2
Aquatic Animal Health

At least 50 different diseases currently affect aquatic animals resulting in high economic losses by the U.S. aquaculture industry each year (70). In 1988 for example, the trout industry cited losses due to disease at $2.5 million; in 1989 the catfish industry reported loss due to disease at $23 million (88,89). A viral epidemic in Texas destroyed an estimated $11 million worth of shrimp in a short period of time in 1995 (149).

Diseases may be caused by many different factors including poor environmental conditions and exposure to infectious agents. Polluted water, contaminants in feed, and various viruses, fungi, bacteria, and parasites are capable of causing disease outbreaks in cultured organisms. Disease outbreaks often occur when poor conditions causing stress are combined with the presence of opportunistic pathogens (134).

Preventing stress in cultured organisms is essential for maintaining healthy populations. Stress weakens the immune system and allows disease organisms to multiply and gain a foothold (134). Stress may be caused by physical damage to the organism, crowding, handling, and poor water quality conditions such as widely fluctuating water temperatures, low dissolved oxygen levels, and high ammonia concentrations (134). Strategies for controlling disease outbreaks rely on good husbandry as well as treatment (127).

CONGRESSIONAL INTEREST

Four major areas of congressional interest in aquatic health management include existing legislation governing interstate transport of aquaculture products, federal regulation regarding use of drugs for cultured organisms, funding and research priorities, and protection of public health and the environment.

Several existing laws directly affect health management in aquaculture. One of the most controversial laws is the Lacey Act (16 U.S.C. 667 et seq., 18 U.S.C. 42 et seq.). Among other goals, this law attempts to restrict the movement of certain pathogens into the United States and into watersheds where a pathogen is not currently found by regulating the movement of fish and wildlife. In addition to a federal list of prohibited fish, wildlife, and pathogens, individual states develop lists of prohibited species to suit their own needs and additionally may require aquaculture products to be certified as disease free for specific pathogens before they can cross state lines. The result is a patchwork of regulation that may impede the movement of aquacultural products.[1]

Similarly, drugs used in aquaculture (box 2-1) must meet numerous safety and efficacy requirements and be approved by the Food and Drug Administration. This process is expensive and approval only can be granted for the specific drug application and species for which the data were generated. This system has resulted in the approval of five drugs for legal use in aquaculture, four of which are currently available (table 2-1). Members of the industry contend that this is too few drugs to address a wide range of potential disease problems and that the risk of catastrophic loss inhibits expansion of the industry (131).

[1] Federal and state roles in the Lacey Act are covered in more depth in the OTA publication, *Harmful Non-Indigenous Species in the United States*, OTA-F-565 (Washington, DC: U.S. Government Printing Office, September 1993).

BOX 2-1: Health Related Definitions

Antibiotic: Substance that may inhibit the growth of or destroy microorganisms and is widely used to prevent or treat diseases.

Bacteria: One-celled microorganisms that have no chlorophyll, multiply by simple division, and can be seen only with a microscope.

Best management practices: Husbandry practices that strive to ensure optimal health, production, and economic performance with minimal adverse environmental impact.

Biologics: Category of health intervention tools which include vaccines and diagnostic test kits.

Chemical prophylaxis: Chemical treatment to reduce disease-causing organisms before outbreak occurs.

Drug: An article that is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or other animals; an article (other than food) intended to affect the structure or any function of the body of humans or other animals.

Extra-label use: The use of an approved new animal drug in a manner that is not in accordance with the approved label directions.

Investigational new animal drug (INAD) exemption: Exemption authorized under the Federal Food, Drug, and Cosmetic Act to permit the shipment of new animal drugs in interstate commerce without an approved new animal drug application.

Low regulatory priority (LRP) substance: Unapproved new animal drug for which FDA has a policy of regulatory discretion that allows the use of such a substance without an approved new animal drug application or INAD (Investigational New Animal Drug) exemption.

New animal drug: Any drug intended for use in animals other than people, the composition of which is not generally recognized among experts qualified by scientific training and experience as safe and effective for use under the conditions prescribed, recommended, or suggested in its labeling.

New animal drug application (NADA): An application package submitted to FDA for review that requests the approval of a new animal drug. The application includes sufficient data to establish the safety and effectiveness of the drug product, along with other requirements.

Parasite: A plant or animal that lives on or in an organism of another species from which it derives sustenance or protection without benefit to, and usually with harmful effects on, the host.

Pathogen: Any agent, especially a microorganism, able to cause disease.

Pesticide: Any substance or mixture of substances intended for preventing, destroying, or repelling any pest, and any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant.

Pharmacokinetics: The study of the absorption, metabolism, and action of drugs.

Prescription (Rx) drug: An animal drug for which adequate directions for safe and effective use by a lay-person cannot be written and which therefore must be prescribed by a licensed veterinarian. The label bears the statement, "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian."

Registration: Under the Federal Insecticide, Fungicide, and Rodenticide Act, the formal listing with EPA of a new pesticidal active ingredient prior to its marketing or distribution in intra- or interstate commerce.

Specific Pathogen Free (SPF): Organism certified free of specific pathogens.

Therapeutant: Term used interchangeably with the word drug; not used by the FDA.

Tissue residue: The drug, pesticide, or toxic breakdown product remaining in edible tissue after natural or technological processes of removal or degradation have occurred.

Box 2-1: (Continued)

Tolerance: The maximum amount of pesticide or drug residue allowed by law to remain in or on a harvested crop or food animal product. EPA sets tolerances for pesticides and FDA sets tolerances for drugs so that treated crops or animals consumed do not pose an unreasonable risk to consumers. Tolerances are set for food-use crops on a per-crop basis. Tolerances are set for animal products on the basis of individual species and tissue (muscle, liver, etc.).

Vaccine: A preparation of killed microorganisms; living attenuated, fully virulent, or related nonvirulent microorganisms; or parts of micro- or macroorganisms that are administered to produce or increase immunity to a particular disease.

Virus: Particles that are composed of genetic material (RNA or DNA) and a protein coat. Viruses can infect animals, plants, and, bacteria. Viruses only can reproduce within living cells.

Withdrawal time: The minimum required period of time between the last drug treatment of an animal and the slaughter or release of that animal.

SOURCES: Joint Subcommittee on Aquaculture, Working Group on Quality Assurance in Aquaculture Production, in cooperation with the Extension Service, *Guide to Drug, Vaccine, and Pesticide Use in Aquaculture*, (Washington, DC: U.S. Department of Agriculture, 1994); G. Stefan, Chief of Industry Programs, Center for Veterinary Medicine, Food and Drug Administration, Rockville, MD; and Webster's New World Dictionary, Third College Ed., V. Neufeld and D.B. Guralink (eds.) (New York, NY: Simon & Schuster, Inc., 1988).

Establishing priorities for aquatic animal health management research, evidenced by the formation of a JSA task force, is another major area of congressional interest. Some have argued that this research is conducted without adequate attention to industry concerns. Others believe that more funding should be provided for extension services, diagnostic facilities, and especially for research to obtain new drug approvals.

Congress also may be interested in aquatic health management to ensure adequate protection of public health. Chemicals and antibiotics used in health management can leave residues in cultured and wild organisms, leading to health problems for consumers as well as harming the environment, and potentially creating antibiotic resistant strains of pathogens. Consumption of products containing antibiotic residues can lead to direct human health problems. For example, the antibiotic chloramphenicol[2] may cause aplastic anemia (a dangerous blood disorder) in some individuals (16). Other antibiotics can cause allergic reactions ranging from a mild skin rash to potentially fatal responses.

Human consumption of low levels of antibiotics, as residues in fish tissue, may contribute to development of antibiotic resistant pathogenic organisms. For example, a bacterial species which causes disease in fish may become resistant to antibiotics and pass this resistance on to human pathogenic bacteria. Such bacteria may be potentially untreatable when they cause disease in humans.[3] It is suspected that long-term, low level exposure of bacteria to an antibiotic may contribute to development of resistance to that antibiotic in that bacterial population. Because of these concerns, antibiotic use must be restricted to approved uses, in accordance with approved dosages, and with adherence to approved withdrawal times before slaughter, to preclude residues in edible tissue (45).

[2] Residues of this chemical have been found in imported shrimp, but it is not used in aquaculture in the U.S. (110).

[3] For more information on problems associated with antibiotic resistant bacteria see the OTA publication, *Impacts of Antibiotic Resistant Bacteria* (Washington, DC: OTA, September 1995).

Thus, if drugs are used as prescribed, residue levels in cultured organisms should not pose health risks (150). Antibiotic use, however, was found to vary by orders of magnitude at different salmon farms in Puget Sound (150). In areas where antibiotics have been used in large quantities, problems have arisen when wild organisms in the vicinity of aquaculture facilities have eaten large amounts of medicated feeds, or taken in excessive antibiotics by filter feeding. Wild fish and mussels caught near net-pen facilities in Norway and red rock crabs caught near net-pens in Puget Sound have had antibiotic concentrations exceeding accepted tolerance levels (84,150). Therefore, consumption of wild fish harvested from the vicinity of net pens may pose human health concerns. Quality

TABLE 2-1: FDA-Approved New Animal Drugs as of July 1995

Trade name	Active drug	Species	Uses
Finquel (MS-222)	Tricaine methanesulfonate	Ictaluridae, Salmonidae, Esocidae, and Percidae. (In other fish and cold-blooded animals, the drug should be limited to hatchery or laboratory use.)	Temporary immobilization (anesthetic)
Formalin-F[a] Paracide-F Parasite-S	Formalin	Trout, salmon, catfish, large-mouth bass, and bluegill	Control of external protozoa and monogenetic tremotodes
		Salmon, trout, and esocid eggs	Control of fungi of the family Saprolegniacae
		Cultured penaeid shrimp	Control of external protozoan parasites
Romet 30	Sulfadimethoxine and ormetoprim	Catfish	Control of enteric septicemia
		Salmoids	Control of furunculosis
Sulfamerazine in fish grade[b]	Sulfamerazine	Rainbow trout, brook trout, and brown trout	Control of furunculosis
Terramycin for fish	Oxytetracycline	Catfish	Control of bacterial hemorrhagic septicemia and pseudomonas disease
		Lobster	Control of gaffkemia
		Salmonids	Control of ulcer disease, furunculosis, bacterial hemorrhagic septicemia, and pseudomonas disease
		Pacific salmon	Marking of skeletal tissue

[a]Only Parasite-S is approved for use in shrimp. Formalin-F and Paracide-F are not approved for use in shrimp (45).
[b]According to sponsor, this drug is not presently being distributed.

SOURCE: Joint Subcommittee on Aquaculture, Working Group on Quality Assurance in Aquaculture Production, in cooperation with the Extension Service, *Guide to Drug, Vaccine, and Pesticide Use in Aquaculture*, (Washington, DC: U.S. Department of Agriculture, 1994).

assurance programs and educational efforts to ensure proper use of antibiotics in the United States attempt to address these problems.

ISSUE IDENTIFICATION

Issue: Establishing Best Management Practices

Good husbandry is a critical factor in managing aquatic animal health. Maintaining proper environmental conditions, selecting healthy organisms, providing a nutritious diet, reducing stress, vaccinating organisms, and rapidly diagnosing, isolating, and treating disease outbreaks all are important aspects of good husbandry. Establishing consistent procedures or Best Management Practices (BMPs) for aquaculture operations may facilitate aquatic health management (120). BMPs, however, will be most effective for systems where control of environmental conditions is more complete, as in recirculating systems. In other systems such as outdoor ponds, where it is more difficult to control environmental parameters, BMPs may be more difficult to identify and implement. For example, research needed to determine water quality management procedures usually is performed in a particular type of pond. Ponds where the research is conducted often have uniform areas, depths, are of the same hydrological type, and generally have similar watersheds (14). Procedures that work well in specific experimental units may yield different results when used in ponds that are physically different. It may be difficult to produce BMPs that are applicable to a wide range of situations due to the large variability from system to system, even from one pond to another (14).

Although many species are raised in U.S. commercial aquaculture, details about their lifecycles, nutritional requirements, environmental tolerances, and diseases are commonly unknown, making it difficult to devise BMPs. Even for species such as catfish, salmon, trout, and oysters, information may be lacking.

Few reliable data exist on the impact of diseases in aquaculture production. Even the precise number of organisms a producer begins with may be unknown. For example, when an aquaculture producer begins an operation with fry or fingerlings, they are often packaged by weight and the producer may never know the exact numbers of organisms purchased. Harvested organisms also may be sold by weight and not number. Stocking ponds that contain organisms left from the previous crop may further complicate precise estimates of numbers of organisms contained in a pond (80). In addition, high losses in early life stages lead many aquaculturists to start the production cycle with fertilized eggs in excess of what they require for final production. High mortality in early production phases is typically accepted as part of the process and, thus, causes may never be fully investigated (89).

In some circumstances, loss of organisms can be attributed to specific causes such as escape of organisms, a natural disaster, or predation. However, it is usually difficult to determine all the reasons for loss of organisms before harvest especially when the number of organisms at the beginning, middle, and end of the cycle has never been accurately measured (80,89).

Issue: Availability of Health Products and Services

Managing the health of aquatic organisms is facilitated by veterinarians, aquatic animal health specialists, diagnostic labs, and specific products such as vaccines. Provision of services and distribution of products, however, is not uniform nationwide. Availability is likely to be high in areas with established aquaculture industries, but low in areas with fewer aquaculture facilities.

Aquatic health management would be facilitated by greater use and availability of appropriately trained veterinarians, diagnostic

and extension services. Veterinarians are important because they are the only people legally able to prescribe antibiotics or make provisions for extra-label drug use (use beyond that described in the drug's initial license). Currently, there is a shortage of veterinarians trained in managing the health of aquatic organisms. A survey conducted in 1993 found that only 17 of 35 states had private or public veterinarians that specialized in aquatic animal health (143). Interest in aquatic health management, however, is on the rise. Twenty four of the thirty one American Veterinary Medical Association (AVMA) accredited veterinary schools in North America now offer classes in aquatic medicine (113). By 1992, thirty seven percent of all graduating veterinary students had taken at least introductory courses in aquatic medicine. Some schools require students to enroll in aquatic medicine classes (113). As opportunities to practice aquatic medicine increase, more students are likely to become interested in this field.

The use and availability of diagnostic services also may be a factor in aquatic health management. Diagnostic, laboratory, and extension services are offered by some federal agencies (for example, APHIS or FWS), by state agencies including state veterinary schools, and in some cases laboratories that offer traditional services for livestock and poultry (113). Not all states have facilities for disease diagnosis; some may offer only partial services. Producers in many states routinely send material out of state for diagnostic services (113). However, the difficulty of properly shipping diseased organisms in some cases may preclude use of such services. Disease diagnosis is usually most effective with live organisms or organisms that have just died. Improper methods of preservation or long time delays until samples reach laboratories may make it difficult to identify the disease. Therefore, on-site diagnostic services may be the most useful but also are the most difficult to provide.

In addition to diagnostic and laboratory services, vaccinations could facilitate aquatic health management. Although numerous vaccines are marketed, the majority are limited as to their applications. Of the 15 products licensed with the U.S. Department of Agriculture, 12 are specifically used for salmonid production, one can be used with catfish, and two are nonspecific and can be used with any finfish (71). Additionally, vaccines are often effective against the causative agent(s) of only one disease (or monovalent).

Vaccines are not widely used in the United States because they are costly, they are only available for a narrow range of cultured organisms and, they commonly provide protection against only one type of disease (89). The degree of protection they provide may be variable depending on environmental conditions at the time of administration (111). They also may be difficult to effectively administer to cultured organisms (89).

Vaccination, however, can be effective in bringing disease outbreaks under control. For example, in the 1980s, cold water vibriosis, a serious problem for Norwegian salmon farmers, largely was controlled by expanded use of vaccines for this disease (101). Moreover, there is evidence that vaccination can be a cost effective measure in limiting disease outbreaks. The cost of vaccinating salmonids against furunculosis in a Norwegian hatchery was estimated to be less than 10 percent of the cost of providing medication after an outbreak according to Leiv Aarflot, president of the Norwegian Association of Aquaculture Veterinarians (111). Similarly, vaccines may be effective at reducing losses due to outbreaks of viral diseases for which there are no treatments. As vaccines gain wider use in the industry other benefits also may appear including reduced damage to the environment from less use of potentially harmful chemicals and safer products due to diminished antibiotic use (101).

Issue: Availability of Approved Drugs

Most individuals involved in aquaculture development describe lack of approved drugs as a major problem for the industry. Currently four drugs are approved and for use in aquatic species (table 2-1 and box 2-1). Another 17 drugs have been given low regulatory priority (box 2-2 and table 2-2) if they are used as prescribed (71). Low regulatory priority substances fit the definition of a drug as stated in the Federal Food, Drug, and Cosmetic Act, but present few safety concerns if used as specified and thus are allowed for such use (44).

Drug approval, performed by the Food and Drug Administration, requires that potential drugs have been established scientifically as safe and effective by the drug sponsor. Data must illustrate that the drug will be consistently and uniformly efficacious; that it will not harm the recipient; that it is safe to consume products derived from the recipient of the drug; that it will not affect people administering the drug or handling the recipient; and that the drug will not have an adverse impact on the environment (141). Generating data to meet these requirements is time consuming and expensive.

It is further required that drugs be approved on a species by species basis for a specific application. A cautious, species by species approach to drug approval has been implemented because many factors influence drug uptake, metabolism, and elimination. Different species may exhibit large differences

BOX 2-2: FDA Comments on Low Regulatory Priority Drugs

Why are garlic, ice, and onion described as low regulatory priority drugs? This question is often asked by aquaculture producers and others when reading over the list of low regulatory priority drugs prepared by FDA. Gary Stefan, Chief, Industry Programs, Center for Veterinary Medicine (as quoted in the July 1994 issue of *The Aquaculture News*) makes the following statements regarding FDA's position on this matter:

> The [Low Regulatory Priority] list has for some time included certain seemingly innocuous substances, such as salt, ice, onion and garlic. [FDA] continue[s] to receive comments and questions as to why such substances are on the list.
>
> The short answer is that we were asked for regulatory determinations on these substances and we wanted to be responsive to the requests. The substances are technically 'drugs' under the Federal Food, Drug and Cosmetic Act when used as proposed. By adding the substances to the LRP list, however, we intended to indicate that we had no regulatory interest in them, and we hoped that would put the matter to rest.
>
> As you may know, the definition of a drug in the Federal Food, Drug, and Cosmetic Act (the Act) is very precise. To paraphrase, any article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals, and any article (other than food) intended to affect the structure or any function of the body of man or other animals, is a drug. The key phrase is "intended use." For example, ice, when used to reduce metabolic rate (a function of the body of fish), would meet the definition of a drug under the Act because of its intended use. The use of ice for the purpose, such as preventing spoilage, would not be considered a drug use.
>
> Due to the precise definition of the term "drug" in the Act, certain seemingly innocuous substances are defined as drugs for certain uses. [FDA] does not have the discretion to define such uses as non-drug uses. The fact that certain substances are common in nature or are found in the human diet does not preclude their being defined as drugs for their intended uses. However, we do have authority to exercise regulatory discretion where the intended use does not raise significant human food safety or other concern.

SOURCE: "FDA Updates, Clarifies Information On Drugs Used In Aquaculture," *Aquaculture News* 2(9):16, July 1994.

TABLE 2-2: Unapproved New Animal Drugs of Low Regulatory Priority

Common name	Permitted use

Acetic acid	Used as a dip at a concentration of 1,000 to 2,000 milligrams per liter (mg/L)for 1 to 10 minutes as a parasiticide for fish.
Calcium chloride	Used to increase water calcium concentration to ensure proper egg hardening. Dosages used would be those necessary to raise calcium concentration to 10-20 mg/L calcium carbonate. Also used to increase water hardness up to 150 mg/L to aid in maintenance of osmotic balance in fish by preventing electrolyte loss..
Calcium oxide	Used as an external protozoacide for fingerling to adult fish at a concentration of 2,000 mg/L for 5 seconds.
Carbon dioxide gas	Used for anesthetic purposes in cold, cool, and warmwater fish.
Fuller's earth	Used to reduce the adhesiveness of fish eggs in order to improve hatchability.
Garlic (whole)	Used for control of helminth and sea lice infestations in marine salmonids at all life stages
Hydrogen peroxide	Used at 250-500 mg/L to control fungi on all species and at all life stages of fish, including eggs.
Ice	Used to reduce metabolic rate of fish during transport.
Magnesium sulfate (Epsom salts)	Used to treat external monogenetic trematode infestations and external crustacean infestations in fish at all life stages. Used in freshwater species. Fish are immersed in a solution of 30,000 mg/L magnesium sulfate and 7,000 mg/L sodium chloride for 5 to 10 minutes.
Onion (whole)	Used to treat external crustacean parasites and to deter sea lice from infesting external surface of fish at all life stages.
Papain	Used as a 0.2 percent solution in removing the gelatinous matrix of fish egg masses in order to improve hatchability and decrease the incidence of disease.
Potassium chloride	Used as an aid in osmoregulation to relieve stress and prevent shock. Dosages used would be those necessary to increase chloride ion concentration to 10-2,000 mg/L.
Providone iodine compounds	Used as a fish egg disinfectant at rates of 50 mg/L for 30 minutes during water hardening and 100 mg/L solution for 10 minutes after water hardening.
Sodium chloride (salt)	Used as a 0.5-1% solution for an indefinite period as an osmoregulatory aid for relief of stress and prevention of shock. Used as a 3 percent solution for 10-30 minutes as a parasiticide.
Sodium sulfite	Used as a 15 percent solution for 5 to 8 minutes to treat eggs in order to improve hatchability.
Thiamine hydrochloride	Used to prevent or treat thiamine deficiency in salmonids.
Urea and tannic acid	Used to denature the adhesive component of fish eggs at concentrations of 15 g urea and 20 g NaC1/5 L of water for about 6 minutes, followed by a separate solution of 0.75 g tannic acid/5 L of water for an additional 6 minutes. These amounts will treat approximately 400,000 eggs.

NOTE: FDA is unlikely to object at present to the use of these low regulatory priority substances if the following conditions are met:

1. The drugs are used for the prescribed indications, including species and life stage where specified.
2. The drugs are used at the prescribed dosages.
3. The drugs are used according to good management practices.
4. The product is of an appropriate grade for use in food animals.
5. An adverse effect on the environment is unlikely.

FDA's enforcement position on the use of these substances should be considered neither an approval nor an affirmation of their safety and effectiveness. Based on information available in the future, FDA may take a different position on their use.

Classification of substances as new animal drugs of low regulatory priority does not exempt facilities from complying with other federal, state, and local environmental requirements. For example, facilities using these substances would still be required to comply with National Pollutant Discharge Elimination System requirements.

SOURCE: Joint Subcommittee on Aquaculture, Working Group on Quality Assurance in Aquaculture Production, in cooperation with the Extension Service, *Guide to Drug, Vaccine, and Pesticide Use in Aquaculture*, (Washington, DC: U.S. Department of Agriculture, 1994).

in processing drugs. For example, catfish treated with oxytetracycline, an approved antibiotic, reduce tissue concentrations of this chemical to acceptable levels within two days (at 27°C or 81°F), while chinook salmon require 30 days to reach the same tolerance level (at 8 to 10°C or 46 to 50°F) (5,110). Moreover, the same species may eliminate substances more slowly if the drug is administered at less than optimal temperatures (11).

The distribution of a drug in body tissues can also be important and may vary from species to species. Drug residues may be higher in internal organs or the skin than in muscle. In some species, such as catfish, this is of little concern because the skin typically is not consumed. In many salmonids, however, the skin may be eaten regularly and, if drug residues are retained at high concentrations in the skin, may pose health concerns to the consumer (110). Further studies of drug distribution in the tissues are needed as well as research on the metabolism of drugs.

Thorough research for drug approval also is required to ensure protection of the environment. Studies have found that antibiotics released into unconfined environments may alter the ecosystem. In some cases, antibiotics released into the water with feeds have adversely affected benthic organisms. In other instances antibiotics have been found in wild organisms in the immediate vicinity of fish farms that were using antibiotics in fish feed (36). For example, in a study conducted in Norway, wild fish caught in the vicinity of a fish farm immediately after drug treatment of the cultured fish contained concentrations of the drug oxytetracycline at levels many times higher than allowed by Norwegian law (84). Cooking the fish for 15 minutes did not reduce the drug residues present in the fish (84). Antibiotic resistant microbes also have been found where antibiotics have been widely used in aquaculture (36,123). There is a danger that human pathogens present in marine environments could become antibiotic resistant and thus adversely affect human health (90). Microbial surveys of aquatic environments near fish farms show that there are approximately 20 groups of microbes, potentially pathogenic to humans, commonly found in these areas (82,90).

Antibiotics or their metabolites are released into the water in feed in feces. High levels of drugs may enter the environment for several reasons. First, antibiotics may not be absorbed well in the gut of the animal requiring higher concentrations of these substances in the food. Oxytetracycline and other antibiotics for example are administered to fish in doses that are five to 10 times higher than doses used for humans (84). Second, sick animals have reduced appetites and generally do not consume the same quantities of food that healthy fish might normally consume (62). Excess food, therefore, may filter out of the cage and end up in the sediments. Once in the sediments, these chemicals may rapidly degrade or, depending on environmental conditions, may persist at low levels for extended periods (for at least one year) of time (123,150). In one experiment conducted in Norway, it took 142 days for initial oxytetracycline levels in the sediments below a net pen to degrade by one half (123).

Introduction of antibiotics into the environment can alter the dynamics of microbial populations as well as affect organisms higher in the food chain (84). In some cases, detrimental effects on fish growth and development have been observed when antibiotic concentrations in the water reached high levels (84). Additionally, chemicals that are toxic or that degrade slowly may build up to high concentrations in the sediments and have detrimental effects on bottom-dwelling organisms.[4]

The main obstacle to obtaining additional approved drugs is the cost of generating necessary data used to prove that the drug is

[4] To date most incidents of environmental impairment caused by use of antibiotics have taken place in situations where antibiotics were used prophylactically. Current regulations and the cost of administering antibiotics restrict this type of antibiotic use in the United States (135).

both effective and safe. Moreover, because this process must be repeated for each species and each disease, only a few drugs are approved and they are only permitted for use in a small number of species. Estimates for obtaining approval for a new animal drug to be used in food fish range from $3.5 million to $20 million dollars (43). Private industry is reluctant to invest these sums due to the market potential for aquaculture drugs in the United States. Federal and state agencies are trying to address this situation by investigating the concept of crop grouping, by conducting research under joint federal-state partnerships, and by allowing some extra-label use of approved drugs (e.g., use in other species).

Crop grouping has been proposed to hasten the development of data required for New Animal Drug Approval. Normally, a drug must be shown to be effective for each species and its disease condition; any other use is illegal. Obtaining separate approvals for each situation is costly (70). Crop grouping allows data obtained for a representative species of a group of species to be used to approve the drug for all members of that group. Species might be grouped according to genetic similarities (e.g., rainbow trout might represent salmonids), or environmental characteristics such as salinity requirements or water temperature (e.g., warm-water fish, cool-water fish, or cold-water fish). Studies showing that the selected groups of organisms metabolize various classes of drugs in a similar fashion will be needed (70).

The National Research Support Project for the Minor Use Animal Drug Program (NRSP-7) is also a mechanism for making additional drugs available to producers. The NRSP-7 program (formerly called the IR-4 program) provides funding for research needed to obtain clearance for animal drugs for minor and specialty crops (91). All cultured aquatic species are considered minor or specialty crops. Since 1990, 30 percent of NRSP-7 funds (totaling $664,500 from 1990 to 1994) have been used for research on drugs for use in aquaculture. Critics of the NRSP-7 program claim that it is not funded at a high enough level to generate the data necessary to gain drug approvals (43).

Recent legislation (Public Law 103-396) addressing extra-label use of drugs, amends the Federal Food, Drug, and Cosmetic Act to permit a veterinarian to order "1) a new animal drug, approved for one use to be used for a different purpose other than a use in or on animal feed; and 2) a new drug approved for human use to be used in animals." Some believe this legislation could help the aquaculture industry gain access to more drugs to aid disease control (132). Conversely, others believe this law may have minimal effect on the industry because of a shortage of suitably trained veterinarians in some areas and because of its potential to restrict FDA's current policy of allowing some extra-label use of medicated feeds (45,132).

Issue: Coordination of Regulation

At least six federal agencies and numerous state agencies are involved in aquatic health management issues (tables 2-3 and 2-4). Many involved in the aquaculture industry believe that the distribution of regulations among so many agencies is confusing. For example, pesticides for aquatic use are governed by the EPA; antibiotics, other drugs, animal feeds, and feed additives are regulated by the FDA (45), and the licensing of vaccines is the responsibility of APHIS. States may have their own laws regulating transport of cultured products across state boundaries as well as other aquatic health management regulations.

In addition, federal and state authorities may be split for some regulatory activities. For example, the EPA may cede authority to issue effluent emission permits to a state agency. The state agency is responsible for making sure that basic federal requirements are met along with any additional state regulations (121). State water-quality programs may help to determine where shellfish can be safely grown (120). Likewise, many states have enacted their own versions of the Food, Drug and Cosmetic Act, making it illegal to transport contaminated or adulterated food within state boundaries (121).

Seafood-safety inspections also may be carried out at the state level, especially in states such as Florida that produce large quantities of seafood (121).

States also may be acceded some authority to administer the Lacey Act. The Lacey Act attempts to restrict the movement of potential pathogens into the United States and into watersheds where the pathogen is not currently found. The Lacey Act attempts to accomplish this goal by formulating a list of "injurious" species or groups of fish, wildlife, and fish pathogens that states are prohibited from importing (139). Oversight of this legislation is the responsibility of the U.S. Department of the Interior, Fish and Wildlife Service. States, however, may develop prohibited species lists that suit their own unique needs. Many states require aquaculture products to be certified as disease free for specific pathogens before they can cross state lines (143). This state by state approach has resulted in a patchwork of regulation. According to many aquaculture producers, the lack of uniformity in Lacey Act requirements established by each state has impeded interstate commerce of aquaculture products.

Some attempts have been made to improve coordination among agencies regulating aquatic health management. The Joint Subcommittee on Aquaculture (JSA) was created to act as a facilitator among all the agencies involved in aquaculture and has been active in aquatic health issues. JSA, has, for example, established a list of priority drugs needed by the aquaculture industry; published information on the use of drugs, vaccines and pesticides in aquaculture; and worked on quality assurance issues.

Examples of state-federal cooperative efforts include the Sea Grant College Program which supports research, education and extension activities funded by the state and the National Oceanic and Atmospheric Administration (NOAA); and the Cooperative State Research Education and Extension Service of USDA, which awards grants to state experimental stations, land-grant colleges, and colleges of veterinary medicine. Recently, 39 states have joined the federal government in an $8 million study of eight drugs determined to be priority needs for disease treatment in state and federal hatcheries as well as in aquaculture systems (148).

TECHNOLOGIES IN AQUATIC HEALTH MANAGEMENT: PREVENTION AND TREATMENT

Disease prevention is accomplished by good husbandry practices such as maintaining optimum environmental conditions, good sanitation, and proper nutrition; by breeding disease-resistant varieties and using certified disease-free stocks; and by chemical prophylaxis, vaccination, and disease diagnosis (127).

Maintaining Proper Environmental Conditions

Poor water quality is a common factor in disease outbreaks. Cultured species have variable tolerance ranges for such parameters as dissolved oxygen, ammonia concentration, and water temperature. Stress and eventually death may occur when these parameters fall outside an optimum range. Proper conditions may be easier to maintain in closed systems than in open pond systems. Continuous monitoring of water quality parameters is essential for maintaining optimum environmental conditions (127).

Various technologies exist for monitoring and upgrading water quality. For example, if dissolved oxygen falls to low levels in a pond, emergency aeration using mechanical aerators will help increase the concentration of dissolved oxygen. Likewise, biofilters can be used to lower ammonia levels in the water. In some systems, such as net pens, the choice of a site can also help to ensure proper water quality: a site where the water exchange rate is high, with specific bottom characteristics or a certain depth and oxygen-rich waters will reduce problems (58). Similarly, choosing a site with the proper

salinity characteristics may diminish disease problems in cultured oysters as some pathogens have narrow salinity tolerances (127).

Sanitation

Disease outbreaks can be reduced by using good sanitation practices. For example, workers should wash all gear as well as their bodies and clothes thoroughly before and after handling diseased organisms. Nets used to retrieve organisms should be dipped in a disinfectant solution before each new use, including use in a neighboring pond or tank (134). Disinfecting ponds by draining and adding lime also helps reduce disease problems from organisms that may survive in pond bottoms (14).

Nutrition

Organisms receiving proper nutrition are less likely to become ill. Lack of specific nutrients, such as vitamins or minerals, may lead to disease. For example, insufficient vitamin E in the diet may cause reduced growth and survival, anemia and exophthalmia (bulging eyes) (134). Paradoxically, excess levels of vitamins also can cause illness. Vitamin E given in excess causes poor growth, toxic liver reaction, or potentially death (134). Lack of information about a cultured organism's nutritional requirements is often a serious constraint to improved disease management in aquaculture (80).

Disease-Resistant Stocks

Breeding and using disease-resistant organisms also may be a mechanism that could help prevent loss. In one study, brown trout (*Salmo trutta*) were selected for resistance to furunculosis--a common disease that affects salmonids. After one generation, offspring from selected parents and control parents were exposed to *Aeromonas salmonicida*, the causative agent of furunculosis. Mortality due to furunculosis six months after hatching was 2 and 48 percent, respectively, in the selected versus the control group (21). Enhanced disease resistance may be an inadvertent feature of other rearing techniques. For example, triploid American oysters (*Crassostrea virginica*) grow faster than normal oysters and thus are capable of reaching market size before being killed by the parasite *Perkinsus marinus* (7).

Certified Disease-Free Stocks

Diseases may be prevented by using eggs, embryos, juveniles or broodstock that have been certified as disease free. Many states now have programs to certify that various organisms are disease-free (89). Similarly, FWS and USDA's Animal and Plant Health Inspection Service (APHIS) provide some diagnostic assistance and export certification for nonmammalian aquatic and aquacultured animals, including gametes and embryos (80).

USDA and a consortium of four other organizations (the Oceanic Institute in Hawaii, the Waddell Mariculture Center in South Carolina, the Gulf Coast Research Laboratory in Mississippi, and the University of Arizona Department of Veterinary Science) formed a program to supply specific pathogen free (SPF) broodstock of the Pacific shrimp (*Penaeus vannamei*) to several commercial hatcheries. Results from commercial pond trials have shown that SPF shrimp exhibit improved growth, survival, feed conversion ratios, and higher production rates than non-SPF shrimp in some areas (120,152).

Chemical Prophylaxis

Chemical treatment to reduce potential pathogens is another technique for reducing disease. For example, treating salmonid eggs with hydrogen peroxide or a formalin solution can remove potentially harmful fungi. Similarly, clams may be dipped in sodium hypochlorite solution to reduce surface-coating bacteria (127).

Vaccines

Significant progress has been made in recent years in the development of vaccines to prevent a wide range of diseases in finfish, shellfish, and crustaceans (31,67). Vaccines can be administered in several ways including by injection, immersion, spraying on the skin of the

organism, and orally (134). Currently, 15 vaccines are registered in the United States, most of which are for use with salmonids (71). Routine use of vaccines has reduced the frequency of disease outbreaks and consequently, the use of antibiotics (31).

Disease Diagnosis

Early and accurate diagnosis also is important for disease control. The first step in disease diagnosis involves constant monitoring of cultured organisms especially after stress-inducing events such as temperature fluctuations, or capture and transport. Variations in behavior, reluctance to eat, discoloration of the skin and the presence of lesions can indicate potential disease problems (134). In addition to constant observation of cultured organisms, tools such as microbiological testing and gene probes can help identify the presence of disease agents (31,74).

Managerial Methods to Treat Disease

Management interventions are generally the first steps taken in treating a disease outbreak. If disease is present, immediate steps should be taken to reduce stress to the organisms and to limit the spread of disease by isolating the sick and removing the dead organisms (134). Restoring optimal environmental conditions could help to reduce the impact of the outbreak. In some cases environmental parameters can be directly altered to reduce parasite levels. For example, the parasite *Ichthyophthirius multifiliis*, which affects freshwater cultured fish, can be controlled by increasing or reducing water temperature or by increasing salinity (134). Biological control methods also may be possible (box 2-3).

Chemical Methods to Treat Disease

Three types of legal chemical disease treatments exist in the United States: two are regulated by the FDA -- approved New Animal Drugs and unapproved New Animal Drugs of Low Regulatory Priority (tables 2-1 and 2-2). The third is EPA-registered pesticides. Drugs can be administered to cultured organisms in several ways: added directly to the water, added to the feed, injected into the organism, or the organisms can be dipped in a solution of the chemical (134).

All legal chemical treatments have strict requirements governing their use. For example, one approved drug[5] can be used only on catfish to treat enteric septicemia or on salmonids to control furunculosis. For any chemical treatment, only specified concentrations may be used, adequate withdrawal times must be adhered to, and tissue residues must be below established levels (71).

CONCLUDING REMARKS

The role of the federal government in aquatic health management is complex. Many agencies have programs or regulations concerning aquatic health management (tables 2-3 and 2-4). The Joint Subcommittee on Aquaculture (JSA) will most likely continue to play an important role in coordinating agency efforts to promote improved aquatic health management and protect consumer interests.

The private sector is playing an increasingly important role in aquatic health management. Frequently, there is collaboration between federal and state agencies and private groups in health related matters. For example, a recent publication, the "Guide to Drug, Vaccine, and Pesticide Use in Aquaculture" prepared by the JSA (August 1994), was funded by a consortium of federal agencies and industry groups (71). Industry groups such as the Catfish Farmers of America (CFA) and the U.S. Trout Farmers Association (USTFA) also have been active in creating quality assurance programs for their members to follow (87).

[5] Sulfadimethoxine and ormetoprim, tradename Romet 30.

BOX 2-3: Biological Control of Sea Lice

Sea lice (various species from the genera *Argulus*, *Caligus*, *Ergasilus*, *Lepeophtheirus* and *Pseudocaligus*) (119) are external parasites that attach to the skin of fish and feed on underlying tissues and blood (125). Sea lice parasites can be transmitted through the water column, from host to host, or from wild fish to cultured fish (119). Skin lesions, reduced growth, and mortality caused by the sea lice reduce the marketability of the fish (125). Infections in wild fish are relatively rare and characterized by small numbers of parasites; however, high densities of fish on fish farms encourage the spread of these parasites (125). Once established in a population, parasite numbers increase and may eventually reach epidemic proportions after several years.

Treatment of sea lice infections has traditionally relied on the use of chemicals, especially dichlorvos, an organophosporous pesticide. Net pens are treated by surrounding the pen with a tarp and then adding the chemical to the water (119). At the end of the treatment period, the tarp is removed and pesticide is released into the environment. Frequent treatments are required (every three to four weeks) because the pesticide is only effective against the adult stages of the parasite and does not affect larval stages in the water column. Additionally, the parasite can be re-transmitted to cultured fish from wild fish (106,119).

Frequent use of chemicals to treat sea lice infestations can cause several additional problems. First, applying chemicals is expensive, time consuming, and labor intensive (101,106). Second, widespread use of chemicals may damage the environment, stress the fish, and cause health problems in cultured and wild fish (66,101,119). Third, treatment efficacy is variable depending on temperature of the water and concentration of the chemical within the water (119). Fourth, parasites have started to show resistance to the main chemical dichlorvos, so increasing amounts of the chemical will be needed to contain the infections. Application levels of dichlorvos, however, can only be increased slightly before toxic effects are seen in the cultured fish (66,119).

To reduce chemical use in the treatment of sea lice tests have been made of biological control agents. For example, fish such as the gold sinny wrasse (*Ctenolabrus rupestris*) will remove and consume external parasites from other fish. Experiments have shown that adding these fish to salmon net pens decreases the need for chemical treatments to reduce sea lice infestation. In one trial, 600 wrasse were added to a sea cage containing 26,000 salmon. The salmon growing in this cage did not require chemical treatment but the control group that contained no wrasse had to be treated several times during the course of the study to reduce sea lice infection (106). Additional experiments evaluating control of sea lice with the gold sinny wrasse are currently taking place in Scotland and Norway (106). Further evaluation of this technique and other biological pest control methods may be able to reduce the use of chemical treatment for sea lice.

SOURCE: Office of Technology Assessment, 1995.

Research on antibiotics also may be performed on a collaborative basis due to the high cost associated with gaining data necessary for drug approval. In one case, the U.S. Fish and Wildlife Service and Abbott Labs have performed joint studies on the metabolism and pharmacokinetics of sarafloxacin, a potential drug candidate for aquaculture,[6] as well as methods to detect sarafloxacin residues in tissues of fish (46,47).

Similarly, researchers from the U.S. Department of Agriculture, Agricultural Research Service (ARS) have developed a test that identifies whether catfish have been exposed to the pathogen, *Edwardsiella ictaluri*, the cause of potentially fatal enteric septicemia in catfish. DiagXotics, Inc., of Wilton Connecticut, a producer of other aquaculture related diagnostic tools, has obtained a license from ARS to produce and market the diagnostic test kit, which is expected to be available in 1996 (62). Private industry has also produced aquatic health management products independently. For example, vaccines are manufactured by two private companies: BioMed, Inc. of Bellevue Washington and Aqua Health, LTD. of Canada. Together, they produce 15 different vaccines primarily for use with salmonids (71).

Private-sector involvement in producing vaccines and offering health related services

[6] As of June 23, 1995, Abbott Laboratories has discontinued development of sarafloxacin for aquaculture use in the U.S. (1).

will likely grow in the future. However, it is unlikely that private industry will invest the large sums of money necessary to generate data required for approval of a wide range of drugs. In many cases, the costs involved are too high and the potential profits too low to justify private-sector initiative. Therefore, collaborative efforts between federal and state agencies, and private industry will continue to be important. Other possibilities also exist, for example, if crop grouping for drug approval is determined to be viable or the FDA agrees to permit drug uses for non-food organisms or classify certain life-stages as non-food, then more drugs may become available for use in aquaculture.

Regardless of whether more drugs gain approval, public acceptance of aquaculture products will derive from the perceived quality and safety of the products. If consumers perceive that drugs are widely used in the industry, then they may be reluctant to purchase these products. To avoid problems of this nature, research could focus on such preventative measures as vaccination; production of genetically improved, high health broodstock, and seedstock for commercially important species; and establishing Best Management Practices (BMP) for reducing disease.

Formulating BMPs requires considerable data on impacts of diseases on aquaculture, especially among marine systems and less prominent animals and plants. To address the current dearth of information, it may be possible to expand present USDA data collection systems to address entire life cycles of cultured animals and plants. Using existing programs such as cooperative extension services to collect data within each state for all cultured species could help to fill information gaps. This might help to determine actual economic losses incurred by aquaculturists, provide data to support requests for federal help, and aid in identification of unrecognized disease problems. If this type of data could be compiled and disseminated it also would be useful for formulating management strategies to reduce mortality due to disease. However, much of these data would be difficult to obtain, especially for outdoor ponds, and likely would require additional funding for training extension workers (89).

Data also are needed to harmonize Lacey Act requirements. Regulations governing the movement of fish and wildlife to control the spread of disease organisms across state and international borders are promulgated by individual states resulting in a patchwork of often conflicting requirements. Congress could request that one federal agency, such as the Fish and Wildlife Service, establish guidelines for uniform health certification procedures among all states and with foreign countries. Attempts could be made to map the disease status of facilities, watersheds, or regions to assist in a uniform program to prevent the spread of disease to new areas (80). Stronger cooperation among states with more federal intervention may be necessary to eliminate the disparity and confusion that exists as an obstacle to interstate trade. A strong, uniform program in the United States may facilitate reasonable agreements with other countries and international trade.