Target Animal Batch Safety Test

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[redacted]

Virus-Serum-Toxin Act

...it is unlawful to:

- Sell **W**orthless, **D**angerous, **C**ontaminated, or **H**armful (**W-D-H-C**) biologics

- Ship biologics unless they are:
  - prepared in compliance with USDA regulations
  - prepared in a licensed establishment

Regulatory Framework

- Virus-Serum-Toxin Act (1913 & 1985)
  (21 U. S. Code, Sections 151-159)
- Title 9 Code of Federal Regulations
  (Parts 101-122)
- Veterinary Service Memorandums and Notices
- General Licensing Considerations

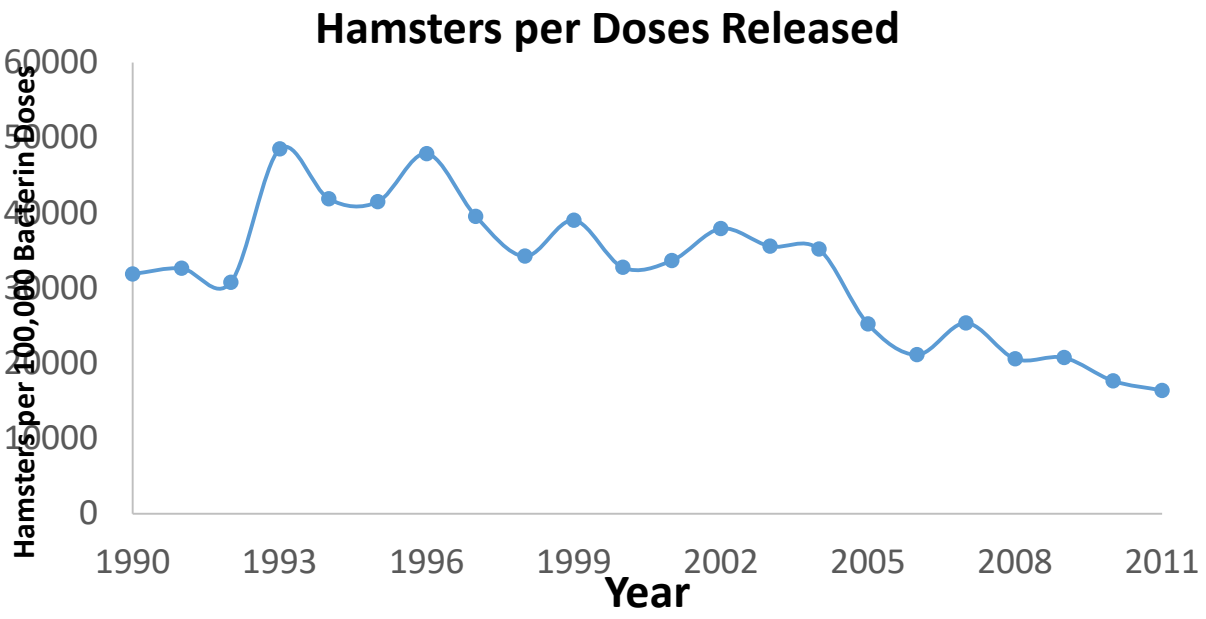
Progress towards 3R Accomplishment

- 1980s/90s – Shift from Host/Lab animal vaccination/challenge to vaccination/serology
- 1980s/90s – Correlation of potency test to protective antigen quantification and host efficacy for killed virus products

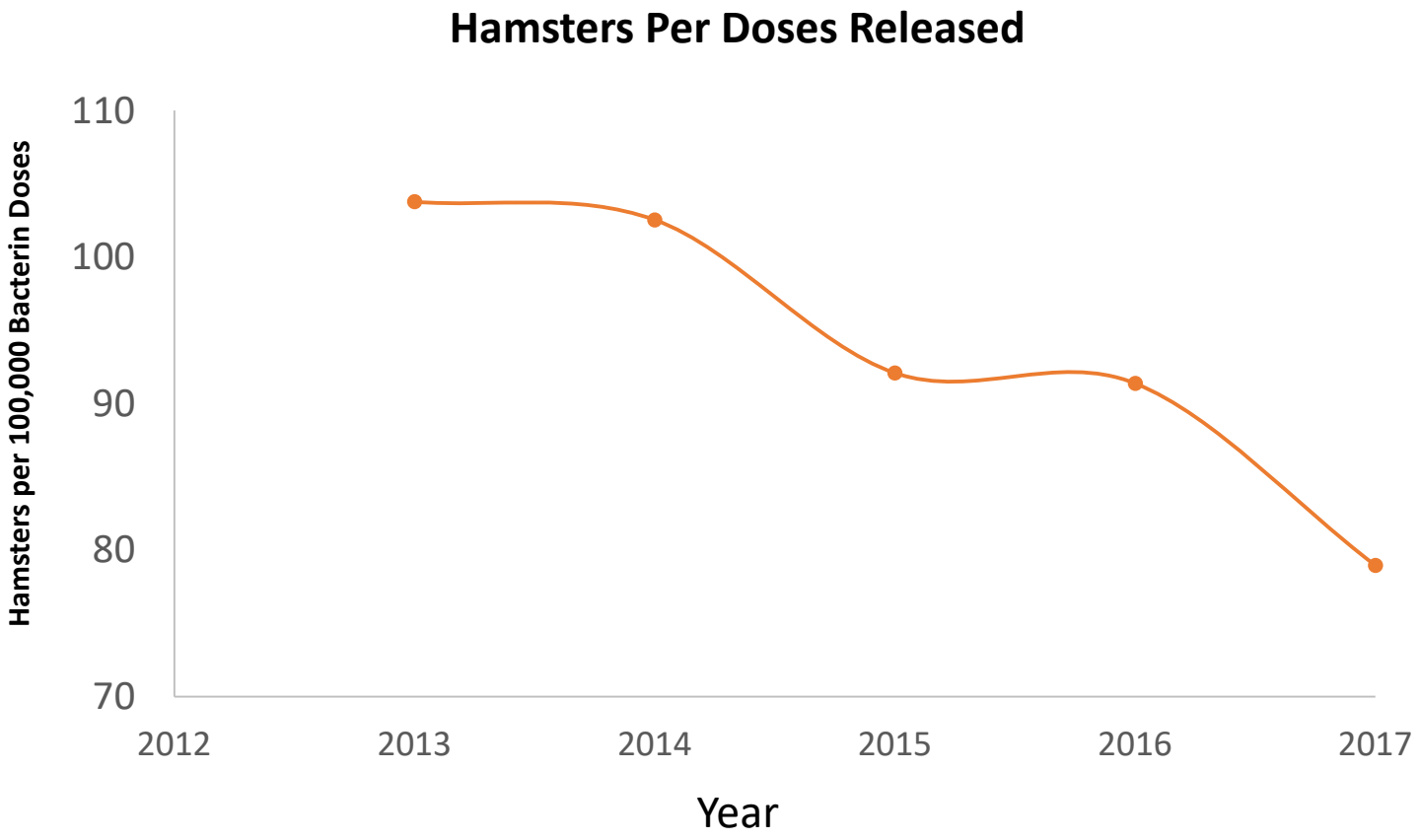
USDA
United States Department of Agriculture

Progress towards 3R Accomplishment

1992 - Relative Potency with ELISA
Leptospira Product Testing



Progress towards 3R Accomplishment



Progress towards 3R Accomplishment

- 1992 - Relative Potency with ELISA
- 1998 - Humane Endpoints acceptance & regulatory change in US.
- 2004 - Exemption to 3-year Master Seed Immunogenicity
- 2006 - Reference qualification & requalification by serology
- 2011 – Extension of reference dating to 15 years
- 2012 – Use of analgesics/anesthesia for IC inoculations

Safety Per 9 CFR

- 9 CFR 101.5(d) *Safe or safety.* Freedom from properties causing undue local or systemic reactions when used as recommended or suggested by the manufacturer.

- 9 CFR 101.5(l)(m) *Healthy* and 9 CFR 101.5(n) *Unfavorable reactions.*

- 9 CFR 113.5(a) No biological product shall be released prior to completion of test prescribed in the Outline of Production or Standard Requirements for the product to establish the product to be pure, safe, potent, and efficacious.

9 CFR Standard Requirements for Safety

9 CFR 113.64: Live Bacterial Products

- **Lab animal –**
  - 113.33(b) except poultry
- **Target animal** - In each of two (2) animals administer a "X" dose & observe for "X" days
  - **10X dose and observation**
  - 113.39 – cats for 14 days
  - 113.40 – dogs for 14 days
  - 113.41 – calves for 21 days
  - **2X dose**
  - 113.44 – swine for 21 days
  - 113.45 – sheep for 21 days

9 CFR Standard Requirements for Safety

9 CFR 113.100 Inactivated Bacterial Products

- **Lab animal**
  - 113.33 (b) or 113.38
- **Target animal for**
  - 9 CFR 113.100(b)(1) Poultry
  - 9 CFR 113.100(b)(3) Fish, Aquatic species, Reptiles

9 CFR Standard Requirements - Serial of Product

9 CFR 113.200 Inactivated Virus Products

- **Lab animal**
  - **113.33 and 113.38**
- **Target animal for 9 CFR**
  - Poultry
  - 113.204 Mink Enteritis Virus
  - 113.209 Rabies Virus
  - 113.210 Feline Calicivirus
  - 113.215 BVDV
  - 113.216 IBR virus

9 CFR Standard Requirements - Serial of Product

9 CFR 113.300 Live Virus Products

- **Lab animal**
  - 9 CFR 113.33
- **Target animal**: In each of two (2) animals administer a "X" dose & observe for "X" days
  - **10X dose & Observe for 14 days**
  - 9 CFR 113.39(b) healthy cats
  - 9 CFR 113.40(b) healthy dogs
  - **10X dose & Observe for 21 days**
  - 9 CFR 113.41 calves
  - 9 CFR 113.44 swine
  - 9 CFR 113.45 sheep

TABST Exemption

- 9 CFR 113.4 request for an exemption
- Veterinary Services Memorandum 800.116 Target Animal Safety Testing Exemption
  - GL50 - *Harmonization of Criteria to Waive Target Animal Batch Safety Testing (TABST) for Inactivated Vaccines*
  - GL 55 - *Harmonization of Criteria to Waive Target Animal Batch Safety Testing for Live Vaccines for Veterinary Use*
- Live or Inactivated veterinary biologics
- Evaluate 10 consecutive serials from different batches or 5 serials if not manufactured in the past 3 years
- Data to support Product Safety and Consistency in Manufacturing

Exemption Criteria

- **Consistency in Product Manufacturing**
  - Product must be produced in accordance with the Outline of Production (OOP)
  - Serials produced with manufacturing deviations - not acceptable
- **Evaluation of Product Safety**
  - Satisfactory target animal safety test results
  - Number of doses sold and years on the market
  - Pharmacovigilance data – Adverse event report
  - Safety of individual antigen component

Post-Exemption Requirements

- **Outline Revision & Documentation**
  - Upper antigen limit
  - Approval of Exemption
- **Adverse Event Report**
  - Submission on an annual basis

TABST Exemption-Suspension

- **Product Safety Concern**
  - Unfavorable Pharmacovigilance data
- **Concern for Consistency in Manufacturing**
  - Nonconformance in manufacturing
  - Major manufacturing changes
  - Nonconformity identification during CVB inspection
- **Suspension**
  - Product – longer term
  - Serial – short term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