



W051: Update on the Regulatory Journey of the AquAdvantage Genetically-Engineered Salmon

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"The mission of the animal genomics and biotechnology extension program is to provide broad, science-based extension programming on the uses of animal biotechnologies in livestock production systems."

<http://animalscience.ucdavis.edu/animalbiotech>





Salmon



- 1996: World farmed salmon production (mostly Atlantic salmon) first exceeded wild salmon harvest
- Americans consume an average of about 0.28 MMT of salmon annually
 - $\frac{1}{3}$ was wild Pacific salmon and $\frac{2}{3}$ was imported, farmed Atlantic salmon
 - 99% of the Atlantic salmon consumed in the US is farmed – almost all from ocean pen aquaculture operations in Canada, Chile, Norway and Scotland
- Atlantic salmon can not interbreed with Pacific salmon – they are different species





There are three types of salmon aquaculture



- ❖ Sea cages or open net pens
- ❖ Sea ranching
 - salmon eggs are fertilized in hatcheries and grown until they are able to live independently, at which time they are released – either into streams or ocean
 - In 2008, the Alaska Department of Fish and Game reported that 146 million Pacific salmon were commercially harvested. Of this, 60 million salmon were identified as ocean ranched. Therefore ocean ranched salmon represented over 41% of the “wild-caught” Pacific salmon commercial catch in Alaska
- <http://www.sf.adfg.state.ak.us/FedAidPDFs/fmr09-08.pdf>
- ❖ Grow fish in inland tanks



SALMON ATLANTIC
FILLET COLOR
ADDED FRESH

Club
Price

6⁹⁹

per lb

Non-Member Price 11⁹⁹/_{lb}

86280485 331

Thru Tue, Oct. 11

Fresh Atlantic
Salmon Fillets
Farm Raised

\$8⁹⁹

With Card

SALMON ATLANTIC
FILLET FRESH

Club
Price

6⁹⁹

lb

October 2011
Davis, CA

Wild Caught
Fresh
KING SALMON
FILLETS

Origin: U.S.A.

\$17.99



Nugget

FISH WISE



Fast growing salmon

The founder female was generated in 1989 – 21 years ago

Nature Biotechnology 10:176 – 181. **1992**



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GROWTH ENHANCEMENT IN TRANSGENIC ATLANTIC SALMON BY THE USE OF AN “ALL FISH” CHIMERIC GROWTH HORMONE GENE CONSTRUCT

Shao Jun Du, Zhiyuan Gong, Garth L. Fletcher¹, Margaret A. Shears¹, Madonna J. King¹, David R. Idler¹ and Choy L. Hew*

Research Institute, The Hospital for Sick Children and Departments of Clinical Biochemistry and Biochemistry, University of Toronto, Toronto, Canada M5G 1L5. ¹Ocean Sciences Centre, Memorial University of Newfoundland, St. John's, Newfoundland, Canada A1C 5S7. *Corresponding author.

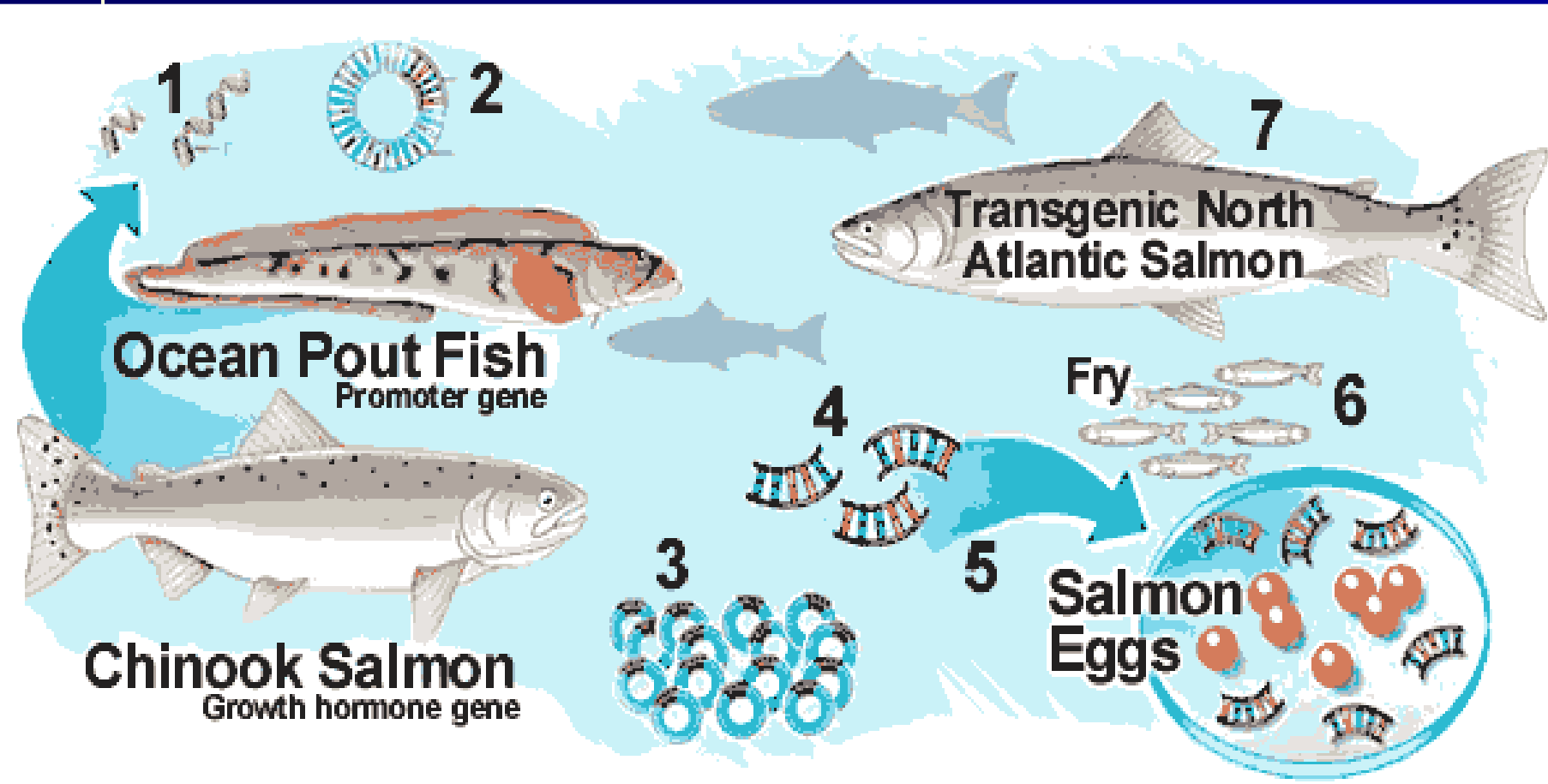
We have developed an “all fish” growth hormone (GH) chimeric gene construct by using an antifreeze protein gene (AFP) promoter from ocean pout linked to a chinook salmon GH cDNA clone. After microinjection into fertilized, nonactivated Atlantic salmon eggs via the micropyle, transgenic Atlantic salmon were generated. The presence of the transgene was



University of Toronto/Memorial University of Newfoundland, Canada

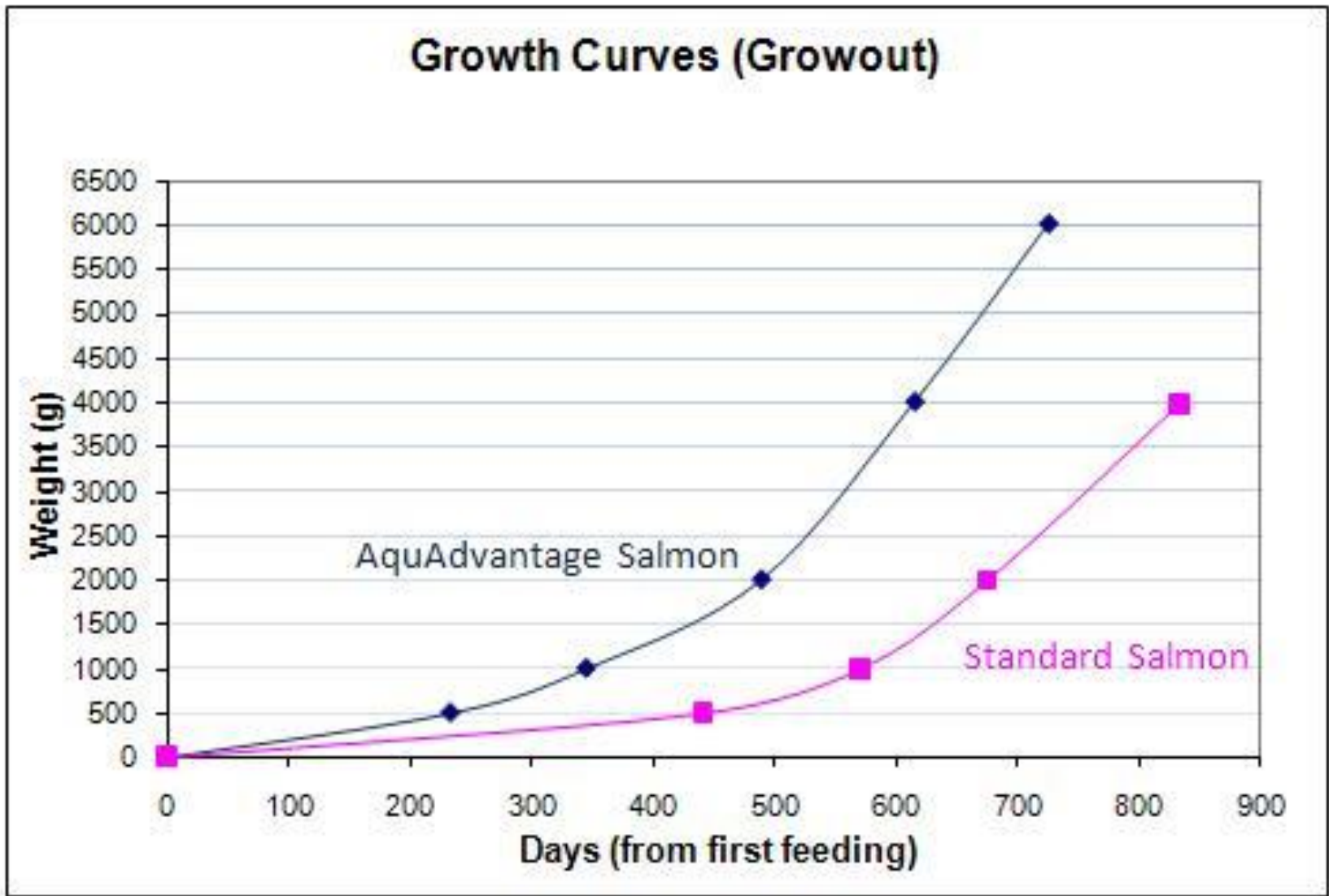


What is the AquAdvantage salmon?





Fish reach adult size in 16 to 18 months instead of 30 months





Same-age siblings – one carrying a hemizygous copy of the transgene





In a letter to the FDA dated April 26, **1993**, AquaBounty Technologies (then A/F Protein) initiated discussions with the FDA seeking regulatory guidance for development and approval of a GE Atlantic salmon intended to grow faster than conventionally bred Atlantic salmon.

- In January 2009, the Food and Drug Administration issued a final guidance for industry on the regulation of genetically engineered (GE) animals (had 28,000 comments on draft!!)
- FDA plans to regulate GE animals under the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA), and the National Environmental Policy Act (NEPA).

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Guidance for Industry

Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs

Final Guidance

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf>





“New Animal Drug” approach

- The recombinant DNA (rDNA) construct is a new animal drug because it is “an article intended to alter the structure or function” of the animal.
- New animal drugs may be approved if they are shown to be safe and effective for the intended use.
- In a hierarchical risk-based multistep scientific review the agency examines the safety of the rDNA construct to the animal, the safety of food from the animal, and any environmental impacts posed, as well as the extent to which the performance claims made for the animal are met.





FDA NEWS RELEASE

FOR IMMEDIATE RELEASE

January 15, 2009

Media Inquiries:

Michael Herndon, (301) 796-4673

Consumer Inquiries:

888-INFO-FDA

FDA Issues Final Guidance on Regulating Genetically Engineered Animals

En Español

The U.S. Food and Drug Administration today issued a final guidance for industry on the regulation of genetically engineered (GE) animals under the new animal drug provisions of the Federal Food, Drug and Cosmetic Act (FFDCA). The guidance, titled "The Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs," clarifies the FDA's statutory and regulatory authority, and provides recommendations to producers of GE animals to help them meet their obligations and responsibilities under the law.

Genetic engineering generally refers to the use of recombinant DNA (rDNA) techniques to introduce new characteristics or traits into an organism. When scientists splice together pieces of DNA and introduce a spliced DNA segment into an organism to give the organism new properties, it is called rDNA technology. The spliced piece of DNA is called the rDNA construct. A GE animal is one that contains an rDNA construct intended to give the animal new characteristics or traits.

"Genetic engineering is a cutting edge technology that holds substantial promise for improving the health and well being of people as well as animals. In this document, the agency has articulated a scientifically robust interpretation of statutory requirements," said Randall Lutter, Ph.D., deputy commissioner for policy. "This guidance will help the FDA efficiently review applications for products from GE animals to ensure their safety and efficacy."

The FDA released the draft guidance in September 2008 with a 60-day public comment period, and received about 28,000 comments. The agency has summarized and responded to these comments on the Web site listed below.

The FDA's Center for Veterinary Medicine (CVM) has been working with developers of GE animals on both early stage and more mature applications.

"At this time, it is our intent to hold public scientific advisory committee meetings prior to making decisions on GE animal-related applications" said Bernadette Dunham, D.V.M., Ph.D., director of CVM.

The FFDCA defines "articles (other than food) intended to affect the structure or any function of the body of man or other animals" as drugs. An rDNA construct that is in a GE animal and is intended to affect the animal's structure or function meets the definition of an animal drug, whether the animal is intended for food, or used to produce another substance. Developers of these animals must demonstrate that the construct and any new products expressed from the inserted construct are safe for the health of the GE animal and, if they are food animals, for food consumption.

The guidance also describes the manufacturer's responsibility in meeting the requirements for environmental review under the National Environmental Policy Act.

For more information:

- [Genetically Engineered Animals](#)



Date	Event
September 1995	AquaBounty submits Investigational New Animal Drug (INAD) application with FDA for fast-growing salmon with intent to commercialize
September 2010	Public Veterinary Medicine Advisory Committee meeting to consider data on safety and efficacy of AquAdvantage salmon Held in Washington DC





Product Definition for the AquAdvantage Salmon

Product Identity

Triploid hemizygous, all-female Atlantic salmon (*Salmo salar*) bearing a single copy of the transgene.

Claim

Significantly more of these Atlantic salmon grow to at least 100 g within 2700 deg C days than their comparators.

Limitations for Use

These Atlantic salmon are produced as eyed-eggs for grow-out only in the FDA-approved physically-contained fresh water culture facility.





Food/Feed Safety: Does food or feed from the GE animal pose any risk to humans or animals consuming edible products from GE animals compared with the appropriate non-transgenic comparators?

Conclusion of food/feed safety evaluations:

*"We therefore conclude the food from AquAdvantage Salmon (the **triploid** ABT salmon) that is the subject of this application is as safe as food from conventional Atlantic salmon, and that there is a reasonably certainty of no harm from the consumption of food from this animal. No animal feed consumption concerns were identified".*

Page 62, AquAdvantage Briefing packet. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM224762.pdf>



Environmental Safety: What is the likelihood that AquAdvantage Salmon will escape the conditions of confinement?

Where will the AquAdvantage Salmon be raised?

If approved, the AquAdvantage Salmon will be raised **in inland tanks**. They will not be raised in ocean net pens. Any change would require a new application and approval.

There are multiple and redundant physical and mechanical barriers in place to prevent the accidental release of eggs and/or fish to nearby aquatic environments... a minimum of three to five mechanical barriers in place for all internal flow streams which release water to the environment. Standards and has been verified by an FDA inspection or site visit. **Therefore, the likelihood is considered very low that AquAdvantage Salmon will escape from confinement at these sites.**





The public meeting held in Washington DC was intended to increase transparency, clarity, and public confidence in the GE animal regulatory process



Wenonah Hauter of Food and Water Watch carries a box with public comments opposing FDA approval of genetically engineered salmon.

10. Frankenfish Aren't Animals, They're "Animal Drugs"

1 of 11

A group of people are gathered outdoors for a protest. A woman in the foreground is speaking into a microphone and making a peace sign. Behind her are several signs, including one that says "something's fishy: STOP G.E. SALMON!", another that says "WRONG GENES", and a banner that says "CENTER FOR FOOD SAFETY". There is also a sign with a picture of a fish and the text "Just Say No To Frankenfish".

Obama's FDA is regulating genetically engineered salmon, a genetically modified organism (GMO) that is the first of its kind, not as an animal, but as an animal drug.



Examples of claims made during the public meeting – not actually supported by what was in the data package that was made public by company to increase transparency

- **More Allergenic:** GMO salmon have mean allergenic potencies that are 20% and 52% higher than normal salmon.
- **More Carcinogenic:** GMO salmon has 40% more IGF1, a hormone linked to prostate, breast and colon cancers in humans.
- **Less Nutritious:** GMO salmon has the lowest omega-3 to omega-6 ratio of any salmon.
- **Likely To Change The Bacteria Of Your Gut:** Horizontal gene transfer, where the bacteria of the human gut takes up modified DNA from GMO foods during digestion, has been shown occur with soy and is likely to happen with GMO salmon, too.
- **All Messed Up:** GMO salmon has increased frequency of skeletal malformations like “humpback” spinal compression, increased prevalence of jaw erosions or “screamer disease,” and multisystemic, focal inflammation in its tissues.





“There is little benefit to society if attempts to increase public participation in the regulatory process are used as an opportunity to vilify technology.”

Transgenic salmon: a final leap to the grocery shelf?

Nature Biotechnology (2011) **29**: 706–710.

Alison L Van Eenennaam & William M Muir

Despite being caught up in regulatory proceedings for 15 years or more, AquAdvantage salmon, the first animal genetically engineered (GE) for food purposes, continues to raise concerns. Are any of these concerns scientifically justified?

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The tortuous passage of AquAdvantage salmon through the US regulatory system provides a stark reminder of the adage that sometimes it is good not to be first. A fast-growing transgenic fish containing a gene encoding Chinook salmon growth hormone under the control of an antifreeze protein promoter and terminator from ocean pout, AquAdvantage salmon has been subjected to one of the most prolonged, if not exhaustive, regulatory assessments in history. This process culminated last September with a meeting of the Veterinary Medicine Advisory Committee (VMAC) as well as a public hearing, together with the release of a comprehensive health and safety briefing and an environmental assessment package on the transgenic animal developed by AquaBounty Technologies of Waltham, Massachusetts. Despite VMAC's determination



AquaBounty Technologies



Less than 2 weeks after the meeting, more than 40 members of Congress signed letters requesting FDA halt the approval of the AquaBounty transgenic salmon.

"The FDA's hastily completed approval process puts American consumers and the environment at risk. GE salmon could be devastating to fishing and coastal communities, our food source, and already depleted wild salmon populations. The FDA should put the interests and safety of American families and our ocean resources above special interests"

Rep. DeFazio (D-OR) September 2010.



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September 1995	AquaBounty submits Investigational New Animal Drug application with FDA for fast-growing salmon with intent to commercialize
September 2010	Public Veterinary Medicine Advisory Committee meeting to consider data on safety and efficacy of AquAdvantage salmon
June 15 th 2011	House of Representatives passed a voice vote amendment that prohibit use of FDA funds to approve any application for approval of genetically engineered salmon. Offered by Reps. Don Young (AK) and Lynn Woolsey (CA).

Young argued that the modified fish are unnatural and their production could create competition for his state's fishing industry. In a statement, Young said he had deep concern about the salmon, which he dubbed "Frankenfish."

"Frankenfish is uncertain and unnecessary," Young said. "Should it receive approval as an animal drug, it clears the path to introduce it into the food supply. My amendment cuts them off before they can get that far. Any approval of genetically modified salmon could seriously threaten wild salmon populations as they grow twice as fast and require much more food."



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The letter was signed by Sens. Daniel Akaka (HI), Mark Begich (AK), Maria Cantwell (WA), Jeff Merkley (OR), Barbara Mikulski (MD), Lisa Murkowski (AK), Patty Murray (WA), and Jon Tester (MT).



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December 15, 2011	<p>The Senate Subcommittee on Oceans, Atmosphere, Fisheries, and Coast Guard is holding a hearing to examine potential environmental risks of genetically engineered (GE) fish. Testifying were:</p> <ul style="list-style-type: none">- Dr. Ron Stotish, president and CEO AquaBounty Technologies, Inc.- Dr. John Epifanio, Illinois Natural History Survey- Paul Greenberg, journalist and author of "Four Fish"- Dr. George Leonard, Aquaculture Program Director Ocean Conservancy



The 12/15/11 hearing was led by a man who has dubbed this bio-engineered creation the “frankenfish”—U.S. Sen. Mark Begich (D-Alaska) chairman of the Subcommittee on Oceans, Atmosphere, Fisheries, and Coast Guard. Begich has been a staunch opponent of the gene-altered salmon and has even introduced legislation to stop it.

U.S. senator and ranking committee member Olympia Snowe (R-Maine) further commented on the regulatory limits of the FDA in its ability to effectively evaluate environmental concerns.

“The FDA is using an approval process originally created to approve new animal drugs that the agency has interpreted to include genetically engineered or modified fish,” said Snowe. “This is an outdated and inadequate approach to evaluating a technology of this magnitude.”

Snowe called on the FDA to halt its approval until the agency establishes a “transparent and comprehensive review process for genetically engineered animals.”

“The FDA has a procedure that is not designed for this type of product in its public review,” said Sen. Begich. “It’s a different ballgame.”

*“I know Dr. Stotish has struggled through years of review, but Congress has had very little conversation about this,” said Begich in his closing comments. “**I will tell you as chair of this subcommittee and someone who comes from a state that produces 60 percent of the wild stock of this country: we are going to be interested in this.**”*

<http://www.theepochtimes.com/n2/united-states/battle-to-put-genetically-engineered-fish-on-dinner-tables-161957.html>



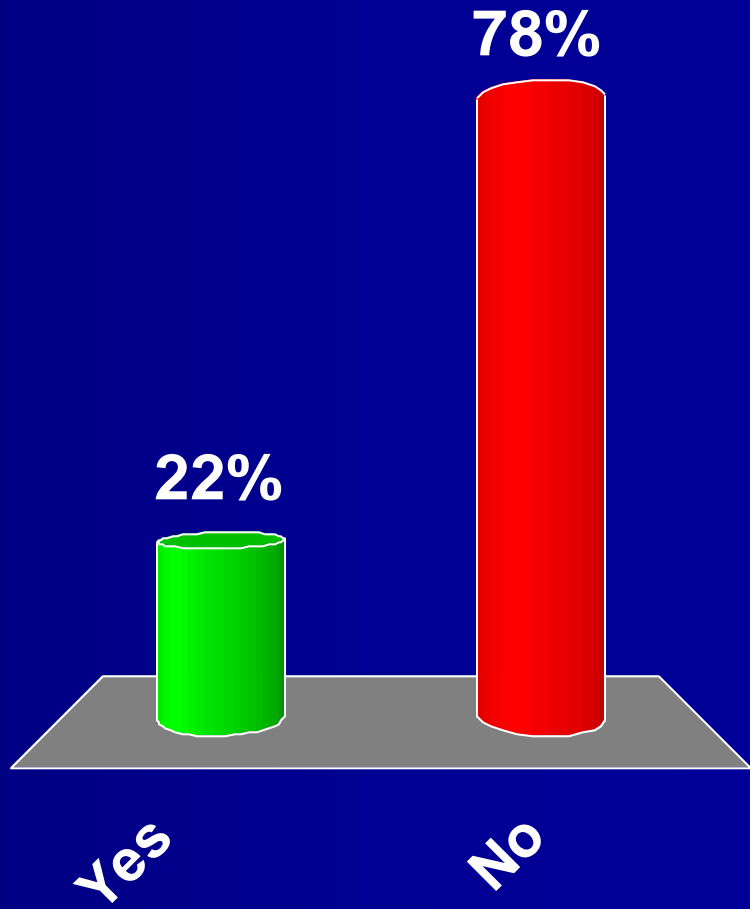


Would you eat Frankenfish?

Results from general public audience at UCD College of Agriculture and Environmental Sciences breakfast 11/05/2011



- 1. Yes
- 2. No





CASE STUDY: SALMON

Which type of salmon would you buy?





Summary of potential advantages of land-based (inland tank) AquAdvantage aquaculture

- Shorter production time – 16-18 months versus 30 months
- Shorter time to harvest diminishes the risk of disease and resultant use of chemotherapeutics/antibiotics
- Culture in a land based, contained system reduces spread of disease in the environment (and wild salmon populations)
- 15% improvement in food conversion ratio (i.e. produce more lbs product per lb feed) –feed is major cost of fish production!
- Does not spawn during growout (more energy available for growth AKA less energy wasted on reproduction!).
- Land based salmon culture systems **could** be located on land adjacent to major markets, reducing freight and the associated environmental impact i.e. locally-grown “**locivovre**” source of fish





1. Wild-caught: \$17.99/lb Pacific salmon





2. Farm-raised: \$6.99/lb net pen imported from Norway/Scotland/Canada





3. Farm-raised: \$6.99/lb land-based GE AquAdvantage Atlantic triploid, female salmon raised in Panama



**ATLANTIC
SALMON FILLET
FRESH
FARM-RAISED
PRODUCT OF CANADA
AND PANAMA**

AND/OR POULTRY. SOME FOOD PRODUCTS MAY CONTAIN BACTERIA THAT COULD CAUSE ILLNESS IF THE PRODUCT IS MISHANDLED OR COOKED IMPROPERLY. FOR YOUR PROTECTION, FOLLOW THESE SAFE HANDLING INSTRUCTIONS.

- KEEP REFRIGERATED OR FROZEN. THAW IN REFRIGERATOR OR MICROWAVE.
- KEEP RAW MEAT AND POULTRY SEPARATE FROM OTHER FOODS.
- WASH WORKING SURFACES (INCLUDING CUTTING BOARDS), UTENSILS, AND HANDS AFTER TOUCHING RAW MEAT OR POULTRY.
- COOK THOROUGHLY.
- KEEP HOT FOODS HOT. REFRIGERATE LEFT-OVERS IMMEDIATELY OR DISCARD.

238767910090

Tare	Store No.	Sell By
0.06 lb	1205	Sep 19, 10
Net Wt/Ct	Unit Price	
1.01 lb	\$9.99/lb	

P 12: Safeway Inc. Pleasanton, CA 94588

SAFeway.

Total Price
\$10.09

CLUB PRICE	YOU SAVE	WITH CARD YOU PAY
\$6.99/lb	\$2.02	\$8.07



4. Farm-raised: \$6.99/lb land-based GE AquAdvantage triploid, female Atlantic salmon locally-grown in land-based tanks



ATLANTIC SALMON FILLET
FRESH
FARM-RAISED
PRODUCT OF USA

269310 91510

SAFE HANDLING INSTRUCTIONS

THIS PRODUCT WAS PREPARED FROM INSPECTED AND PASSED MEAT AND/OR POULTRY. SOME FOOD PRODUCTS MAY CONTAIN BACTERIA THAT COULD CAUSE ILLNESS IF THE PRODUCT IS MISHANDLED OR COOKED IMPROPERLY. FOR YOUR PROTECTION, FOLLOW THESE SAFE HANDLING INSTRUCTIONS:

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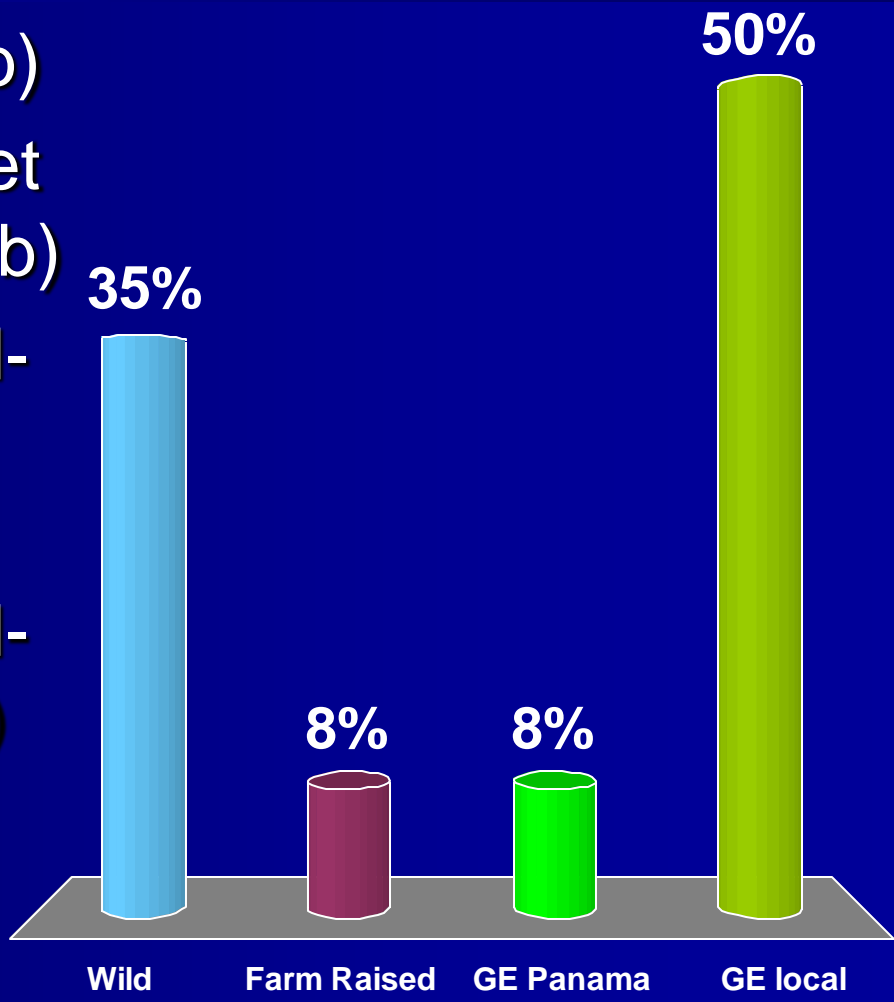


Which type of salmon would you buy?

Results from general public Audience at UCD College of Agriculture and Environmental Sciences breakfast 11/05/2011




- 1. Wild-caught (\$17.99/lb)
- 2. Farm-raised, ocean net pen, imported (\$6.99/lb)
- 3. Farm-raised, GE, land-based, imported (\$6.99/lb)
- 4. Farm-raised, GE, land-based, local (\$6.99/lb)



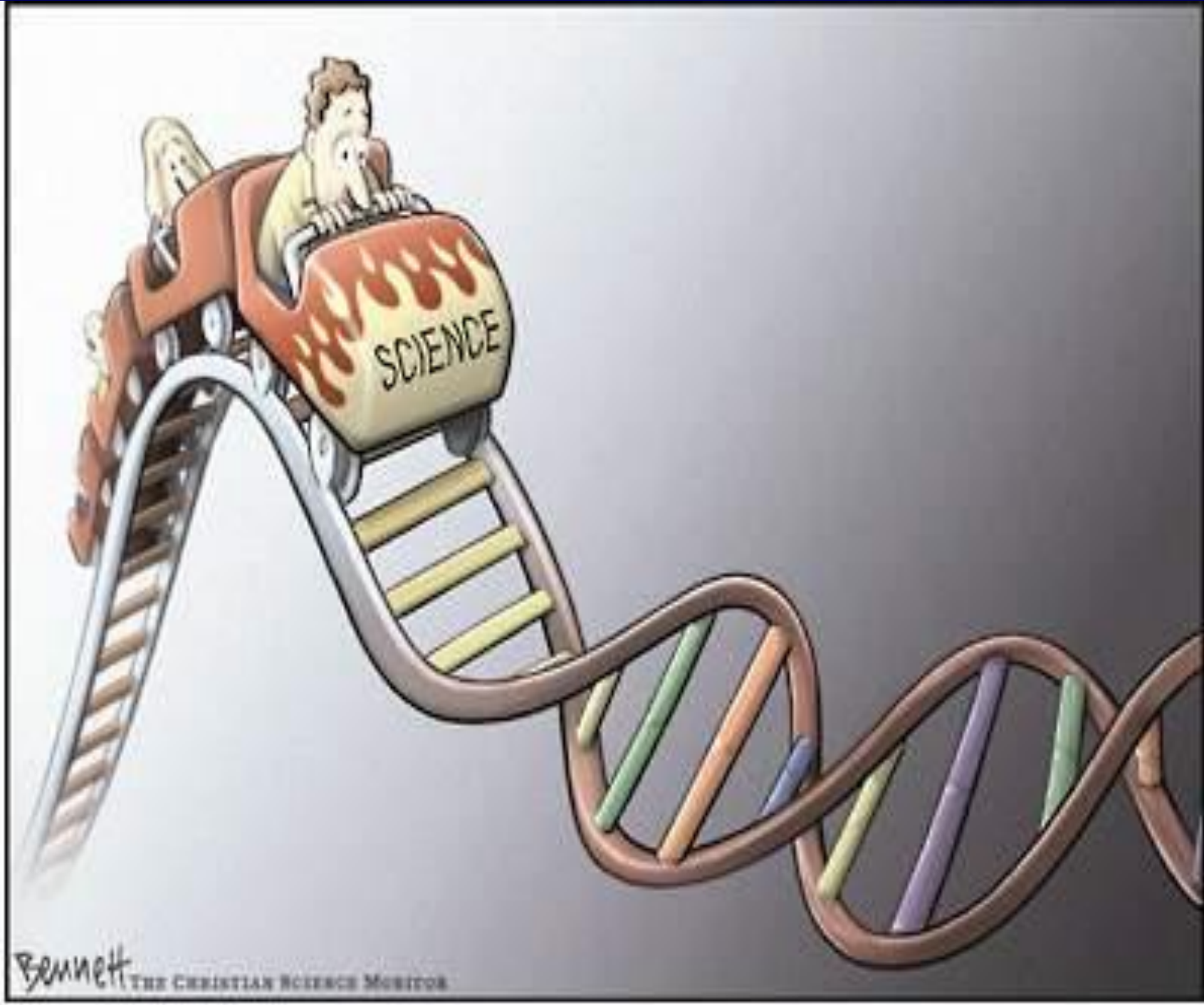


Dr. Calestous Juma, Harvard's Kennedy School of Government, at a 6/23/11 hearing to examine the benefits of agricultural biotechnology held by the House Agriculture Committee's Subcommittee on Rural Development, Research, Biotechnology, and Foreign Agriculture



“. . It is not this particular fish that is at stake. It is the principle behind the amendment (to prohibit use of FDA funds to evaluate any application for approval of genetically engineered salmon) and its wider ramifications. It sends the message to the rest of the world that the science-based regulatory oversight as embodied in the FDA review process is subject to political intervention.

Furthermore, it signals to the world that the United States may cede its leadership position in the agricultural use of biotechnology. . . I believe it is imperative that the United States stay the course it has set in not letting politics interfere with its science-based regulatory system”



Bennett
THE CHRISTIAN SCIENCE MONITOR

