*Aquabyte* is the Newsletter of the Network of Tropical Aquaculture Scientists



**Editorial**

To bridge the increasing gap between supply and demand for aquaculture products, scientists on the one hand are working to produce super animals through genetic improvement and biotechnology, while farmers on the other hand are introducing exotics. Billions of dollars are being spent in developed countries for genetic engineering of plants and animals. Biotechnology is allowing scientists to cross the barriers set by nature. All these efforts are raising concerns among activists about the possible implications of intellectual property rights and the economic, social and environmental impacts of biotechnology in developing countries. While the activists agree that genetic engineering has many useful applications in pharmaceutics and agriculture, what they are questioning is the lack of regulatory limits on its advances. This issue includes an interesting article on bioethics and biotechnology and a paper on the introduction of redclaw crayfish in Ecuador.

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# Bioethics and Biotechnology

E.M. Hallerman

## Introduction

The development of biotechnology, including gene transfer, chromosome set manipulation, and interspecific hybridization techniques,while benefitting aquaculture and fisheries management, also raises a range of ethical and social issues (Office of Technology Assessment 1995). Discussions on biotechnology tend to focus on techniques and application, leaving aside the ethical and social issues. This reflects the feeling of many biotechnologists that ethical and social issues are irrelevant, unimportant, or simply not their responsibility. For wider acceptance of biotechnology by society, biotechnologists will have to address those ethical and social issues that are genuine and effectively argue against those that are not legitimate.

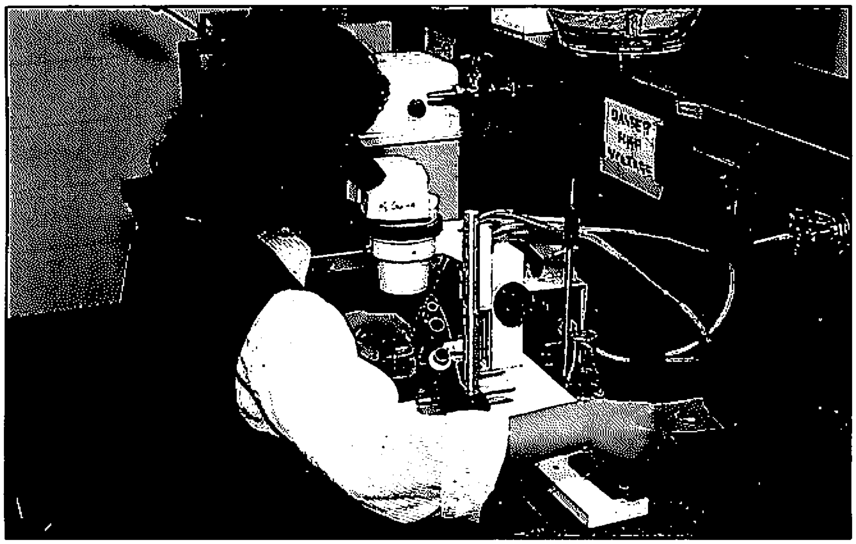
This paper examines the practice and products of biotechnology from the viewpoint of bioethics, looking at four cases where aquatic biotechnology and bioethics intersect. For purposes of this article, ethics is defined as: "(i) the principles of morality, including both the science of the good and the nature of the right; and (ii) the rules of conduct recognized in respect to a particular class of human actions, e.g., bioethics" (Barnhart and Stein 1959). In this context, the related concept of values may be defined as: "(i) Social: the things of social life (ideals, customs, institutions, etc.) toward which the people of the group have an affective regard and (ii) Ethics: any object or quality desirable as a means or as an end in itself."

## *Case I. Genetic Modification of Animals*

The first case involves genetic modification of animals and the ethical issues that arise from genetic modification per se. Why would biotechnologists modify animals? Genetically modified animals provide: (i) unique scientific model systems for studying gene expression; e.g., the "oncomouse" which expresses the ras oncogene under the control of the promoter from the mouse mammary tumor virus; (ii) bioreactors for producing pharmaceutical compounds, e.g., pigs secreting a coagulant, protein C, into their milk; and (iii) more efficient agricultural or aquacultural production, e.g., transgenic coho salmon exhibiting growth rates 11 times that of non-transgenic controls.

These applications all sound laudable. What ethical concerns are at issue? Expression of a novel gene, or expression of a host gene at heightened levels, in unusual tissues or at unusual times, can lead to unintended direct or indirect effects on the health and well-being of the animal. The ethical issue is one of causing animal suffering. The best known example is the case of Beltsville pigs, which suffered from a number of health problems. The unintended, pleiotropic effects of transgenes in pigs, and also in mice, have their parallels in aquatic organisms. Among transgenic coho salmon, individuals expressing the transgene exhibited an abnormal green coloration, and transgenic individuals showing the highest levels of growth enhancement exhibited dramatic deformities of the body, opercles, and jaw (Devlin et al. 1995).

Any potential benefit to science, medicine, and agriculture posed by production of genetically modified animals must be balanced with the suffering of the animals so modifed. For cases where animals are modified for biomedical applications, the goal of the



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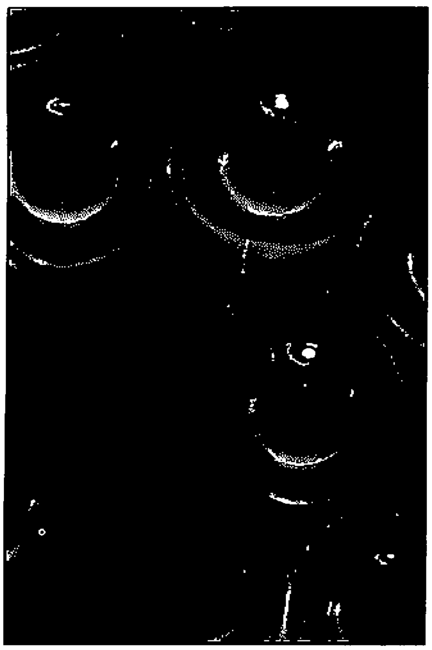

***Using a dissecting microscope and a microinjector, a gene transfer experiment is initiated: (a) looking through the microscope; (b) a glass needle is inserted and a small amount of DNA-bearing solution is injected into a one-celled walleye* (Stizostedion vitreum) *embryo.***

line of research is relief of human suffering, on which many societies place paramount importance. In other contexts, however, the determination of what is ethical is much less clear. Asked whether animals have rights that people should not violate, over 80% of 1 200 US adults surveyed "agreed" (Hoban and Kendall 1993). Asked about genetic modification of animals, 42% of the respondents felt that it was "not wrong," while 53% felt that it was morally "wrong." However, there are differences among cultures regarding ethical issues associated with genetic engineering of animals per se (Custers and Sterrenberg 1992). The general public in France is not very interested in matters concerning genetic modification of animals or animal welfare. In contrast, the Netherlands has a public policy concerning genetic modification of large animals, including case-by-case assessment of whether the experiments should be undertaken, taking into account ethical, as well as health and welfare, considerations. The Netherlands, and to a lesser extent, Denmark and Germany, are reticent about genetic modification of animals and their use for the production of meat or milk. To the author's knowledge, no surveys of public attitudes about genetic modification of animals have been conducted in developing countries.

Seeking a balance between economic considerations and animal welfare, Rollin (1996) proposed an ethical principle termed the Conservation of Welfare: "Genetically engineered animals should be no worse off than the parent stock would be were they not so engineered, and ideally should be better off." Genetic engineering for disease resistance is a good example of the latter. I suggest that Conservation of Welfare is a useful test of the ethics of a wide range of experiments in aquatic biotechnology.

## *Case II. Genetically Modified Organisms as Food*

The second case where biotechnology and bioethics intersect is where genetically modified organisms (GMOs) are produced and marketed as food. Three major reasons for the attraction in using GMOs for human food are: (i) more efficient production in agriculture or aquaculture through faster growth or improved feed conversion efficiency, e.g., fast-growing transgenic common carp; (ii) novel production qualities, e.g., Calgene's Flavr Savr tomato; and (iii) heightened yield of compounds of interest, e.g., red alga, *Gracilaria tikvahiae*, modified to increase the yield of phycocolloids.

All these applications where GMOs are produced and marketed for food seem positive. What are the areas of potential conflict? Foods derived from genetically modified organisms will contain novel proteins not normally found in the parent species, some subset of which may prove allergenic to some consumers. There is particular concern about unforeseen allergenicity of proteins from sources that have not been part of the food supply. Many consumers may want to avoid biotechnologically-derived food for reasons other than safety, such as religious or ethical reasons. Certain biotechnological methods conflict more directly with religious traditions or with ethical or aesthetic convictions, e.g., crossing of species boundaries. The perception of food safety associated with aquaculture products might be compromised if the animals express non-native or heightened levels of hormones or other gene products.

What are consumers' attitudes towards food biotechnology? If it improved quality or taste by 10%, 43% of American respondents were more willing to buy a food produced through biotechnology, but 48% were less willing (Hoban and Kendall 1993). However, if it made the product 10% cheaper with no impact on quality, 59% were more willing to buy the food produced through biotechnology, and only 31%

less willing. Asked what types of information would be very important on a food label, 85% wanted to know whether biotechnology was used; the only issues of greater interest were the use of pesticides, food additives, and type and amount of fat.

Trust may be the key issue for acceptance of food biotechnology. The key ethical principle seems to be full disclosure for the consumer to make an informed decision. Recognition of this by national regulatory agencies overseeing agriculture and food safety, in which the public would like to place its trust, has been very uneven. The definitive example was the initial public outcry in the United States accompanying the Food and Drug Administration (FDA) policy not to require labeling of whole foods produced through biotechnology and its approval for marketing the Flavr Savr tomato. Consumer groups complained of the lack of opportunity to comment on rulemaking generally and on the approval decision for the particular product. Major restaurant chefs pledged a boycott of the Flavr Savr tomato. FDA refused to change its labeling policy. In the face of all the negative publicity, Calgene agreed to voluntarily label the Flavr Savr tomato. Subsequent approvals have not been as contentious and few companies have undertaken voluntary labeling.

Summing up this case, the benefits of biotechnology in food production can be realized in an ethical fashion if companies recognize the desirability of full disclosure and informed choice, and thereby maintain the public's confidence in quality and safety of their food supply.

## *Case III. Environmental Applications of GMOs*

A third case where ethical concerns arise is when GMOs are to be produced and maintained not in well confined laboratories or greenhouses, but instead, in the open environment. In the context of aquaculture and fisheries management, reasons to produce or release GMOs in the environment include: (i) improved production efficiency, e.g., transgenic fish expressing introduced growth hormone genes to exploit faster growth and improved feed conversion, (ii) expression of novel traits, e.g., sterile triploid grass carp, and (iii) combination of favorable traits of the parent species, e.g., hybrid striped bass which combine the hardiness of white bass with the large size and angler appeal of striped bass.

Benefits to aquaculture and fisheries management must be balanced with any risks such application might pose. But before discussing potential risks of environmental application of biotechnology, let us consider the conflicting values systems that color our views of any risks.

*Values systems:* The first value system, termed the Utilitarian value system, emphasizes human utilization of natural resources. Pinchot (1947) expressed the Utilitarian value system quite succinctly: "There are just two things on this material earth - people and natural resources." For example, in debate over whether and how to protect an endangered species, Utilitarians might ask, "What good is this minnow or chub, anyway?" (Callicott 1991).

The contrasting value system emphasizes the intrinsic value of natural resources. Leopold (1949), who was a key inspiration for the environmental movement, expressed the evolutionary-ecological Land Ethic, "A thing is right when it tends to preserve the integrity, stability, and beauty of the biotic community. It is wrong when it tends otherwise." Those espousing the evolutionary-ecological land ethic would never question the desirability of protecting any species (Callicott 1991).

American respondents to the survey by Hoban and Kendall (1993) expressed considerable concern over environmental degradation and strong support for environmental protection. However, attitudes about nature and the environment differ greatly among cultures.

*Ecological risk:* Returning to the issue of risks posed by environmental release of aquatic GMOs, we can anticipate ecological risks to a range of species with which the GMO interacts in the accessible ecosystem, and genetic risks to conspecific natural populations. Ecological risks include the possibility of heightened predation or competition, colonization by or persistence of modified organisms in ecosystems outside the native range of the species, and possibly, alteration of population or community dynamics due to activities of the GMO. Should GMOs be fertile, they could interbreed with natural populations. Any impacts would depend on the fitness of novel genotypes in the wild. Reproduction of GMOs would also prolong any ecological effects beyond the one generation at issue in the case of sterile GMOs.

Interspecific hybrids of many aquatic species are fertile. Release of such hybrids into an ecosystem containing either or both parental species introduces the genetic risks of backcrossing and introgressive hybridization. One example of interspecific hybrids posing risk to parental species arises from the stocking of hybrid striped bass to establish sport fisheries in US reservoirs. Evidence of introgressive hybridization has been documented in Morone stocks in the Chesapeake Bay (Harrell et al. 1993), Savannah River (Avise and Avyle 1984), and Lake Palestine, Texas (Forshage et al. 1988).

Use of sterile GMOs reduces, but does not eliminate risk. Even sterile organisms compete with conspecifics. For small natural populations, this could limit the number of potential spawners, causing a population bottleneck. Male triploids of at least some species undergo steroidogenesis, produce functional spermatozoa, and may attempt to spawn, leading to losses of the resulting aneuploid broods.

How can we quantify any risks posed by production or release of aquatic GMOs in the environment? No single experimental approach is likely to lead to the full range of needed data. We'll need to pursue a combination of laboratory, field, and simulation modelling approaches. The first experiments approaching risk assessment are yielding results.


Photo by E. Hallerman

*Fishes expressing introduced growth hormone genes have been produced in the hope of enhancing growth rate to result in larger fish.*

Should we go ahead? Given our desire to ethically pursue research with incomplete information, how should we approach biotechnology R&D? The USDA Agricultural Biotechnology Research Advisory Committee (1995) adopted Performance Standards for Safely Conducting Research with Genetically Modified Finfish and Shellfish. The performance standards help researchers identify any risk posed by a proposed experiment, and help manage risk cost-effectively, if any is identified. Computer software has been developed to support use of the Performance Standards, and is available through the Internet at http://www.nbiap.vt.edu (or through the author).

Certain key issues posed by scaling up production of aquatic GMOs to full commercialization have not been adequately addressed. In the interim, and maybe over the long term, on-shore tank culture may be the appropriate mode of production for transgenic stocks posing risk. Certain biotechnologies have already led to commercial application, including: monosex rainbow trout, triploid grass carp, and triploid Pacific oysters. These particular applications pose little or no risk; indeed, application of biotechnology in these cases minimizes genetic risk.

Though many societies exhibit deep conflicts between Utilitarian and Land Ethic values systems, many people value environmental quality and want to strike a sensible balance between economic development and ecological integrity. To quote Roe (1990), a US Congressman, "The success of biotechnology will rely on obtaining the public's confidence that these new products of biotechnology can be used in the environment safely and beneficially."

## *Case IV. Intellectual Property Protection for GMOs and DNA Sequences*

The fourth case to be discussed is the intellectual property protection for GMOs and DNA sequences, which pose several ethical issues.

*Patenting of GMOs:* Key precedents for patenting of GMOs were set in the United States. The concept of intellectual property protection can be found in Article I of the US Constitution. The legal basis for patenting of non-plant life forms can be traced back to key rulings on particular patent applications (Office of Technology Assessment 1989). In 1980, the Supreme Court ruled that genetically modified microrganisms, in this case, oil-metabolizing bacteria, were patentable. In 1987, the Board of Patent Appeals declined application for triploid oysters because they felt the invention was "obvious," but ruled that animals were, in principle, patentable. In 1988, the Patent Office issued the first patent on a living animal for oncomouse, mentioned earlier.

The granting of a patent on an animal was highly controversial. The religious community, in particular, was outraged that an animal could be patented. Biotechnology and pharmaceutical companies wanted to dismiss such ethical arguments as a smoke screen for objections to genetic engineering per se. This point of view was summed up by William H. Duffey (quoted in Crawford 1987), "The act of issuing patents is morally neutral and ought to be kept that way."

Because patented animals are inventions that can reproduce themselves, the issue of users' royalty obligations is an important one for the aquaculture sector. After having paid royalties for acquisition of patented stock, would aquaculturists be expected to pay royalties when the stock reproduces and the progeny bought or sold? Current law fails to address adequately the respective rights of patent holders and animal owners over the offspring of patented animals (Merges 1988).

Some patent claims have been very broad, and they are being challenged in the US courts. The granting of such broad patents has a chilling effect on research and on the testing and commercialization of GMOs, especially by individual researchers and small companies not ready for long, expensive court battles.

Patenting policies differ among nations (Office of Technology Assessment 1989). The European Patent Convention permits patenting of certain elements of life forms, providing they are novel, inventive, and industrially applicable, but it also imposes restrictions that "the invention should not be contrary to "order public" and morality, and should not cover plant nor animal varieties per se." Certain nations have no patenting laws, and are not party to multilateral patenting conventions, although the General Agreement on Tariffs and Trade may impact this area.

To resolve issues posed by patenting of GMOs, I quote ethicist George Annas (Office of Technology Assessment 1989): "The real issue is not whether animals can or should be patented, but what things it is reasonable to permit humans to do to animals. Patenting simply adds another incentive to profit-making organizations to pursue certain lines of animal experimentation, and makes this pursuit seem more legitimate."

*Patenting of genes and gene products:* Intellectual property protection poses a second set of ethical issues stemming from the patentability of genes and gene products. An ethical issue posed by patenting of molecules is one of exploitation of natural resources of developing countries by the biotechnology and pharmaceutical firms of developed countries, enriching the corporations and returning nothing to native people (Stone 1992).

Patenting of genes and gene products was recently a central issue in international relations, affecting adoption of the United Nations-sponsored biodiversity treaty. The United States was one of a handful of countries that refused to sign the treaty. This is because Patent Office officials and the biotechnology industry were concerned that portions of the treaty concerning technology transfer implied compulsory licensing for marketing a product developed from a native species to the country where the species originated.

There is an excellent model of an ethical and practical way to deal with the respective rights of patent holders and native people. Merck and Company is analyzing biological samples collected by Costa Rica's National Institute of Biodiversity, or INBio, in exchange for an up-front payment and royalties, half of which Costa Rica will invest in conservation (Stone 1992). To bring the case for intellectual property protection to a close, a wide range of observers feel that this arrangement is a model for intellectual property protection benefiting both corporate and societal interest.

## Conclusion

Forthright discussion of ethical issues is important for the development of biotechnology and for society. Convincing biotechnologists, who like all scientists, are professional skeptics, that this is true, is not easy. And it is not easy to interest entrepreneurs in ethical and social issues. The political leadership of nations and international groups have been highly uneven in their attitude toward oversight of biotechnology. But, to quote Leopold (1949), "No important change on ethics was ever accomplished without an internal change in our own intellectual emphasis, loyalties, affections, and convictions."

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