FDA's Oversight of Heritable Intentional Genomic Alterations in Animals

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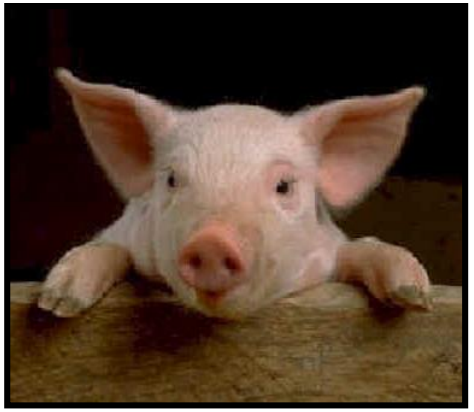
What is FDA Regulating?

- FDA regulates the heritable intentional genomic alteration (IGA) in the animal.
- The IGA is the specific DNA alteration at each site where it occurs; multiple alterations can be part of one review
- The animal itself is not what FDA approves or makes a risk determination for

Oversight Objective

FDA review of the IGA is focused safety:

- Safe to the animal
- Safe to anyone that consumes food from the animal
- Does what it claims to do



GFI 187: History

- Final Guidance issued in 2009 “Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs”
  - Regulated article = rDNA construct
  - Did not refer to IGAs other than those made using rDNA constructs (e.g deletions and base pair substitutions produced using genome editing technology)
  - FDA regulates under existing statute and regulations

GFI 187 History, continued

- Revised draft issued in 2017
  - Scope clarified to include non-transgenic IGAs such as deletions or base pair substitutions created using genome editing
  - Regulated article = change to genomic DNA (intentional genomic alteration or IGA)
- Currently in clearance: 187 split into 2 parts
  - Final #187A explains risk-based oversight framework
  - Draft #187B clarifies how approval process applies to IGAs
    - In draft to solicit comment on further updating regulatory process and making as efficient as possible

Enforcement Discretion

- Decision not to enforce a requirement
  - Not possible to enforce every requirement at all times given limited resources
- Case law: "involves a complicated balancing of a number of factors," including the best use of agency resources, policy
- “These are all factors that should be considered on a case-by-case basis.”

Risk-Based Approach

The scope of FDA's review process is based on the product's risk-profile:

Approval application not expected based on determination of low risk

Example: IGAs in laboratory animals

Example: IGAs in food animals that exist in conventionally-bred animals and have a history of safe use

Example: IGAs in food producing animals with human health claims

FDA Process

- FDA may indicate a category (e.g. animal model) is appropriate for determination of low risk, but still do case-by-case review
- First, determine if the IGA/intended use is low risk
  - Low risk to: humans, animals, environment
- Then, if it is, decide whether to exercise enforcement discretion, which means…
- FDA does not expect the developer to submit an approval application for the IGA

Veterinary Innovation Program (VIP)

- Available for IGAs in animals and ACTPs that provide a benefit to animal or human health, food production, or animal well-being
- 46 products enrolled

Benefits:
- VIP Toolkit
- Frequent Interaction: Meetings Early and Often
- Dedicated Review Team
- Alternative Data Discussions
- CVM Senior Management Involvement
- Feedback on Assay Development
- Pre- and Post-review Feedback
- Stopping/Re-starting the Clock
- Hands on Help with Post-approval Requirements

FDA/CVM Approvals

Name	Traits	Purpose	Approval Date
Atryn Goat	IGA produces recombinant human antithrombin in milk for use in anticlotting agent for individuals with hereditary clotting disorders in high risk situations	Biopharm	2009
AquAdvantage Atlantic Salmon	IGA results in Atlantic salmon that reaches market size more quickly than non-IGA farm-raised Atlantic salmon	Food	2015
SBC LAL-C chicken	IGA produces a recombinant form of human lysosomal acid lipase protein in their egg whites for treatment of patients with lysosomal lipase deficiency	Biopharm	2015
LFB R69 rabbit	IGA produces human recombinant Factor VII zymogen in the rabbit milk for the treatment of patients with hemophilia A or B disorders	Biopharm	2018
GalSafe Pigs	IGA results in non-detectable levels of alpha gal sugar on cell surfaces to be used for food and as a source of human therapeutics	Food/ Biopharm	Dec 2020

Contact Information

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