What might a risk assessment for a genetically modified food producing animal look like?

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Two guidelines of the Codex Alimentarius Commission…

- CAC/GL 44-2003, Principles for the risk analysis of foods derived from modern biotechnology.

- CAC /GL 68-2008, Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA animals

A food safety risk assessment should take into account:

- The nature of the recombinant (or edited) DNA and its expression product(s), if any
- The health status of the recombinant-DNA (genetically modified) animal
- The composition of foods produced from the recombinant-DNA (genetically modified animal), including key nutrients

Framework of a food safety assessment

a) General description of the recombinant –animal (or otherwise genetically modified animal)

b) Description of the recipient animal (genetically modified animal) prior to the modification and its use as food or for food production

c) Description of the donor organism or other source(s) of any introduced recombinant-DNA

d) Description of the genetic modification(s) including the construct(s) (if any) used to introduce the recombinant DNA (the genetic modification)

e) Description of the methods used to produce the initial recombinant-DNA animal (initial genetically modified animal) and the processes to produce the recombinant-DNA animal (genetically modified animal) ultimately used as food or for food production

Framework of a food safety assessment

f) Characterization of the genetic modification(s) in the recombinant-DNA (genetically modified) animal ultimately used as food or for food production.

g) Safety assessment:
   a) Health status of the recombinant-DNA (genetically modified) animal;
   b) Expressed substances (non-nucleic acid substances);
   c) Compositional analysis of key components;
   d) Food storage and processing; and
   e) Intended nutritional modifications

h) Other considerations

What might this look like? Based on our current best thinking…

FDA Guidance for Industry #187. Regulation of Intentionally Altered Genomic DNA in Animals. Draft Guidance. January 2017.

Basic categories of information

1. **Product Identification/Definition**
2. Molecular characterization of the altered genomic DNA
3. Molecular characterization of the lineage of animals whose genomes have been intentionally altered
4. Phenotypic characterization of the animals whose genomes have been intentionally altered
5. Genotypic and phenotypic durability assessment
6. Food safety and environmental safety
7. Safety/Effectiveness

Product Identification/Definition

Product Identity:

A single copy of the α-form of the opAFP-GHc2 rDNA construct at the α-locus in the EO-1α lineage triploid, hemizygous, all-female Atlantic salmon (Salmo salar) known as AquAdvantage Salmon.

What is the genetic modification intended to do?

Significantly more AquAdvantage Salmon grow to at least 100 g within 2,700 ^{0}C-days than their comparators.

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Molecular characterization

What are the components and composition of the article

What are the changes to the genomic DNA in the animal lineage to be introduced into commerce

- Details of how the genomic alteration(s) was achieved
- Description of the source of the functional components of the altered genomic DNA
- Sequence of the altered genomic DNA or of nucleotides surrounding the alteration (for a deletion)
- Purpose of the alteration
- Intended function(s) of the genomic alteration
- Purity of the preparation containing the materials introduced into the recipient animal or cells
- Location and nature of the genomic alteration in the animal
- Depending on the product and technology, whole genome sequencing may become important (particularly for off target effects)
- Breeding strategy used to produce the lineage progenitor

Basic categories of information

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4. **Phenotypic characterization of the animals whose genomes have been intentionally altered**
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Phenotypic characterization

Informs potential risks to humans, animal health, or environment

- Data whether the genomic alteration(s) or its expression product(s) cause direct or indirect toxicity
  - Detailed data on animal health
    - Veterinary & treatment records, growth rates, reproductive function, behavior
  - Detailed data on physiological status
    - Clinical chemistry, hematology, histopathology, post-mortem results
- Data should come from a generation close to that intended for use in commerce

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Food safety

- A general standard of reasonable certainty of no harm.
- Direct toxicity
  Is there any direct toxicity as a result of consumption of the expression product (or other materials introduced into the animal)?
  - Characterize the toxicological hazard, including allergenicity
  - Establish an acceptable daily intake, if necessary establish a tolerance with an analytical method

Food safety

- Indirect toxicity
  Is there any other toxicity as a result of intentional or unintentional changes on the animal's physiology?
  - Build on the genotypic and phenotypic characterization.
  - Compositional analyses of key components
  - Comparison of the GE animal to conventional counterpart


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