USDA United States Department of Agriculture

Animal and Plant Health Inspection Service

Licensing Requirements for vaccines: US perspective

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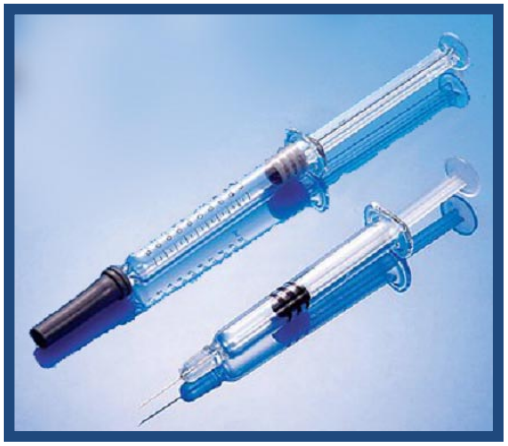
CVB Mission

The Veterinary Biologics Program implements the provisions of the Virus-Serum-Toxin Act to ensure the veterinary biologics available for the diagnosis, prevention and treatment of animal diseases are pure, safe, potent, and effective.



Primary Missions (linked to VSTA)

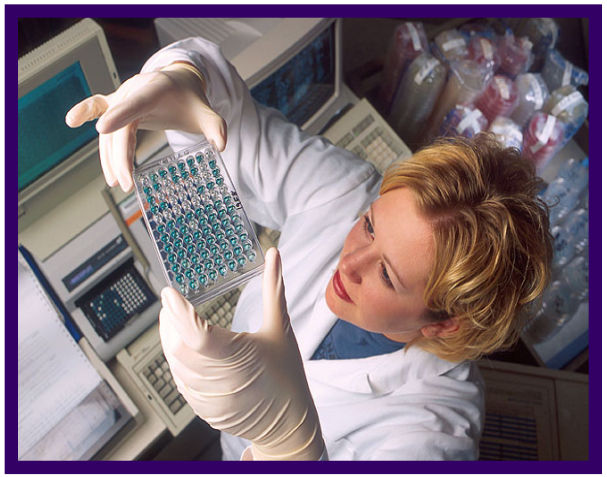
- Licensing/Permitting Veterinary Biological Products
- Evaluating product dossiers
- Evaluating (testing) products and product critical components
- Program documentation (notices, memorandum, regulations, licensing considerations)
- Facility inspections

Product Types

- Vaccine
- Bacterin and Bacterial Extract
- Toxoid
- Bacterin-Toxoid
- Antitoxin
- Antiserum and Antibody
- Diagnostic Test Kits
- Immunomodulator and Immunostimulant
- Allergenic Extracts

Testing Activities

- Confirmatory and Investigatory Testing (pre- and post-license)
  - Seeds and cells
  - Final Product (check and surveillance)
- Test development and standardization
- Reference/reagent production and distribution
- Technical harmonization
- Quality Assurance
- Training and scientific advice



Confirmatory and Investigative Testing

- Pre-license
  - Seeds
  - Cells
  - First Serials

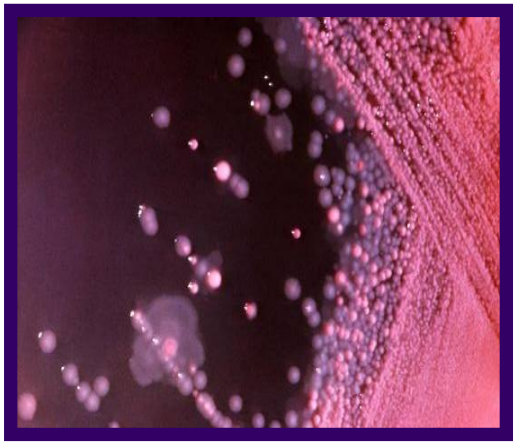
- Post-license
  - Random selection of samples prior to release
  - Problem, surveillance, stability, dating extension, reprocess
  - First serials after change
  - Investigation of field reports

Confirmatory and Investigative Testing

- Efficacy (Pre-license)
  - Host Vaccination-Challenge
  - Minimum antigenic dose, highest passage
  - Route, Age, etc.
  - Duration of Immunity
- Field performance (Post-license)

Confirmatory and Investigative Testing

- Potency - correlated to Efficacy
  - Live
    - Enumeration
  - Killed
    - Vaccination-challenge/Vaccination-serology
      - Host Animal
      - Laboratory Animal
    - *In Vitro*
      - Validated with *in vivo* testing



Confirmatory and Investigative Testing

- Safety
  - Pre-license
    - Controlled animal studies
      - Backpassage
    - Field trials
  - Post-license
    - Laboratory animals
    - Target animals

Licensing Exemptions

- Official USDA Program, emergency disease situation, or USDA experimental use
- Veterinarian-client-patient relationship
- Animal owners
- Products under State license
  - *Currently, no active state programs*
- FDA Export Reform and Enhancement Act of 1996
  - No U.S. Establishment # on the label
  - Not approved for distribution in the U.S.
  - Claims not allowed in the U.S.

Types of Product Licenses

Standard

- Autogenous
- Conventional
  - Breakout or fall-out
- Genetic modified

Conditional

Autogenous Product

Requirements:

- Outline of Production
- If killed viral Autogenous Vaccine
  - CVB confirmatory testing and approval of Master Cell Stock (MCS)
- Labels

Risks:

- Unknown efficacy
- Unknown potency
- Minimal safety

Conventional Products

Requirements (VS Memorandum 800.50):

- Outline of Production
- CVB confirmatory testing Master Seed(s)
  - If modified-live: reversion-to-virulence and shed-spread studies
- If viral vaccine
  - CVB confirmatory testing of MCS
- Efficacy studies
  - Establish minimum dose
  - Duration of immunity studies
  - Immunological interference studies
  - Studies in maternal antibody-positive animals

Conventional Products

Requirements (continued):

- Safety studies
  - Field Safety
  - If Killed vaccine:
    - Inactivation kinetics
  - establishment of slaughter withholding period for adjuvant
- Potency test validation data
  - Reference qualification & stability monitoring
  - Sensitivity/specificity
- CVB confirmatory testing prelicense batches
- Labels

Conventional Products

Risks:

- Minimal

Breakout of Conventional Products

Requirements:

- Combination products may be blended into smaller fraction products following same manufacturing procedures and release criteria
- Outline of Production
- Labels

Risks:

- Safety-excess antigen concentrations

Genetic Modified Products

Same requirements as conventional products plus:

- Summary Information Formats (SIF). For Master Seeds produced by recombinant DNA technology, additional safety and identity data
  - Publication of an environmental release risk assessment before conducting Field Safety
  - CVB confirmation of recombinant seed

Risks:

Safety-Recombination of Live Vectored products

Conditional Licensed Products

Requirements:

- All are mono-fraction majority Killed Products
- Outline of Production
- CVB confirmatory testing Master Seed(s)
- If viral vaccine
  - CVB confirmatory testing of MCS
- Reasonable expectation of efficacy study
  - Serology
  - Small host animal vaccination/challenge
- Safety studies
  - Field Safety
  - Inactivation kinetics
  - establishment of slaughter withholding pe
    for adjuvant
- Labels

Conditional Licensed Products

Risks:

- Unknown efficacy
- Potency not correlated to efficacy

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