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-IN AD 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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