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# A Day on the Fish Farm: FDA and the Regulation of Aquaculture

by

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*NOTE*

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## I. INTRODUCTION

Aquaculture is the art of rearing aquatic organisms.[1] Although fish farming is over 3,500 years old,[2] the industry only came to the United States during the 1950s.[3] Since that time, the practice of industrial aquaculture has exploded in this country and around the world. Aquaculture is the fastest growing area of agriculture in the U.S. and exists in every state.[4] However, despite the current prevalence and economic importance of the industry, there are still many neglected questions concerning aquaculture regulation. Issues such as monitoring antibiotic resistance, reducing environmental impact and determining the appropriate role of genetic technologies have garnered a great deal of regulatory scrutiny with regard to agriculture generally, yet seem to be neglected in the realm of fish farming. The set of federal agencies involved in creating and implementing policies that govern aquaculture includes the United States Department of Agriculture (USDA), the Environmental Protection Agency (EPA), the National Marine and Fisheries Service (NMFS) and the Fish and Wildlife Service (FWS). But perhaps the most interesting regulatory questions currently facing the industry must be answered by the Food and Drug Administration (FDA).

This note examines certain human health and environmental concerns currently faced by aquaculture, evaluates the FDA's current regulatory practices and considers possible policy changes for the future. Throughout this note, aquaculture will refer to the practice of raising fish as food for human consumption in open

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[1] Aquaculture is defined by the Food and Agriculture Association of the United Nations as "[f]arming of aquatic organisms including fish, mollusks, crustaceans and aquatic plants. Farming implies some sort of interventionist rearing process to enhance production, such as regular stocking, feeding and protection from predators. Farming also implies individual or corporate ownership of the stock being cultivated. For statistical purposes, aquatic organisms which are harvested by an individual or corporate body which has owned them throughout the rearing period contribute to the aquaculture while aquatic organisms which are exploitable by the public as common property resources, with or without appropriate license, are the harvest of fisheries." Joint FAO/NACA/WHO Study Group, *Food Safety Issues Associated with Products from Aquaculture,* 883 World Health Organization Technical Report Series 1, 4 (1999) [hereinafter *Products from Aquaculture*] (quoting FOOD AND AGRICULTURE ORGANIZATION OF THE U. N., AQUACULTURE PRODUCTION STATISTICS 1986-1995, FAO FISHERIES CIRCULAR NO. 815, REV. 9 (1997)).

[2] Ronald J. Rychlak & Ellen M. Peel, *Swimming Past the Hook: Navigating Legal Obstacles in the Aquaculture Industry,* 23 ENVTL. L. REV. 837, 837 (1993) (explaining that the Chinese practiced various forms of aquaculture between 3,500 and 4,000 years ago).

[3] Mary Liz Brenninkmeyer, *The Ones That Got Away: Regulating Escaped Fish and Other Pollutants from Salmon Fish Farms,* 27 B.C. ENVTL. AFF. L. REV. 75, 75 (1999).

[4] *Id.*

water netpens.[5] Part II addresses the increase in antibiotic resistance arising from aquaculture practices, illustrates why aquaculture medication practices should be of concern, explains how the FDA currently regulates the use of antibiotics in aquaculture and evaluates the latest proposal for the approval of new antimicrobial animal drugs. Part III looks at how the FDA should regulate the use of genetic engineering techniques in aquaculture facilities, specifically focusing on a recent request to market a transgenic salmon. This section discusses the use of genetically modified organisms (GMOs) in agriculture, illuminates concerns about genetic engineering, outlines how the FDA regulates genetically modified (GM) products, describes how these regulatory practices would be applied to a transgenic salmon and inquires whether or not the FDA's current policy is sufficient to protect human health and the environment. Part IV explores policy considerations the FDA should consider in evaluating transgenic salmon products, recommends that the FDA require product labeling for foods derived from transgenic fish, explains why a labeling requirement could be statutorily justified, documents a wide scope of concerns regarding current industrial aquaculture techniques and exhorts the FDA to exercise diligence in its regulatory activity in order to keep human health and environmental problems from getting out of control.

## II. AQUACULTURE AND ANTIBIOTIC RESISTANCE

### A. *Antibiotic Resistance*

Bacteria, also known as microbes, are pervasive throughout the world. Humans and animals alike carry millions of these tiny one-celled organisms.[6] Some bacteria cause health problems such as tuberculosis, typhoid fever, diphtheria, pneumonia and food poisoning, while others are essential to normal biological functioning.[7] Starting with the discovery of penicillin, modern medicine has had at its disposal multiple classes of antimicrobial drugs (or antibiotics) capable of controlling harmful bacteria.[8] The use of these drugs has been and will continue to be critical to curing diseases

[5] *See id.* at 79 (describing a standard aquaculture facility as follows: "[a] coastal salmon fish farm typically consists of a group of open mesh net-cages (or netpens) suspended from anchored metal cage frames.").

[6] Robyn L. Goforth & Carol R. Goforth, *Appropriate Regulation of Antibiotics in Livestock Feed,* 28 B.C. ENVTL. AFF. L. REV. 39, 42 (2000) [hereinafter Goforth].

[7] *Id.*

[8] Michael Misocky, *The Epidemic of Antibiotic Resistance: A Legal Remedy to Eradicate the "Bugs" in the Treatment of Infectious Disease,* 30 AKRON L. REV. 733, 734-35 n.12 (1997) [hereinafter Miscocky].

and fighting infections.[9] However, after repeated exposure, microbes can develop a resistance to antibiotics.[10] Resistance is understood as follows: "[b]acterial strains can be termed resistant if they can function, survive or persist in the presence of a higher concentration of an antimicrobial than the parent population can support."[11] Simply stated, the existence of antibiotic resistance means that current drugs used in both human and veterinary medicine are not as effective as they once were in controlling pathogenic bacteria. The Centers for Disease Control (CDC) has estimated that more than half of the deaths due to bacterial infection in the United States involve resistant bacteria.[12] Many national and international health organizations recognize the severity of the resistant microbe problem.[13] Limiting the spread of antibiotic resistance is essential to maintaining human and animal health.

Despite almost unanimous recognition of the development of antimicrobial resistance, there continues to be a great deal of controversy over the best way to stop this crisis. One reason for the disagreement is the complexity of resistance phenomena.[14] A simple way in which resistance can be created occurs when an antibiotic kills many microbes in a population but spares less susceptible individual bacteria, thereby creating a propagating population of organisms against which the antibiotic is ineffective.[15] Tracking and understanding microbial resistance is very complicated, however, because there are many causes of resistance within an individual microbe and many different mechanisms for the spread of that resistance. Some bacteria simply inactivate antibiotics, others flush antibiotics from their cells, while still others mutate so that their target sites are unrecognizable to antimicrobial drugs.[16] Once an individual organism develops a resistant characteristic it can spread

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[9] Goforth, *supra* note 6, at 42.

[10] Sergio Paone, FARMED AND DANGEROUS: HUMAN HEALTH RISKS ASSOCIATED WITH SALMON FARMING, A REPORT PREPARED FOR FRIENDS OF CLAYOQUOT SOUND 6 (2000), *available at* http://www.eurocbc.org/salmon_farming_health_risks.pdf (last visited Aug. 17, 2004) [hereinafter Paone].

[11] *Products from Aquaculture*, *supra* note 1, at 4.

[12] Misocky, *supra* note 8, at 744.

[13] Paone, *supra* note 10, at 6.

[14] U.S. DEP'T OF HEALTH AND HUMAN SERVS., FOOD AND DRUG ADMIN. & CTR. FOR VETERINARY MEDICINE, GUIDANCE FOR INDUSTRY #152: EVALUATING THE SAFETY OF ANTIMICROBIAL NEW ANIMAL DRUGS WITH REGARD TO THEIR MICROBIOLOGICAL EFFECTS ON BACTERIA OF HUMAN HEALTH CONCERN 1 (2002) [hereinafter GUIDANCE DOCUMENT #152], *at* http://www.fda.gov/cvm/guidance/fguide152.pdf (last visited Aug. 17, 2004).

[15] Goforth, *supra* note 6, at 42.

[16] *Id.* at 43.

this trait vertically, through reproduction, but bacteria can also pass their traits horizontally, directly from one bacterium to another through conjugation, transformation and transduction.[17] The spread of resistance characteristics causes great concern among health professionals. Bacteria's ability to pass their traits horizontally means that antibacterial resistance in any kind of microbe can be dangerous. While it is clear that antimicrobial resistance in a human pathogen can be detrimental to human health, resistance in other bacteria is also a concern since those microbes can pass the resistance to different strains that pose a direct threat to humans. A microbe that only affects a cow or a fish can spread its resistance to a microbe that affects humans.[18] Resistance is accordingly a concern with respect to human pathogens, pathogens that only affect animals and shared human and animal pathogens.[19]

Resistance transfer can happen through environmental contact, when humans eat animals with resistant bacteria and when they merely come in contact with these animals or animal products.[20] Dr. Stuart B. Levy, Director of the Center for Adaptation Genetics and Drug Resistance at Tufts University School of Medicine, has said that "[t]he exchange of genes is so pervasive that the entire bacterial world can be thought of as one huge multicellular organism in which the cells interchange their genes with ease."[21]

A final twist to the complexity of antibacterial resistance involves determining to what specific antibiotics particular bacteria are resistant. Some bacteria can show resistance to antibiotics that they have never even encountered. Resistance to one form of antibiotic can also lead to resistance to other classes of antibiotics.[22] A pathogen that builds up resistance to one medication can also be less susceptible to other drugs. Significant arguments rage in scientific circles over the nature of resistance, the causes of resistance, and the particular effects of different resistance transfer

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[17] *See id.* (providing a detailed description of conjugation, transformation and transduction).

[18] T. Midtvedt & E. Lingass, *Putative Public Health Risks of Antibiotic Resistance Development in Aquatic Bacteria*, CHEMOTHERAPY IN AQUACULTURE: FROM THEORY TO REALITY 302, 305-06 (C. Michel & D.J. Alderman eds., 1992) [hereinafter Midtvedt]; *see infra* Part I.C (discussing how fish microbials may spread resistance to human microbials).

[19] Paone, *supra* note 10, at 7; Sherwood L. Gorbach, *Antimicrobial Use in Animal Feed – Time to Stop*, 345 NEW ENG. J. MED. 1202 (2001).

[20] Goforth, *supra* note 6, at 44-45.

[21] Paone, *supra* note 10, at 8.

[22] GUIDANCE DOCUMENT #152, *supra* note 14, at 1.

pathways. However, most epidemiologists would agree that antibiotic resistance poses a significant threat to human health and that any use of antibiotics can contribute to this problem. While it is acknowledged that human use of antibiotics plays the most important role in creating antibiotic resistance in human pathogens, use of antibiotics in agriculture and aquaculture is a part of the problem as well.[23] Therefore it is important to monitor, evaluate and perhaps restrain the use of antimicrobial agents on terrestrial and aquatic farms.

### *B. Overview of Antibiotics in Agriculture*

Farmers use astronomical amounts of antibiotics in agriculture. Animals receive approximately half of the over 50 million pounds of antibiotics produced in this country.[24] In the last thirty years the amount of penicillin-type antibiotics used by farmers has grown by an estimated 600%, while the use of tetracycline, another antibiotic, has grown 1500%.[25] The beneficial results from farm antibiotic use are preventing and curing disease, and enhancing animal growth.[26] These uses are known respectively as prophylactic, therapeutic and promotional applications. During prophylactic and promotional applications, antibiotics are given to animals at subtherapeutic levels, or in smaller doses.[27] With regard to resistance, dispensing smaller amounts of antibiotics is thought to be more problematic; bacteria that are least susceptible to the drugs will not be killed by the application and will live to spread their resistance characteristics.[28] This prevalent and varied use of antibiotics on farms contributes significantly to bacterial resistance.[29] Already, as a result of ever-increasing resistance, farmers must use ten to twenty times more antibiotics than they did only ten years ago to achieve the same level of growth benefits in farm animals.[30]

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[23] Paone, *supra* note 10, at 6.

[24] Goforth, *supra* note 6, at 47-48.

[25] Alex Kirby, *Why Farm Antibiotics Are a Worry,* BBC NEWS (Oct 8, 1999), *at* http://news.bbc.co.uk/1/hi/health/background_briefings/antibiotics/436398.stm (last visited Aug. 18, 2004).

[26] Goforth, *supra* note 6, at 45-46.

[27] *Id.*

[28] *Id.* at 51.

[29] Paone, *supra* note 10, at 6 (citing WORLD HEALTH ORG., THE MEDICAL IMPACT OF ANTIMICROBIAL USE IN FOOD ANIMALS (1997)).

[30] Goforth, *supra* note 6, at 47 (citing John W. Harrison & Timothy A. Svec, *The Beginning of the End of the Antibiotic Era? Part I. The Problem: Abuse of the "Miracle Drugs,"* 29(3) QUINTESSENCE INT'L 151, 157 (1998)).

Furthermore, antibiotic resistance generated on farms can negatively affect our ability to fight human diseases. Concerns often focus on the direct impacts of resistant farm animal pathogens, such as salmonella, on humans and animals alike.[31] However, resistant bacteria found in animals are principally dangerous because they can be transferred to any human pathogen when consumers eat the animals containing the resistant bacteria,[32] by mere contact with these animals[33] or perhaps through other pathways in the greater environment.[34] This spread of resistance is of paramount concern because of the many varieties of antibiotics used on farms; most are either identical or closely related to the drugs prescribed to treat humans.[35] A study of the top ten drug resistant microbes concluded that many of the drugs used in medicine and agriculture are now less effective at treating human disease than in the past.[36] Human diseases are becoming stronger and harder to cure because of agricultural uses of antibiotics.[37]

The problem of antibiotic resistance, caused by the agricultural use of antimicrobials, is severe. Much of current scientific research and legal scholarship, however, has focused exclusively on the development of antimicrobial resistance on the traditional farm, ignoring prolific antibiotic use in aquaculture. Mounting evidence indicates that resistance is fostered on fish farms and that the use of antibiotics in aquaculture deserves careful scrutiny.

### C. *Problems Associated with the Use of Antibiotics in Aquaculture*

The Center for Veterinary Medicine (CVM), the division of the FDA responsible for regulating the manufacture and distribution of food additives and animal drugs, has promulgated various rules governing the use of antibiotics in aquaculture. Before an antibiotic may be used on a fish farm, the manufacturer must first submit

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[31] Goforth, *supra* note 6, at 54-55.

[32] GUIDANCE DOCUMENT #152, *supra* note 14, at 1.

[33] Goforth, *supra* note 6, at 53.

[34] Paone, *supra* note 10, at 8.

[35] Gorbach, *supra* note 19, at 1202 (noting that these antimicrobials include penicillins, tetracyclines, cephalosporins (including ceftiofur, a third-general cephalosporin), fluoroquinolones, avoparcin (a glycopeptide that is related to vancomycin) and virginiamycin (a streptogramin that is related to quinupristin-dalfopristin)).

[36] Ann Gibbons, *Exploring New Strategies to Fight Drug-Resistant Microbes,* 257 SCIENCE 1036 (Aug. 1992).

[37] Goforth, *supra* note 6, at 51-65 (summarizing numerous scientific journals tying antibiotic resistance in human pathogens to the use of antimicrobials in agricultural settings).

an Investigational New Animal Drug Application (INADA) in order to receive permission to do a pre-market study with the drug, and then submit a New Animal Drug Application (NADA) illustrating that the drug is safe and effective.[38] There are currently three antibiotics approved by the CVM for use on fish farms: oxytetracycline, sulfadimethoxine and sulfamerazine.[39] These drugs are marketed and sold as Fish Grade products under the respective names of Terramycin,[40] Romet-30[41] and Sulfamerazine.[42] Romet-30 is approved to control furunculosis in trout and salmon,[43] while Sulfamerazine in Fish Grade is approved for treating furunculosis in trout only.[44] Terramycin is approved for marking skeletal tissue of Pacific salmon, controlling ulcer disease, furunculosis, bacterial hemorrhagic septicemia and pseudomonas diseases in salmonids, and controlling bacterial septicemia and pseudomonas diseases in catfish.[45] The CVM specifies dosage amounts and withdrawal times that must be followed when using medications and medicated feeds. All three of these drugs are available over-the-counter (OTC), but their labels require that they be used only under veterinary supervision.[46] It is illegal to use any antibiotic or other drug in a manner inconsistent with its approved uses.[47]

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[38] General Provisions for New Animal Drug Applications, 21 C.F.R. § 514.1 (2003).

[39] CTR. FOR VETERINARY MEDICINE, FOOD AND DRUG ADMIN., DRUGS APPROVED FOR USE IN AQUACULTURE (POIKILOTHERMIC FOOD SPECIES) [hereinafter DRUGS APPROVED] (guidance document specifying the appropriate uses and limitations of aquaculture drugs), *at* http://www.fda.gov/cvm/index/aquaculture/appendixa6.htm (last visited Aug. 17, 2004).

[40] *New Animal Drug Application: 038-439*, PRODUCT INFORMATION FOR THE NRSP-7 DATABASE [hereinafter *NADA: 038-439*], *available at* http://www.nrsp-7.org/mumsrx/tn/ (last visited Aug. 17, 2004).

[41] *New Animal Drug Application: 125-933*, PRODUCT INFORMATION FOR THE NRSP-7 DATABASE [hereinafter *NADA: 125-933*], *available at* http://www.nrsp-7.org/mumsrx/tn/ (last visited Aug. 17, 2004).

[42] *New Animal Drug Application: 033-950*, PRODUCT INFORMATION FOR THE NRSP-7 DATABASE [hereinafter *NADA: 033-950*], *available at* http://www.nrsp-7.org/mumsrx/tn/ (last visited Aug. 17, 2004).

[43] *NADA: 125-933*, *supra* note 41.

[44] *NADA: 033-950*, *supra* note 42.

[45] DRUGS APPROVED, *supra* note 39, at 1.

[46] *NADA: 038-439*, *supra* note 40; *NADA: 125-933*, *supra* note 41; *NADA: 033-950*, *supra* note 42.

[47] OFFICE OF REGULATORY AFFAIRS, FOOD AND DRUG ASS'N, COMPLIANCE POLICY GUIDE; COMPLIANCE POLICY GUIDANCE FOR FDA STAFF, SEC. 615.115: EXTRA-LABEL USE OF MEDICATED FEEDS FOR MINOR SPECIES 2 [hereinafter EXTRA-LABEL GUIDE] (explicating regulations codified at 21 C.F.R. § 530 (2004) promulgated under the Animal Medicinal Drug Use Clarification Act of 1994), *available at* http://www.fda.gov/ora/compliance_ref/cpg/cpgvet/cpg615-115.html (last visited Aug. 18, 2004).

However, since 1994, the FDA has indicated that it will not take regulatory action against either fish farms or drug or medicated feed manufacturers for using drugs in a manner inconsistent with their labeling if they conform to extra-label use policies.[48] The CVM created extra-label use provisions because it recognized the significant disparity between the number of available medications, the number of diseases that each medication was approved to treat and the needs of the aquaculture industry.[49] Furthermore, inadequate financial incentives deterred manufacturers from submitting new drugs for approval or testing current drugs for new uses.[50] The CVM felt that, without the extra-label use provisions, the lack of available medication would limit the treatment of diseased fish.

In order to avoid regulatory action when using medications in a manner not specifically approved by the CVM, aquaculturists must conform to several broad requirements. Extra-label use of medication is allowed only when the following conditions exist: (1) the health of the animal is seriously threatened, or death is a possible consequence of failing to initiate treatment; (2) the medication is approved for other uses with aquatic species; (3) a veterinarian oversees and prescribes the treatment in the context of a valid veterinarian-client-patient relationship, making sure that there is no approved new animal drug already labeled for such treatment, carefully documenting the treatment and creating safe withdrawal times; and (4) the treatment is therapeutic rather than promotional in nature.[51] CVM has a variety of enforcement measures at its disposal under the Federal Food, Drug and Cosmetic Act (FDCA) that it may use in order to ensure that only approved drugs are used at aquaculture sites in either an approved or acceptable extra-label manner. However, despite the CVM's current regulation of antibiotics in aquaculture, a range of possible problems still exist regarding antibiotic resistance.

The specific disbursement methods, quantities and types of antibiotics used in fish farms have raised growing concerns that the aquaculture industry unnecessarily contributes to the problem of resistant microbes. The American Society of Microbiology, for example, has warned that the use of antibiotics in aquaculture is

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[48] *Id.*

[49] Telephone Interview with Dr. Susan Storey, Veterinary Medical Officer, Aquaculture Drug Team, Office of New Animal Drug Evaluation, Center for Veterinary Medicine, Food and Drug Administration (April 21, 2003).

[50] *Id.*

[51] *See* EXTRA-LABEL GUIDE, *supra* note 47, at 2-5.

potentially one of the primary causes of antibiotic-resistant bacteria.[52] The U.S. aquaculture industry uses between 204,000 and 433,000 pounds of antibiotics annually,[53] usually to counter bacterial disease breakouts.[54] However, additional uses of antibiotics are commonly found in aquaculture notwithstanding their illegality. For example, aquaculturists use antibiotics for growth promotion, even though such a use is not authorized by any antibiotic label or by CVM's extra-label use policy.[55] Industry observers claim that antibiotics are also used on fish farms to prevent disease, affect reproduction and growth and tranquilize fish during transit.[56] Such use of antibiotics, particularly in ways not sanctioned by the CVM, increases the likelihood that these drugs will contribute to antibiotic resistance.

In fact, even if aquaculturists only use antimicrobial drugs according to their label indications and the extra-label use policy, the administration of these drugs will still contribute to the problem of antibiotic resistance in several ways. First, aquaculture's use of antibiotics creates antibacterial resistance in fish. Recent studies illustrate that depositing medicated feed into netpens can create antibiotic resistance in the intestinal bacteria of farmed fish and even in the guts of wild fish surrounding aquaculture sites.[57] A study of *V. salmonicida*, the microbe that causes furunculosis in salmon, found that approximately one third of the 463 isolates

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[52] REBECCA GOLDBERG AND TRACY TRIPLETT, ENVIRONMENTAL DEFENSE FUND, MURKY WATERS: ENVIRONMENTAL EFFECTS OF AQUACULTURE IN THE U.S. 45 (1997) (citing PUB. AND SCIENTIFIC AFFAIRS BD., AM. SOC'Y FOR MICROBIOLOGY, REPORT OF THE AMERICAN SOCIETY FOR MICROBIOLOGY TASK FORCE ON ANTIBIOTIC RESISTANCE (1995)), *available at* http://www.environmentaldefense.org/pdf.cfm?ContentID=490&FileName=AQUA.pdf (last visited Aug. 18, 2004).

[53] DR. CHARLES M. BENBROOK, THE NORTHWEST SCIENCE AND ENVIRONMENTAL POLICY CENTER., ANTIBIOTIC DRUG USE IN U.S. AQUACULTURE 5-14 (2002) (illustrating specific use of antibiotics on salmon and catfish farms), *available at* http://www.iatp.org/fish/library/uploadedFiles/Antibiotic_Drug_Use_in_US_Aquaculture.doc (last visited Aug. 18, 2004).

[54] Paone, *supra* note 10, at 4 (stating "[a]ntibiotics are administered to farmed salmon only when a bacterial disease outbreak is identified.").

[55] EXTRA-LABEL GUIDE, *supra* note 47, at 4 ("[i]t is inappropriate under any circumstances to use a medicated feed in an extra-label manner for improving weight gain, feed efficiency or other production purposes.").

[56] BENBROOK, *supra* note 53, at 5 (claiming "[d]espite the often-encountered claim that there are no antibiotics used for growth promotion in aquaculture, a National Seafood HACCP Alliance for Training and Education Compendium identifies 'growth' as one of the reasons why producers administer antibiotics (FDA 1998). In Chapter 22, the compendium lists the following reasons for use of drugs in aquaculture production: 1. Affect reproduction and growth; 2. Treat and prevent disease; 3. Control parasites; 4. Tranquilization.").

[57] *Id.* at 4.

were resistant to tetracycline and 81% were resistant to sulphonamides.[58] The more antibiotics used in treating fish and other animals, the stronger bacterial resistance becomes.[59]

Second, in addition to antibacterial resistance propagated in farmed fish themselves, current aquaculture practices can create antibacterial resistance elsewhere in the aquatic environment. These practices allow significant amounts of antibacterial agents to pass directly into open waters and settle in bacterial sediments below fish farms. Fish farmers normally administer antibiotics to fish through their food, usually fish pellets.[60] This practice is problematic because as fish pellets are thrown into the water, fragments containing antibiotics can break apart and pass undigested directly into the aquatic environment.[61] Even pellets that do not break apart may pass straight through the fish farm cages because fish suffering from bacterial disease have decreased appetites and will consume less of the antibiotic-coated food pellets than are provided for treatment.[62] Antibiotics ingested by fish often end up in the environment as well, as fish do not metabolize antimicrobial agents completely.[63] Some estimates indicate that due to poor metabolism, as much as 75% of the antibiotics eaten by fish end up in the water through excretion.[64] Oxytetracycline in particular is poorly absorbed by the intestinal tract of fish.[65] Allowing such large amounts of antibiotics to pass into open aquatic environments is detrimental because it can create resistance in the bacte-

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[58] Henning Sorum, *Antibiotic Resistance in Aquaculture*, 92 ACTA VETERINARIA SCANDINAVICA SUPPLEMENTUM 29, 30 (1999).

[59] H.C. Wagener et al., *Transfer of Antibiotic Resistant Bacteria from Animals to Man*, 92 ACTA VETERINARIA SCANDINAVIA SUPPLEMENTUM 51, 56 (1999).

[60] *Products from Aquaculture, supra* note 1, at 24 (noting that "[f]or finfish and crustaceans, antimicrobials are usually administered in feed, either compounded during manufacture or surface-coated onto feed pellets. Antimicrobials are usually added with a small quantity of oil, either by the feed manufacturer or at the farm.").

[61] B.T. Lunestad, *Fate and Effects of Antibacterial Agents in Aquatic Environments*, CHEMOTHERAPY IN AQUACULTURE: FROM THEORY TO REALITY 151, 153-54 (C. Michel & D.J. Aldermand eds., 1992).

[62] O.B. Samuelsen, *The Fate of Antibiotics/Chemotherapeutics in Marine Aquaculture Sediments*, CHEMOTHERAPY IN AQUACULTURE: FROM THEORY TO REALITY 162, 163 (C. Michel & D.J. Alderman eds., 1992).

[63] Lunestad, *supra* note 61, at 154 (stating "[t]he standard dose [of oxytetracycline (OT)] recommended for treatment of fish is five to ten times higher than doses commonly used in medical practice, indicating that OT is poorly absorbed by the fish. This is especially true for fish held in seawater; there the intestinal uptake is substantially reduced as compared to fish in fresh water. To compensate for the poor intestinal uptake higher amounts of OT are used during medication, giving an increased environmental load of this agent.").

[64] BENBROOK, *supra* note 53, at 5.

[65] Samuelsen, *supra* note 62, at 163.

rial flora found in underlying aqueous sediments.[66] Although sediments under aquaculture netpens are exposed to a lot of antibiotics, the concentration of these antibiotics is relatively small because they quickly disperse in open water. This creates ideal conditions for the development of resistance; low concentrations of oxytetracycline, for example, do not kill all bacteria, but do offer favorable conditions for resistant strains of bacteria to evolve through natural selection.[67] Current aquaculture practices allow significant amounts of antibiotics to pass into sediments and the greater aquatic environment, thereby significantly contributing to antimicrobial resistance.

Whether in farmed fish, sedimentary bacterial flora or the open water, antibacterial resistance caused by aquaculture practices is principally dangerous because affected bacteria may transfer their antibiotic-resistant characteristics. There is only a remote possibility of resistant fish pathogens directly affecting humans, though the risk may be slightly higher in tropical climates.[68] The primary danger associated with antibiotic-resistant bacteria in fish relates to an eventual transfer of antibacterial resistance to human pathogens. Transfer of antibiotic resistance can occur even between different kinds of bacteria that are not closely related through evolution or ecology.[69]

When a human eats a farmed salmon, antibiotic-resistant strains of bacteria can transfer their resistance to bacteria carried in that person.[70] Extensive transfer of antimicrobial-resistance can take place in the human colon, thereby creating a reservoir of antibiotic-resistant genes that can be acquired by deadly human pathogens.[71] The Centers for Disease Control (CDC) found that bacteria from aquaculture sites also could be transferred directly to humans simply by handling the fish.[72] The same general risk of transferring antibiotic resistance applies to bacteria found in aquatic environ-

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[66] Ruth-Anne Sandaa et al., *Transferable Drug Resistance in Bacteria from Fish Farm Sediments*, 38 CANADIAN J. OF MICROBIOLOGY 1061, 1064-65 (1992) (finding that sediment bacteria possessed increased resistance to oxytetracycline after the fish farms were treated with the antibiotic after a disease outbreak); Lunestad, *supra* note 61, at 157.

[67] Sandaa, *supra* note 66, at 1064-65.

[68] *Products from Aquaculture*, *supra* note 1, at 26 (stating that in warmer climates fish pathogens such as *A. hydrophila* and *Edwardsiella spp.* may pose a risk to human health).

[69] H. Kruse, *Indirect Transfer of Antibiotic Resistance Genes to Man*, 92 ACTA VETERINARIA SCANDINAVICA SUPPLEMENTUM 59, 59-65 (1999).

[70] BENBROOK, *supra* note 53, at 4.

[71] Gorbach, *supra* note 19, at 1202-03.

[72] NATIONAL AQUACULTURE ASSOCIATION, NAA & ANTIBIOTIC USE IN AQUACULTURE: CENTER FOR DISEASE CONTROL REBUTTAL 4 (1999) [hereinafter ANTIBIOTIC USE

ments or related sediments. A recent study concluded that "the occurrence of bacteria with transferable resistant plasmids and fish pathogenic bacteria in sediments creates situations where a transfer of resistance bacteria is possible."[73] Another study found that the transfer of resistant genetic material between bacteria at aquaculture sites and bacteria found in humans is so fluid that "we should consider the two environments (fish farm and hospital) one interactive compartment."[74]

Antibiotic-resistance anywhere in the environment can be detrimental to human health if resistance-causing genes are transferred to human pathogens. The risk becomes even more profound for antibiotic-resistant microorganisms found in foodstuffs consumed by humans. With regards to aquaculture, antibiotic-resistance creates especially critical concerns because of the close relationship between antimicrobial agents used for treating fish and similar agents still used for treating humans; tetracyclines, especially, are of considerable medical importance.[75] Considering the findings of recent scientific studies, the FDA should recognize that antibiotic-resistance is a serious problem. The Agency must regulate aquaculture closely in order to ensure that fish farming practices do not unduly exacerbate antibiotic-resistance problems.

### *D. Evaluation of FDA's Regulation of the Use of Antibiotics in Aquaculture*

As discussed above, the CVM must approve any drug under a NADA before it may be used in agriculture or aquaculture. In order to receive CVM approval, manufacturers must demonstrate, through carefully enumerated methods, that their drugs are both safe and effective.[76] "Safe," according to FDA policy, means "there is reasonable certainty of no harm to human health from the proposed use of the drug in food-producing animals."[77] In the past, the CVM approved a number of antibiotics for use in agriculture and aquaculture before the danger of antimicrobial resistance

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IN AQUACULTURE], *available at* http://www.natlaquaculture.org/pdf/CDC%20Response%20to%20the%20Record.pdf (last visited Aug. 19, 2004).

[73] Sandaa, *supra* note 66, at 1065.

[74] Glenn Rhodes et al., *Distribution of Oxytetracycline Resistance Plasmids between Aeromonads in Hospital and Aquaculture Environments: Implication of Tn1721 in Dissemination of the Tetracycline Resistance Determinant Tet A*, 66 APPLIED & ENVTL. MICROBIOLOGY 3883, 3889 (2000).

[75] Midtvedt, *supra* note 18, at 306.

[76] General Provisions for New Animal Drug Provisions, 21 C.F.R. § 514.1 (2003).

[77] GUIDANCE DOCUMENT #152, *supra* note 14, at 2.

was fully appreciated. Accordingly, the agency recently initiated a review of its drug approval policies regarding antimicrobial agents. The findings and new policy arising out of that review currently appear in *Guidance for Industry #152: Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern.*[78] This new proposed policy advocates several important steps toward stopping the spread of antibacterial resistance.

The most important regulatory decision included in the new guidance document is the FDA's stated intention to pay special attention to "the potential human health impact of all classes of antimicrobial new animal drugs intended for use in food-producing animals."[79] In order to actualize this new emphasis, the FDA must consider not only whether new antimicrobial animal drugs will create antibiotic-resistant bacteria, but it must also pay attention to pathogen load effects (the total amount of bacteria found in food-producing animals) and the effects of drug residues on human intestinal microflora in order to determine whether unprocessed antibiotic residues can directly create resistance in bacteria found inside the human body.[80]

The FDA will focus on the pathway by which antibiotic-resistance is transferred through ingestion of bacteria found in animals used for food.[81] The technical methodology outlined in the new guidance document demands that the applicant conduct three assessments: a release assessment, an exposure assessment and a consequences assessment. Pursuant to the assessments, the applicant must then determine whether a "low," "medium" or "high" risk exists with respect to each assessment.

The release assessment asks the applicant to describe the probability that use of the new animal drug will result in the emergence of antibiotic-resistant bacteria in the animal. This assessment should consider the characteristics of the product, its intended use, possible mechanisms of antibiotic-resistance in target bacteria, transferability of antibiotic-resistance, specific antibiotic-resistance selection pressures and several other factors.[82]

The exposure assessment requires the applicant to evaluate the likelihood that humans will be exposed to the antibiotic through

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[78] *Id.*
[79] *Id.* at 3.
[80] *Id.* at 2-3.
[81] *Id.*
[82] *Id.* at 10-14.

specific pathways. The applicant should consider the probability of exposure to antibiotic-resistant bacteria through particular food commodities as well as the strength of any resistance that a consumer may encounter.[83]

The consequence assessment mandates that the applicant consider the consequences of exposure based primarily on the importance of the specific antibacterial drug to human medicine.[84]

After arriving at a risk estimation of "low," "medium" or "high" for each of the three assessments, the guidance document provides a table used to calculate the total risk estimation of "low," "medium" or "high."[85] The total risk estimation is then used to determine whether new antibacterial drugs are approved and, if they are, under what circumstances they can be used. In *Guidance Document # 152*, the FDA provides the following table outlining likely limitations placed on the use of antibacterial drugs with various levels of risk:

TABLE 5. EXAMPLES OF POTENTIAL RISK MANAGEMENT STEPS ASSOCIATED WITH THE APPROVAL OF NEW ANTIMICROBIAL ANIMAL DRUGS IN FOOD-PRODUCING ANIMALS BASED ON THE LEVEL OF CONCERN (1, 2 OR 3) AS ESTIMATED BY A QUALITATIVE ANTIMICROBIAL RESISTANCE RISK ASSESSMENT.

| | Category of concern | | |
|---|---|---|---|
| Approval conditions | Category 1 | Category 2 | Category 3 |
| Marketing Status[1] | Rx | Rx/VFD | Rx/VFD/OTC |
| Extra-label use (ELU) | No ELU | Restricted in some cases[3] | ELU permitted |
| Extent of use[2] | Low | Low, medium | Low, medium, high |
| Post-approval monitoring | NARMS[4] | NARMS | NARMS |
| Advisory committee review considered | Yes | In certain cases[3] | No |

[1] Prescription (Rx), Veterinary Feed Directive (VFD), Over-the-counter (OTC).
[2] *See* Table 4 [in *Guidance Document # 152*] for characterization of extent of use.
[3] These risk management steps may be appropriate for certain Category 2 drugs that were ranked high for consequence assessment *and* ranked high for release *or* exposure assessment.[86]
[4] A designation of "NARMS" indicates new antimicrobial animal drugs would be subject to post-approval monitoring through the National Antimicrobial Resistance Monitoring System (NARMS).[87]]

[83] *Id.* at 14-18 (see Table 2, appearing at page 17 of the document, in order to understand how these two different factors should be considered when determining whether to designate the risk of exposure as high, medium or low).

[84] *Id.* at 19 (see Appendix A of the guidance document for a general ranking of different classes of antibiotics and their relative importance to human medicine).

[85] *Id.* at 20-21.

[86] *Id.* at 25.

[87] *Id.*

An antibiotic medication meeting the other NADA requirements for approval with a "high," "medium" or "low" risk would receive approval as a Category 1, Category 2 or Category 3 drug respectively. These new approval policies most likely represent the FDA's current and future approach to managing new antibacterial agents for use in agriculture and aquaculture. Furthermore, the FDA intends to apply these review procedures to previously approved antibiotic agents if their dangers to human health through antibacterial resistance have not yet been adequately considered.[88]

Despite the FDA's significant efforts to try and control the ballooning problem of antibiotic-resistant bacteria, a number of issues still cause concern, specifically within the realm of aquaculture. The FDA should formally commit to reexamine the use of currently approved aquaculture antibiotics in a regimented manner to ameliorate the problem.

If the CVM does reexamine the use of antibiotics in aquaculture, its new policies will require significant regulatory reform. With the previously discussed scientific studies in mind, it is likely that the antibiotics currently used at fish farms would be given a "high" rating under the release analysis. Resistant bacteria are present or are forming in fish and the sediment surrounding aquaculture sites. This resistance has been shown to be transferable.[89] These two facts are enough to earn a "high" rating according to the criteria stated in the release analysis. It is also likely that these antibiotics would receive a "high" rating for the exposure assessment, given evidence indicating that antibacterial resistance spreads to humans from aquaculture through ingesting or handling farmed fish.[90] Although it is difficult to be certain of the risk ratings that current aquaculture antibiotics would receive without performing the kinds of studies mandated by the FDA, an exposure assessment rating of "high" seems reasonable given the direct use of fish from aquaculture in foodstuffs consumed by humans. Regarding the consequence assessment, tetracyclines are given a ranking of "medium" by the CVM.[91] Modern medicine continues to consider tetracyclines to be of considerable importance.[92]

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[88] *Id.* at 3-4.

[89] *See* discussion *supra* Part I.C.

[90] ANTIBIOTIC USE IN AQUACULTURE, *supra* note 72, at 3.

[91] GUIDANCE DOCUMENT #152, *supra* note 14, at 32.

[92] Midtvedt, *supra* note 18, at 307.

According to the CVM's method of calculating a new antibiotic's total risk estimation, a designation of "high" risk for release, "high" risk for exposure and "medium" risk for consequence would earn current aquaculture medications a total risk designation of "high" and likely lead to their classification as Category 1 drugs.[93] Assuming the validity of this analysis, current aquaculture antibiotics should only be available by prescription (not over-the-counter), should be used sparingly and should not fall under the allowances of extra-label use provisions. Even if current aquaculture drugs were given a total risk estimation of "medium," their use should still be strictly curtailed. According to the principles of the FDA's latest proposed policies, the CVM should reexamine and more strictly regulate the current and future use of antibacterial agents in the aquaculture industry.

Under the FDA's proposed guidelines, the use of antibiotics in aquaculture would probably be curtailed to some degree; however, other industry observers suggest that use of these medications should be sharply curtailed. Midtvedt and Lingass suggest that only drugs meeting the following requirements should be used in fish farming:

1. the compound must be rapidly broken down to non-toxic components;
2. it should not give rise to a plasmid-mediated resistance;
3. it should not give rise to any cross-resistance to other groups of antimicrobial drugs; and
4. it should not be medically important.[94]

Tetracyclines do not meet any of these requirements,[95] and according to Midtvedt and Lingass's recommendations, should not be used in aquaculture. Robyn and Carol Goforth maintain that sub-therapeutic applications of antibiotics should not be administered anywhere in agriculture, because such treatments add to the total amount of antibiotics administered and create ideal conditions for the development of resistant bacteria.[96] The Goforth article also presents a cost/benefit analysis on a proposed prohibition of sub-therapeutic treatments of antibiotics in agriculture, and finds that the advantages of prohibition outweigh its expenses.[97]

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[93] GUIDANCE DOCUMENT #152, *supra* note 14, at 21.

[94] Midtvedt, *supra* note 18, at 307.

[95] *Id.*

[96] Goforth, *supra* note 6, at 64.

[97] *Id.* at 65-68.

It seems likely that a similar analysis would result in a comparable conclusion in the field of aquaculture. The CVM already prohibits the sub-therapeutic use of antibiotics both as a means of promoting fish growth and as a preventive health measure.[98] However, as mentioned earlier, industry observers maintain that, regardless of the CVM's regulations, aquaculturists continue to employ sub-therapeutic treatments of antibiotics for fish tranquilization and to affect reproduction and growth.[99] In order to prevent these offenses and to find drugs that would not cause significant harm, the FDA needs to restrict the use of antimicrobial agents in aquaculture to a greater degree than suggested by *Guidance Document # 152.* The CVM should consider prohibiting the extra-label use of antibiotics in fish farms in order to better prevent sub-therapeutic uses of these agents. The FDA should also revoke the OTC status of these antimicrobial medications, making them available by prescription only.

Antibiotic resistance is a growing threat to human health. As fish, animal and human pathogens become resistant to antimicrobial agents, modern medicine may lose its ability to fight serious bacterial diseases. Antibiotic use on farms and at aquaculture sites significantly contributes to the problem of antimicrobial resistance. To counter this growing threat, the FDA must carefully enforce policies to evaluate new antimicrobial drugs for animals and stringently apply these policies to current aquaculture practices as well. The CVM should curtail the use of antibiotic agents in aquaculture by reviewing their properties, classifying them as Category 1 medications, preventing sub-therapeutic applications and possibly prohibiting their extra-label use. Only by taking significant measures to more carefully regulate the use of antibiotics in aquaculture can the FDA fulfill its obligation to curb ever- increasing antimicrobial resistance and thus protect human health.

## III. FDA AND THE REGULATION OF TRANSGENIC FISH

### *A. Introduction*

In addition to the regulatory challenges created by the use of antibiotics in aquaculture, the FDA must also address the role of genetic engineering on the fish farm. The impact of genetic engineering on traditional agriculture has received significant attention, but an analysis of the impact on aquaculture is critical. Genetic

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98 EXTRA-LABEL GUIDE, *supra* note 47, at 2-5.

99 BENBROOK, *supra* note 53.

engineering has the potential to significantly benefit the modern farm. For example, transgenic plants that exhibit natural pesticides or resistance to chemical pesticides can increase productivity. Transgenic fruit with delayed ripening may result in fresher foods in grocery stores. Soybeans and other products can be genetically engineered to provide greater nutritional value.[100] While many exciting agricultural improvements are soon to be made, some have already hit grocery store shelves. In the year 2000, 38% of the corn crop, 57% of the soybean crop and 70% of the canola crop in the United States were expected to be produced from genetically engineered seeds.[101] In light of these developments, controversy has surrounded the introduction of genetically modified organisms (GMOs) into the marketplace. Consumer safety advocates, scientists and public interest groups raise concerns regarding the place of GMOs in our food supply. They question the presence of toxicity, allergens, increased antibiotic resistances and environmental impacts.[102] The FDA plays a crucial role in the genetic engineering controversy. It is responsible for ensuring food safety under the Food, Drug and Cosmetic Act (FDCA),[103] and its screening and labeling policies regarding GMOs have been closely scrutinized.

A debate about GMOs squarely focuses on aquaculture as the FDA is presently considering a controversial application to produce a genetically engineered salmon, a transgenic fish, for human consumption.[104] The approval process of the FDA should include a careful analysis of policy and the characteristics of the transgenic salmon. The FDA's handling of this crucial decision could have profound ramifications for the production and marketing of other genetically engineered animals in the near future.

### *B. Genetic Engineering Generally*

Farmers have been altering the genes of plants and animals for centuries. Until recently this was a very slow process. Prior to the

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[100] Michael A. Whittaker, *Reevaluating the Food and Drug Administration's Stand on Labeling Genetically Engineered Foods,* 35 SAN DIEGO L. REV. 1215, 1219-20 (1998).

[101] Kelly A. Leggio, *Limitations on the Consumer's Right to Know: Settling the Debate Over Labeling of Genetically Modified Foods in the United States,* 38 SAN DIEGO L. REV. 893, 905 (2001).

[102] *Id.* at 906-07.

[103] Federal Food, Drug and Cosmetic Act (FDCA), 21 U.S.C. §§ 301-395 (2003).

[104] Lester M. Crawford, D.V.M., Ph.D., Deputy Commissioner, U.S. Food and Drug Administration, Speech before the American Enterprise Institute (June 12, 2003), *available at* http://www.fda.gov/oc/speeches/2003/aei0612.html (last visited Aug. 19, 2004).

advent of modern genetic engineering, farmers were able to modify the characteristics of domesticated plants and animals only through selective breeding.[105] This process involved breeding organisms with desirable traits to create offspring with a combination of those traits. These traditional methods produced such advantageous qualities as higher productive yields and pest resistance.[106] However, breeders were faced with slow reproduction times and characteristics that, to some degree, were pervasive in a species.[107] Genetic engineering has remedied such hardships. Genetic engineering essentially works as follows: certain qualities in plants or animals are first traced to particular genes—the stretches of DNA that code for, or direct the production of, a particular protein.[108] Then, scientists select the desired genes and insert them into the genome of another organism, thus leading to the expression of the original trait in a new individual plant or animal.[109] This process eliminates the need to wait for slow natural reproduction and provides farmers with a greater pool of characteristics from which to draw. Genes can be inserted from one species into another; for example, from a fish into a tomato.[110] In many ways genetic engineering is similar to traditional breeding. It ultimately accomplishes the same goal of identifying specific desirable traits and ensuring that these traits appear in future generations. However, technological advancements, such as the acceleration of genetic change, the ability to use the characteristics of more far-reaching species and the creation of new pharmaceutical uses for animals (drug production, for example), concern genetic engineering opponents.

### *C. Concerns Regarding Genetic Engineering in Agriculture*

There are essentially five basic concerns regarding the use of genetic engineering in agriculture: allergenicity; toxicity; environmental impact; moral, ethical and religious objections; and possible undiscovered consequences of genetically engineered organisms.

The first objection concerns the potential for allergic reactions to genetically engineered agricultural products. While there is noth-

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105 Whittaker, *supra* note 100, at 1218.

106 Diane Thue-Vasquez, *Genetic Engineering and Food Labeling: A Continuing Controversy*, 10 SAN JOAQUIN AGRIC. L. REV. 77, 81 (2000).

107 *Id.*

108 Leggio, *supra* note 101, at 902.

109 *Id.* at 904.

110 *Id.*

ing unique about DNA inserted through genetic engineering that makes it inherently allergenic, some fear exists that genes from foods that do cause allergic reactions could be inserted into otherwise safe foods. Consumers may then unknowingly ingest allergenic foods.[111] There has already been one case that demonstrates the validity of this fear. A scientific study conducted by the *New England Journal of Medicine* recently demonstrated that when certain genes from Brazil nuts were inserted into soybeans to improve nutritional content, people with nut allergies had significant reactions.[112] In addition to concerns about transplanting known allergens into other foods, there is concern that imprecise insertion of a particular gene into a new genome could create previously undocumented allergens.[113] There have not yet been any scientifically recorded cases of new allergens created through genetic engineering, but such a scenario remains a possibility.[114] Approximately ten percent of the adult population suffers from food allergies, so concerns about allergens are significant.[115] Because of the risk of possible allergic reactions, the FDA should screen GMOs for potential allergens and label products that carry an allergenic risk.

The second fear regarding genetically engineered food concerns the presence of toxins. Many plants currently being genetically engineered for human consumption are created with increased levels of inherent natural toxins to deter pests.[116] These elements pose a human health risk even greater than those from traditional pesticide residues.[117] Toxicity may especially affect segments of the population that eat large amounts of the same genetically engineered foods.[118] Although fears regarding toxicity seem largely speculative, concerns may be sufficient to warrant toxicity screening.

The third objection to genetically modified crops relates to the possible ecological impact of these organisms. The principal concern is that genetically modified material will spread to natural plants, animals and/or other organic or non-GM farmed species.

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111 Whittaker, *supra* note 100, at 1221.

112 Julie A. Nordlee et al., *Identification of a Brazil-Nut Allergen in Transgenic Soybeans*, 334 NEW ENG. J. MED. 688, 688 (1996).

113 Susan D. Borowitz, *Biotech Breakdown*, TERRAIN (Summer 2000), *available at* http://www.i-sis.org.uk/terrain.php (last visited Aug. 25, 2004).

114 Leggio, *supra* note 101, at 907.

115 Thue-Vasquez, *supra* note 106, at 93.

116 *Id.* at 97.

117 *Id.*

118 *Id.*

This issue recently became prominent when it became known that genetically modified seeds from a Monsanto strain of GM corn were inadvertently mixed with seeds used for organic farming.[119] The transfer of genetically modified material can frustrate the intentions of organic farmers, and causes further concern because characteristics like resistance to certain herbicides or pests may also be transferred. These qualities may have negative environmental impacts in their own right.

Today the most common forms of GMOs on the market are those known as "Round-up Ready."[120] These crops are engineered to be resistant to the herbicide glyphosate, known as Round-Up, and their use enables farmers to apply more of the herbicide to their field without endangering their crops.[121] Increased use of herbicides leads to increased resistance to herbicides in weeds which, in turn, necessitates the use of even more herbicide.[122] Meanwhile, herbicides themselves can leave residues in food, end up in ground water and endanger wild animals.[123] Similar arguments to those against the use of genetically engineered herbicide resistant crops also apply to the use of organisms that are resistant to pests or pesticides.[124] Many genetically engineered characteristics intrinsically threaten the environment and further transfer their properties to non-genetically engineered species.[125] While all of these problems are serious, they are not of principal concern to the FDA.[126] Other agencies such as the EPA and the USDA bear primary responsibility to make sure that agricultural activities are not a threat to the environment.[127] However, in certain situations, such as when it evaluates a NADA or completes a required Environmental Assessment, the FDA needs to consider environmental

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119 JOSEPH MENDELSON, III, CENTER FOR FOOD SAFETY, COMMENT ON USDA/APHIS ENVIRONMENTAL ASSESSMENT ACCOMPANYING APHIS DECISION ON MONSANTO PETITION 01-137-01P SEEKING A DETERMINATION OF NONREGULATED STATUS FOR Bt *cry3Bb1* INSECT RESISTANT CORN LINE MON 863 (May 13, 2002), *available at* http://www.centerforfoodsafety.org/pubs/commentsmonsantocornrootworm5.13.2002.pdf (last visited Aug. 9, 2004).

120 Thue-Vasquez, *supra* note 106, at 100.

121 *Id.*

122 *Id.*

123 *Id.* at 98-99.

124 *Id.* at 102.

125 Whittaker, *supra* note 103, at 1220-21.

126 *Id.* at 1221.

127 *Case Study No. I. Growth-Enhanced Salmon*, CEQ/OSTP ASSESSMENT: CASE STUDIES OF ENVIRONMENTAL REGULATION FOR BIOTECHNOLOGY 1, 10-13 [hereinafter *Case Study*], *available at* http://www.ostp.gov/html/ceq_ostp_study2.pdf (last visited Aug. 18, 2004).

impacts. Considering the circumstances mentioned above, potential transfers of genetically modified characteristics and possible interactions between GMOs and the natural environment should be serious concerns to the FDA in regulatory proceedings.

The fourth area of concern regarding genetically modified organisms does not relate to consumer or environmental safety issues *per se*, but to non-utilitarian objections to genetic techniques. Many people are opposed to GMOs regardless of their safety levels.[128] Some theologians have stated that tampering with God's creations through genetic engineering is morally wrong.[129] Furthermore, in some religious traditions, it is a violation of doctrinal law to eat certain foods; mixing the genes from one organism into another could make compliance with such religious laws impossible.[130] Many animal rights supporters, such as People for the Ethical Treatment of Animals (PETA), feel that it is wrong to manipulate an animal's genes in the service of human needs.[131] Finally, there are many people, regardless of their religious or philosophical opinions, who feel that genetic engineering is simply wrong and unnatural.[132]

Arguments can be made against all of the previously described positions. First, genetic engineering is arguably similar to selective breeding, which most people find inoffensive and which has progressed unhindered for centuries. Second, religiously-based opinions can cut both ways: one could argue that the teachings of the Book of Genesis that provide humankind with "dominion," "rule" or "complete authority" over plants and animals allow for genetic engineering technologies.[133] Many individuals will inevitably continue to have reservations regarding genetic engineering despite rational counterarguments, and it is virtually impossible to address all of these concerns in an objective, universal or scientific manner. Nonetheless, a secular federal agency should not consider sectarian religious doctrines in deciding whether or not to approve GMOs. If any of these beliefs or values are held by a significant

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[128] *See* Mark Sagoff, *Biotechnology and the Environment: Ethical and Cultural Considerations*, 19 ENVTL. L. REP. 10,520 (1989).

[129] Dorothy W. Bisbee, *Preparing for a Blue Revolution: Regulating the Environmental Release of Transgenic Fish*, 12 VA. ENVTL. L.J. 625, 641 (1993).

[130] *Id.*

[131] *Id.*; Carol Lewis, *A New Kind of Fish Story: The Coming of Biotech Animals*, FDA CONSUMER MAGAZINE, Jan.-Feb. 2001, at 4 [hereinafter *Fish Story*], *available at* http://www.fda.gov/fdac/features/2002/101_fish.html (last visited Aug. 25, 2003).

[132] *Id.*

[133] *Genesis* 1:26.

portion of society, then a ban or limitation on genetic engineering should be drafted in a congressional, rather than in an administrative, forum. While some argue that the FDA should consider these concerns with regard to *labeling* GMOs (as discussed below), non-utilitarian values should not determine whether to approve or screen genetically engineered foods.

A final objection to GMOs is manifest in all of the previous concerns. This final protest focuses on the perception that an inadequate knowledge base exists regarding possible consequences of genetic engineering, including unforeseeable allergic reactions, toxicity or environmental impacts that might result from our current practices. In considering the more than 50,000 comments gathered in response to the FDA's proposed labeling policy for GMOs in 2000, the Agency found that most of the concerns were directed at possible unknowns.[134] Some opponents of genetic engineering suggest that the FDA follow a precautionary principle according to which the FDA would not approve any GMO until proven to be 100% safe. Many new technologies or products, such as nuclear power or the pesticide DDT, seem safe at first but actually present significant dangers. Opponents of genetic engineering believe that adherence to the precautionary principle avoids significant risks posed by this type of product.[135] Observing the precautionary principle might be especially warranted in the case of genetic engineering because genes may spread and be transferred throughout the natural environment, and once they are expressed they cannot be "turned off."[136] However, others argue that no product can be demonstrated to be 100% safe and that the costs of delaying the development of genetic engineering overwhelm any benefits to be gained from stalling for additional testing.[137] While a complete prohibition of GMOs might be an extreme reaction, genetic engineering features many unknown elements and possible consequences. Arguably, the FDA should take extra steps in the screening process to demonstrate the safety of GMOs to the greatest reasonable extent possible, while not wholly sacrificing the potential benefits to be derived from genetic engineering.

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134 Leggio, *supra* note 101, at 907.

135 *Id.* at 908.

136 *See* Scott Anderson, *Who Needs Sex?*, SCIENCE FOR PEOPLE, May 20, 2004, *at* http://www.scienceforpeople.com/Essays/gene_transfer.htm (last visited Aug. 14, 2004).

137 Leggio, *supra* note 101, at 908-09.

### D. Overview of the FDA's Regulation of Genetically Modified Organisms

After considering all of the previous arguments, the FDA adopted a controversial position on the regulation of GMOs. Before evaluating that position, it is important to understand the basic statutory framework within which the FDA regulates. Under the FDCA[138], if a food is considered to be of "natural biological origin," then the only general requirement of the FDCA is that producers use good manufacturing practices and provide correct labeling.[139] A food of "natural biological origin" is defined as a food commonly consumed in the United States prior to 1958 and not modified by a process introduced after 1958.[140] If a food, such as a GMO, does not meet this definition, then it may be subject to additional regulation. A food may be prohibited if it is adulterated or if it carries any "poisonous or deleterious substance;"[141] or it may be strictly scrutinized if it contains a food additive or any unsafe substance that might reasonably be expected to affect the characteristics of the food.[142] A product avoids both of these types of regulation, however, if it has been approved as a Generally Recognized As Safe (GRAS) food.[143] A food may be recognized as GRAS if it was in common use prior to 1958 or deemed such by "experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food."[144]

In 1992, the FDA indicated that it would generally consider GMOs as GRAS; the fact that foods were produced with genetic engineering was not considered material.[145] Additionally, as the FDA does not anticipate any serious questions regarding the safety of GMOs, it has stated that it will allow producers of genetically modified foods to determine independently if their specific products should be given GRAS status.[146] Because of their GRAS status, genetically modified foods undergo little pre-market screening.

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138 Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§ 301-395 (2003).

139 Thue-Vasquez, *supra* note 106, at 83; *see also infra* Part IV for a discussion of labeling of GMOs.

140 FDCA, 21 U.S.C. § 321(s) (2003).

141 FDCA, 21 U.S.C. § 342(a)(2)(A) (2003).

142 FDCA, 21 U.S.C. § 321(s) (2003).

143 Thue-Vasquez, *supra* note 106, at 86.

144 *Id.* (discussing eligibility for classification as Generally Recognized As Safe under 21 C.F.R. § 170.30(a) (2003)).

145 Statement of Policy: Foods Derived From New Plant Variety, 57 Fed. Reg. 22,984, 22,990 (May 29, 1992).

146 Thue-Vasquez, *supra* note 106, at 86-87.

The only step required of GMO manufacturers before going to market is mandatory FDA consultation.[147] This consultation does not require any specific testing or screening mechanisms.[148] However, the FDA has reserved a right to initiate an enforcement action against any product that it discovers not to be GRAS; the manufacturers are responsible for ensuring that their product meets all of the safety requirements of the FDCA and are liable for their mistakes.[149] The FDA has not yet initiated any such enforcement proceeding against a GMO producer.

Although the FDA has not published any formal policy on the regulation of transgenic animals, indications from numerous publications signal that genetic modifications inserted into animals will be treated as drugs.[150] Genetic modifications to animals seem to receive slightly higher FDA scrutiny than genetic modifications to plants. When the manufacturer of a new animal drug, or in this case, a transgenic animal, wants to earn approval for the new product, the manufacturer must first submit an Investigational New Animal Drug Application (INADA) while conducting research and then a New Animal Drug Application (NADA) before using the product commercially.[151] For example, before being able to use recombinant bovine somatotropin (rBST) to increase milk production in dairy cows, manufacturers had to submit an NADA and await CVM approval.[152] To be approved, an NADA must show that the drug in question is safe and effective for its stated use.[153] Under the FDCA, "safety" refers to the "health of man or animal."[154] The FDA also includes environmental safety within its definition of "safety," if environmental impacts could directly or indirectly affect the safety of humans or animals.[155]

Environmental concerns, although not the chief focus of the FDA approval process, must also be considered by the Agency

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147 FDA consultation was made mandatory in 2000. Leggio, *supra* note 101, at 911.

148 *See* Statement of Policy: Foods Derived From New Plant Variety, 57 Fed. Reg. 22,984 (May 29, 1992).

149 *Id.* at 22,989.

150 Margaret Ann Miller and John C. Matheson, *Food Safety Evaluation of Transgenic Animals,* 9(2) FDA VETERINARIAN NEWSLETTER, Mar.-Apr. 1996, at 15, *available at* http://www.fda.gov/cvm/index/fdavet/1996/march96.html (last visited Aug. 25, 2004); *Case Study*, *supra* note 127, at 13.

151 *Case Study*, *supra* note 127, at 14.

152 *Id.* at 15.

153 General Provisions for New Animal Drug Applications, 21 C.F.R. § 514.1(b)(8) (2003).

154 21 U.S.C. § 321(u) (2003).

155 *Case Study*, *supra* note 127, at 14.

through an Environmental Assessment (EA) or an Environmental Impact Statement (EIS) as required by the National Environmental Policy Act (NEPA).[156] NEPA is the "basic national charter for protection of the environment."[157] The act is intended to "promote efforts which will prevent or eliminate damage to the environment and biosphere and stimulate the health and welfare of man."[158] The FDA is responsible under NEPA for conducting an EA to examine the environmental risks of any major federal action.[159] If the EA shows that there are significant effects related to public health, safety or the environment, under NEPA the FDA must also complete a more comprehensive environmental analysis in the form of an EIS.[160] If the EIS shows that approving a NADA could cause significant harm to the environment, the FDA requires, when appropriate, environmental safety instructions on the drug's label or certain precautions to mitigate environmental harms. The FDA can refuse approval if immitigable environmental impacts will affect human or animal health or safety.[161]

Finally, under the Endangered Species Act (ESA), the FDA must determine if approval of a NADA may affect endangered species and take measures to avoid, minimize or compensate for any impacts on those species.[162] Therefore, while environmental concerns are not normally considered part of the FDA's purview, there are a number of ways that the Agency must consider environmental issues during the approval process for a GMO.

Considering the concerns over genetically modified foods (e.g., allergenicity, toxicity, ecological impacts, non-utilitarian concerns and possible unknown impacts), it is easy to see why the FDA's current regulatory structure could be considered inadequate. Most GMOs are GRAS and consequently require almost no pre-market screening. Although the mandatory consultation process may reveal some problems and trigger additional FDA review, GMOs that contain allergens or higher levels of toxins may still slip into the market without due examination. Similarly, there are still

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156 *Id.*

157 Council on Environmental Quality: Purpose, Policy and Mandate, 40 C.F.R. § 1500.1 (2003).

158 National Environmental Policy, 42 U.S.C. § 4321 (2003).

159 Procedures for Implementing the National Environmental Policy Act, 33 C.F.R. § 230.7(a) (2003).

160 Categorical Exclusions for Environmental Analysis of Army Exclusions, 32 C.F.R. § 651.29 (2002).

161 *Case Study*, *supra* note 127, at 14-15.

162 *Id.* at 12.

many unknowns surrounding genetic engineering, and under the current regime the FDA does not always take the time to examine specific GMOs for hidden dangers.

Conversely, it seems that the NADA process, with its safety, effectiveness and limited environmental impact requirements, may provide adequate pre-market review to evaluate most concerns regarding genetically modified animals. Genetically engineered changes to animals are considered to be new drugs, and as such undergo a much more intensive screening process than comparable genetically engineered changes to plants. This process is now being tested by an application to market a transgenic fish.

### *E. The Transgenic Salmon*

In order to protect manufacturing trade secrets, the FDA does not disclose the filing of an INADA or NADA application.[163] Because the FDA regulates transgenic animals as new animal drugs, the public may not know about new GMOs until the FDA has already approved them for market. It is impossible to tell how many such transgenic animal drug applications the FDA is currently considering. However, one company, Aqua Bounty Farms, a subsidiary of A/F Protein, has publicly disclosed that it has filed an INADA for a new GMO; thus, the FDA can freely discuss this product and its regulatory status.[164] Aqua Bounty submitted the INADA and initiated research to fulfill the requirements of an associated NADA in order to market a transgenic salmon.[165]

Aqua Bounty's transgenic salmon is remarkable because of its increased rate of growth. Some claim that the altered fish can grow as much as ten to thirty times faster than a normal salmon at some points during its life span.[166] Dr. Choy Hew discovered the science behind the fish almost 20 years ago. Hew accidentally froze an aquarium full of pout, a type of flounder, in his lab. To his surprise, Hew found that the fish were still alive when thawed. Hew discovered that the pout had a gene that turned on and off the production of an anti-freeze protein. He isolated the on-off switch mechanism in this gene, altered it to remain in the "on" position and then connected it to a growth-stimulating hormone gene from a chinook

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163 General Provisions for New Animal Drug Applications, 21 C.F.R. § 514.11 (2003).

164 General Provisions for New Animal Drug Applications, 21 C.F.R. § 514.12 (2003).

165 *Case Study*, *supra* note 127, at 14.

166 Dan Bacher, *Sacramento USDA Ministerial Wild Salmon Fisheries Threatened by Genetically Engineered Fish*, DISSIDENT VOICE, ¶ 14 (June 16, 2003), *at* http://www.dissidentvoice.org/Articles5/Bacher_GE-Fish.htm.

salmon. Hew then inserted this genetic apparatus into the genome of an Atlantic salmon. These actions produced a line of transgenic Atlantic salmon that grow to market weight in only 18 months, compared to 24 to 30 months for a normal Atlantic salmon.[167] This new kind of fish could dramatically reduce time and costs of fish farmers in bringing salmon to market. However, as with other GMOs, a number of concerns exist regarding the production of the transgenic salmon and the FDA policies that will regulate that production.

The FDA has indicated that it would regulate the Aqua Bounty salmon in the same way as it would regulate a new animal drug.[168] According to the regulations described above, this means that the FDA must approve the transgenic fish before it can be marketed. In order to receive the FDA's approval, Aqua Bounty must demonstrate that its transgenic salmon is effective for its stated purpose and safe for humans, animals and the environment. There have already been some doubts raised as to whether Aqua Bounty Farms can meet this burden. First, questions have arisen as to whether the genetic modification on the Atlantic salmon actually results in increased growth.[169] The FDA should not approve the use of Aqua Bounty's transgenic salmon unless increased growth can be demonstrated. However, this concern seems like an elementary stumbling block. It is unlikely that Aqua Bounty would incur the cost of monumental administrative procedures, or that the FDA would publicize its current evaluations so extensively, if the transgenic salmon did not actually possess rapid growth characteristics. The most significant issues surrounding FDA approval of the transgenic fish will probably relate to its safety for humans, safety for animals and environmental impact.

Human safety concerns related to Aqua Bounty's transgenic salmon mostly involve fears of potentially undiscovered characteristics of the fish or consequences of its use. As yet, no scientific studies suggest that transgenic salmon pose any specific risk. No known allergens are being introduced into the Atlantic salmon, and the genetic manipulation to affect size does not trigger the

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[167] Lewis, *supra* note 131, at 1.

[168] CTR. FOR FOOD SAFETY, EXECUTIVE SUMMARY OF THE CENTER FOR FOOD SAFETY'S GENETICALLY ENGINEERED FISH LEGAL PETITIONS 1, *available at* http://www.centerforfoodsafety.org/pubs/execsummpetition5.9.2001.pdf (last visited Aug. 18, 2004).

[169] Robert H. Devlin et al., *Growth of Domesticated Transgenic Fish,* NATURE, Feb. 15, 2001, at 781 (stating that transgenic salmon do not necessarily grow faster than normal fish).

kind of toxicity questions raised by engineering certain kinds of resistance.

Even in the absence of documented hazards, fears still exist that inserting new genetic material into the salmon could result in mutations, novel proteins, unintended expression, creation of new allergens or toxicity.[170] People have never been exposed to many of the proteins created through genetic engineering, and these proteins could cause negative reactions.[171] Relatively little is known about the effects of genetic engineering; therefore the FDA should be careful to include allergenicity and toxicity tests in its human safety evaluation. However, unless something unexpected occurs, an FDA rejection of Aqua Bounty's salmon based upon human safety concerns appears unlikely. While increased testing is justified, the possible economic benefits of moving forward with GMOs should not be lost if test results provide no indication of danger.

The most serious concerns regarding the production of transgenic salmon relate to possible environmental effects. As discussed above, the FDA must regulate the environmental impacts of GMOs through the NADA approval process, as required by NEPA and possibly by the ESA. There are many environmental objections to the aquaculture industry even without the introduction of transgenic salmon. These objections include (1) algal build up under aquaculture sites due to nutrient fish feed and fish excretion,[172] (2) an increased occurrence of diseases in farmed fish,[173] (3)

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[170] Roberto Versola, *The Genetic Engineering Debate (v1.02)*, at 5 *available at* http://www.bwf.org/gedebate.html (last visited Aug. 19, 2004).

[171] Sarah L. Kirby, *Genetically Modified Foods: More Reasons to Label Than Not,* 6 DRAKE J. AGRIC. L. 351, 360-61 (2001).

[172] *See* Craig Emerson, *Aquaculture Impacts on the Environment,* CULTURE IMPACTS ON THE ENVIRONMENT: HOT TOPICS SERIES, CAMBRIDGE SCIENTIFIC ABSTRACTS (Dec. 1999) (stating "[a]n increasingly significant effect of intensive fish culture is eutrophication of the water surrounding rearing pens or the rivers receiving aquaculture effluent. Fish excretion and fecal wastes combine with nutrients released from the breakdown of excess feed to raise nutrient levels well above normal, creating an ideal environment for algal blooms to form. To compound the problem, most feed is formulated to contain more nutrients than necessary for most applications . . . . [O]nce the resulting algal blooms die, they settle to the bottom where their decomposition depletes the oxygen. Before they die, however, there is the possibility that algal toxins are produced. Although any species of phytoplankton can benefit from an increased nutrient supply, certain species are noxious or even toxic to other marine organisms and to humans."), *available at* http://www.csa.com/hottopics/aquacult/overview.html (last visited Aug. 14, 2004).

[173] Wild Salmon Rapidly Being Wiped Out by Fish Farm Diseases, Escapes, EARTH CRASH EARTH SPIRIT, ¶ 2 (Feb. 14, 2001) (quoting Professor Trygue Poppe as follows: "I think we have seen in recent years a number of diseases that we could call productional diseases, that is, kind of man-made diseases, made through the way we handle these fish and the way we farm them. There are some bacterial, some viral and some parasitological

an increased occurrence of diseases in wild fish,[174] (4) the interference of netpens with the natural ecosystem[175] and (5) epidemic outbreaks of sea lice, affecting both farmed and wild salmon.[176] All of these environmental concerns apply to the farming of transgenic fish as well. However, the greatest environmental concern regarding transgenic fish is that they will be released into the open ocean and disrupt the natural ecosystem. Fish will almost inevitably escape from their netpens.[177] In fact, there have been several instances of unintentional mass releases of hundreds of thousands of salmon from aquaculture sites.[178] Escapes can be caused by operational errors, containment failures caused by heavy weather events, or damage from ships or predators.[179] Accordingly, if the FDA allows Aqua Bounty Farms to produce transgenic salmon, it is, more than likely, also allowing the introduction of thousands of GM fish into the natural ecosystem.

Releasing transgenic fish into the environment could be problematic because of their potential to interact and interbreed with

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diseases. We see the diseases in wild fish as well, but never to such an extent and such seriousness as in farming conditions, because the farming condition itself caters in a way for infectious diseases to occur."), *at* http://www.eces.org/articles/static/98213040084031.shtml (last visited Aug. 25, 2004).

174 Alexandra Morton, *Whales Don't Eat Farm Salmon, Why Should We?*, NATURAL LIFE MAGAZINE, Nov.-Dec. 1997, at 1-2, *available at* www.life.ca/nl/58/fishfarming.html (last visited Aug. 14, 2004).

175 INKA MILEWSKI, CONSERVATION COUNCIL OF NEW BRUNSWICK, IMPACTS OF SALMON AQUACULTURE ON THE COASTAL ENVIRONMENT: A REVIEW, *available at* http://epbea.org/downloads/mmilewski.pdf (last visited Aug. 14, 2004).

176 Graham Shaw, *Sea Lice* (stating "[w]ith the advent of sea cage fish farming the presence of sea lice has a more sinister connotation in that unprecedented levels of sea lice infestation has accompanied the collapse of sea trout populations in areas where fish farms are present . . . . [H]eavily infested sea trout return prematurely to fresh water, perhaps in an effort to shed the lice which causes them severe head and fin damage and ultimately kills them . . . . [I]t has been clearly established that sea lice infestation from fish farms is the primary cause of sea trout population collapses since sea trout populations will begin to recover if the farms are fallowed or if they control lice to very low levels during the crucial March - May period while sea trout and salmon are migrating to sea."), *available at* http://www.loughswilly.com/Facts/Sealice.htm (last visited Aug. 19, 2004).

177 Eric M. Hallerman and Anne R. Kapuscinski, *Ecological Implications of Using Transgenic Fishes in Aquaculture,* 194 INT'L COUNCIL FOR EXPLORATION OF THE SEA MARINE SCI. SYMP. 56, 59 (1992).

178 Letter from Tracie Letterman, Fish Program Director, Center for Food Safety, to Marta Jordan, Office of Water, Engineering and Analysis Division, U.S. Environmental Protection Agency, 2 (Jan. 8, 2003) (stating "Between 1987 and 1997, over a half-million Atlantic salmon escaped off the West Coast of North America"), *available at* http://www.centerforfoodsafety.org/pubs/CommentsEPAnon-nativefish1.8.2003.pdf (last visited Sept. 15, 2004).

179 *Case Study*, *supra* note 127, at 23.

native fish populations.[180] This interaction could threaten many endangered species, including the Atlantic salmon.[181] Interbreeding transgenics that escape can cause a rapid loss of genetic variation and reduce adaptability to native ecosystems.[182] In addition to the simple genetic disruption of endangered wild salmon, which is problematic in its own right and already occurs with the farming of non-native species, several scientific studies have concluded that because of specific characteristics, Aqua Bounty's salmon could quickly cause the extinction of natural populations.[183] This is known as the "Trojan gene effect."[184] Aqua Bounty will attempt to sterilize transgenic salmon to minimize this type of risk. Although current methods provide high levels of reproductive sterility, they are not 100% effective.[185] Escaped non-sterile transgenic salmon could cause the extinction of endangered natural species. Even if transgenic fish do not interbreed with natural fish populations, they could still cause harm by aggressively competing for limited food supplies as mega-predators.[186] Aqua Bounty's transgenic fish will have environmental impacts that endanger the safety of many animals. These environmental concerns seem to violate the environmental safety requirements of the NADA process.

The FDA is aware of the environmental concerns regarding Aqua Bounty's transgenic salmon.[187] In fact, the FDA bears a significant responsibility in evaluating the environmental impact of transgenic fish. While other agencies like the EPA and FWS take a hand in regulating aquaculture, and Aqua Bounty Farms is responsible for illustrating environmental safety under the NADA, the FDA itself must complete an Environmental Assessment, an Environmental Impact Statement and consider the ESA.[188] It reflects well on the screening process for transgenic animals that the FDA is prepared to take into account environmental ramifications when

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[180] *Id.* at 24.

[181] U.S. FISH & WILDLIFE SERVICE, THREATENED AND ENDANGERED SPECIES SYSTEM, (listing the Atlantic salmon, *Salmo salar,* as an endangered species), *available at* http://ecos.fws.gov/tess_public/TESSWebpage (last visited Aug. 25, 2003).

[182] *Case Study*, *supra* note 127, at 23.

[183] Tony Reichhardt, *Will Souped Up Salmon Sink or Swim?*, NATURE, July 6, 2000, at 10.

[184] William M. Muir & Richard D. Howard, *Possible Ecological Risks of Transgenic Organism Release When Transgenes Affect Mating Success: Sexual Selection and the Trojan Gene Hypothesis,* PROC. OF THE NAT'L ACAD. OF SCI., Nov. 1999, at 13,853-56.

[185] Crawford, *supra* note 104.

[186] *Id.* at 20-21.

[187] *Case Study*, *supra* note 127, at 18-24.

[188] *Id.* at 12-14.

approving GMOs. However, it remains to be seen if the FDA will approve Aqua Bounty's application to produce transgenic salmon and what limitations on production techniques might condition the approval. Under NEPA and the ESA, the FDA could approve transgenic salmon while placing certain constraints on Aqua Bounty Farms in an attempt to limit environmental impacts.[189] One such technique might require Aqua Bounty Farms to sterilize their transgenic salmon to prevent breeding with natural populations,[190] but again, sterilization techniques are not 100% effective.[191] Additionally, even if the transgenic salmon could be effectively sterilized, individual sterilized fish would still cause environmental impacts when released into the environment as discussed above. Another option is to require Aqua Bounty Farms only to raise their transgenic fish in enclosed, land-based sites such as large tanks or man-made ponds. Aqua Bounty is currently making use of such facilities to raise and test their unapproved transgenic salmon.[192] With the previous environmental concerns in mind, the FDA is legally required under the NADA requirements, NEPA and the ESA to prohibit transgenic salmon from disrupting the natural environment and threatening endangered species.[193] It seems that the only possible way for the FDA to fulfill its environmental protection obligations is either to deny Aqua Bounty's NADA or require that transgenic salmon be raised in land-locked facilities.

### *F. Conclusion*

The use of genetic engineering is on the rise in agriculture. Farmers currently use genetically modified species in products to increase nutritional content, create herbicide resistance and increase shelf life. Applications of this technology will probably continue to grow in quantity and breadth. The next GMO to appear on grocery store shelves could be the transgenic salmon. However, a number of concerns persist regarding the use of genetic engineering technologies. Consumer advocates and scientists raise objections relating to allergenicity, toxicity, environmental concerns, moral, religious and ethical considerations, and unknown effects. It is unclear whether the FDA's current policies of recog-

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189 *Id.* at 15.
190 *Id.* at 31.
191 Bisbee, *supra* note 129, at 637.
192 *Case Study*, *supra* note 127, at 1.
193 *Id.* at 17.

nizing most GMOs as GRAS, compelling mandatory consultation sessions with industry and requiring some products to undergo NADA approval as animal drugs are sufficient for protecting public health. In the case of Aqua Bounty's application to market a transgenic salmon, the screening requirements seem adequate regarding limited fears of allergenicity, toxicity and potential unknown factors. However, it remains to be seen whether the FDA will abide by the NADA environmental safety requirement, NEPA and the ESA to uphold its public protection obligations. In order to effectively control the environmental impact of transgenic salmon, the FDA should consider either preventing their production altogether or requiring that they be raised in land-locked facilities. Time will tell whether the pre-market screening process for transgenic salmon will reflect these conclusions or signal an ominous future for the regulation of genetically modified food products.

## IV. Labeling of the Transgenic Salmon

### *A. Introduction*

If the FDA decides to approve Aqua Bounty's application to market genetically engineered salmon, even with some limitations on production techniques, the FDA must still address the question of consumer labeling. Many critics of genetic engineering demand that GMOs be removed from our food supply until more research is done on safety issues. However, there are a number of other consumer advocates who simply want people to have the option to avoid GMOs; they want all genetically engineered foods to be labeled. The FDA has refused to compel GMO labeling, claiming that neither section 201(n) nor section 403(a) of the FDCA require the labeling of every genetically engineered product on the market. However, it seems that Aqua Bounty's transgenic salmon is different from previously approved GMOs; it could be the first genetically engineered product that the FDA requires to be labeled under the FDCA. Producers of non-transgenic fish can also act to give consumers a choice by labeling their products as being free of genetically modified substances. Alternatively, if the FDA decides not to compel transgenic salmon labeling under any current statute, individual states or Congress might pass consumer notification laws. It remains to be seen whether consumers will know when they are eating a transgenic super fish rather than a natural Atlan-

tic salmon, and if so, how any labeling requirements will be statutorily supported.

### *B. FDA's Current Labeling Policy for GMOs*

Critics of genetic engineering want GMOs to be labeled for the same reasons that they think the screening process should be more stringent. Many consumer advocates feel that the FDA is not going to adequately take into account allergenicity, toxicity, environmental impact, non-utilitarian objections and concerns regarding undiscovered hazards in its approval process of GMOs. They support GMO labeling so that they may easily avoid products containing GMOs.[194] However, if the FDA requires GMOs to be labeled as such, it must have a statutory justification for doing so. The FDA's relevant food labeling authority is found in sections 403 and 201(n) of the FDCA.[195] Parts of section 403 have been in effect for nearly a hundred years, but the current version of the section was adopted in 1938.[196] The purpose of section 403 is to prohibit false and misleading labeling and require that certain essential and material information appears on food labels.[197] Section 403 requires the name of the manufacturer of the food, the net weight and contents of the food, the ingredients used to create the food and the name of the food all to appear on the label.[198] Section 201(n) of the FDCA is ancillary to section 403 and gives the FDA power to prevent a label from being misleading by requiring information to appear on a label that is material and essential but is not otherwise compulsory.[199] The text of section 201(n) is as follows:

> [i]f an article is alleged to be misbranded because the labeling or advertising is misleading, then in determining whether the labeling or advertising is misleading there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to

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194 Whittaker, *supra* note 100, at 1222-24; Kirby, *supra* note 171, at 356-58.

195 FDCA, 21 U.S.C. §§ 321(n), 343 (2003) (FDCA §§ 201(n), 403 (2003)).

196 Fred H. Degnan, *Biotechnology and the Food Label: A Legal Perspective,* 55 FOOD DRUG L.J. 301, 302 (2000).

197 *Id.*

198 21 U.S.C. § 343(e), (g), (i) (2003) (FDCA § 403(e), (g), (i) (2003)).

199 Degnan, *supra* note 196, at 304.

> which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.[200]

There are two prongs of this section. The first part enables the FDA to require that any representations made regarding the product not mislead consumers, while the second requires the provision of "material" information relating to usual and customary product use. For example, the second prong of section 201(n) could require the manufacturer of a non-fruit juice containing product branded as "Fruit Juicy Popsicles" to state that the product actually does not contain any real fruit juice. In that example, the lack of any fruit juice in the popsicles is made material by the producer's branding. This second prong of section 201(n) functions to reduce the likelihood of misleading labeling. To date, the FDA has taken the position that the genetically modified character of a food product does not trigger any of the basic labeling requirements of section 403, nor is it material to the consequences of use under section 201(n).[201]

Under the FDCA, production methods, safety concerns, consumer demand or environmental ramifications generally connected to genetic engineering could each be an independent basis for the FDA to require GMOs to be labeled as such. However, the FDA has decided to treat genetically modified products just as it treats all other food products. The FDA has stated that it considers genetic engineering to be a simple extension of traditional farming methods.[202] The agency does not consider plant production techniques such as chemical or radiation-induced mutagenesis, protoplast fusion, embryo rescue, somoclonal variation or "any other method" of genetic engineering to be material information within the meaning of section 201(n).[203] Additionally, the FDA neither considers the introduction of GMOs without disclosure misleading, nor construes the disclosure of the presence of GMOs as falling under the "ingredients" labeling requirement.[204] Regarding safety concerns such as allergenicity or toxicity, the FDA deems GMOs as GRAS and does not consider them, as a class, to pose any special

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200 FDCA, 21 U.S.C. § 321(n) (2003).

201 Kirby, *supra* note 171, at 353-54.

202 Degnan, *supra* note 196, at 307.

203 Foods Derived from New Plant Varieties, 57 Fed. Reg. 22,984, 22,991 (May 29, 1992).

204 Degnan, *supra* note 196, at 306-07.

threat to consumers.[205] While, cultural, religious or ethical concerns can be a factor in the FDA's decision to label a product,[206] it has not to date heeded the call of consumer demand to label all genetically modified products. Finally, while environmental concerns could affect the FDA's decision to label a GMO as an instance of consumer demand, there is no indication that the FDA separately considers environmental impact as material information under sections 403 or 201(n). The FDA has decided that as a class, GMOs are not materially different from traditional agricultural products and do not require labeling under the FDCA for any reason. However, it is also clear that as with any kind of food, the agency will consider nutritional, safety and other specific material concerns when deciding whether or not to label an individual genetically modified product. The FDA will soon have to decide how to apply the requirements of sections 403 and 201(n) to Aqua Bounty's transgenic salmon.

### *C. Mandatory Labeling of Transgenic Salmon*

It is unlikely that section 403 of the FDCA would either mandate or justify labeling to identify transgenic salmon. While there is some chance that the FDA would require that transgenic salmon be given a new name for labeling purposes, it is unlikely that natural and transgenic salmon are different enough to be considered two separate food products.[207] Another possible reason for mandatory labeling is that Aqua Bounty's transgenic salmon contain significant levels of a growth hormone. It is possible that the FDA could mandate the inclusion of the growth hormone in the

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[205] Leggio, *supra* note 101, at 911. However, the FDA has asserted that if any GMO were shown to have allergic properties it would be labeled as such just like any other food product. *See* Degnan, *supra* note 196, at 308.

[206] Thue-Vasquez, *supra* note 106, at 90 (describing how the presence of protein hydrolysate, a protein derived from milk, is a material fact regarding labeling; the FDA deemed it material not only because of its effect on compositional and functional properties, but also because of dietary constraints observed by members of the public, some of which derive from religious doctrine).

[207] CTR. FOR FOOD SAFETY AND APPLIED NUTRITION, FOOD AND DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY: VOLUNTARY LABELING INDICATING WHETHER FOODS HAVE OR HAVE NOT BEEN DEVELOPED USING BIOENGINEERING 1, 2 (Jan. 2001) [hereinafter VOLUNTARY LABELING] (stating "[i]f a bioengineered food is significantly different from its traditional counterpart such that the common or usual name no longer adequately describes the new food, the name must be changed to describe the difference."), *available at* http://www.cfsan.fda.gov/~dms/biolabgu.html (last visited Aug. 25, 2003).

ingredients list.[208] However, this is also unlikely, given the traditional understanding of the term "ingredient." Thus, the FDA will probably not require transgenic fish to be labeled under section 403. Moreover, the second prong of section 201(n) probably will not be implicated. Aqua Bounty will probably be careful in its labeling to avoid misleading statements or any indication that its fish is not genetically engineered.

Yet it is possible that the first prong of section 201(n) could mandate the labeling of transgenic fish. Aqua Bounty's salmon are different from normal Atlantic salmon in many ways. While these differences may not be so extreme as to deem transgenic salmon a new food product, they may be significant enough to be considered material. First, Aqua Bounty's fish are different from other Atlantic salmon in that they grow many times faster.[209] While this difference is extreme, it is unlikely to be considered material because the speed at which a fish reaches its final size has little to do with the consequences of its use. The transgenic salmon's final size is identical to natural Atlantic salmon. Second, transgenic salmon can have deformed heads and jaws.[210] This may be more significant. Third, organoleptic differences between transgenic and normal salmon may be considered material. It is possible that Aqua Bounty's fish differs in taste, color, smell or texture when compared to a normal salmon. The only difference between the two kinds of fish currently known, however, is that the transgenic salmon has a different coloration; the increased growth hormone causes the transgenic fish to lose their dark vertical bars and develop a silver coloration earlier than normal salmon.[211] While differences do exist between transgenic and natural salmon, it is unlikely that these differences, even when viewed together, will be considered a material fact under section 201(n). However, the case for labeling transgenic fish is strengthened when evaluation of these differences is linked with strong consumer sentiment.

A consumer desire for information can determine whether or not the characteristics of a certain product are material to the extent that the product should be labeled under section 201(n). A

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[208] ENVIRONMENTAL MEDIA SERVICES, EMS REPORTERS' GUIDE TO GENETIC ENGINEERING IN AGRICULTURE 37-38, *available at* http://www.ems.org/biotech/media_guide_3.pdf (last visited Aug. 18, 2004).

[209] Lewis, *supra* note 131, at 3.

[210] ENVIRONMENTAL MEDIA SERVICES, GENETICALLY ENGINEERED SALMON, *available at* http://www.ems.org/salmon/genetically_engineered.html (last visited Aug. 18, 2004).

[211] OFFICE OF TECHNOLOGY ASSESSMENT, CONGRESS OF THE UNITED STATES, SELECTED TECHNOLOGY ISSUES IN U.S. AQUACULTURE 35 (1995).

key example is how consumer demand affected the FDA's choice to label irradiated food.[212] Although the organoleptic changes to irradiated food are minor, consumer demand made irradiation a material fact.[213] A vast majority of people believe that GMOs should be labeled.[214] As discussed above, there are many religious, ethical and moral reasons that certain people want to avoid genetically engineered products.[215] While a consumer right-to-know argument must be based on more than groundless fears or idle curiosity,[216] and the FDA has already decided that the numerous non-utilitarian objections to genetic engineering do not require all GMOs to be labeled,[217] there are real differences between transgenic fish and natural salmon. Deciding whether or not to label transgenic salmon is more like deciding to label irradiated foods than deciding to regulate all GMOs. With the real, albeit not overwhelming, differences between Aqua Bounty's salmon and natural fish in mind, the FDA should heed consumer demand and label the transgenic fish.

A final possibility for requiring the labeling of GM fish under section 201(n) involves a novel legal argument. Facts are considered to be material in their relation to "consequences which may result from the use of the article."[218] Consequences are the direct effects on a consumer resulting from eating a certain food.[219] How-

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[212] Irradiation in the Production, Processing and Handling of Food, 51 Fed. Reg. 13,376, 13,388 (April 18, 1986) (stating that "[t]he large number of consumer comments requesting retail labeling attest to the significance placed upon such information by consumers. Moreover, several comments argued irradiation of food altered the organoloepic properties of food thereby reducing its nutritional value. These changes in the food, the comments asserted, make the irradiation of the food a material fact that must be disclosed under section 403(a) and 201(n) of the Act.").

[213] *Id.* (stating that "[i]n determining whether labeling is misleading, the agency must take in to account the extent to which labeling fails to reveal material facts in light of representations made about the food or consequences that may result from the use of such food. Therefore, the agency must decide whether the changes in the organoloepic properties of irradiated foods constitute a material fact or *whether the information that a food has been irradiated constitutes information that is material to a consumer even if the organoleptic changes were not significant.*") (emphasis added).

[214] AMERICAN VIEWPOINT, GENETICALLY ENGINEERED FOOD STUDY 1 (2002) (stating that 88.4% of people polled said that they agree with the following statement: "[t]he federal government should require labels on all food products that have been genetically engineered." Over 68.3% of individuals polled said that they strongly agreed), *available at* http://www.centerforfoodsafety.org/pubs/OregonPollResult11.5.2002.pdf (last visited April 27, 2003).

[215] *See supra* Part III.C.

[216] *See* Indus. Dairy Foods Ass'n v. Amestoy, 92 F.3d 67, 73 (2d Cir. 1996).

[217] *Id.*

[218] FDCA, 21 U.S.C. §§ 321(n) (2000).

[219] Degnan, *supra* note 196, at 304.

ever, the FDA could also interpret this clause to refer to the consequences that would result from the manufacturing practices used in creating food that were enabled or encouraged by a consumer purchasing a specific product. A consequence of using transgenic salmon would be their continued production, thereby endangering the environment in all the ways discussed above. If the FDA interpreted section 201(n) in this way, it could consider as a "consequence" the environmental or economic impact of rearing transgenic salmon, which would easily qualify as material. The FDA could thus construe section 201(n) to require labeling to identify transgenic fish. This novel approach, however, does seem unlikely.

It appears that the choice whether or not to label transgenic fish as such belongs to the FDA. Based on the real, but not overwhelmingly significant, differences between normal salmon and Aqua Bounty's fish, strong consumer sentiment and a possible consideration of environmental ramifications, the FDA could justify requiring transgenic salmon labeling. The characteristics of the GM fish are not obviously dangerous to human health or otherwise so distinct that the FDA *must* label transgenic salmon. Yet a liberal interpretation of section 201(n) would support such a decision. The intent behind sections 403 and 201(n) is to prevent consumers from being misled about what foods they are eating, and consumers may feel misled if they unwittingly eat transgenic fish. Some individuals feel so strongly about genetically modified foods that where any difference exists, the FDA should enable consumers to make their own decisions. With such strong consumer demand for labeling in mind, the FDA should follow the precedent set by its decision to label irradiated foods and require Aqua Bounty's salmon to be labeled as genetically modified.

### *D. Voluntary Labeling of Non-Genetically Modified Fish*

Even if the FDA does not require transgenic fish to be labeled, there is a chance that consumers will be able to make an informed choice. The FDA has created a draft guidance for industry entitled *Voluntary Labeling: Indicating Whether Foods Have or Have Not been Developed Using Bioengineering.*[220] It is unlikely that producers of GMOs would volunteer the fact that their products have been created through genetic engineering when significant public apprehension exists regarding genetically modified foods. Unless

[220] VOLUNTARY LABELING, *supra* note 207.

compelled, Aqua Bounty Farms would probably not label its salmon as transgenic. However, manufacturers and farmers of natural products may very well take advantage of the FDA's guidance on this matter in labeling their products. Natural Atlantic salmon may be labeled as *not* being genetically engineered. However, according to the FDA's guidelines, manufacturers who want to claim that their products have not been genetically modified must be careful.[221] Section 201(n) requires that food labels not be misleading. The FDA asserts that "GM Free," for example, might be misleading as nearly all food products have some form of selective breeding in their genetic histories and could be construed as being genetically modified in a broad sense.[222] The FDA accordingly suggests that manufacturers use statements similar to the following to avoid such pitfalls: "[w]e do not use ingredients that were produced using biotechnology;" "[t]his oil is made from soybeans that were not genetically engineered;" or "[o]ur tomato growers do not plant seeds developed using biotechnology."[223] The label for non-GM Atlantic salmon might say "this salmon was not developed using biotechnology." However, the FDA also warns that manufacturers choosing to put such labels on their products must be careful not to imply that their products are better than GMOs if this is not the case; such a label would also be misleading. Natural aquaculturists and fishermen should avoid such statements. Finally, the FDA requires manufacturers to be able to substantiate any voluntary claim that they make.[224]

If the FDA does not require labeling and producers do not label voluntarily, consumers who wish to avoid transgenic salmon may buy salmon labeled "organic." According to the National Organic Program's new labeling requirements, any product marked organic will not be genetically modified.[225] However, organic foods are typically significantly more expensive than other products, so consumers must incur a high cost for their certainty.[226] Additionally, manufacturers wishing to put the label "organic" on their food must comply with a number of requirements.[227]

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221 *Id.* at 5.

222 *Id.*

223 *Id.* at 6.

224 *Id.* at 7.

225 National Organic Program, 7 C.F.R. § 205.2 (2004), *available at* http://www.ams.usda.gov/nop/NOP/standards/FullRegTextOnly.html (last visited Aug. 25, 2003).

226 Leggio, *supra* note 101, at 931.

227 National Organic Program, 7 C.F.R. § 205.300 (2004).

Voluntary labeling creates the possibility that consumers wishing to avoid genetically modified fish can do so even if the FDA does not require Aqua Bounty Farms to label their transgenic fish. However, a voluntary labeling scheme is far from ideal. Voluntary labeling does not ensure that consumers will be adequately informed. If a shopper encounters salmon in a grocery store without a "GM Free" label, the consumer will not know if it is transgenic or not. Furthermore, labeling has direct and indirect costs. A manufacturer must bear the risk that its label will not meet the FDA requirements and face possible regulatory action. Additionally, the vast majority of salmon currently on the market are not genetically engineered, and the producers of these salmon should not have to change their practices to inform consumers properly. A voluntary labeling scheme does not inform consumers as well or distribute costs as equitably as mandatory labeling of transgenic fish.

### *E. Statutory Reform*

In the end, the question whether or not the FDA should require transgenic fish to be labeled might very well become moot. It is possible that states or Congress will pass new laws requiring GMOs generally, or transgenic salmon specifically, to be labeled as such. Several bills that would require GMOs to be labeled have been introduced in Congress already. California Senator Barbara Boxer introduced the Genetically Engineered Food Right to Know Act to Congress in 2000.[228] This act would require mandatory labeling for all genetically modified foods and give new labeling regulation responsibilities to the FDA. Dennis J. Kucinich introduced similar legislation in the House of Representatives.[229] However, no bill on this issue has been passed into law. It is more likely that GM-labeling legislation will arise in at least one state. There already have been instances of such law making. In response to the FDA's NADA approval of rBST, Vermont passed a law requiring the labeling of any dairy products that came from rBST-treated cows.[230]

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[228] The Genetically Engineered Food Right-to-Know Act, S. 2080, 106th Cong. § 2 (2000), *available at* http://www.foe.org/safefood/boxer-s2080.htm (last visited Aug. 25, 2004).

[229] *Id.*

[230] Indus. Dairy Foods Ass'n v. Amestoy, 92 F.3d 67, 73 (2d Cir. 1996).

Yet any such constraint on free commercial speech must pass the four-part test created in *Central Hudson Gas & Electric Corp. v. Public Services Commission of New York*:[231]

1. the expression is not protected under the First Amendment (speech is unlawful and misleading);
2. a substantial government interest can be identified;
3. the regulation "directly advances" the asserted interests; and
4. the regulation is "not more extensive than is necessary to serve that interest."[232]

The Vermont rBST labeling law did not pass this test.[233] The Second Circuit Court of Appeals found that Vermont did not demonstrate a "substantial government interest."[234] The only reason that Vermont gave for the legislation was to serve a strong consumer interest and the public's right to know. This rationale was found insufficient to overcome the dairy farmers' interest in free commercial speech.[235]

Nevertheless, a state likely could craft a law requiring the labeling of transgenic salmon that would pass constitutional muster. A state could argue that the government interest lies in protecting the environment, serving the consumer interest, and preventing economic harm to local fisheries and natural aquaculture sites. Additionally, a law requiring transgenic fish to be labeled would be more likely to succeed than the Vermont law discussed above because GM salmon are distinguishable from natural fish, while rBST milk is impossible to differentiate from normal milk. While the third and fourth elements of the *Central Hudson* test might pose some difficulty in developing new laws, a carefully crafted state statute could probably overcome these requirements. Whether or not the FDA requires Aqua Bounty's fish to be labeled, consumers may not have to depend on voluntary labeling if state legislatures choose to act.

Critics of genetic engineering feel that GMOs should be labeled so that individuals can avoid these products if they so desire. Despite significant consumer pressure, to date the FDA has not required any genetically modified food product to be labeled. The FDA has declared that, as a class, there is no reason under either

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231 447 U.S. 557, 566 (1980).
232 *Id.*
233 *Amestoy*, 92 F.3d at 74.
234 *Id.* at 73.
235 *Id.* at 74.

section 403 or section 201(n) of the FDCA to require that GMOs be labeled. The Agency feels that there is generally no material difference between genetically modified and natural foods. However, there is some possibility that the FDA will elect to label transgenic fish. Aqua Bounty's salmon are different from natural Atlantic salmon. Coupled with strong consumer interest, this difference should provide a material reason to label the new fish under section 201(n). If the FDA fails to take such action, consumers will have to depend on either voluntary labeling or new legislation in order to avoid genetically modified salmon. The FDA should act to protect consumer interests.

## V. Conclusion

The FDA should reexamine its regulation of aquaculture. The problems of ever-increasing antibiotic resistance and the development of genetic engineering technologies pose special problems that require agency supervision. The use of antibiotics in aquaculture contributes to the existence of resistant strains of bacteria that could cause serious human health problems. Antibacterial resistance that develops in either fish or sediment bacteria can be transferred to human pathogens and make standard medical treatments less effective. In order to fight this problem, the FDA should apply the review procedures outlined in *Guidance Document #152* to drugs currently used in aquaculture. In line with this proposed policy, the FDA should prevent sub-therapeutic use of antibiotics and probably should prohibit the extra-label use of these drugs.

In the near future, the FDA must also consider how to regulate the introduction of transgenic fish into the aquaculture industry. There are many fears regarding the use of GMOs in agriculture, including concerns over human health and safety, environmental ramifications and moral, ethical and religious objections. All of the concerns shaping agriculture regulation apply to the developing aquaculture industry as well. With regard to Aqua Bounty's transgenic salmon, environmental impact and non-utilitarian concerns are the considerations that most support FDA regulation. In accordance with its pre-market review requirements under the NADA process, NEPA and ESA, the FDA should either refuse to approve the application to market transgenic salmon or approve their production under limited circumstances. Moreover, if the FDA does allow genetically modified fish to be sold, it should ensure that they are properly labeled. Under section 201(n) of the FDCA, the FDA should evaluate the real differences between

transgenic salmon and natural fish, consider consumer demand and find that there is a material reason to provide consumers with information regarding genetic engineering. The FDA's voluntary labeling guidelines and possible future legislation may alert consumers to the presence of transgenic salmon, but, by requiring such notice, an FDA labeling requirement would be the most ideal system. The fish farm should not be ignored. The FDA must scrutinize the aquaculture industry more closely in order to prevent serious human health and environmental problems in the future.