Issue 3-Policy Considerations for Different Product Types

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

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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 ≈16X's ($+1.2\log_{10}$) the efficacy serial and must maintain ≈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?