Animal Biotechnology and FDA Regulation

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Topics for Discussion

- What laws apply?
- FDA Guidance #187: Current and Draft Revised
- Regulatory Process

Statutory Authority

Federal Food, Drug, and Cosmetic Act (FD&C Act)

- Products are regulated; not processes

National Environmental Policy Act (NEPA)

- Procedural; agencies must evaluate impacts of “agency actions”

Federal Food, Drug, & Cosmetic Act

- Section 201(g): “the term drug means … (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals...”
- Section 201(v) “The term ‘new animal drug’ means any drug intended for use for animals other than man …”

FD&C Act New Animal Drug Provisions

- § 512(a): In general, an unapproved animal drug is unsafe
  - § 512(b)(3), 512(j) Exception for investigational new animal drugs
- § 501(b)(5): An unsafe new animal drug is adulterated

National Environmental Policy Act (NEPA)

- Requires Federal agencies to consider the environmental impact of their major and final agency decisions.
- Relevant implementing regulations:
  - CEQ
  - FDA
  - Approvals are among the major agency actions triggering environmental assessment under the National Environmental Policy Act (NEPA)
- Endangered Species Act analysis also required where relevant.

Current Guidance for Industry 187: GE Animals

- Issued in 2009
- Definition of “article”
  - rDNA construct intended to affect the structure or function of the animal
- All GE animals in a lineage are covered
- Event-based, case-by-case evaluation
- Enforcement discretion for some animals
- Most animals require approval prior to marketing
- Post-market surveillance

What's New Since FDA Issued GFI 187?

- Emergence of new technologies; genome editing technologies such as CRISPR
- Need to understand risks
- Lower bar to entry: DIY

Draft Revised GFI 187: Regulation of Intentionally Altered Genomic DNA in Animals

- Issued in January, 2017. Comment period closed 6/19/17.
- Scope expanded to “animals whose genomes have been intentionally altered”

What is the Regulated Article?

- 2009 GFI 187: the subject of the NADA is “the rDNA construct at a specific site in the genome”
- Draft revised GFI 187:
  - “For purposes of this Guidance, ‘altered genomic DNA’ refers to the portion of an animal’s genome that has been intentionally altered.
  - “Unless otherwise excluded…[it] is an animal drug within the meaning of section 201(g) of the FD&C Act because such altered DNA is intended to affect the structure or function of the body of the animal…
  - Altered genomic DNA may result from rDNA technology (i.e., non-specific gene insertion), genome editing technology (i.e., targeted DNA sequence changes including nucleotide insertions, exchanges, or deletions), or other technologies that introduce sequence-specific and/or site-specific changes to the genome of the animal.

Request for Comment

- NOA said we intend to modify regulatory approach based on comments/submission of evidence of low risk
- We asked for comments on:
  - Terminology: How do we refer to these animals?
  - Is there any existing empirical evidence demonstrating that certain types of genome editing may pose minimal risk?
    - Categories with no significant target animal, user safety, food safety, environmental risk?
    - Categories where evidence shows durability?
    - Degrees of introduced changes with less risk?
    - Degree of taxonomic relationship between introduced gene and animal influences health or trait expression?

Enforcement Discretion

- Enforcement Discretion:
  - Non-food animals regulated by other agencies
  - Animals raised in contained and controlled conditions, i.e. lab animals
  - Animals evaluated on a case-by-case basis, for risk, including environmental
- FDA's expectation ranges from no notification to submission of information demonstrating limited risk

What are Approval Requirements?

- Investigations: INAD requirements apply, 21 CFR Part 511
- Approval: NADA requirements in 512(b) of the act and 21 CFR Part 514 apply. Must demonstrate:
  - Safety to animal
  - Food safety (for food animals)
  - Effectiveness (ensure the article meets the sponsor claims)
- Environment: NEPA applies

NEPA Process for New Animal Drugs

- Sponsor submits claim of categorical exclusion or draft EA for INAD and NADA.
- Thus far, there have been no categorical exclusions for GE animals.
- Because the existence of an INAD or NADA is confidential, FDA does not typically publish a draft EA for comment; GE salmon and Oxitec mosquito are exceptions.
- EA leads to either finding of no significant impact or preparation of EIS.

Review Process

- Case-by-case evaluation
- Risk-based, phased review
  - Each of the major data-based sections reviewed when submitted
  - CVM issues a “section complete” letter when review is completed and found acceptable
  - Last section is “all other information,” providing any new information obtained or published since the completion of the previous major sections
- Once all sections are completed, sponsor requests an administrative NADA (i.e., no NADA pending until then)
- Once application submitted, FDA has 60 days to make a decision

Food Derived From Animals with Intentionally Altered Genomic DNA

- Regulation of NADs involves determining food safety
- Investigational animals: Must have prior authorization (21 CFR 511.1(b)(5))
- NADA: Same legal standard (reasonable certainty of no harm), regulations, and guidances apply
- Labeling: Regulated by CFSAN

Questions?

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Thank you!