estuarine/marine fish (sheepshead minnow), and a marine mollusk (Eastern oyster) are used to evaluate pesticides. Sheepshead minnows and mysid shrimp are placed into separate aquariums containing specific concentrations of the pesticide for 96 hours. The mortality data generated is used to calculate the LC_{50} and/or the EC_{50} .

Typically, one end pointthe pesticide concentration that inhibits shell growth by 50 percentis sought to estimate the impact of a pesticide on mollusk species. The shell growth of young Eastern oysters is assessed by placing them in a series of pesticide concentrations in water for 96 hours each. The concentration that inhibits shell growth by 50 percent is calculated. Such a study is regarded as an indirect measure of the impact of the pesticide on the nutritional status of the animal. A mollusk that closes its shell in the presence of a pesticide cannot feed; thus, shell growth is severely limited.

Testing for Adverse Effects on Mammals

Testing on wild mammals normally is not required. Data from testing for human health

risks (using rats, mice, dogs, and rabbits) typically are used to predict toxicity to wild mammals. A situation where wild mammal toxicity testing may be required is when a highly toxic rodenticide or predacide is used as a broadcast bait; minks often are used as test subjects to determine the potential for secondary toxicity (toxic effects in predators that have consumed poisoned animals).

The honeybee *(Apis mellifera)* is used as the principal insect pollinator. Tests used to measure effects of a pesticide on nontarget insect pollinators are the *honeybee acute contact* LD_{50} and the *honeybee toxicity of residues on foliage.*

Testing for Adverse Effects on Nontarget Insect Pollinators

The *acute contact* LD_{50} *test* requires that honeybees be anesthetized to facilitate placement of the pesticide directly on the abdomen or thorax. Afterward, the bees are monitored for 48 or 96 hours; the LD_{50} is calculated and expressed in micrograms (mg) of active ingredient per bee.

The *honeybee toxicity of residue on foliage test* determines how honeybees can receive a toxic dose from dislodgeable residues on foliage. The pesticide is applied to foliage which is then harvested over a number of days. Harvested foliage is placed into cages containing worker bees, and the number of bees that die from contact with the foliage is

recorded and compared with controls.

Testing for Adverse Effects on Plants

Nontarget Terrestrial Plant Toxicity

Corn, soybeans, root crops, tomatoes, cucumbers, lettuce, cabbage, oats, ryegrass, and onions often are used to test effects on nontarget plants. The soil is treated or the pesticide applied to the foliage at the maximum rate allowed by the label, or at a concentration three times the expected environmental concentration. Data collected in specific tests include

- root length,
- percent germination,
- percent emergence,
- time to emergence,
- plant height,
- dry plant weight, and
- percent of plants exhibiting phytotoxic (morphologic) changes.

The NOEC is determined for each end point, such as growth and root length. The most sensitive NOEC may be used in risk assessment.

Nontarget plants studies. Plants of various species are monitored for seedling emergence and vegetative vigor.

Nontarget Aquatic Plant Toxicity

Tier 1

The two aquatic plant species most commonly tested for nontarget plant toxicity are *Selenastrum capricornutum* (a freshwater green alga) and *Lemna gibba* (a macrophyte duckweed). Water containing the two species is treated with either

- a single dose representing the maximum allowed rate, or
- a concentration three times the expected environmental concentration.

Tier 2

Five aquatic plant species are used for Tier 2 testing: *S. capricornutum*, *L. gibba;* *Anabaena flos-aquae* (a blue-green alga); *Skeletonema costatum* (a marine diatom); and *Navicula pelliculosa* (a freshwater diatom). The focus is on growth rate data measured either as increases in cells, or as fronds. Effects are expressed as EC_{50} (the concentration of pesticide that reduces cell growth by 50 percent). Follow-up tests determine if the effects are temporary, permanent, or lethal.

Exposure Characterization

Environmental processes result in transformation, transfer, and transport of pesticides. And the characterization of environmental fate assesses *what the environment does to the chemical* so that environmental exposurethat is, concentrations an

organism might actually encountercan be estimated. Knowledge of pesticide environmental fate and transport characteristics is essential to accurate estimation of the form and amount of the chemical that wildlife and aquatic organisms might encounter in the environment. Laboratory and field studies make it possible to predict how much of a molecule and its metabolites might reach nontarget organisms.

Understanding how a pesticide can be modified by the environment also is critical in judging how it will affect its intended target. For instance, a herbicide may offer great promise, in the laboratory, in suppressing hard-to-control perennial weeds found in cantaloupe and tomato fields. But if environmental factors in the field break down the herbicide before the weeds can absorb a sufficient dose, weed control is diminished. Conversely, if the pesticide is somewhat resistant to environmental breakdown, concerns are raised about the product's residual action impacting water quality, wildlife, soil, and rotational crops.

Complex Interactions Must Be Studied

The environment plays a major role in determining

- how much pesticide residue remains;
- how long it remains;
- where it goes, ultimately;
- what form it might assume; and
- the toxicity of the molecule as it is modified, over time.

How a pesticide reacts within a specific environment (the site of application) is dependent on its physical and chemical characteristics as well as environmental properties such as soil type, landscape position, and weather. Soil properties such as pH, temperature, moisture, and nutrient concentrations influence how chemicals are changed in the environment. Similarly, climatic factors such as temperature and rainfall impact pesticide persistence and movement.

Site-specific differences such as how a pesticide reacts, over time (when applied in a Louisiana sugarcane field versus an Indiana corn field, for example) are critical in estimating environmental exposure. The circumstances of use and the uniqueness of each chemical molecule make predicting environmental exposure across the United States very complex.

How will the pesticide be used?

Application rates and techniques have direct bearing on how a pesticide enters the environment. Thus, a pesticide applied at a

rate of *ounces or less* per acre has a lower potential for exposing fish and wildlife than the same chemical applied at a rate of *pounds* per acre.

A pesticide may be so sensitive to sunlight that it decomposes soon after application. If the same product is protected from sunlight by incorporation into the soil, however, its persistence in the environment may be extended.

An incorporated product is less likely to impact wildlife than one which is left exposed on the soil surface. For instance, a granular pesticide presents greater exposure potential for birds than does the same chemical applied as a liquid. Thus, formulation is considered a critical factor in estimating environmental exposure.

How will the pesticide be transformed by the environment?

Research has shown that the environment often alters pesticide molecules dramatically. The original (parent) molecule often is modified as it enters and interacts with the environment. Pesticides often are degraded in water (hydrolysis), by sunlight (photodegradation), and by soil and aquatic microorganisms (microbial degradation). Knowledge of transformation rates and the

products and toxicity of transformation is key to assessing ecological risk.

Chemical properties of pesticides, such as volatility or water solubility, influence their transfer in the environment. For instance, the initial distribution of a pesticide in soil and water, or between soil particles and the air that surrounds them, might be 90 percent in soil and 10 percent in water. The physical characteristics of a molecule, in combination with chemical properties of the environment, influence whether a pesticide molecule resides mainly in soil, air, or water.

How long will the pesticide persist in the environment?

A pesticide's continued presence in the environment*persistence*is a key factor in predicting potential exposure of wildlife. Persistence is generally described as a half-life, that is, the length of time it takes for the disappearance of one half of the applied pesticide from an environmental compartment. Biological and chemical processes that degrade or dissipate the pesticide influence its persistence.

How will the pesticide be transported from the

original application site to off-site environments?

Pesticides and their metabolites (breakdown products) move in a number of ways. They can

- leach downward into ground water,
- attach to soil particles and be washed away in surface water runoff,
- volatilize into the atmosphere, or
- drift off-target.

Leaching, runoff, volatilization, and drift often are modeled to show how pesticides move in the environment. Compounds that do not readily adsorb to soil particles often have a high potential for leaching to ground water or entering streams via surface water runoff. Highly volatile pesticides may escape the soil environment and dissipate into the atmosphere; when redeposited later, via rainfall, they may interact with nontarget plants and animals.

What is the range of pesticide concentrations expected to come in contact with biological systems?

Knowledge of the application rate and an understanding of how a pesticide can be transformed, transferred, and transported within the environment facilitate prediction of the range of concentrations that will actually interact with other organisms.

Development of expected environmental concentrations depends on information developed from a host of environmental fate and residue chemistry studies that describe transformation, transfer, and transport. The lists of studies on the following page demonstrate the extensive laboratory and field data required for estimation of environmental concentrations.

Gambrel's quail with radio transmitter. Studies with free-ranging but trackable birds, conducted to monitor effects on survival and reproductive performance.

What organisms are expected to be exposed to a pesticide?

Characterization of environmental exposure requires consideration of the inhabitantswildlife, aquatic organisms, and nontarget plantsof sites where a pesticide is likely to occur. An understanding of the natural history (distribution, abundance, breeding habits, and food sources) of nontarget species facilitates identification of the predominant route of exposure.

Laboratory and Field Data Required for Estimation of Environmental Concentrations of Pesticides

Environmental Fate Data Requirements

- Hydrolysis
- Photodegradation in water
- Photodegradation in air
- Aerobic soil metabolism
- Anaerobic soil metabolism
- Anaerobic aquatic metabolism
- Leaching and adsorption

- Laboratory volatility
- Field volatility
- Field dissipation, terrestrial uses
- Field dissipation, aquatic uses
- Forestry field dissipation
- Confined rotational crop
- Field rotational crop
- Accumulation in irrigated crop
- Accumulation in fish
- Accumulation in aquatic nontarget organisms

Residue Chemistry Data Requirements

- Chemical identification
- Nature of residue in plants
- Residue analytical methods, plants/animals
- Magnitude of the residue in potable water
- Magnitude of the residue in fish

Spray Drift Data Requirements

- Droplet size spectrum
- Drift field evaluation

Estimated Environmental Concentration: A Key Environmental End Point

Potentially, all pesticides pose some risk to

nontarget organisms; and environmental concentration estimates are critical in estimating ecological risk. Data developed on the environmental fate of a pesticide, along with use information as stated in the proposed pesticide labeling, are used to generate a value known as an Estimated Environmental Concentration (EEC). The EEC is an estimate of how much of a pesticide might reach nontarget areas, potentially exposing wildlife, bees, worms, aquatic animals, and plants. EECs generally are predicted for ground and surface water, soil, and nontarget food items.

The key word in *Estimated Environmental Concentration* is *estimated*. Scientists cannot measure actual concentrations for every conceivable environmental situation. An actual concentration measured today most likely would not match measurements taken sometime earlier or later. Therefore, EECs should not be viewed as *hard* or *fixed* values, but as *estimates* based on data availability. Actual concentrations can and do fluctuate according to numerous variables: time of year, geographic location, weather patterns, soil conditions, cropping systems, etc.

Mathematical models that simulate the fate of pesticides in the environment are used for developing EECs. But initial models based on preliminary data, very early in the pesticide development and testing processes, leave a window of uncertainty. This initial lack of specific pesticide informationthe unknownleads to this uncertainty in determining accurate EECs. Therefore, the degree of uncertainty is compensated by very conservative assumptions.

As researchers gain a better understanding of the molecule through refined laboratory data and in-depth analysisand as it becomes known what influence factors such as weather conditions and soil characteristics might haveinput assumptions are modified and new EECs determined that are less

uncertain, that is, refined.

The challenge in refining the EEC is to provide greater scientific certainty and improved interpretations of the available data. In this way, an improved understanding and approximation of the actual environmental concentration is achieved. The better the prediction, the better the risk estimate.

Developing Estimated Environmental Concentrations for Aquatic Organisms

There are four basic tiers used to estimate environmental exposure concentrations for aquatic systems. Each tier requires additional data or more refined data analysis than lower tiers. The higher tiers employ sophisticated models where principal parameters and site-specific scenarios have been developed.

Aquatic EEC Tier 1: Single Event EEC Based on a High-Exposure Scenario

The *Generic Estimated Environmental Concentration (GENEEC)* model was developed by EPA to determine a generic EEC for aquatic environments. EECs derived from GENEEC models reflect the pesticide concentration expected under worst-case conditions: an application on a highly erosive and very steep upland slope, with heavy rainfall occurring immediately after. The watershed model is essentially ten acres of surface area. It is assumed that the entire area is treated, and that the treated area has uniformly high slopes so that runoff drains directly into a six-foot-deep, one-acre pond.

The GENEEC model utilizes environmental fate parameters identified by laboratory

testing protocols, as well as information obtained from the proposed pesticide labeling. It also includes fixed soil and weather parameters. The model estimates pesticide runoff to the pond on the basis of rate and method of application, water solubility, soil binding (adsorption) characteristics, and persistence of the pesticide; spray drift is also a factor.

Aquatic EEC Tier 2: Single Site, Variable Weather

Tier 2 assessments determine EECs based on geographic areas nationwide and use sites (e.g., corn) in close proximity to ponds; many input variables are the same as those for GENEEC models, but additional parameters more descriptive of use site may be factored, as well. These data are used in more comprehensive models (PRZM/EXAMS). Conditions typical of product use sites, including specific soils and weather information (a distribution of weather, including a one-in-ten-year high-runoff incidence) are used. Single median values for chemical characteristics are selected from laboratory-derived environmental half-lives in the upper ten percent of the statistical distribution. Contributions from spray drift also are factored into the estimate. The goal of Tier 2 analysis is to better define the *range* of EEC--as compared to the single, worst-case Tier 1 assessment--that can be reasonably expected under variable weather conditions. Frequently, a case more typical of the intended site is analyzed, as well, for comparison against the worst case scenario.

Aquatic EEC Tier 3: Multiple Sites, Multiple Weather Conditions

Tier 3 differs from tiers 1 and 2 in that both use-site and weather parameters are varied. Tier 3 assessments examine hypothetical

circumstances representative of the regions in and conditions under which the pesticide is likely to be used. Tier 3 modeling results in development of a distribution of EECs that might be expected across use markets, recognizing that both soil properties and weather patterns will vary significantly by market region and years of use. Tier 3 analysis is used by pesticide registrants to address environmental exposure concerns that arise during product reregistration processes.

Aquatic EEC Tier 4: Watershed Site Assessment

Tier 4 assessments are complex analyses that investigate how pesticides are likely to interact with a landscape composed of hundreds of thousands of acres. The landscape has diverse soils and climates, varied proximities of treated fields to receiving waters, and randomly distributed bodies of water.

Geographic Information Systems (GISs) are commonly used at Tier 4. GISs allow graphical evaluation of concurrent risk factors (within the regions of use) that heighten concerns. In other words, GISs distinguish high risk versus low risk areas of use on a regional basis.

Tier 4 procedures sometimes shift from risk characterization and modeling to actual environmental residue monitoring. Risk assessment equations and exposure estimates for EECs are validated by actual measurements in the environment, called *Actual Environmental Concentrations (AECs).* Although sampling provides actual residue data, each set of data is valid only for the point in time when the corresponding samples are taken. And each sample yields only a hint as to the scope of residue incidence. Modeling and monitoring often are combined within Tier 4 to provide a fuller understanding of the distribution of exposure occurring within treated watersheds.

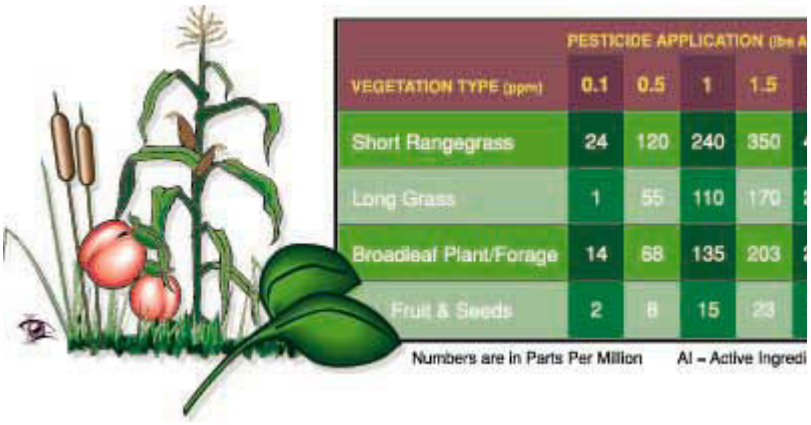
Predicting Environmental Concentrations for Terrestrial Organisms

Terrestrial (unlike aquatic) wildlife are exposed to pesticides primarily through the plant or animal material that they consum as food. Other routes of exposure, such as dermal, inhalation, a ocular, are considered less important and difficult to measure, a effects are thought to at least resemble those associated with or and dietary routes. For birds, the primary route of exposure is dietary exposure to residues on food items, although there is a potential to ingest granular pesticides. EECs are developed for these routes of exposure.

Exposure estimates for wildlife vary according to the amount o pesticide residue on food items and the actual consumption of those items. In determining EECs for terrestrial organisms, it is assumed that residue levels on food items increase as applicatio rates per acre rise.

Predicting Concentrations on Food Items

EPA and pesticide manufacturers, in performing Tier 1 risk assessments, use a series of tables that establish guidelines on h much pesticide residue might be expected on various types of plants and insects. The original tables were developed by Fred Hoerger and Gene Kenega and refined by John Fletcher, James Nellessen, and Thomas Pfleeger.



Predicting the total amount of residue available on vegetation depends on two variables: application rate and plant type. Plant types are assigned to a simple plant characterization scheme:

- Short rangegrass
- Long grass
- Broadleaf plants/forage
- Fruits
- Seeds

A portion of the revised Kenega table (p. 37), illustrates maximum expected residues per plant species as a function of application rate. For instance, the table predicts a maximum EEC of 240 parts per million (ppb) on rangegrass immediately after a pesticide application at one pound per acre.

EECs also are calculated for birds and mammals consuming pesticide-treated insects. It is important to note that these EECs are based on application rates without regard to the characteristics of the pesticide. When actual residue data are not available, EECs of 58 and 135 (based on pounds applied per acre) can be used as estimates of residues on large and small insects.

Models Can Account for Residue Declines

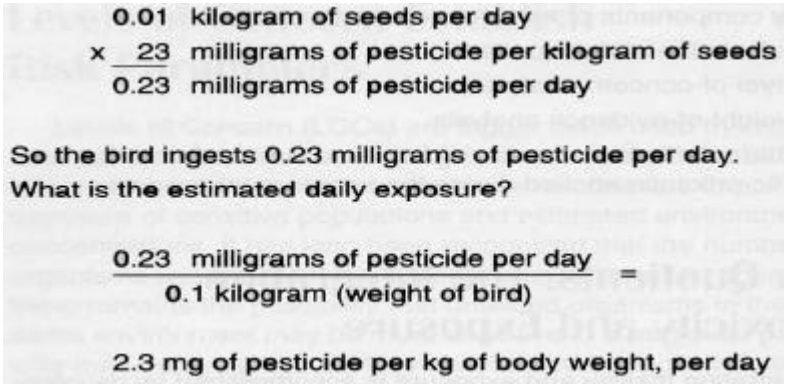
Residue levels from the Kenaga table can be refined. First, the most appropriate environmental fate half-life value is selected. Then degraded residue values are calculated, considering multiple applications and time intervals between repeat applications. These values can be used as more realistic

estimates of terrestrial residues. Further refinements can factor in more specific feeding habits, food sources, body weights, and ingestion rates for sensitive species likely to inhabit or infiltrate the treated area.

Food Consumption Patterns Dictate the Amount of Exposure

Exposure of birds or mammals can be refined by incorporating weight of the animal, percentage of food consumed relative to body weight, and amount of pesticide residue on the food item.

Example: A 100 gram (0.1 kilogam) bird is known to consume seeds in an amount equivalent to 10 percent of its body weight each day. The estimated EEC was predicted to be 23 ppm by using the Kenega table for fruits and seeds, with 1.5 pound of active ingredient applied per acre. We assume that this avian species feeds exclusively on the seeds. What is the EEC (total amount of pesticide per kilogram of seeds consumed daily)?



Granular Product LD_{50} Per Square Foot

There is a potential for birds and mammals to ingest pesticide g initial risk assessment of oral exposure of terrestrial vertebrates insecticide considers an estimated number of unincorporated gr square foot in relation to the number per square foot that result mortality, that is, LD_{50}. This procedure is based on

- application rate,
- concentration of the pesticide per granule,
- a laboratory-derived LD_{50}, and
- body weight of the bird or mammal in question.

The procedure assumes that the bird or mammal will ingest all available within one square foot of treated area, and that all gra consumed within a short period of time. The greater the LD_{50} the greater the presumed risk. If a high level of risk is indicated research may be conducted to either confirm or refute the origi

Risk Characterization

Risk characterization is the summarizing step of a risk assessme (EEC) and toxicity are assembled, the overall ecological risk fo exposure and toxicity characterizations are integrated into a co

description of the potential risk to the environment from use of

Key components of risk characterization include

- calculation of risk quotients,
- level-of-concern analysis, and
- weight-of-evidence analysis.

Risk characterization should yield clear, concise information on scientific rationale applied during the assessment process.

Risk Quotients: The Integration of Toxicity and Exposure

Integrating toxicity and exposure is accomplished by developing an index called the risk quotient (RQ). This begins with a conservative Tier 1 assessment that utilizes the highest EEC and the most sensitive end point to determine the quotient. An RQ provides general guidance on potential risks posed by a pesticide. It is derived by dividing the EEC for a particular environmental compartment (such as water) by a toxicological end point (such as LC_{50}) for an organism (e.g., fish) subject to exposure in that compartment.

In other words, an EEC for *water* may be divided by an LC_{50} for *fish* to determine the risk quotient. An RQ of less than one indicates an estimated exposure concentration below the toxicity end point. Risk quotients greater than a level of concern indicate that exposure may exceed levels shown in laboratory tests to produce adverse effects; it may lead to refined

estimates of exposure and effects to gain a better understanding of the risks which are likely to occur in the environment.

Levels of Concern Establish Risk Parameters

Levels of Concern (LOCs) are trigger ratios used by regulatory comparison against calculated RQs. LOCs incorporate (into risk uncertainties due to possible exposure of sensitive populations a environmental concentrations. It has long been recognized that organisms used to examine adverse effects is limited; thus, there possibility that untested organisms in the same environment may sensitive to a particular pesticide than those tested. EPA establi values to ensure adequate protection for more-sensitive, unteste endangered species.

There are two general categories of LOCs (acute and chronic) f nontarget fauna groups; and there is one category (acute) for ea floral group. To determine if an LOC has been exceeded, a risk determined and compared to trigger values. The following table quotients and LOCs.

Level of Concern (LOC)

End Point and Scenario	Risk Quotient	Nonendangere
Mammalian acute (granular)	LD_{50}/FT^2	0.5

LOCs are regulatory triggers used to categorize whether the potential risk is of low, medium, or high concern. For instance, a risk quotient less than 0.5 developed for an avian acute response is of minimal concern to nonendangered species, while a quotient of 0.5 or greater suggests potentially higher acute risk.

LOCs differ among biological indicators and types of tests, as well as between nonendangered and endangered species. If the risk quotient is categorized as minimal for a chemical where no LOC is triggered, the use of the pesticide is predicted to cause no adverse effects when used in accordance with the label; and registration or reregistration generally is granted. A moderate risk quotient indicates that applicators should be educated on use of the pesticide to minimize the likelihood of adverse environmental effects; pesticides with moderate RQs usually are granted restricted-use registration.

Registrants of pesticides with risk quotients that generally exceed the LOC supported by the weight of evidence face extensive risk mitigation requirements prior to product registration. Optimally, mitigation efforts lower potential risk concerns below the LOC, frequently through a refined EEC. Reduced rates of application and number of applications, buffer strips, in-furrow application (vs. broadcast), and ground application (vs. aerial) are examples of measures that can be taken to minimize fish and wildlife exposure.

The following is an example of the use of toxicological data and EEC values to calculate a risk quotient; it is based on an application rate of one pound of active ingredient per acre.

The data and assessment show that the risk quotients for pesticide A do not exceed LOCs of acute and chronic exposures for fish and birds; thus, no additional testing or mitigation is required. For pesticide B, which is more toxic, the risk quotients are greater than the threshold for presumption of risk for both acute and chronic exposure. Additional testing, or more extensive evaluation of the EEC, may be required to demonstrate a reduced risk; or, risk mitigation measures might be adopted. This example illustrates how two pesticides with different toxicological properties but similar application rates can have different presumptions of risk, based on their toxicity.

Calculated Risk Quotients (application rate 1lb/acre)

Organism	Toxicity Test	Pesticide A	Pesticide B	Estimated Environmental Concentration (EEC) Water Residue	Estimated Environmental Concentration (EEC) Soil Surface or Food Residue	Risk Quotient A	Risk Quotient B
Fish	Acute LC_{50} (mg/L)	2	0.125	0.08 mg/L		0.04[a]	0.64
	Chronic NOEC (mg/L)	0.5	0.03	0.08 mg/L		0.16	2.67
Bird	Acute LD_{50}[c] (mg/kg)	1000	75		10.41 mg/ft^2	0.06[b]	0.78
	Dietary LC_{50} (ppm)	1000	75		120 ppm	0.12	1.60
	Reproduction NOEC (ppm)	350	25		50 ppm	0.14	2.0

[a]RQ=EEC/Toxicity; thus, 0.08/2=0.04

[b]$RQ = \frac{\text{Application rate (lb active ingredient per acre) x (453,590 mg/lb/43,560 ft}^2\text{/acre)}}{LD_{50}\text{ mg/kg x weight of bird (grams)/1000g/kg}}$

[c]Bobwhite quail with a mean weight of 178 grams

Calculated Risk Quotients (application rate A=1lb/acre, B=.33lb/acre)

Organism	Toxicity Test	Pesticide A	Pesticide B	Estimated Environmental Concentration (EEC) Water Residue	Estimated Environmental Concentration (EEC) Soil Surface or Food Residue	Risk Quotient A	Risk Quotient B
Fish	Acute LC_{50} (mg/L)	2	0.125	A=0.08 mg/L B=0.025		0.04[a]	0.2
	Chronic NOEC (mg/L)	0.5	0.03	A=0.08 mg/L B=0.025		0.16	0.83
Bird	Acute LD_{50}[c] (mg/kg)	1000	75		A=10.41 mg/ft^2 B=3.47	0.06[b]	0.26
	Dietary LC_{50} (ppm)	1000	75		A=100 ppm B=33	0.10	0.44
	Reproduction NOEC (ppm)	350	25		A=60 ppm B=20 ppm	0.17	0.80

[a]RQ=EEC/Toxicity; thus, 0.08/2=0.04; 0.025/0.125=0.2

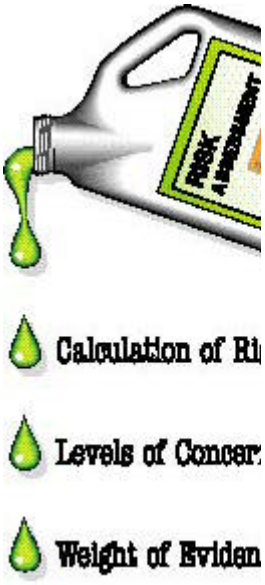
[b]$RQ = \frac{\text{Application rate (lb active ingredient/acre) x (453,590 mg/lb/43,560 ft}^2\text{/acre)}}{LD_{50}\text{ mg/kg x weight of bird (grams)/1000g/kg}}$

[c]Bobwhite quail with a mean weight of 178 grams

Application rates also influence risk assessment. The toxicological data provided (p. 43), assuming that Pesticide A has an application rate three times that of Pesticide B, illustrate that, although Pesticide B is more toxic to fish and birds, its presumption of risk is similar to less toxic Compound A. In the second illustration (p. 43) neither pesticide's RQ value exceeds the triggers for presumption of risk, although pesticide B is acutely toxic to fish and birds.

Weight of Evidence Analysis

Strengths, limitations, and uncertainties, as well as magnitude, frequency, and spatial and temporal patterns of previously identified adverse effects, are discussed. Monitoring data and reported incidents of wildlife kills are included to help confirm risk potential. Dissipation and application characteristics of the pesticidedistance from application site, duration of effects, and time of year at which wildlife and aquatic organisms may be most susceptibleare discussed in terms of likelihood of the pesticide to affect wildlife and aquatic organisms. Very often, discussions suggest a number of potential mitigation measures that may be used to reduce risk while maintaining benefits from continued registration of the pesticide.



Finally, potential risks of pesticide use are compared to potential risks from pesticides already used on the same site and, typically, for the same pests. This helps decision makers to view the overall picture of potential ecological risk while making registration and reregistration decisions. The process ends with a summary statement on the likelihood of adverse effects based on evidence analysis and professional judgment.

Conclusions

Pesticides provide significant benefits to the American public by controlling pests that invade agricultural crops, industrial sites,

homes, schools, restaurants, and hospitals. Public health is enhanced when pesticides are targeted against mosquitoes, ticks, and rodents that carry disease; head lice; fleas; and allergy-producing cockroaches. Antimicrobial products disinfect drinking water supplies and reduce hazards from organisms that cause human diseases such as cholera. The motoring public and transportation industries benefit when herbicides eliminate plants that obscure roadway signs and encroach on rights-of-way. Pesticides are instrumental in protecting native habitats and indigenous flora from non-native plant species. Other pesticides protect and preserve homes, museums, and historic buildings from wood-destroying insects such as termites and carpenter ants.

But there are risks associated with pesticide use, as well, and they draw public attention. Obviously, in order to be useful, most pesticides are toxic to the target pest. It is very difficult to develop a chemical that will affect *only* the targeted pest and carry *no* potential to harm nontarget wildlife species. No pesticide is risk-free, and certainly no pesticide is "safe" in all situations: All carry the potential to cause adverse effects.

Ecological risk assessment is a process where scientific information is used to address potential environmental risks associated with pesticide use. Good regulatory decisions depend on documented scientific research, an understanding of the strengths and weaknesses of the specific risk assessment, and sound professional judgment in drawing conclusions from compiled data. Risk assessments should clearly identify pertinent facts *and* any assumptions deemed necessary to accurately evaluate the pesticide. If ecological risk assessments are clear, concise, and thorough, they add a vitally important dimension to EPA's decision making process. Clarity and openness in the risk assessment process permit informed debate on pesticide use; ultimately, the registration of a pesticide must withstand scientific inquiry, public scrutiny, and legal review.

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