Environmental Assessment of Genetically Engineered Animals at CVM (FDA)

Animal Biotechnology Interdisciplinary Group
Center for Veterinary Medicine
U.S. Food and Drug Administration
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Major Statutes Governing Regulation of GE Animals

Federal Food, Drug, and Cosmetic Act (FD&C Act)
- Products are regulated; not processes

National Environmental Policy Act (NEPA)
- Procedural; orders agencies to evaluate impacts of “agency actions”
Guidance for Industry 187*

- Definition of “article”
  - rDNA construct intended to affect the structure or function of the animal
- Covers all types of GE animals
- All GE animals in a lineage are covered
- Event-based, case-by-case evaluation
- Enforcement discretion and approval paths
- New Animal Drug Application (NADA) means mandatory approval prior to marketing
- Post-market surveillance

Statutory/Regulatory Requirements

- Sponsor must submit Environmental Assessment/supporting data under INAD/NADA

- National Environmental Policy Act (NEPA) requirement triggered by “agency action”
  - EA $\rightarrow$ FONSI? (finding of no significant impact)
  - If no FONSI, EIS (environmental impact statement)
NEPA Process Overview

- **Regulated Article**
- **Categorical Exclusion**
  - Meets Criteria
- **Environmental Assessment (EA)**
  - No Significant Effects
  - May Significantly Affect
- **Environmental Impact Statement (EIS)**
- **Finding of No Significant Impact (FONSI)**
- **Record of Decision (ROD)**
Hierarchical Risk-Based Evaluation

Post-Approval Reporting

Claim Validation

Environmental/Food/Feed Safety

Genotypic and Phenotypic Durability Plan

Phenotypic Characterization of the GE Animal

Molecular Characterization of the GE Animal Lineage

Molecular Characterization of the Construct

Product Definition

Are there significant direct or indirect effects from introduction of the GE animal into the environment?

Basis for satisfying NEPA requirements.
Definitions, Relationships, Standards

**Harm** ≡ an adverse outcome

**Hazard** ≡ substance or activity that has the potential to cause a harm

**Risk** ≡ conditional probability of an adverse outcome provided that exposure to a **receptor** has occurred

...or

\[
\text{Risk } \propto f_{\text{outcome}} (\text{exposure, hazard}),
\]

...or

“the likelihood of harm”

**Receptor** ≡ individual or population experiencing risk

**Safety** ....reasonable certainty of no harm (established standard)
### Potential Environmental Hazards and Risks

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Risk</th>
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<tbody>
<tr>
<td>Use of viral sequences, including vectors</td>
<td>Increased probability of new pathogenic recombinants</td>
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<tr>
<td>\textit{(Characterized in Molecular Characterization steps)}</td>
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<tr>
<td>Traits increasing species fitness or adaptation</td>
<td>Increased probability of disruption of existing ecosystems due to</td>
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<tr>
<td>\textit{(Characterized in Phenotypic Characterization)}</td>
<td>establishment of a GE animal in the environment</td>
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<td>Altered population dynamics due to horizontal transfer of gene</td>
<td>Specific risk is a function of the nature of the trait</td>
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<tr>
<td>construct(s)</td>
<td></td>
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<tr>
<td>\textit{(Likelihood of transfer; part of Molecular Characterization}</td>
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Environmental Assessment: General Risk Questions

For a specific GE animal (population) containing a specific rDNA construct….

- What is the likelihood of escape?
  - Containment/redundancy
- What is the likelihood of survival if escape occurs?
- What is the likelihood of establishment and reproduction?
- What are the potential consequences/effects associated with escape?

Considered in context of an appropriate comparator on a case-by-case basis
Consequences of Introduction, Escape, and Dispersion

Will depend largely on:
- Specific physical locations of production or release
- Extent of containment (if applicable)
  - Physical/mechanical
  - Biological (e.g., sterility, monosex)
  - Geographical/geophysical (environmental conditions)
  - Domestication of species (ability to become feral)
- Mobility of species
- “Net fitness”
Areas of interest

- Containment effectiveness and ways to ensure containment of GE animals
  - Physical/mechanical
  - Biological (e.g., sterility, monosex)
  - Geographical/geophysical (environmental conditions)
- Fitness
- Case by case evaluation of GE animals
Areas of interest

- Biological containment
  - Commercial production
  - Control of released GE animals or invasive species
Questions?

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