AFS Policy Statement #21:
Transgenic Fishes
(Full Statement)

Issue Definition

The advent of gene transfer techniques has introduced the development of lines of fishes, as well as other aquatic organisms, bearing introduced genes. Such modifications are typically aimed at substantial changes of performance characters (e.g., faster growth), extension of environmental tolerance (e.g., cold resistance), or expression of novel proteins. Most fisheries professionals would agree that (1) traits other than those targeted by gene transfer are likely to be affected, (2) overall phenotypic performance of such fishes is virtually uncharacterized, and (3) introduction of such fishes into natural aquatic communities is likely to cause ecological impacts.

Because the performance and ecological impacts of transgenic organisms in natural ecosystems are unknown, uncontrolled release of transgenic fishes is undesirable. Public policies for regulating development and release of transgenic organisms are currently being formulated. It is important that fisheries scientists become involved in evaluations of the performance and ecological impact of transgenic fishes, and in development of relevant public policies to ensure that rational, carefully considered decisions are made regarding development and release of transgenic fishes. While position statement focuses on transgenic fishes the concerns and recommended courses of action apply equally to au transgenic aquatic organisms.

Technical Background
Transgenic Fish

Within their cellular genetic material, transgenic fish bear copies of novel DNA produced by recombinant DNA methods. Such fish are produced by insertion of copies of the novel DNA into newly-fertilized eggs or by reproduction of the individuals so produced. Production of some 14 species of transgenic fishes has been carried out as of July 1989. Genes that have been transferred into fish of different species have included those coding for growth hormone, antifreeze protein, and a variety of easily detected marker proteins. An increase in types of transgenic fishes is expected because the number of isolated single genes is rapidly increasing. In cases where transgenic fish have been reared to sexual maturity, germline transmission of the inserted genes and normal fertility have been observed. Besides the expected direct effects of inserted DNA, indirect phenotypic effects might occur as a consequence of uncontrolled genomic integration or expression of the introduced DNA. Although performance data for transgenic fish are limited, predictions of indirect effects are supported by findings in other transgenic animals.

Ecological Impacts

The potential impacts of transgenic fishes on natural ecosystems might be manifested through a large number of pathways. Impacts will result from altered performance of such fish. At least three conceptual classes of phenotypic changes for transgenic fish might be anticipated. These include changes in: physiological rates, tolerance of physical factors, and behavior. Based on current understanding of community-level impacts of stocking non-transgenic piscivorous fish, the release of certain transgenic fishes, especially those exhibiting substantially altered performance, could destabilize and reorganize aquatic ecosystems. Because aquatic ecosystems function through complex interactions involving transfers of energy, organisms, nutrients, and information, it is reasonable to expect difficulty in predicting the community-level impacts of releasing transgenic fishes that exhibit one or more type of phenotypic change.

Ecological risks of releasing transgenic fishes could be reduced by making them sterile, although sterilization itself may cause other problems. Sterility may be accomplished by ploidy manipulation, hormone treatment, hybridization, surgery, or combinations of these methods. When sterilization is accomplished via induction of triploidy or administration of hormones, there is the added risk that not all individuals are truly sterile. Phenotypic effects of these sterilization methods could be confounded with effects of the introduced gene, thus making it difficult to evaluate performance effects of transgenes. Surgery also has its drawbacks, since some fishes have regenerated gonads and viable urogenital ducts following complete gonadectomies. Sterilization procedures may pose practical problems when applied on a large scale or when used upon some species. Releases of sterile transgenic fish would still involve short-term, risks because sterile fish can alter community dynamics through processes such as competition and altered predation.

Legal Background

Regulation in the United States

Development of animals bearing recombinant DNA molecules is regulated under the Coordinated Framework for the Regulation of Biotechnology, a policy document directing various federal agencies to oversee such development activities. Promulgation of the Coordinated Framework was an administrative attempt to regulate development of a technically broad field in a comprehensive manner, and its coverage consequently included a number of oversights which could prove problematic, as discussed below. Certain state agencies also may have regulatory jurisdiction over transgenic animals.

Under the Coordinated Framework different federal agencies have promulgated their own definitions of transgenic organisms. The definitions -ere supposed to be made consistent by an interagency committee, but this has not been accomplished as of June 1990. These definitions share the feature of being product rather than process oriented, hinging upon the origin and nature of the DNA introduced. Under the Framework, a new organism has been defined as one containing "an intergeneric combination of genetic material." Specifically "excluded are organisms that have resulted from the addition of intergeneric material that is well characterized and contains only nonbonding regulatory regions."

Thus, transgenic organisms that contain DNA constructs bearing such regulatory regions and intrageneric protein-encoding sequences are not le ally considered transgenic, and hence might prove more readily certifiable for deliberate release, distribution, or final use. Yet, regardless of the source of the expression-regulating or protein-encoding sequences in the introduced DNA, alterations of gene expression and gross phenotype are possible and form the bases for the novel performance and ecological impact of transgenic animals. From the viewpoint of environmental impact, distinctions about the particular sources of introduced DNA are largely irrelevant.

Research with transgenic animals at institutions receiving federal support is regulated under guidelines promulgated by the National Institutes of Health (NIH) or, for USDA funded projects, under guidelines being developed by USDA. These guidelines specify proper laboratory practices and levels of biological containment for work involving recombinant DNA methodology. Among institutions not receiving federal funding, voluntary compliance with NIH guidelines is expected under terms of the Coordinated Framework.

The natural environmental conditions required for the attainment of sexual maturity in certain species and the normal culture conditions required for identification of high performance lines dictate the need for environmental release (i.e., outdoor containment) during development of transgenic lines in many fish species. Provisional policy guidelines for outdoor testing of transgenic animals have been promulgated by the USDA Office of Agricultural Biotechnology. It is noteworthy that these guidelines specifically regulate environmental release of only those animals produced as part of USDA-funded research. After reviewing a research proposal involving release of transgenic carp into a secure, outdoor research facilities the release was recommended for approval in spring 1989 by the USDA Agricultural Biotechnology Research Advisory Committee. The proposal was not funded by USDA and, thereafter, transgenic broodfish were stocked into research ponds.

Within the next decade the first genetic lines of transgenic fish will likely emerge from held testing and development and become potentially available for distribution and final use in aquaculture or fisheries management. As transgenic fish are distributed for final use, they will enter a wide range of less secure containments, from which entry into natural systems and impacts upon natural aquatic communities will become more likely. Under the Coordinated Framework, public policy regulating distribution and final use of transgenic animals is not -well defined, with a number of federal agencies responsible for particular aspects of such oversight, but *none with* overall responsibility as a lead agency.

Regulation in Canada

There are a number of Canadian Federal Acts that might regulate the development of biotechnology product. The National Biotechnology Advisory Committee (1989) has urged the federal government to clarify the coverage of biotechnology, products under such legislation. Although the process is well underway, several fundamental issues remain.

Production of transgenic animals is regulated under guidelines promulgated by the Medical Research Council (MRC). The guidelines clearly apply to laboratory research but are not intended to cover environmental release, or distribution and final use of transgenic organisms. Compliance with the guidelines is required only in projects funded by MRC or the Natural Sciences and Engineering Research Council. Furthermore, the guidelines are not enforced by either Council, except by withholding of funds.

The application of existing legislation (such as the Food and Drug Act, the Quarantine Act, and the Animal Disease and Protection Act) to biotechnology hinges upon specific product categories (e.g., veterinary biologics, foods, or drugs) without regard to the process of manufacture. Biotechnology products, specifically transgenic animals, intended for use in the open environment are not well covered by existing legislation.

The recently-enacted Canadian Environmental Protection Act (CEPA) is intended to have wide applicability covering safety in the research, production, use, and disposal of a wide range of products. The Act will ostensibly cover situations where regulatory coverage under existing legislation may be absent or unclear. Draft regulations promulgated under the Act are still in development. For example, criteria are still being developed for assessing permit applications for field trials and for containment during testing. Apparently, regulations covering distribution and final use of transgenic organisms have not yet been addressed by Agriculture Canada.

Courses of Action

Development of public policies on transgenic organisms is at a pivotal stage. It is important that fisheries professionals participate in development of public policies with possible impacts on fisheries resources. Advocacy by the American Fisheries Society of policies endorsed by the membership will provide a powerful impetus towards development of sound policies. We suggest advocacy of the following positions regarding transgenic fishes, in the areas of research, regulation, and proprietary rights:

1. Support research to provide data for rational policy decisions.

Timely progress of scientific understanding and production technology will fill critical needs for development of environmentally sound uses of fertile or sterile transgenic fishes. Needs include: phenotypic characterization of transgenic lines, evaluation of the performance of transgenic lines, improvement of sterilization techniques, and development of ecological risk assessment models and protocols.

2. Advocate caution in uses of transgenic fishes.

Because evaluations of the performance of transgenic fishes will provide meaningful and needed data for assessing the benefits and risks associated with uses of such animals, well-defined studies in secure indoor and outdoor research facilities should be encouraged and approved.

To introductions of transgenic fishes into production aquaculture facilities, whether public or private, should be permitted until completion of risk assessment studies and demonstration of minimal environmental risk on a case by-case basis.

Criteria should be developed for containment of fertile transgenic broodstocks. Whenever practical, transgenic fishes used in aquaculture should be sterile.

Stockings Of transgenic fishes into natural waters should be barred unless and until a body of research strongly indicates the merits of and ensures the ecological safety of stocking a particular transgenic fish into a particular receiving natural system, and only following public comment and approval by the appropriate fisheries management agencies.

3. Advocate regulations improving Comprehensiveness of the Coordinated Framework in the United States.

The American Fisheries Society should support full application of the existing NIH and USDA guidelines regulating production and handling of transgenic organisms, and should support revisions of the guidelines to address the following concerns:

The definition of a transgenic animal within the Coordinated Framework must be changed to hinge upon the process by which the novel animal was produced rather than upon sources of introduced DNA. The definition must be made consistent across the various federal agencies involved in the Coordinated Framework.

Introduction of transgenic animals in non-federally funded laboratories should be required, rather than simply, expected, to follow NIH guidelines. Monitoring and enforcement provisions of the guidelines should be strengthened.

The scope of regulations regarding environmental release of transgenic animals should be expanded to include experiments not specifically funded by USDA.

The American Fisheries Society should advocate mandatory federal regulatory review of proposed releases of transgenic fishes. An AFS committee of technical experts should monitor both the regulatory process and early releases of transgenic fishes. As experience with releases of transgenic fishes accumulates, the degree of federal review should be reassessed. A greater degree of public involvement should be incorporated into decision-making upon release permit requests.

The American Fisheries Society should advocate and participate in early development of policies regulating distribution and final use of transgenic fishes, pressing for adoption of an ecologically conservative philosophy. Granting of separate permits for distribution and final use of transgenic organisms should be considered on a case-by-case basis, as set out in H. R. 1557, the proposed Transgenic Animal Regulator Reform Act. Evaluation of permit applications should include review of results from an environmental risk

assessment that considered the particular genetic and phenotypic modifications and the receiving environment at issue.

The American Fisheries Society should advocate designation of a lead agency, including Society representation on appropriate advisory committees, for development of policy and enforcement of regulations regarding distribution and uses of transgenic fishes. Federal regulatory authority must be established over release of transgenic fishes by the private sector and over transport of such animals within states.

4. Advocate further consolidation of Canadian regulatory authority over development of transgenic organisms.

The American Fisheries Society should advocate further definition or extension of the Canadian Environmental Protection Act or other regulatory instruments to specifically address these areas of concern:

The definition of terms within existing legislation needs to be reviewed to determine whether transgenic organisms are covered and whether they are adequately controlled within the scope of such laws. For example, it may be appropriate to broaden the definition of "substances" under the Canadian Environmental Protection Act. As in the U.S., regulation of transgenic organisms should be built upon a process-based definition.

Field testing of transgenic animals is not subject to a clearly defined regulatory framework. Nonetheless, a 365-day notification for field experimentation is required, lending to complaints from the Canada biotechnology community. Greater definition and streamlining of regulatory process is called for.

Explicit incorporation of transgenic animals into Agriculture Canada's regulations covering distribution and final use of biotechnology is crucial. Encouragement for developers of transgenic animals to contact Agriculture Canada for preparation and planning of such developmental activities is too weak a regulatory approach.

The Canadian provinces and territories play a prominent role in regulation, sharing responsibility with the federal government for environmental protection. However, the applicability of existing regulations to biotechnology products is uncertain and may van, from province to province. Consistency in approach among jurisdictions is essential for effective regulatory control.