**Issue 3**-Policy Considerations for Different Product Types

**Product--Specific Considerations, e.g. Viral Vaccines (live, killed, vectored), Bacterins, Bacterial Extracts, Toxoids**

David M. Dusek  
Staff Reviewer  
Center for Veterinary Biologics/USDA  
Ames, Iowa
What is this issue about?

Should the potency requirements of different veterinary biologicals (vaccines and therapeutics) be treated the same or different based on:

- **Category**
  - Virus or bacterial or parasite
  - Live or inactivated
  - Toxoids
  - Recombinant
  - Immunomodulator
Is it this simple?

Some factors to consider

- Species treated
  - Production animal (bovine, porcine, poultry, minor species)
  - Companion animal (canine, feline, equine)
- Adjuvanted vs none
- Type of adjuvant
- Single fraction vs multi-fraction
- Purpose—Herd immunity versus individual protection
- Disease agent (*e.g.* Canine Coronavirus vs Rabies)
Is it this simple?

- Study design (Experimental clinical vs Field efficacy)
  - Representative of the disease transmission in the field vs artificial but convenient
  - Number of animals
  - Effectiveness of challenge strain
  - Route of challenge
  - Primary outcome
  - Case definition
What is the Typical Study Design?

Pivotal efficacy studies are conducted with small numbers of animals using firm devised/CVB reviewed protocols or the 9CFR Standard Requirements.

- Typically 20 treated and 20 controls
- Experimental clinical study
- Usually no dose titrations
- Naïve animals, at youngest age
- Sometimes immunocompromised
  - CD/CD
  - Steroids
- Challenge/route procedure varies
  - Natural vs Convenient
What is the typical efficacy serial and How is it tested?

- Production serial or bench-top in R&D or in process development
- One serial or one of many, evaluated for potency in a validated or un-validated assay
- Maybe the result of a series of proof-of-concept studies or not
Is it this simple? Probably not!
Current release and throughout dating specifications

- Quantal assays *e.g.* titrations of live virus products are set at $\approx 16X$’s ($+1.2\log_{10}$) the efficacy serial and must maintain $\approx 5X$’s ($+0.7\log_{10}$) is required throughout dating.

- Quantitative counts *e.g.* live bacteria must maintain 2x the CFU of the efficacy serial throughout the dating of the product.

- Inactivated products the efficacy, release, and throughout dating are traditionally the same.
Why are they treated differently?

History?
- History is indeed the witness of the times, the light of truth. (Cicero)
- Seemed like a good idea at the time (anonymous)
The reason for revisiting our potency policy and evaluation of stability monitoring and the rationale for setting expiration dates

- A long term process
- CVB is in the early stages
Should there be Product-Specific considerations for setting release and throughout dating potency specifications?

- Perhaps certain categories could be established based on product type, according to some rational criteria.
- But note that the divisions are complex because of the diversity of the products
- Possibilities?
  - Risk-based? (What does this mean?)
  - Category within a species e.g. Bovine
    - Dairy
    - Passive immunity products
  - Feed lot
  - Companion animal (Canine, Feline, Equine)
How do you bring consistency to the situation?

Regardless of possible divisions a common starting point is essential:

- Validated potency assays...... regardless of the product.
- Take into account the variation in the potency assay, manufacturing process, the vial-to-vial variation and the product stability......... regardless of the type of product.
- This is essentially what is proposed by the VSM Draft DOC No. 440.
- A science based approach in line with the plan initiated in 2004 as part of CVB’s long term comprehensive approach to potency testing.
Questions?