Regulatory Perspective on Trends in Veterinary Biologics

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Predominating Trends

• Increased pressure to bring products to market more quickly
• Increased interest in customized biologicals to meet regional or individual needs
• National regulatory authority and global trade
Regulating at the Speed of Commerce

- Increased pressure to bring products to market as quickly as possible:
  - Highly mutable agents
  - Emerging diseases
  - Novel technologies
  - Acceptance of other regulatory approaches 

vs.

- USDA’s mission to ensure licensed products are pure, safe, potent, and effective
Time to market

• Several approaches have been useful in the U.S. to reduce the time for a new product to gain marketing approvals
Conditional Licenses

• 9 CFR 102.6

• To meet emergency conditions, limited market, local or special circumstance

• Reduced requirements for proof of efficacy ("reasonable expectation") but otherwise must meet all licensing requirements for full licensure

This product license is conditional. Efficacy and potency test studies in progress.
Conditional Licenses:
Limitations

• Special labeling to disclose conditional status, no trade names
• Restricted distribution—requires permission from State or importing authorities
• Annual or biannual license renewal
• Conditionally licensed fractions cannot be mixed with fully licensed fractions
• Once a similar product has full license, no additional conditional licenses are issued
Influenza virus changes

• Veterinary Services Memorandum 800.111, first published in 2007
• Arose from need to keep vaccine Seeds up to date with rapid, frequent virus shift/drift
• Once manufacturer has a full license for killed product, can add, remove, exchange Seeds of same HN type(s) in expedited manner
• Requires only similar serological response. No large-scale field safety
• Updated product receives full license
Platform Technology

- VS Memorandum 800.213, first published 2013
- Inactivated, non-replicating protein or nucleic acid vaccines (any agent) from recombinant technology
- Unchanging part of vector construct + consistent manufacturing method = production platform
- Can prepare limitless vaccine constructs differing only in inserted gene sequence
Production Platforms

• First license using a defined platform--traditional requirements
• Subsequent licenses for same platform expedited
• Depending on similarity of new insert to licensed insert(s):
  – Abbreviated inactivation kinetics
  – Abbreviated field safety studies
  – Abbreviated risk assessment
Production Platforms

• Platform-based Seeds (vector + gene insert) that only have reasonable expectation of efficacy ("conditional" license) may be combined with fully licensed Seeds from same platform

• May be eligible for conditional license even if similar full licenses exist
Emerging Diseases

• Recent examples: Pandemic H1N1 influenza (2009), porcine epidemic diarrhea virus (2013), H3N2 canine influenza viruses (2015)

• To expedite product licensure, USDA obtained, tested Master Seeds for direct distribution to biologics manufacturers. Applicants could use these Seeds in product development with minimal or no additional testing.

• Provided challenge virus and standardized challenge protocol for PEDV
Products for Grave Diagnoses

• Niche products for diseases with grave diagnoses (e.g., cancer) may be conditionally licensed on limited efficacy and safety data with expectation more will be gathered

• Typically evaluated in well-controlled clinical trials with rolling enrollment
Products for Emergency USDA Use

- Foreign animal diseases
- *Can* be used under exemption with no license/permit (9 CFR 106.1)
- BUT current goal is to use only licensed product in emergencies
- Increased reliance on pre-existing foreign dossiers and other streamlined processes to justify conditional licenses or restricted import permits for emergency use
Customized Biologicals

• To meet distinct needs in:
  – A geographic region
  – An integrated animal production system
  – Individual animals
Autogenous Products

- 9CFR 113.113 and VS Memo 800.69
- Traditional Seeds
- Open-ended license to make conventional vaccine from an isolate from a source herd
- Purity tested only. No efficacy or safety testing.
- Can only be used in source herd and adjacent premises
Prescription Products

• VS Memo 800.213 (added 2015)
• Open-ended license to create custom recombinant formulations based on established production platform
• Requires prescribing veterinarian
• Serials (batches) tested for safety, purity. Vet assumes liability for efficacy.
• Gene sequence for platform Seed may be obtained from prescribing veterinarian or other epidemiological data
Prescription Products

- May be used in geographically distant sites, as veterinarian deems appropriate.
- May include gene sequences animals are at risk for exposure but not yet in herd
- Prescription fraction may be combined with fractions licensed for non-prescription products
Prescription products

- Restricted labeling—similar to conditional
- Restricted distribution—only by State permission
- Individual serial (batch) release by USDA
- License issued for 2 years, subject to renewal
Autologous cancer therapeutics

- Immunotherapy as an adjunct to other cancer treatment
- Vaccines prepared from patient’s tumor cells stimulate immune response against same cells
- Custom products prepared in small quantity solely for administration to the same patient are considered a laboratory service and NOT regulated as biologicals by the USDA
Accept other regulatory approaches

• Mutual recognition / regulatory convergence / harmonization
  – All requires a relationship

• National sovereignty and the VICH approach
  – Standardized data/testing vs. standardized decisions
  – Ultimately, will a result be acceptable?
  – Political consequences for failures
Summary

• **Expediting time to licensure**
  – Conditional licenses
  – Streamlined updates of influenza strains
  – Production Platforms
  – USDA provides Seeds for emerging diseases
  – Products for USDA emergency use
  – Products for grave diagnoses

• **Custom Products**
  – Autogenous products
  – Prescription products
  – Autologous cancer therapeutics

• **Regulatory approaches in a global environment**
  – It will continue to be a challenge
Questions?