



Environmental Assessment of Genetically Engineered Animals at CVM (FDA)

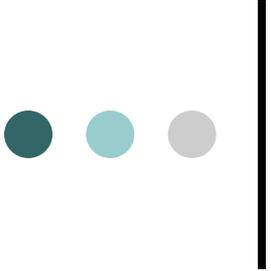
Animal Biotechnology Interdisciplinary Group

Center for Veterinary Medicine

U.S. Food and Drug Administration

Evgenij A. Evdokimov, PhD





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)

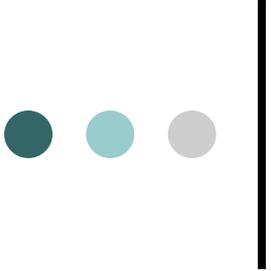
- Procedural; orders agencies to evaluate impacts of “agency actions”

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



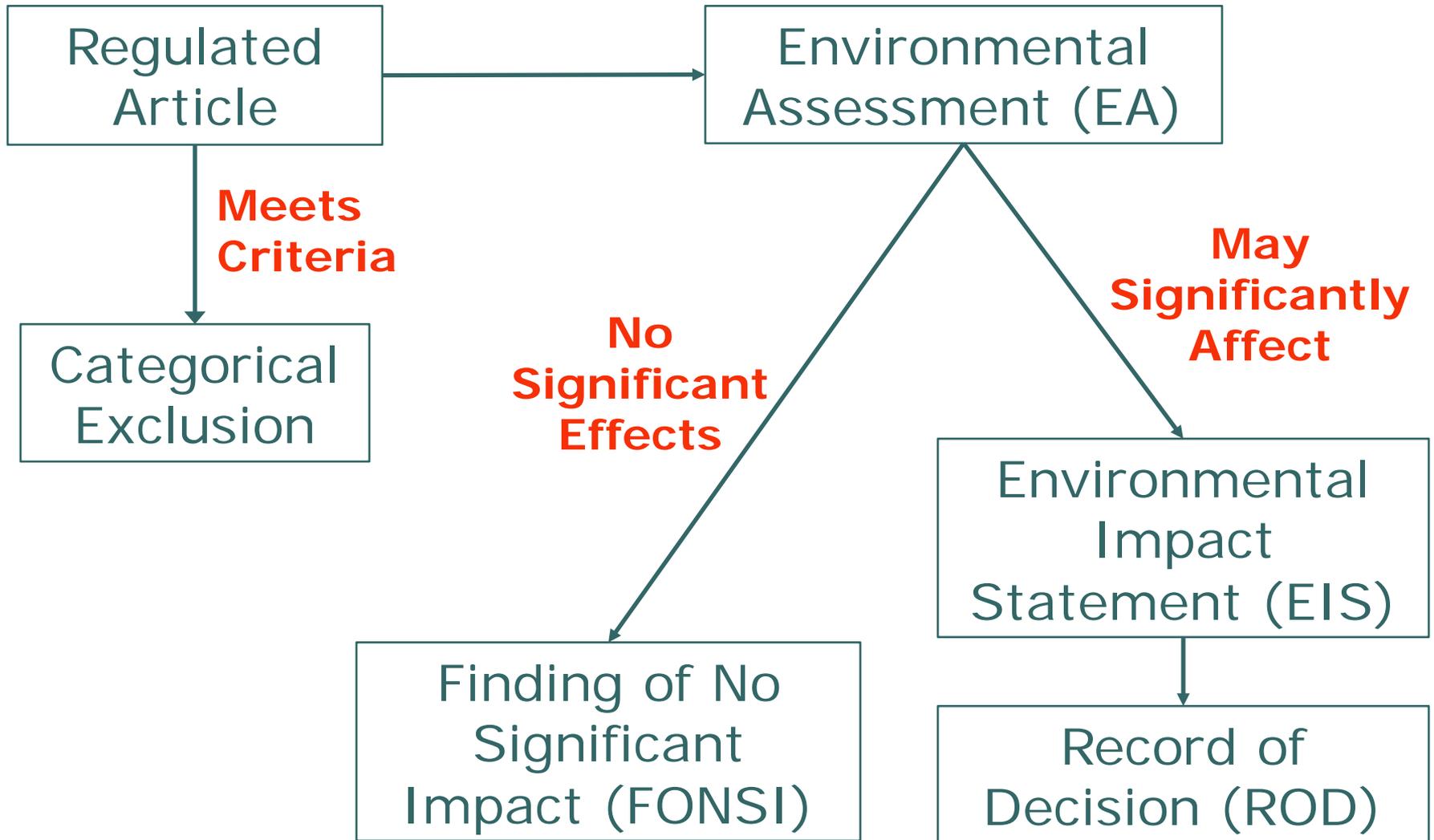
*<http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/default.htm>



Statutory/Regulatory Requirements

- Sponsor must submit Environmental Assessment/supporting data under INAD/NADA
- National Environmental Policy Act (NEPA) requirement triggered by “agency action”
 - EA → FONSI? (finding of no significant impact)
 - If no FONSI, EIS (environmental impact statement)

NEPA Process Overview



Hierarchical Risk-Based Evaluation

Post-Approval Reporting

Decision

Claim Validation

Environmental/Food/Feed Safety

Genotypic and Phenotypic Durability Plan

Phenotypic Characterization of the GE Animal

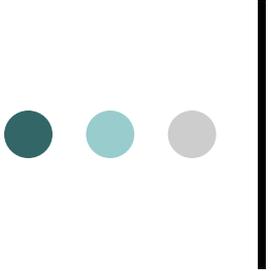
Molecular Characterization of the GE Animal Lineage

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 \equiv an adverse outcome

Hazard \equiv substance or activity that has the potential to cause a harm

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

...or

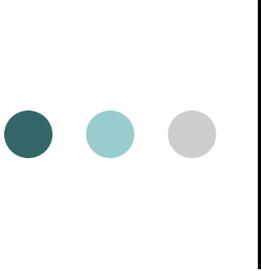
$$\text{Risk} \propto f_{\text{outcome}}(\text{exposure}, \text{hazard}),$$

or

“the likelihood of harm”

Receptor \equiv individual or population experiencing risk

Safetyreasonable certainty of no harm (established standard)



Potential Environmental Hazards and Risks

Hazard	Risk
Use of viral sequences, including vectors <i>(Characterized in Molecular Characterization steps)</i>	Increased probability of new pathogenic recombinants
Traits increasing species fitness or adaptation <i>(Characterized in Phenotypic Characterization)</i>	Increased probability of disruption of existing ecosystems due to establishment of a GE animal in the environment
Altered population dynamics due to horizontal transfer of gene construct(s) <i>(Likelihood of transfer; part of Molecular Characterization steps)</i>	Specific risk is a function of the nature of the trait

Environmental Assessment: General Risk Questions

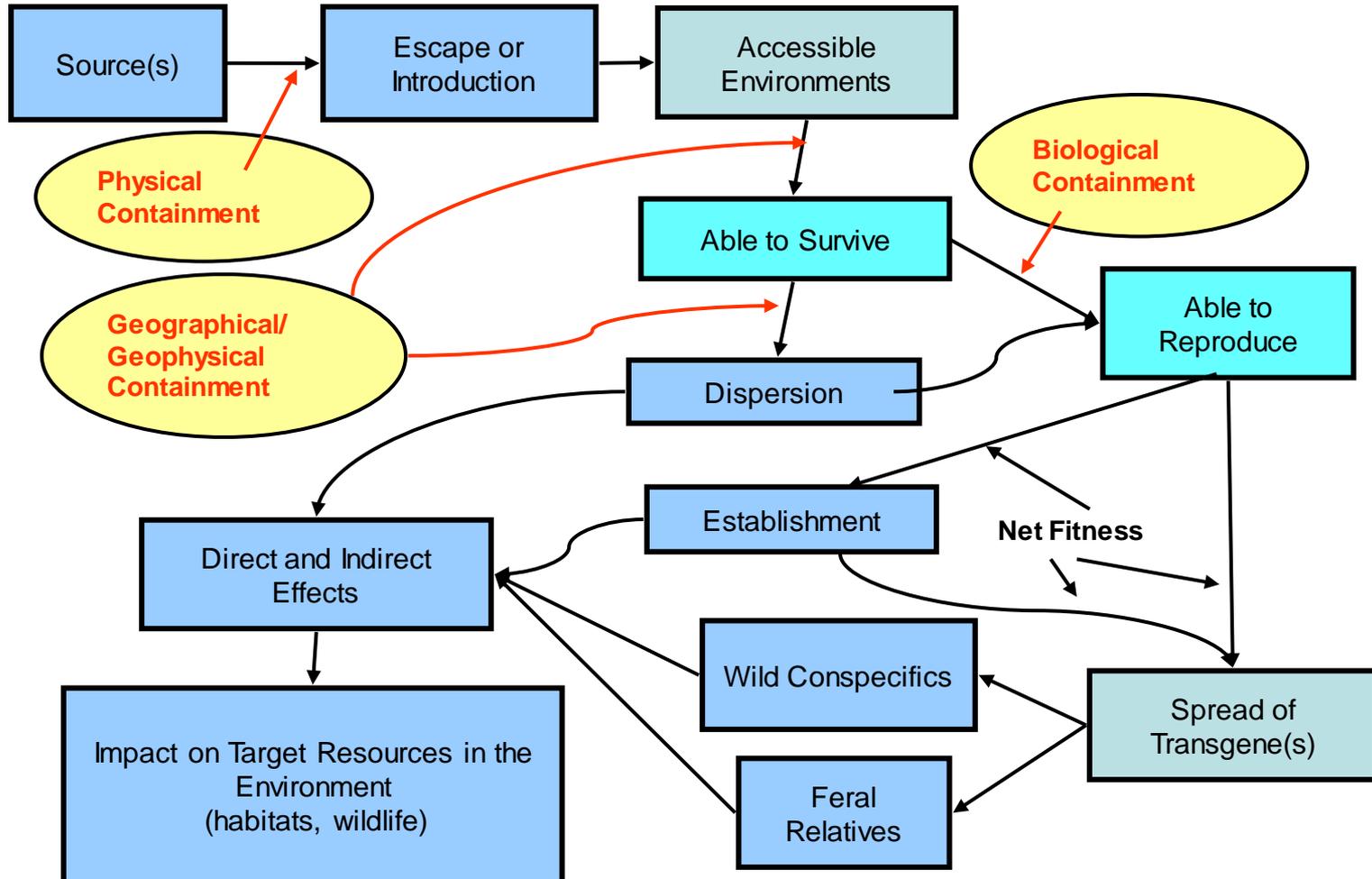


For a specific GE animal (population) containing a specific rDNA construct....

- 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

Conceptual Framework for Environmental Assessment

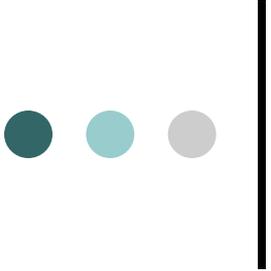


Consequences of Introduction, Escape, and Dispersion

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?

Contacts at CVM:

Dr. Eric Silberhorn eric.silberhorn@fda.hhs.gov

Dr. Evgenij Evdokimov evgenij.evdokimov@fda.hhs.gov