Regulation of Novel New Animal Drugs

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Terminology

Novel:

New and not resembling something formerly known or used (Merriam-Webster)

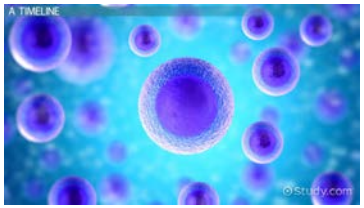
Innovation:

The introduction of something new

(Merriam-Webster)

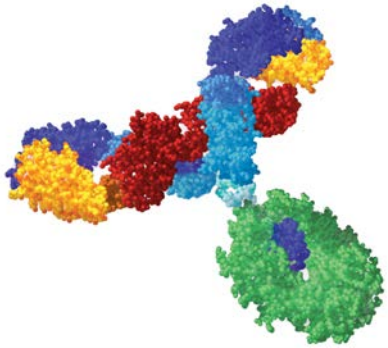
What do these terms mean to CVM and our stakeholders?

Examples



Improvest®

(Gonadotropin Releasing Factor Analog-Diphtheria Toxoid Conjugate, 0.2mg/mL)



AquaBounty TECHNOLOGIES

Definition of a New Animal Drug (FD&C 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)

- In general, an unapproved animal drug is unsafe
  - Exception for investigational new animal drugs
- An unsafe new animal drug is adulterated
- **Must meet standard of approval**
  - safety (human food, target animal, human user, environmental impact)
  - effectiveness
  - quality manufacturing
  - properly labeled

Coordinated Framework

- FDA regulation is based on the rational and scientific evaluation of products, and not on *a priori* assumptions about certain processes.
- Congress has provided FDA authority to regulate products regardless of how they are manufactured.
- Review of products using biotechnology is based on the intended use of each product on a case-by-case basis.
- FDA will evaluate products in cooperation with USDA and EPA, where appropriate.

ONADE's Vision/Mission

- Expeditiously approve quality safe and effective new animal drug products through a science-based approach in a regulatory environment
  - Employ applicable science to make high quality safety and effectiveness decisions
  - Keep unsafe and ineffective drugs off of the market
- Communicate with our stakeholders and understand the forces that affect them
  - Understand the economics of the animal health industry as it pertains to drug availability
- Protect human, animal, and environmental health and promote a safe and abundant food supply

How we measure success of our public health mission

Put in the hands of the end-user

- approved,
- safe and effective,
- quality manufactured,
- properly labeled

new animal drugs to meet therapeutic and production need of animals

Regulatory Strategies for Novel Products

- Same statutory requirements apply, but can require innovative thinking on how to address them
- Unique technical sections (e.g. product characterization, durability, etc.)
- Early interactions with sponsors (PID, EI, Tech Teams)
- Guidance/policy development
- Collaboration/communication with other Offices; Centers within FDA; external agencies such as USDA, EPA; international regulatory bodies (EMA, VDD, etc.)
- Communication/Outreach

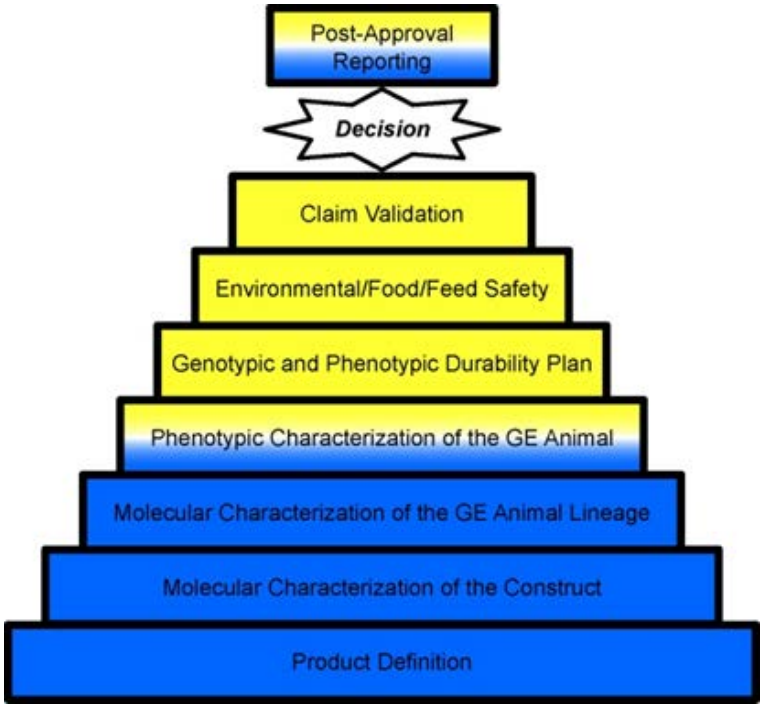
Genetically Engineered Animals

- Growing field
- Regulatory framework developed
  - GFI #187 published, recently updated to include genome editing (draft)
- Three approvals (1 food animal, 2 biopharm animals)
- Regulation based on risk (e.g. GloFish, animal models of human disease, research animals)

AquaBounty TECHNOLOGIES

GE Animal Review Process

- Alternative approach to review
  - AND it Satisfies the statutory requirements for safety and effectiveness
  - Follows NADA regulations with adaptations for technology/expertise



Regulatory Challenges- GE animals

- Public Perception of GE
- Ease of use of CRISPR/Cas-9 technology (e.g. biohackers)
- New technology, limited amount of data available
- Need for additional policy and guidance
- Outreach/Education

Cell-Based Products

- Science is rapidly evolving
- Product Characterization prior to clinical trials (unique technical section)
- risk-based approach to creating a predictable and efficient pathway to approval and regulation of cell-based products throughout their life-cycle

Regulatory Challenges- Cell-based products

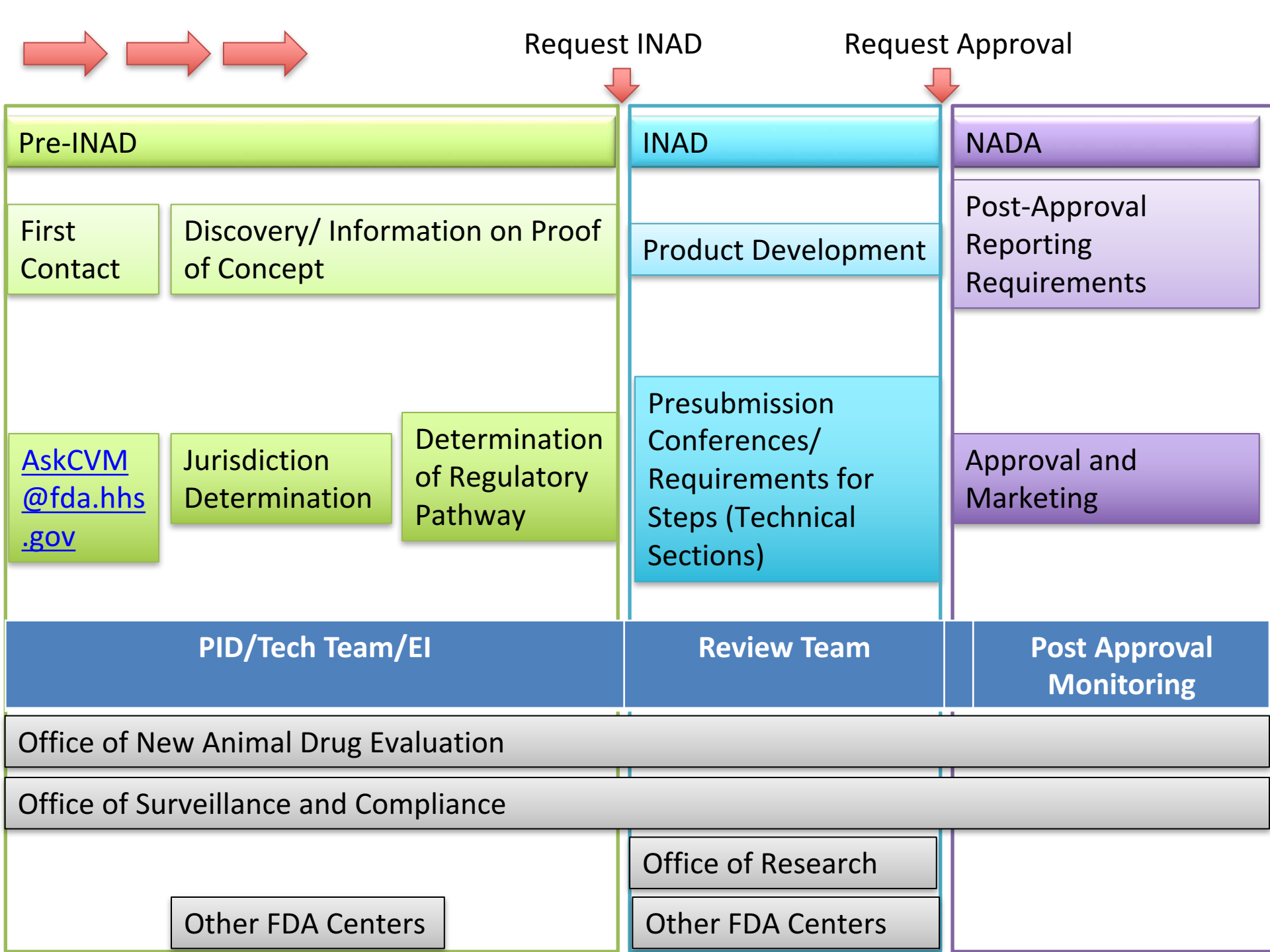
- Rapid growth in industry
- Public perception of miracle cures
- Scientific limitations
  - Adequate characterization
  - Veterinary specific reagents and assays
  - Bioassays and clinical comparability

Regulatory Challenges- Cell-Based Products

- Communication with industry
  - Lack of group representation
- Need for product-specific policy and guidance
  - Rapidly growing industry
  - Unique aspects to cell-based products
- Education for industry and public

Early Interactions with Sponsors

- Pre-Investigational Development/Tech Teams
- Early Information


Request INAD
Request Approval
Pre-INAD
INAD
NADA
First Contact
Discovery/ Information on Proof of Concept
Product Development
Post-Approval Reporting Requirements
AskCVM @fda.hhs .gov
Jurisdiction Determination
Determination of Regulatory Pathway
Presubmission Conferences/ Requirements for Steps (Technical Sections)
Approval and Marketing
PID/Tech Team/EI
Review Team
Post Approval Monitoring
Office of New Animal Drug Evaluation
Office of Surveillance and Compliance
Office of Research
Other FDA Centers
Other FDA Centers

Early Information

- Available to all sponsors
- Focus is on a single proposed product
- CVM provides earlier answers to sponsor's specific questions, allowing the sponsor to propose a development plan more acceptable to CVM
- Usually during the INAD process
- For alternatives to antibiotics, can happen prior to opening and INAD
- Example:
  Discussion on novel experimental designs

Pre-Investigational Development/Tech Teams

- Early interactions between CVM and the sponsor during development/proof of concept work
- Typically utilized for novel technologies (stem cells, GE animals, etc.)
- Submissions can be filed under a VMF, not subject to user fees
- Allows for information exchange/discussion of any potential regulatory hurdles prior to the approval process
- No binding decisions/agreements
- Goal is to provide for a more efficient and seamless approval process for novel products

Focus Groups

- internal teams used to address broad topic areas.
- may be technology-focused, such as biomarkers, or process improvements.
- These might be formed based on conversations with a sponsor.

Collaboration with other Centers/Agencies

- CVM/CBER working group (cell-based products and GE animals)
- Dual approval for “biopharm” animals; coordination between Centers
- Close interaction with CFSAN/USDA/EPA
  - Guidance/policy development
  - Jurisdictional decisions
  - GE animals used for food

Guidance/Policy Development

- Examples of recent guidance documents created to address novel products
  - GFI #187 Regulation of Intentionally Altered Genomic DNA in Animals
  - GFI #218 Cell-Based Products for Animal Use
  - GFI #236 Clarification of FDA and EPA Jurisdiction over Mosquito-related Products
- Ongoing efforts to publish additional GFI/regulations
- Development of Compliance Programs specific to the technology

International Collaboration

- Veterinary Drug Directorate (VDD)
  - Regulatory Cooperation Council (RCC) – simultaneous review VDD and FDA
- European Medicines Agency (EMA)
  - meet quarterly, scientist-to-scientist
  - Parallel Scientific advice available
- VICH – Chairs, EWGs
- CODEX- CVM chairs the Codex Committee for Residues of Veterinary Drugs in Food setting maximum residue limits (MRLs) for residues in food
- Other opportunities for regulator-to-regulator collaboration (MOU/confidentiality agreements with other countries)

ADVENT

- Ad Hoc Expert Group on Veterinary Novel Therapies – EMA
- Current EMA ADVENT groups :
  - Monoclonal antibodies for veterinary use (specific questions to be addressed by ADVENT)
  - Cell-based products for veterinary use (2 documents focusing on sterility/donor eligibility)

Communication/Outreach

- Websites
- Webinars
- Meetings/Conferences
  - BIO
  - NAVRMA
  - USDA/FAS
  - DARPA (Safe Genes)
  - NIH

When should you contact CVM?

- Early in development/proof of concept studies
  - Call/email
  - General discussion
  - Jurisdiction determination
  - Invite you for a meeting
  - Make a recommendation as to whether/when you should open an INAD or submit to a VMF
  - Walk you through your general obligations and responsibilities
    - Regulatory
    - User Fee

Take Away Message

- We welcome innovation as a regulatory agency
- Come in early and often to talk to us
- Bring data
- We intend to exercise enforcement action on fraudulent, unsafe products

Contact Information

- AskCVM@fda.hhs.gov (all inquiries)
- Animal Bioengineering and Cellular Therapies Team
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  - Project Manager: Sarah Bembe, Sarah.Bembe@fda.hhs.gov, 240-402-0599


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