Case Study 1: Fish – Enhancing Productivity and Environmental Containment
Summary of Discussions

Myostatin KO Tilapia

1. In your own words, what is the intended purpose of modifying the myostatin gene in tilapia? What is the claimed benefit for fish farmers and consumers based on the case study summary?

- ***Increased yield. Faster production; shorter production cycles. Feed efficiency. Lower production cost = higher profits***
- ***Larger meatier fish for the consumers.***

2. The scientists targeted the mstnb gene, not the mstna gene. Based on the summary, which describes that mstnb is primarily expressed in muscle while mstna is expressed in the brain, why was this specific gene chosen? What does this tell us about the precision required in gene editing to achieve a desired outcome without affecting other systems?

- ***mstnb expressed in muscles – targeting the edit to the tissue of interest (muscle).***
- ***Avoid off-target physiological disruption (mstna)***
- ***Design principle in GnEd for production trait: essential – knowledge of gene family members, tissue-specific expression***

3. This technique is a "knockout," meaning a gene is inactivated, but no new genetic material from another species is added. How might this be different from a "transgenic" animal from a scientific and public perception standpoint?

- ***Absence of foreign DNA | same as conventional = loss-of-function variant same as naturally occurring mutations***
- ***Public perception is country-dependent: what does it look like? Maybe viewed differently from GM, need for communication***

Sterile Salmon

1. What is the primary agricultural and environmental problem that creating sterile salmon aims to solve? How does this relate to the sustainability of large-scale aquaculture?

- ***Problem: possibility of cross-breeding***
- ***Biological containment – addressing genetic introgression from farm escapees into wild stocks***

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PART 2: Potential Pathways to Harm (30 mins)

Human Health

1. For the Myostatin KO Tilapia, could inactivating a growth-regulating gene lead to unintended changes in the fish's composition (e.g., new proteins, altered nutrients, or potential allergens)? What kind of data would you, as a regulator, need to see to be confident in its food safety?

- ***No effects | No need for data requirement in composition***
- ***No new DNA – doesn't warrant composition data | may vary by jurisdiction***

2. For the sterile salmon, are there direct human health risks from consuming a fish that cannot reproduce? Or are the risks primarily indirect and related to environmental safety and animal welfare?

- ***No additional risk (same as conventional) – sterility not inherently a food safety hazard***

Animal Welfare

1. The Myostatin KO Tilapia has an increased number of muscle fibers and overall muscle mass. Could this muscle growth affect the fish's ability to swim, breathe, or behave normally? How do this differ from the naturally occurring myostatin mutations that occur in cattle (e.g. Belgian Blue breed), and how are the welfare implications of conventional breeding currently addressed? What specific welfare indicators should be monitored throughout the animal's life cycle?

- ***Behavior change, locomotion; respiratory capacity [if they cannot breathe, they will not survive]***
- ***A standards issue (GnEd vs conventional); country-to-country variation [assessment - follow National standards, data-driven]***

2. What are the potential welfare implications, both positive and negative, of producing sterile salmon? Consider effects on the animal's natural life cycle, maturation, and behavior.

- ***None***

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Environmental Impacts

1. If Myostatin KO Tilapia escaped into the wild, what potential impacts could they have on wild tilapia populations or the broader ecosystem? Would their faster growth give them a competitive advantage for food and habitat, potentially displacing native populations?

- ***Outcompeting wild populations for food and habitat***
- ***Altering ecosystems – would require multiple releases of huge batches***
- ***Potential control – addon trait (biological control via sterility) or physical containment***

2. The primary goal of sterile salmon is to prevent environmental impact. What could go wrong with this strategy? What if the sterility method is not 100% effective? What level of certainty (e.g., 99%, 99.99%) would a regulator require before approving its use in open-net pens? How does this compare to the current situation where fertile conventionally-improved salmon escape net pens?

- ***If sterility is not 100% effective – possible genetic introgression from escaped farmed salmon to wild stocks***
- ***Unlikely to impact wild populations – not many left out there***
- ***Level of certainty – 95% would be good enough***

- ***Relative to current situation – higher-efficacy sterility (99%, 99.99%) represents a substantial risk reduction***

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PART 3: Regulatory Approaches and Trade Implications (90 mins)
Regulatory Triggers

1. In your country's current legal framework, would a gene-edited fish with an inactivated gene (like the tilapia) be considered a "Genetically Modified Organism" (GMO) and be subject to specific regulations? Why or why not?

- Argentina – No; no foreign DNA
- Canada – Yes; GM food; considered a new substance
- Costa Rica – No; Considered 'as conventional' – no foreign DNA
- Japan – No; organism obtained from GnEd – risk assessment process leading to ->> non-GM determination
- Germany – Yes; GnEd = GMO
- Uruguay – No; Considered 'as conventional' – no foreign DNA
- Vietnam – No; Considered 'as conventional' – no foreign DNA
- Thailand – No; no foreign DNA (as of 2024)
- Nigeria – No; no recombinant DNA
- USA – Yes; 'Intentional Genetic Alteration'; Considered GMO; subject to regulation
- Paraguay - No; Considered 'as conventional' – no foreign DNA
- Kenya – No; no foreign DNA, case-by-case product-based approach

2. Does your country's regulatory framework distinguish between an animal with a gene "knocked out" (an edit) versus an animal with a gene "added" from another species (a transgene)? Should it?

- ***Most countries – Yes. Knockouts differ from transgenes – no foreign DNA.***
- ***Fewer unknown risks. Laws should distinguish them to allow proportional oversight.***

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Data Requirements

1. Imagine you are the regulator reviewing a formal application for the commercial farming of Myostatin KO Tilapia. What specific studies and data would you require from the developer to assess its safety for humans, animals, and the environment? Consider molecular characterization, compositional analysis, and long-term environmental monitoring.

- Vietnam – molecular characterization;
- USA – (all three); personal – none
- Uruguay – molecular and phenotypic characterization; → to determine decision pathway
- Thailand – molecular; compositional; absence of foreign DNA; & off-targets
- Paraguay – molecular; absence of foreign DNA
- Nigeria – no experience with GnEd
- Japan – method of edit; absence of foreign DNA; WGS; new allergens; impact on metabolism; reproductive physiology 魚
- Germany – EU (all three); personal – only animal welfare
- Costa Rica – molecular; phenotypic characterization
- Canada – compositional analysis; background genetics
- Argentina – Editing technique used; absence of foreign DNA; phenotype
- Kenya – molecular characterization

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- **Comparative Models and National Adaptation**
- 1. The **US** FDA regulates all intentional genomic alterations (IGAs) in animals using a risk-proportionate approach that includes interaction with USDA. The extent of the review process is highly case specific; data requirements vary based on the risk of the product.
- 2. **Brazil and Argentina** would likely not consider it a GMO if no foreign DNA is present, following a case-by-case consultation that could lead to it being treated as a conventional animal.
- 3. **Australia** explicitly exempts this type of modification (known as SDN-1) from GMO regulation.

- ***Which of these models (or a hybrid) seems most appropriate and feasible for your country's context?***

- Nigeria – Brazil/Argentina
- Japan – US + Brazil/Argentina hybrid
- Germany - US + Brazil/Argentina hybrid
- Costa Rica – Argentina
- Canada – animals (US), plants [?]
- Argentina – Brazil/Argentina + Australia hybrid
- Kenya – Currently Brazil/Argentina; could be Australia-like
- Paraguay – currently (Brazil/Argentina); preferable Australia
- Thailand – Australia
- Uruguay - Brazil/Argentina
- US – Australia
- Vietnam - Australia

- ***What resources (scientific, legal, administrative) would be needed to implement each?***

  - Canada – Legal, Communication
  - Argentina – Legal, Scientific
  - Costa Rica – Legal, Scientific
  - Germany – EU member states consensus
  - Japan – Successful models (justification for change), political will
  - Nigeria – none
  - Paraguay – scientific, legal
  - Thailand – scientific (justification)
  - Uruguay – scientific, legal, administrative
  - US – none
  - Vietnam – scientific (justification)
  - Kenya – Scientific

Trade and Labelling

If your country approves this fish for human consumption but a major trading partner does not, what are the potential consequences for your national seafood industry? How would you manage the traceability and segregation of products to prevent unapproved products from entering the export chain? Is this a role for government or for the industry?

- Argentina – No labeling. Gov't (provide clarity);
- Canada – Work with processors to ensure segregation; developer's responsibility. No special label.
- Costa Rica – No label required
- Germany – importing:~ label it, should be traceable; govt responsibility
- Japan – voluntary labeling; industry responsibility
- Paraguay – no consequence; no labeling requirement
- Thailand – no labeling
- Uruguay – no concerns; --; no special labeling
- US – potential consequences for the seafood industry; --; role for the industry
- Vietnam – case-by-case management;