Chapter 8. Developing and Registering a Piscicide

by Terrance D. Hubert

It is important that those involved in managing aquatic systems have as many different tools as possible for the control and eradication of nonnative aquatic species. In earlier chapters, it has been noted that only four chemicals are registered as piscicides. While development of additional chemical tools may be worthwhile, it is important to know what is involved before embarking on an effort to develop and register a piscicide.

The need to regulate pesticides became apparent in the late 1940s. In 1947, Congress passed the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) that regulated the licensing and application of pesticides, primarily for agriculture. Initially, the U.S. Department of Agriculture (USDA) was given the responsibility of registering pesticides. The responsibility passed to the EPA when it was created in 1970. Amendments to FIFRA were made in 1980 and 1988, with the latter amendment requiring that all pesticides registered before 1984 undergo a reregistration process. This was largely done because testing methodology had improved significantly, and Congress felt this necessitated repeating the registration process for older chemicals. Finally, Congress passed the Food Quality Protection Act in 1996, which placed emphasis on chemicals used directly on food crops and feed, and required risk assessments on the basis of cumulative effects from pesticides of similar modes of action, provided special consideration for infants, elderly, and other sensitive groups, required the EPA to establish a program to determine the endocrine disrupting characteristics of pesticides, and required reassessments of pesticide tolerances.

It is estimated that from initial discovery through developmental research to final product, the development of a pesticide can take 8 to 10 years and cost $35 to $50 million (American Crop Protection Association 2001). Registration of the pesticide, which is a critical subcomponent of the development process, may require more than 100 different tests and can cost up to $10 million (USDA 2002). Appendix E lists the current guidelines for studies required for the registration of a pest control product. The number and types of tests required depends on the intended use. For instance, pesticides applied to ornamental plants in an enclosed environment will be subjected to less testing than those applied to food crops raised outdoors. This is because the risk associated with potential exposure in the former circumstance is lower than in the latter.

There are three types of registrations that may be granted by the EPA depending on the circumstances. The most common registration is a full, or Section 3(c), registration (EPA 1996*a*). Section 3 registrations require a full battery of data to support the registration and are renewed on an annual basis. This type of registration is usually obtained by the product manufacturer, although there are circumstances in which a third party would obtain such a registration for a use not supported by the manufacturer's registration.

The second type of registration is known as a Special Local Needs, or Section 24(c), registration (EPA 1996*a*). These types of registrations generally cover situations where individual states apply for registration of an additional use of a federally registered pesticide, or a new end-use product to meet special local needs. For example, Florida has a special local needs registration to apply the molluscide Bayluscide® to ornamental ponds to control snails. In most instances, because this involves a currently registered pesticide, minimal additional data requirements are necessary to register a pesticide for a special local need. Generally, data submitted to support the federal registration are sufficient to support the special local needs registration. Applications for special local needs registrations must be accompanied by an unreasonable adverse effects assessment (defined later in this chapter). The state registration may be disapproved by EPA if the use is not covered by the necessary tolerances or has been previously denied, disapproved, suspended, or canceled by the administrator of EPA. Special local needs registrations are also renewed on an annual basis.

The final type of registration is a Section 18 Emergency Exemption (EPA 1996*b*). Section 18 registrations are sought when a control need is identified in which registered pesticides will not be effective. Section 18 requests most frequently involve pesticides registered for other uses. Occasionally, however, requests are made for pesticides for which registrations have been cancelled. In situations where an emergency exemption is required, the EPA has the authority to grant an exemption from the provisions of FIFRA to a state or federal agency. Also, Section 18 regulations allow a state to issue a crisis exemption for the use of a pesticide when there is not sufficient time to formally request a specific exemption or, if formal application has been made, for the EPA to complete the review of the request.

All data submitted to support the registration of a pesticide, regardless of the intended use, must meet strict standards of record-keeping and documentation known as Good Laboratory Practice (GLP) guidelines. Failure to comply with these guidelines not only will result in rejection of the submitted data, but can also result in fines and/or imprisonment for the offending parties. It is therefore important to carefully review the record-keeping practices of laboratories under consideration for conducting registration-related research.

Development of a pesticide is generally a lengthy process and involves the broad steps of (1) developing a treatment strategy, (2) developing a specific chemical, (3) developing formulations of that chemical, (4) producing, and (5) registering the chemical and formulations of the chemical. In the pages that follow, the components of each of these steps will be discussed.

8.1 Developing a Treatment Strategy

Selecting Critical Life Stage for Control

It is important in developing a chemical control strategy to have a sound understanding of the biology of the organism to be controlled. Thorough study of the organism's life cycle, breeding habits, and habitat preferences may identify a life stage that is particularly susceptible to chemical control. Identification of the larval stage of the sea lamprey as being the most

vulnerable was pivotal in the development of a control strategy for sea lampreys in the Great Lakes (see Chapter 11 for a thorough discussion of sea lamprey control in the Great Lakes).

Selecting Candidate Chemicals

Sixty years ago, labor-intensive screening of thousands of chemicals was necessary to identify a taxon-specific chemical to control nonnative fishes (e.g., 6,000 chemicals were screened to find effective lampricides for sea lamprey). Today, models based on the actions of specific classes of chemicals are available to help identify candidates, and requirements for laboratory screening are reduced. In addition to biological activity and effectiveness, ease of handling, safety, and cost should be considered when selecting potential piscicides (Appendix D).

Toxicity Screening

Once the candidate chemicals have been selected, toxicity screening is initiated to define an effective concentration range over which mortality of the target life stage can be achieved (Lennon and Walker 1964). The types of toxicity tests that can be used in this phase are described in a guide from the American Society of Testing Materials (1980). The number of concentrations initially tested is a matter of convenience. Six concentrations, each differing by a factor of 10, is an appropriate starting point. If no mortality is observed at the highest concentration or total mortality is observed at the lowest concentration, the range should be adjusted and a new test conducted. This procedure is repeated until mortality is observed at the highest concentration and not at the lowest concentration. Effective concentrations are then refined by further toxicity testing on the target organism within this concentration range. Toxicity testing on phylogenetically diverse nontarget organisms is done to determine which of these may be sensitive to the chemical at the concentrations effective on the target organism. If any nontarget organisms are determined to be sensitive at the concentrations toxic to the target organism, then subsequent toxicity screening is conducted to determine if there is a concentration range over which mortality of the target organism may be achieved with minimal mortality to nontarget organisms.

8.2 Active Ingredient Development

Decision to Develop

The decision to develop a particular chemical or group of chemicals as selective piscicides should be based primarily on sound science, although economic considerations will also play a role. Research to register the product with the EPA will cost millions of dollars. Since most piscicides in use today have been developed with public funds, good stewardship of public monies must play a central role in the decision-making process.

Safety Considerations

Perhaps the most important consideration in the development of any piscicide is safety. From a human safety perspective, the chemical must be safe to those who apply the piscicide as well as to those who may come into contact with it following applications. Additionally, nontarget organisms exposed to the piscicide or to its degradation products should not be adversely affected. The piscicide label, the document that describes precisely how the piscicide is to be used, provides explicit instructions on the application methods, dose or application rates, and specific instructions on its safe use. Safety considerations include, but are not limited to, protective clothing for applicators, applicator training, instructions and warning statements

regarding specific hazards, restrictions on water usage during and after treatment, environmental warnings, proper storage and disposal of containers, and procedures for handling spills.

Registration Process

Once the decision to develop a pesticide has been made, the process of registration with the EPA begins with a series of complex, long-term research studies (Appendix E). These studies are designed to provide data related to product chemistry, animal toxicology, residues in food and feed, environmental fate, ecological effects, and efficacy. Although the list of studies is extensive, it is possible through modeling that the requirements for some studies may be satisfied or waived. For example, data from studies such as the physical and chemical properties of the active ingredient may be used in models that predict the environmental fate of the piscicide. The results could reduce the number of studies required, for example, in the Series 850 guidelines (Appendix E).

The EPA places submitted data into two categories: data submitted to support the registration of the active ingredient of the pesticide (generic data) and data submitted to support the registration of a specific formulation of the active ingredient (product-specific data). It is critical that studies to support the registration of the active ingredient and formulations be conducted according to GLP standards**.**

Field Testing and Experimental Use Permits

A critical component of the registration process is field testing. This usually begins late in the registration process because field testing generally requires an experimental use permit and data generated during the registration phase are used to support the application for the permit. Field testing occurs on large-scale plots under normal conditions and should cover all proposed uses. Data from field trials must be submitted to the EPA and are also subject to GLP standards. It is at this point in the piscicide development process that a manufacturing source for the active ingredient and formulations is explored if one does not already exist. Manufacturing process development studies are conducted once a manufacturer is identified. This is in preparation for full production of the pesticide once the registration has been granted by the EPA. Data from the process development studies are also submitted to the EPA and, as with all other data, are subject to GLP standards.

Product Chemistry, Toxicological, and Environmental Assessments

Tests conducted to satisfy product chemistry requirements center on the physical characteristics of the active ingredient and the formulated products. For example, tests include solubility in water and organic solvents, color, melting point, boiling point, octanol-water partition coefficient, and storage stability. Exactly which tests are required depends on the nature of the active ingredient and the formulation and the manner in which the formulation will be used. For example, a test to determine viscosity would not be required if the product is a solid.

Toxicological assessments in mammals to ensure human safety and minimize harm to other nontarget organisms are made to determine the acute effects of single doses, the chronic effects from long-term exposures, mutagenic effects, and carcinogenic effects. Acute studies examine the toxicity from oral exposure, dermal exposure, and inhalation. Acute eye and dermal irritation studies are also generally required. Subchronic tests involve 90-day feeding studies and dermal exposure studies that run from 21 to 28 days. Developmental and reproduction studies are also conducted. Finally, there is a battery of studies conducted to determine potential mutagenic, carcinogenic, and neurotoxic effects.

Environmental testing determines the fate of the chemical in water and soil. Some examples of environmental fate studies are hydrolysis, aerobic or anaerobic aquatic or soil metabolism, and photolysis. Studies of this type are generally conducted with radiolabeled material so that the fate of the parent chemical and its degradates can be followed. Use of radiolabeled chemicals can be costly depending on the ease of their synthesis.

Residue Chemistry and Residue Tolerances

Pesticide residue studies are conducted to determine whether residues would persist in an organism that could potentially be consumed by humans. In the case of registration of a piscicide, residue studies in fish or shellfish are generally required. Livestock and plant metabolism studies may also be required if water from a treated stream or pond could potentially be used for irrigation or watering livestock. If it is practical to place use restrictions on treated pond or stream water, the livestock or plant metabolism studies may be waived by the EPA. As a general rule, the first set of these studies should focus on determining the qualitative nature of the residues in the exposed organisms. Once this is known, field studies are conducted to determine levels of the residues that might be expected from a typical treatment. An assessment of the biological activity of the residues is made, and studies are conducted on those residues that might cause toxicity. The EPA will then set residue tolerances for the food portion of the organism on the basis of those studies. It is the responsibility of the manufacturer or registrant to demonstrate that the residues in a commodity are at levels that provide a reasonable margin of safety for human consumption. Monitoring is conducted and any food or feed commodities having residues that exceed the tolerance are destroyed. For a piscicide, it is not likely that residue tolerances would be set unless the piscicide is used on a contained food fish that will be shipped to market. Tolerance enforcement is the responsibility of the FDA.

Risk Assessment

Risks from the use of pesticides (American Crop Protection Association 2001) are assessed by the equation:

$$\text{Risk} = \text{Hazard} \times \text{Exposure}$$

Toxicology studies provide estimates of the hazards and the residue studies provide estimates of the exposures. In determining the risk associated with pesticide use, the EPA estimates the Reference Dose, also known as the Acceptable Daily Intake (ADI). This factor is arrived at by taking the No Observable Effect Level determined from animal feeding studies and dividing by a safety factor, usually 100 or greater. The ADI is taken as the amount of residue that can be ingested by the average person every day for a lifetime with a reasonable expectation of no ill effects. Typically the ADI is set well below levels that affect the most sensitive test animals. Considering that residue tolerances are also set such that residue exposures from all sources fall well below the ADI, a significant margin of safety is incorporated into the risk estimate.

The Federal Registration Package

The process of conducting the appropriate tests to support the registration of a pesticide takes 6 to 7 years and typically results in the accumulation of several thousands of pages of data. Registration packages are reviewed by the scientific and administrative branches of the EPA's Office of Pesticide Program, and the process of review can take 6 months to 1 year for each individual piece of the submission (e.g., product chemistry, toxicology, etc.). While the review is in progress, the registrant begins preparations for pesticide production. A product label will be approved once the data supporting the registration are judged to be adequate by the EPA.

Registration of Pesticide by States

The process of pesticide registration by state agencies was reviewed for the states of Arizona, New Mexico, Nevada, and Utah. In registering a pesticide, New Mexico, Nevada, and Utah do not conduct full data reviews (New Mexico Statutes 1978, Nevada Pesticides Act 1955, Utah Pesticide Control Act 1979). Rather, these states rely on the assessment of the EPA that makes its Registration Eligibility Decisions available to the public on its Web site. For each of these states, registration of a pesticide requires payment of an annual registration fee, ranging from $35 to $70, along with a completed application form containing information regarding the registrant's name and address, the name of the pesticide, the EPA registration number, and a complete copy of the pesticide label. Statutes of all states contain clauses that indicate that the state may request additional information or data in making its assessment.

Registration of a pesticide in Arizona requires more detailed applications than in New Mexico, Nevada, or Utah. Pesticide registration in Arizona is regulated under two separate statutes, which include the Arizona Revised Statute Title 3 on Agriculture (Arizona Revised Statutes 1988*a*) and Title 49 on the Environment (Arizona Revised Statutes 1988*b*). The Arizona Department of Agriculture generally requires information that is similar to the states of New Mexico, Nevada, and Utah in granting a registration along with a $100 registration fee. Federal, state, and county offices are exempt from paying the registration fee.

In contrast to New Mexico, Nevada, and Utah, Arizona has a specific statute governing pesticides in groundwater that falls under Title 49. In this section of the Arizona Revised Statutes, there are additional rules governing the registration of pesticides written in Section 2, Article 6, Water Quality Control: Pesticide Contamination Prevention (Arizona Revised Statutes 1988*b*). The intent of these statutes is to determine the potential of a pesticide and/or its residues to contaminate groundwater. As a consequence, data on water solubility, vapor pressure, octanol-water partition coefficient, soil adsorption coefficient, Henry's Law constant, and all dissipation data including hydrolysis, photolysis, aerobic and anaerobic soil metabolism, and field dissipation are required. With the exception of studies to determine Henry's Law constant, most of the above data will probably have been submitted to the EPA to support a pesticide registration and can therefore be easily obtained for submission to Arizona regulatory agencies. In addition to these data, any other data that were submitted to the EPA to support a pesticide registration may also be requested under Arizona statute. If any of these data do not exist or if the registrant does not provide them, the pesticide automatically is placed on the groundwater protection list. A pesticide registrant is subject to a penalty of up to $10,000 for each day a groundwater protection data gap exists. While the pesticide is on the groundwater protection list, the director of the Department of Environmental Quality has the authority to regulate the use of the pesticide.

8.3 Formulation Development

Safety Considerations

As with the development of the active ingredient in a pesticide product, the safety of a formulation is a critical consideration. Similar safety considerations that apply to active ingredient development also apply to selecting formulants. As with active ingredients, formulants are required to undergo a testing process similar to, but not as extensive as, active ingredients. The EPA maintains a list of accepted inert ingredients for pesticide formulations (http://www.epa.gov/opprd001/inerts/lists.htm).

Field Testing and Experimental Use Permits

The type of formulation developed will depend on the intended use and how the pesticide is best applied. Generally, more than one formulation of the pesticide is developed for application in different environments.

Once a formulation has been developed, it must undergo additional field testing under experimental use permits as required for active ingredient development. This testing is designed to establish that the proposed formulation is efficacious and will not result in adverse effects under typical use conditions.

Toxicological Testing and Product Chemistry

Registration of a specific formulation of a pesticide does not require the formulation to undergo the same battery of tests as the active ingredient. Tests on the formulation are generally limited to acute toxicology and product chemistry testing to determine formulation characteristics, such as viscosity (if the product is a liquid), flammability, corrosiveness, or explodibility.

Risk Assessment

Once the required data are compiled, they are submitted to the Registration Division of the EPA for review along with a proposed label for the formulation. The EPA reviews the submission to ensure that the formulants are on the registered inert ingredients list and that the proposed use will not result in an unacceptable risk either to applicators or nontarget organisms. The EPA reviews the proposed label and provides guidance regarding specific statements concerning safety to humans and nontarget organisms that must appear on the label. Once the label has been approved, the product is cleared for sale and use.

8.4 Production

Identification of Sponsor

A sponsor, as defined by GLP guidelines, can be (1) a person who initiates and supports a study by provision of financial or other resources; (2) a person who submits a study to the EPA in support of an application for a research or marketing permit; and (3) a testing facility, if it both initiates and actually conducts the studies (40 CFR Part 160). Therefore, the sponsor of a pesticide can be either the manufacturer of a chemical or a third party. Not many chemical manufacturers produce piscicides. In most circumstances, a product that is found to be an efficacious piscicide has been developed for other uses, such as an herbicide. Manufacturers of such chemicals are not usually motivated to register the product for use as a piscicide because it is a minor use and is not profitable and because more tests are required for a chemical used on water. Guiding the registration of a piscicide consequently falls on the party interested in the registration from financial and technical perspectives. Once identified, the sponsor has the responsibility to secure and provide funding to develop and register the piscicide and monitor all testing facilities involved in the conduct of registration studies for regulatory compliance and for study progress. The sponsor also has the responsibility of securing funding to produce the active ingredient and formulations. Once registered, the sponsor is responsible for maintaining the registrations of the active ingredients and formulations with the EPA and the states.

Manufacturing

The producer of a piscicide may be willing to manufacture the piscicide and formulations of the piscicide to the specifications of the party interested in the registration. If not, then it will be necessary for the registrant to identify an additional facility that can manufacture the formulation. It is usually wise, depending on the volume of chemical that needs to be acquired, to have more than one manufacturer of the active ingredient under contract so that a constant source is available and costs can be controlled.

Labels and Product Classification

Registrations of products fall into two broad classifications: manufacturing-use products (MUP) and end-use products (EUP). Manufacturing-use products may either be the active ingredient or a formulation, if that formulation is used in the production of yet another formulation. The product label for such a material will specifically state that the product is an MUP and can only be used in the production of another product. End-use products are formulations that are only used to control pests and may not be used in the production of another formulation unless a specific registration and label have been developed for that purpose. For example, Bayluscide® 70% WP has two registrations, one for use in sea lamprey control (EUP), and one for use in the production of Bayluscide® 3.2% Granular Formulation (MUP).

Registration Maintenance

Once an active ingredient and formulations of the active ingredient have been registered, activities turn toward registration maintenance. The registrant remains in contact with the EPA to pay annual fees, to renew the registrations, and provide any additional information that the EPA may require. One important aspect of registration maintenance is the monitoring and reporting of unreasonable adverse effects of the pesticide that falls under Section 6(a)(2) of FIFRA. The EPA has defined unreasonable adverse effects 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" (EPA 1998*a*). Information provided to the EPA under the adverse effects rule is critical. While such information could result in the suspension or cancellation of a product, it is more likely that it will be used to modify the terms and conditions of the registration on the basis of a review of the risks and benefits.

The burden of submission of adverse effects information falls solely on the registrant of a product, and only information that is additional and factual must be submitted. Any pertinent information that comes to the attention of the registrant directly, or to any party under contract to the registrant so that the registrant might reasonably be expected to receive the information, must be submitted. For example, if a university study finds that a pesticide causes tumors in an avian species and the registrant, or an agent for the registrant, becomes aware of the information, then a 6(a)(2) report must be filed with the EPA. The information must be factual. For instance, if someone is alleged to have become ill after swimming in a pond treated with a pesticide and the allegation is reported by a neighbor or friend, that in itself is not sufficient to warrant a 6(a)(2) report. On the other hand, if the person is treated medically for the condition and the symptoms are consistent with expected toxicity, a 6(a)(2) report to the EPA is required provided the incident is reported by the attending physician to an appropriate authority.

Costs to maintain pesticide registrations vary from year to year and are based on appropriation legislation. For example, in 2003 the legislation authorized the EPA to collect $21.5 million in pesticide maintenance fees (J. Jones, EPA, personnel communication). Consequently, the fee to a company for the first registration of a product was set at $1,675, and $3,350 was charged for

each subsequent product registered. So if Company A has three registered products, the fee would be $1,675 + (2 × $3,350) or $8,375. Fee caps are also set by the appropriation legislation, and for this year the caps were set at $70,000 for the first 50 registrations and a maximum of $121,000.

8.5 Laboratories for Development of Regulatory Data

There are more than 2,000 laboratories in the United States that generate regulatory data for submissions to the EPA (D. Garvin, Society of Quality Assurance, personal communication). Laboratories that have submitted data in support of registrations to the EPA are listed in Table 8-1. Because of the breadth and diversity of data required to register a pesticide, there is no single laboratory that can conduct all of the required studies. Most laboratories have expertise in one particular field. Because of the great number of testing laboratories that can conduct GLP studies, a detailed list of the laboratories and their areas of specialization is not provided.

Whichever laboratories are chosen to perform the required studies, it is imperative that a careful review of the laboratories' capabilities and study proposals be conducted. Because the studies will be submitted to regulatory agencies, it will be necessary to review the quality assurance capabilities and GLP conformance of the laboratories. Laboratories that can conduct the appropriate field studies for environmental or residue studies are less easily identified. The additional effort required to conduct studies in the field that conform to GLP is not usually undertaken by most contract laboratories.

8.6 Time Line and Cost Estimates

Figure 8-1 shows an approximate time line for the stages of developing and registering a pesticide. Actual times will vary depending on the chemical selected and the registration requirements. As stated above, conducting all the studies required to register a pesticide can take 8-10 years and can cost up to $10 million. To register a piscicide, the time line may be closer to 5 years and the cost closer to $5 million. If the active ingredient is one that is already registered, the actual final time required and cost associated with registration will depend on the availability of data from the current registrant. While it is desirable to form a cooperative agreement with the producer of a chemical to register their product as a piscicide, by law they are required to cooperate and supply the data if requested.

Table 8-1. Alphabetical listing of analytical and toxicology laboratories that have had data submitted to the U.S. Environmental Protection Agency. This list is only a small portion of the estimated 2,000 testing laboratories in the United States. This list does not represent an endorsement by either the U.S. Geological Survey or the U.S. Environmental Protection Agency.

Name	Address	Phone number	FAX number
	Analytical Laboratories		
ABC Laboratories, Inc.	7200 East ABC Lane, Columbia, Missouri 65202	573.474.8579	573.443.9033
Adpen Laboratories	11757 Central Parkway, Jacksonville, Florida 32224	904.645.9169 888.428.3784	904.641.8423
Analytical Development Corporation	4405 Chestnut Street, Suite D, Colorado Springs, Colorado 80907-3875	719.260.1711	719.260.0695
Compliance Services International	1112 Alexander Avenue, Tacoma, Washington 98421	253.272.6345	253.272.6241
Midwest Research Institute	425 Volker Boulevard, Kansas City, Missouri 64110	816.753.7600	816.753.8420
Morse Laboratories, Inc.	1525 Fulton Avenue, Sacramento, California 95825	916.481.3141	916.481.2959
National Food Laboratory	6363 Clark Avenue, Dublin, California 94568-3097	925.828.1440	925.833.9239
North Coast Laboratories	5680 West End Road, Arcata, California 95521	707.822.4649	707.822.6831
	Toxicology Laboratories		
Argus Research Laboratories	935 Horsham Road, Horsham, Pennsylvania 19044	215.443.8710	215.443.8587
Battelle Memorial Institute	505 King Avenue, Columbus, Ohio 43201	614.424.7948	614.424.3268
Bell Laboratories	3647 Kinsman Boulevard, Madison, Wisconsin 53704	608.241.0202	608.241.9631
Bio Research	1071 North Fulton Avenue, Fresno, California 93728	559.455.5660	559.455.5661
Biocon, Inc.	15801 Crabbs Branch Way, Rockville, Maryland 20855	301.762.3202	800.826.8426
Celsis Laboratories, Inc., New Jersey Division	165 Fieldcrest Avenue, Edison, New Jersey 08837	732.346.5100	732.346.5115
Chemical Industry Institute of	6 Davis Drive, PO Box 12137, Research Triangle Park,	919.558.1341	919.558.1300

Table 8-1. Continued

Name	Address	Phone number	FAX number
Toxicology	North Carolina 27709-2137		
Consumer Product Testing, Inc.	70 New Dutch Lane, Fairfield, New Jersey 07004-3404	201.808.7111	201.808.7234
Cosmopolitan Safety Evaluation, Inc.	PO Box 71, Stateville Quarry Road, Lafayette, New Jersey 07848	973.383.6253	973.383.0383
Covance Laboratories	9200 Leesburg Pike, Vienna, Virgnia 22182	703.893.5400	703.759.6947
Covance Laboratories	3310 Kinsman Road, Madison, Wisconsin 53704	608.241.4471	608.241.7227
Fermenta Animal Health, Inc.	1512 Webster Court, Fort Collins, Colorado 80524	970.221.2050	970.221.5049
Primedica Redfield Laboratories	100 East Boone Street, PO Box 308, Redfield, Arkansas 72132	501.397.2813	501.397.2002
Genesis Laboratories	10122 NE Frontage Road, Wellington, Colorado 80549	970.568.7059	970.568.3293
Gibraltar Laboratories	122 Fairfield Road, Fairfield, New Jersey 07004-2405	973.227.6882	973.227.0812
Huntingdon Life Sciences	PO Box 2360, Mettlers Road, East Millstone, New Jersey 08875-2360	732.873.2550	732.873.3992
IIT Research Institute	10 West 35th Street, Chicago, Illinois 60616-3799	312.567.4883	312.567.4842
Inhausen Research Institute	2601 South Lemay, Suite 7-505, Fort Collins, Colorado 80525-2247	970.221.1090	970.221.4730
MB Research Laboratories	PO Box 178, Steinsburg and Wentz Roads, Spinnerstown, Pennsylvania 18968	215.536.4110	215.536.1816
MPI Research Laboratories	54943 North Main Street, Mattawan, Michigan 49071	616.668.3336	616.668.4151
OREAD Biosafety, Inc.	400 Farmington Avenue, Farmington, Connecticut 06032	860.674.6300	860.676.9443
Product Investigations, Inc.	151 East 10th Avenue, Conshohocken, Pennsylvania 19428	610.825.5855	610.825.7288

Table 8-1. Continued

Name	Address	Phone number	FAX number
Product Safety Laboratories, Inc.	725 Cranbury Road, East Brunswick, New Jersey 08816	732.254.9200	732.254.6736
Research Triangle Institute	PO Box 12194, 3040 Cornwallis Road, Research Triangle Park, North Carolina 27709-2194	919.990.8347	919.541.6003
Ricerca, Inc.	PO Box 1000, 7528 Auburn Road, Painesville, Ohio 44077-1000	216.357.3722	216.354.6276
SGS US Testing	75 Passaic Avenue, Fairfield, New Jersey 07004	973.575.5252	973.244.1694
SRI International	333 Ravenswood Avenue, Menlo Park, California 94025	650.859.2412	650.859.3344
Sitek Research Laboratories	15235 Shady Grove Road, Suite 303, Rockville, Maryland 20850	301.926.4900	301.926.8891
Springborn Laboratories	640 North Elizabeth Street, Spencerville, Ohio 45887	419.647.4196	419.647.6560
Stillmeadow, Inc.	12852 Park One Drive, Sugarland, Texas 77478	281.240.8828	281.240.8448
TKL Research	4 Forest Avenue, Paramus, New Jersey 07652	201.587.0500	201.587.0209
Tox Monitor Laboratories	33 West Chicago Avenue, Oak Park, Illinois 60302	708.345.6970	708.382.0591
Toxikon Corporation	15 Wiggins Avenue, Bedford, Massachusetts 01730	617.275.3330	617.271.1137
White Eagle Toxicology Laboratories	2003 Lower State Road, Doylestown, Pennsylvania 18901	215.348.3868	215.348.5081
WIL Research Laboratories	1407 Montgomery Township, Road 805, Ashland, Ohio 44805-9281	419.289.8700	419.289.3650

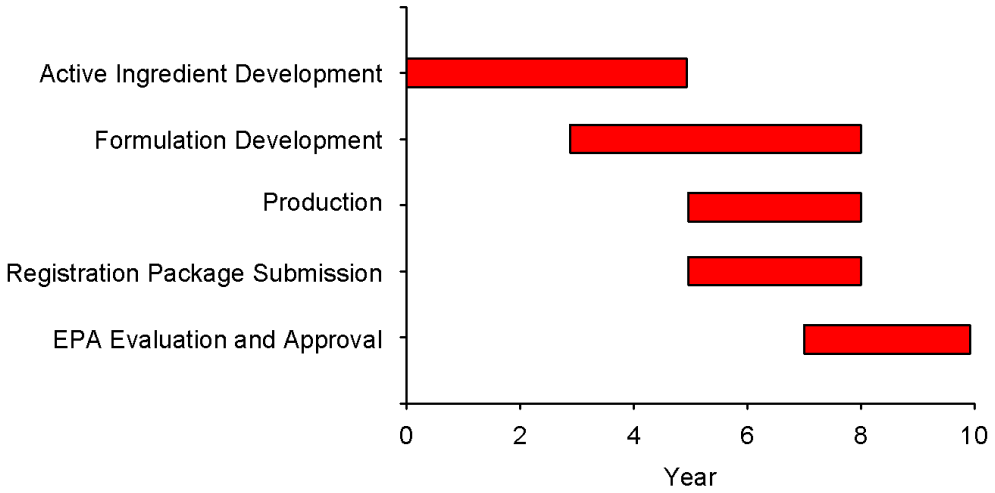
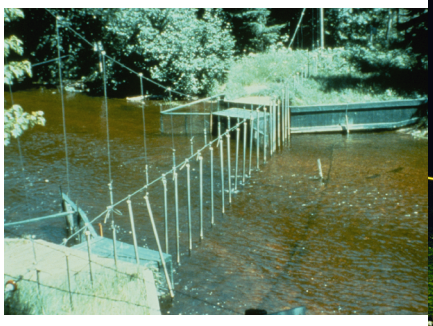


Figure 8-1. Time line for development and registration of a piscicide.



Chapter 9. Developing an Integrated Pest Management Strategy

by Terrance D. Hubert and Verdel K. Dawson

The concept of integrated pest management has been around in various forms for several centuries. It was probably in the late 1950s, however, when the concept started to evolve from a casual combination of techniques into a cohesive strategy of pest management (Forney 1999). The evolution of integrated pest management has been driven primarily by agriculture, and few examples of a complete integrated pest management system for aquatic pests exist. Published definitions of integrated pest management are therefore naturally agriculturally oriented. The USDA defines integrated pest management as follows:

> "a management approach that encourages natural control of pest populations by anticipating pest problems and preventing pests from reaching economically damaging levels. All appropriate techniques are used, such as enhancing natural enemies, planting pest-resistant crops, adapting cultural management, and using pesticides judiciously" (USDA 1994).

In his book on integrated pest management, Dent (1995*a*) states that there are several principles that form the framework of an integrated pest management program. These principles are crop husbandry, ecology, socioeconomics, ecological genetics, principles of control, and control technologies. Crop husbandry, which is changed to resource husbandry for this review, is the practice of growing and harvesting to provide a viable resource in as economically efficient a manner as possible. Ecology is generally defined as the interactions that determine the distribution and abundance of organisms. Socioeconomics describes the aspects of human behavior involved with choices between alternatives on the basis of resources. Ecological genetics examines the changes in genetic composition of populations on the basis of environmental interactions. Principles of control are a move away from the classification of control measures on the basis of their characteristics and a move toward a more functional classification on the basis of the criteria affecting the selection and the use of the control measures. Control technologies are, of course, the various specific methods of control that make up an integrated pest management program.

The first step toward developing a focused integrated pest management strategy is to determine the type and form of integrated pest management system to achieve the required pest control goals (Dent 1995*b*). In doing so, the following questions must be answered: (1) who will be using the integrated pest management control techniques, (2) on what scale will the program be

conducted, (3) what control measures will be used, (4) in what way will the control measures be applied, (5) what will be the perceived benefits, and (6) over what time scale will these perceived benefits be realized? The answers to these questions will determine how research on the integrated pest management program is to proceed and how the integrated pest management system is developed.

Another critical aspect of developing an integrated pest management strategy is the availability of resources (Dent 1995*c*). The availability of human, institutional, temporal, and financial resources will ultimately determine what can or cannot be done as part of the integrated pest management system. Human-resources subcomponents include finding individuals with the appropriate skills, knowledge, and experience to participate in an integrated pest management control program. Subcomponents of the institutional category are vehicles/machinery, land, facilities, and equipment, whereas financial category subcomponents include running costs, consumables, capital, salaries, overhead, and travel.

There are varying opinions regarding the components of an integrated pest management system. Dent (1995*d*) lists pesticides, host plant resistence, biological control, cultural control, and interference methods as components of control. Host-plant resistence and interference methods, i.e., the use of semiochemicals (defined as any of a class of substances produced by organisms, especially insects, that participate in regulation of their behavior in such activities as aggregation of both sexes, sexual stimulation, and trail following; Parker 1994), could be grouped within biological control, and interference methods could also be grouped under chemical control since it is chemical based. Forney (1999) suggests that biological control, cultural control, strategic control, and chemical control are the four major components of an integrated pest management control system and places the use of semiochemicals into the biological control category. For the purposes of this discussion, integrated pest management control systems will be divided into three components: chemical, biological, and physical control.

9.1 Chemical Control

Pesticides have been used in pest control for about 60 years. The effectiveness of pesticides combined with their low cost makes them an attractive part of a control strategy. Drawbacks have included persistence in the environment, deleterious effects on nontarget organisms, and development of chemical resistence in insects. To address the first two harmful effects, research has focused on developing a new generation of more environmentally benign pesticides. On the basis of past experience with invasive species, it is unlikely that an effective integrated pest management strategy can be developed that does not rely to some degree on the use of pesticides.

Rotenone and antimycin are two examples of chemicals that can play key roles in an integrated management of nonnative fishes. In Australia, common carp have contributed to declining water quality, bank erosion, and the disappearance of native species (Carp Control Coordinating Group 2000). Rotenone has been used as part of the national management strategy in this control program (Harris 1995). Also, the use of rotenone in fisheries management in California has been outlined in good detail by Finlayson et al. (2000). Schneider and Lockwood (1997) demonstrated the utility of antimycin in an 8-year study designed to thin out small bluegills from selected lakes in Michigan and enhance the numbers of bluegill larger than 15 cm. The study was conducted on 16 lakes in the southern portion of the state. Antimycin in combination with stocking of walleye, antimycin in combination with catch and release, and walleye stocking only were the strategies tested. Study results indicated that the best responses were obtained by using antimycin in combination with catch and release**.** New piscicides and new formulations of existing piscicides will continue to be avenues of growth in chemical control strategies.

9.2 Biological Control

Over time, biological control has come to mean the use of living organisms as pest control agents. For this review, we expand biological control to include the use of semiochemicals and biochemicals (e.g., pheromones). Dent (1995*b*) suggests that there are five types of biological control strategies: introduction, augmentation, inoculation, inundation, and conservation. Examples of successful biological control involve the introduction of a nonnative natural enemy to control an accidentally introduced pest. Augmentation involves increasing populations of natural enemies present at a given site year-round. One example of augmentation to manage fish populations is the introduction of walleye to complement the use of antimycin to improve bluegill populations in selected Michigan lakes (Schneider and Lockwood 1997). Young walleye were used either alone or in combination with antimycin treatments to thin bluegill populations. In contrast, inoculation is used in situations where seasonal control is desired. The natural enemy is absent from a given area and cannot survive long term under normal circumstances. In this situation, natural enemies are planted at the beginning of the season to prevent buildup of the pest. Inundation involves large releases of native or introduced natural enemies in response to pest levels that have reached damaging proportions. Inundative control is usually a short-term measure. Stocking large numbers of predatory fish is a commonly used biological control method to provide partial control of an undesired species of fish (e.g., attempted control of Eurasian ruffe in Duluth Harbor; Mayo et al. 1998). Finally, conservation involves the use of techniques to conserve populations of natural enemies so that a developing pest population can be controlled.

Biopesticides are materials derived from natural sources, such as animals, plants, bacteria, and certain minerals (EPA 2002). Baking soda, which is used as a fungicide (Kuepper et al. 2002), and canola oil, which is registered by the EPA as an insecticide (EPA 1998*b*), are examples. According to the EPA (2002), biopesticides fall into three major categories: (1) microbial pesticides, (2) plant-incorporated-protectants, and (3) biochemical pesticides. Examples of microbial pesticides include fungi that kill certain weeds or specific insects. Probably the best known example of a plant-incorporated-protectant is incorporation of the Bt® pesticidal protein from *Bacillus thiurengsis* into plant genetic material resulting in the plant's own ability to produce the protein. Biochemical pesticides, or semiochemicals, are naturally occurring substances that control pests by nontoxic mechanisms.

Chemical attractants and repellents have been proposed as means of keeping fish out of specific areas or as means of congregating populations for easier removal (Dawson et al. 1998, Hogue 1999). Specific types of attractants and repellents that have recently received a lot of attention are pheromones. These are species-specific chemicals that can be secreted as attractants to aid in mating or as repellents in the case of alarm pheromones (Maniak et al. 2000, Li et al. 2002). Pheromones could be used to interrupt mating behavior or to lure pest fishes to traps.

Some chemicals that are not naturally occurring also fall under the category of biological control. Some chemicals that have been developed to cause the sterilization of males or females fall into this category. One such chemical is bisazir that is currently being used in the sea lamprey sterile male release program to contribute to the reduction of sea lamprey populations in the Great Lakes (Hanson and Manion 1978). Adult males are sterilized by exposure to bisazir and then released to compete with fertile males during spawning (Figure 9-1). Sterilization can also be achieved by exposure to radiation.

Figure 9-1. U.S. Fish and Wildlife Service technician preparing an adult spawning phase male sea lamprey for sterilization with bisazir.

Genetic manipulations of organisms also fall under the category of biological control. Production of monosex populations of fish is a potential management tool for undesired fishes. This result can be produced by one of two means. The first means is through a process called gynogenesis (development of an ovum after penetration by a spermatozoan but without incorporation of the paternal genome in the zygote). Gynogenesis can be achieved by irradiation of milt and by exposing eggs to thermal shock or hydrostatic pressure (Stanley et al. 1975). Another means of producing monosex fish populations is the use of "daughterless" technology (Carmody 2003, Stucky 2003). Daughterless technology is a strategy in which a promotor is used to activate the daughterless gene to express only in females. The gene triggers the inhibition of production of a key enzyme required for the fish to develop into a female. The fish defaults to a male, and consequently the population is reduced because fewer and fewer females are produced. This approach is being investigated for the control of common carp and Northern Pacific seastar (*Asterias amurensis*) in Australia (Joint Standing Committee on Conservation/Standing Committee on Fisheries and Aquaculture 1999).

Fertility control is being proposed as a fishery management tool in which an immuno-contraceptive agent would provide species-specific management. The target reproductive protein (or antigen) must be specific, that is, show no cross-reaction with nontarget species. The antigen would be delivered in a bait that contains the antigen or a nondisseminating pathogen specific to the species to be controlled (Hinds and Pech 1997).

Specific viruses, such as *Rhabdovirus carpio* that causes the disease Spring Viraemia in carp, is another biological control mechanism that is under investigation (Crane and Eaton 1997). To be effective for this purpose, an infectious agent must be (1) species specific, (2) not capable of

genetic adaptation to new hosts, (3) not affected by environmental conditions, and (4) highly virulent with predictable outbreaks of the disease.

Another area of biological control being debated as a possible fishery management tool involves molecular biological techniques including chromosomal manipulation, gender manipulation (by way of hormones and transgenic methods) and the introduction of inducible fatality genes by way of transgenic methods (Grewe 1997). There is likely to be resistance to gaining approval of these techniques by the public and the scientific community until more is learned about the ecological ramifications of the release of transgenic fish.

9.3 Physical Control

Physical control of undesired species includes management practices, such as the addition of structures to keep the species from infesting a given area and physical removal of individuals of the undesired species. Water-level manipulation can be an effective physical-control strategy when undesired species emigrate differentially from desirable species during the drawdown. This technique has also been used to destroy egg masses of undesired species, such as northern pike, after their deposition in littoral shallows (Harris 1995). Barriers are another example of physical control that may be used in an integrated pest management program. The advantages of high- and low-velocity barrier screens have been described (Miller and Laiho 1997). Barriers of these types were under consideration for control of nonnative fishes in the upper Colorado River. Also considered were electrical, acoustical, and light barriers. An electrical barrier has been installed in the Illinois waterway near Chicago, Illinois, in an attempt to prevent the movement of the invasive round goby from the Great Lakes into the Mississippi River drainage as well as to prevent the upstream migration of Asian carp into the Great Lakes. Two electrical barriers have also been installed on two Central Arizona Project distributary canals to prevent Colorado River fishes from moving upstream into the Gila River drainage (Clarkson 2003). Physical barriers are an important part of the program to control sea lamprey in the Great Lakes (Great Lakes Fishery Commission [GLFC] 2001) and have played an important role in recovery efforts for western trout species (Rinne and Turner 1991). However, barriers have drawbacks as well, related to initial construction costs, maintenance costs, environmental impacts, and preventing desirable fishes from upstream migration.

Examples of other potential physical-control techniques include netting, electrofishing, traps, and explosives. In Lake Davis, California, where northern pike have reduced rainbow trout populations, purse seining was used as one method of control (Lee 2001). The mesh size allowed for the capture of northern pike approximately 20 cm or larger and nontarget species were safely returned to the water. Generally, electrofishing has been thought of as a means of sampling fish for population estimates. However, this method of collecting fish has also been used as a control method in Australia's efforts to control common carp (Harris 1995). The Wisconsin Department of Natural Resources used a combination of chemical treatment with rotenone and placement of traps to control common carp in the Horicon Marsh (Wisconsin Department of Natural Resources 1999), and trap nets have been used to remove bullhead, common carp, and goldfish from diked wetlands on Lake Erie (Wiggins 1999). Detonation cords have been suggested as a possible method of removing nonnative fish stocks, but no examples of this have been reported (Shepard, in press). Physical removal is another approach to controlling undesirable fishes. Targeted fishing or overharvesting of specific species of fish either recreationally or commercially has been used to regulate fish populations, but it has not resulted in elimination of a species. In southeastern Australia, events called "Carpathons" were sponsored, and commercial fishing was encouraged as a means of control of common carp (Harris 1995).

Another important component of nonnative species control is educating the public about the destruction caused by invasive species and how to prevent the spread of the organism. In Australia, part of the National Management Strategy for Carp Control concerns educating the public on the impact of common carp on community assets and resources and how these impact the individual and then encouraging them to participate in eradication and control efforts (Carp Control Coordinating Group 2000). In the United States, the effort to control the spread of the zebra mussel has used an education program sponsored by the U.S. Fish and Wildlife Service and the Great Lakes Sea Grant Network that describes the life cycle of the mussels and emphasizes the importance of making sure that boats that have been in waters infested with zebra mussels are thoroughly cleaned before moving them to another body of water. The Alaska Department of Fish and Game has advised the public on rules and regulations regarding fish transport and stocking laws, particularly to stop the illegal stocking of northern pike (Alaska Department of Fish and Game 2001). The University of Minnesota Sea Grant Program has prepared a small brochure that describes the threat posed by the round goby and what the public can do to control its spread. In some instances, federal or state agencies have enlisted the assistance of private enterprises to assist in the education process. Mercury Marine, manufacturer of outboard motors, has published a brochure on curbing the spread of nonnative species.