



United States Department of Agriculture

# Veterinary Services

## General Licensing Requirements in the United States

Center for Veterinary Biologics  
U.S. Department of Agriculture  
Animal and Plant Health Inspection Service  
Veterinary Services  
2014



# Mission

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

# "Biological Product" - Definition:

- All viruses, serums, toxins, or analogous products.....which are intended for the use in the treatment of animals and which act primarily through.....the immune system or immune response.

# Virus-Serum-Toxin Act of 1913



# Virus-Serum-Toxin Act

## ...it is unlawful to:

- Sell worthless, dangerous or contaminated biologics
- Ship biologics unless they are:
  - prepared in compliance with USDA regulations
  - prepared in a licensed establishment

# Types of Veterinary Biologics Licenses

- Establishment License & Product License
  - Regular [Diagnostic Test Kits and Vaccines]
    - with or without restrictions
  - Conditional (reasonable expectation of efficacy)
  - For further manufacture
  - For export only
- Exemption: Official USDA Program, emergency disease situation, or USDA experimental use

# Types of Veterinary Biologics Permits

- Establishment License & Product Permit
  - Regular [Diagnostic Test Kits and Vaccines]
    - with or without restrictions
  - ~~Conditional~~
- Permits for Research & Evaluation

# Ensuring Quality of Veterinary Biologics in the U.S.

- Licensing Requirements
- Quality Manufacturing Standards
- Inspection
- Testing (pre- and post-licensure)
- Serial (batch) Release
- Compliance Actions
- Vaccinovigilance

# Ensuring Quality of Veterinary Biologics in the U.S.

- Extensive prelicense review of purity, safety, potency, and efficacy data
  - Science-based
  - Risk-based
  - Data-driven
- Established licensing standards
- Established product standards (production, testing, stability, duration of immunity, etc.)

# Ensuring Quality of Veterinary Biologics in the U.S.

- Requirements for manufacturers to prepare products in accord with standards established at the time of licensure
  - Outline of Production
- Requirements to follow good manufacturing practices
- Prelicensure testing of ingredients (seeds and cells) and consistency serials
  - USDA confirmatory testing

# Ensuring Quality of Veterinary Biologics in the U.S.

- USDA check testing prior to release to monitor manufacturer's quality processes
- USDA Compliance testing (investigatory, stability, etc.)
- Monitoring each batch for purity, safety, and potency (APHIS release)



# Licensing of Veterinary Vaccines



# Licensing Requirements for Vaccines

- Purity
- Safety
- Potency/Efficacy

# Purity - Supporting Data Must Demonstrate Purity of:

- Master Seed
- Master Cell Stock
- Ingredients
- Completed Product
  - bacterial/fungal contamination
  - inactivation

# Master Seed Concept

- Applies to conventional, recombinant, and monoclonal antibody products
  - Master Seeds undergo extensive testing for purity and safety
  - Resulting products are, therefore, free of extraneous agents, provided that good manufacturing practices are employed
  - Adherence monitored by inspections and product testing

# Master Sequence Concept

- Applies to Synthetic DNA and Peptide products
  - DNA/Peptide sequence of material used in pivotal efficacy study establishes Master Sequence
  - Prelicense evaluation
  - Manufacturing methods are validated to ensure that the Master Sequence is maintained throughout the production process

# **Safety - Supporting Data Must Demonstrate Safety in:**

- Laboratory animals
- Host animals
- Environment
- Field studies
- Completed product
  - varies by product

# Safety - Supporting Data:

- Master Seed reversion to virulence
  - live products
- Field Safety (3 distinct locations)
  - all classes of animals on the label
- Other Safety
  - effect on food animal production
- Serial Release Safety
  - varies by product

# Potency & Efficacy - Supporting Data:

- Support of all label claims (age, route, etc.)
- Master Seed immunogenicity
  - Most often host animal vaccination/challenge
- Established laboratory animal or in-vitro minimum potency levels for each serial
  - Completed product potency
- Stability

# Potency & Efficacy - Supporting Data:

- Product prepared in production facilities on scale representative of normal production
- Must be conducted using product produced at or below the minimum potency provided in the Outline of Production
- Duration of immunity for new products
- Must support efficacy in each species

# Potency & Efficacy - Supporting Data:

- Must use product produced at highest passage from the Master Seed provided in the Outline of Production
- Interference studies (if appropriate)
- Duration of immunity for new products
- All data must be reported
- Data must demonstrate significant clinical effect

# Review – Basic Licensing Requirements

- Characterization of Master Seeds and Cells
  - USDA confirmatory testing
- Host animal efficacy
  - Controlled studies
  - Adequate number of animals to provide statistical evidence that product provides protection claimed on labels

# Review – Basic Licensing Requirements

- Safety trials
  - Backpassage tests (live)
  - Field safety (minimum of 600 animals, 3 different geographic locations)
- Validated potency assay for serial release (confirmed stability through dating)
- Prelicense serials
  - 3 consecutive (USDA confirmatory testing)

# Good Licensing Practices

- Veterinary Services' licensing process is well defined
- Work with manufacturer early
  - Know the pitfalls
  - Early involvement expedites later review
- Work with Veterinary Services early
  - Information on requirements
  - Review of protocols supports later review

# *The Goal:* Tools for Animal Health

