U.S. Food and Drug Administration

Department of Health and Human Services

CENTER FOR VETERINARY MEDICINE

FDA Guidance 218: Cell-Based Products for Animal Use

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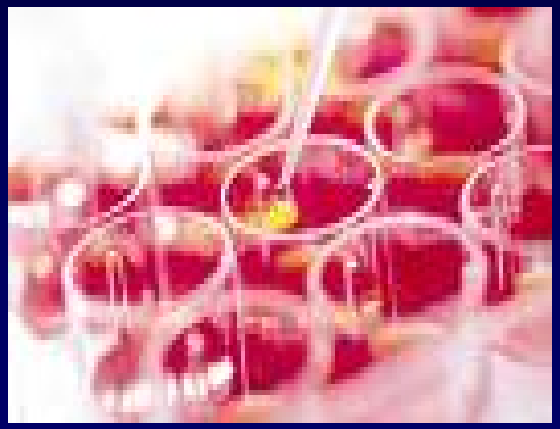
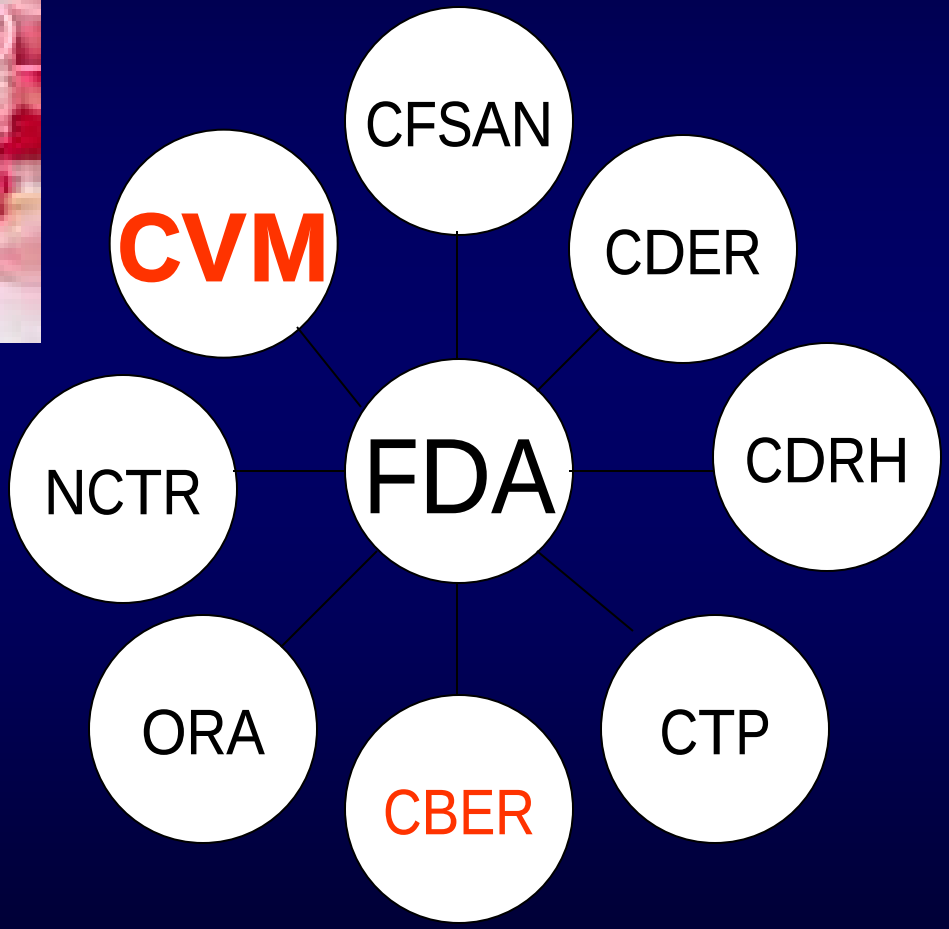
What is the FDA?

The Food and Drug Administration (FDA) is a federal agency within the Department of Health and Human Services.

What does FDA regulate?





What is CVM?

The Center for Veterinary Medicine

- Consumer protection organization, fostering public and animal health
- Authority derived from the Federal Food, Drug, and Cosmetic Act
- CVM is responsible for assuring that animal drugs and medicated feeds are safe and effective and that food from treated animals is safe to eat.

GFI 218 Cell-based Products for Animal Use

- Clarify FDA's jurisdiction
- Existing regulations apply
- Common vocabulary
- Risk-based categories
- Encourage communication

Cell-based Products

Articles containing, consisting of, or derived from cells that are intended for implantation, transplantation, infusion, or transfer into an animal recipient

Animal stem cell products (ASCPs) are a subset of cell-based products

Drug vs Biologic

- FDA regulates new animal drugs
- USDA regulates veterinary biologics
- Most cell-based products are drugs

What Regulations Apply?

- Existing animal drug laws and regulations apply
  - Food Drug and Cosmetic Act
  - New Animal Drug Regulations

Legal Marketing Status

- FDA Approved Application
  - NADA-new animal drug application (pioneer)
    - ANADA-abbreviated NADA (generic)
    - CNADA-conditionally approved NADA
    - Indexed minor species products

Categories of ASCPs

- Xenogeneic
- Allogeneic
- Autologous Type I
- Autologous Type II

Categories of ASCPs

- All cell-based products require premarket review and FDA approval to be legally marketed
- Autologous Type II are a lower enforcement priority – see GFI 218

Autologous Type I

More than minimal manipulation

Non-homologous use

Dependent on metabolic activity

Combined with another article, drug, or device

Use in food producing animals

Autologous Type II

Only if all of these criteria are met:

- Minimally manipulated
- Homologous use
- Not combined with other articles, drugs, or devices
- Use in non-food animals only

Autologous Type II

FDA expects:

- GMPs
- Manufacturing facility registration
- Labeling that is truthful and not misleading
- Adverse event reporting

Contact CVM

- **EARLY**
- Prior to studies in client-owned animals
- Determine the regulatory status of your product
  - Work together with CVM
  - Share information
  - Determine path to approval

Path to Approval

- Safety
- Effectiveness
- Quality

Cell-based Product Considerations

- Product characterization
- Demonstrated control of manufacturing
  - Reliability of tissue handling and cellular isolation
  - Preserve cellular function and integrity
  - Prevent contamination
- GMPs
- Principles of GTPs

Cell-based Product Considerations

- Donor selection criteria
- Tumorigenicity or unintended tissue formation
- Immunogenicity
- Long term safety
- Cell survival
- Biodistribution
- Product, indication, or species-specific considerations

Pre-INAD meetings

- Prior to opening an Investigational New Animal Drug (INAD) file
  - Inform CVM about the product
  - Learn about the approval process
  - Discuss considerations for cell-based products that may impact early stages of your development plan

Pre-INAD Research: Lab Animals

- Investigational exemption for studies in laboratory research animals
- (21 CFR 511.1(a))
  - Does not include animals intended to produce food
  - Does not allow for marketing
  - Labeling, records
  - Talk to CVM early

INAD

- Open the INAD
  - Prior to studies in client-owned animals
  - Allows for detailed product discussion and review
- Request a meeting to discuss product characterization, donor eligibility, and development plan

ADUFA Fees

- Animal Drug User Fees are fees paid by sponsors to support the review of animal drugs
- Waivers:
  - Barrier to Innovation
  - Strongly recommend applying before opening INAD

INAD Research: Client-owned animals

- Investigational exemption for clinical studies (Client-owned animals)
- (21 CFR 511.1(b))
  - Comply with clinical INAD regulations
  - Preliminary studies may inform development plan and study design
  - Safety and Effectiveness studies
  - Talk to CVM early

Clinical Investigation Requirements

- Drug delivery notices submitted to INAD
- Record keeping, monitoring, labeling
- Authorization for use of edible products
- Report serious adverse events
- No commercial distribution or test marketing
- Do not represent as safe and effective

Product Characterization

- Mutual understanding of the product and process
- Informs risk-based approach to development plan and study design
- Characterizes manufacturing, safety and effectiveness profile
- Can be submitted when the INAD is opened

Donor Eligibility Criteria

- Ensure health of donors
- Prevent transmission of disease agents
- Can be submitted when the INAD is opened

Presubmission Conference

- Approval process is risk based and product specific
- Work together on development plan

Protocols

- May be submitted to CVM for review
- CVM concurrence means we fundamentally agree with the study design

Major Technical Sections

- Manufacturing-GMP, principles of GTPs
  - Identity, strength, quality, purity
- Safety-GLP
  - Target animal, special studies
- Effectiveness-GCP
  - Substantial evidence, field study, conditions of use
- Human Food Safety
- Environmental

Minor Technical Sections

- Labeling
- All Other Information
- (Freedom of Information)

Administrative NADA

- Administrative New Animal Drug Application (NADA)
- **Completion of Administrative NADA = FDA approved product**
- Non-administrative NADA

References

- CVM website http://www.fda.gov/AnimalVeterinary/default.htm
- FOI summaries
- CVM guidances
- New animal drug regulations
  - 21 CFR 511 and 21 CFR 514
- CBER regulations and guidances

Contact Information

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