Food Safety Considerations for Animals with Intentional Genomic Alterations

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Intentional Genomic Alterations (IGAs) in Animals

- Produced using various technologies
  - Genetic engineering (e.g., recombinant DNA constructs)
  - Genome editing (e.g., TALENs, CRISPR/Cas, ZFNs)
- Various intended uses
  - Food production
  - Production of biopharmaceutical products
  - Disease resistance
  - Reduced allergenicity

Basic Categories of Information

1. Product Identification/Definition
2. Molecular Characterization of the IGA
3. Molecular Characterization of the Lineage of Animals with IGAs
4. Phenotypic Characterization of the Animals with IGAs/Animal Safety
5. Genotypic and Phenotypic Durability Assessment/Post-Approval Plan
6. **Food Safety**
7. Environmental Impact
8. Effectiveness/Claim Validation

Food Safety Evaluation

- The safety concerns associated with consumption of the edible tissues derived from the animals with IGAs are assessed
- A general safety standard of reasonable certainty of no harm
- An integrated approach is followed
- Substantial equivalence -comparison of the food derived from the animal with an IGA to conventional counterpart

Food Safety Assessment 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

Hazard Identification and Characterization

- Direct toxicity
  - Is there any direct toxicity as a result of production (or other materials introduced into the animal) that will remain in the tissues of the animals?
  - Is there any direct toxicity resulting from the IGA (based on the purpose and intended function)?
  - Is there any direct toxicity resulting from the IGA based on the molecular changes? (e.g., location, copies, and sequence of the DNA or of nucleotides surrounding the alteration)
  - Is there any direct toxicity as a result of consumption of an expression product?
    - Characterize the toxicological hazard, including allergenicity
    - Establish an acceptable daily intake, if necessary establish a tolerance with an analytical method

Phenotypic Data

Informs potential risks to humans

- Data used to determine whether the IGA or its expression product(s) cause direct or indirect toxicity
  - Data on animal health
    - Veterinary & treatment records, growth rates, reproductive function, behavior
  - Data on physiological status
    - Clinical chemistry, hematology, histopathology, post-mortem results
- Data should come from a generation(s) close to that intended for use in commerce
- Is the change stably inherited and a consistent and a predictable phenotype expected?

Hazard Identification/Characterization

- Indirect toxicity
  Is there any other toxicity as a result of intentional or unintentional changes on the animal's physiology?
  - Data from genotypic and phenotypic characterization
  - Animal health status
  - Compositional analyses of foods including key nutrients

Food safety

- An analytical method for a tolerance may or may not be needed
- Unique for animals with IGAs, an analytical method that can identify the altered genomic DNA in the resulting animals or their edible tissues

U.S. Import of Food Derived from Animals with IGAs

- For animals with IGAs registered in other countries, an import tolerance must be requested to allow for import of food-derived from unapproved animals with IGAs
- Food Safety criteria are similar to for an approval of an animal with IGAs in the U.S.


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