CVB Public Meeting

THE ONE-TIER LABEL CLAIM

VACCINE EFFICACY

- **Efficacy**-Efficacy is the direct effect of a medical intervention on an individual subject. The effect of an intervention program in the population is often termed effectiveness. The notion of effectiveness includes both direct effects and the indirect effects of the intervention at the herd or population level. Vaccine efficacy may be isolated from effectiveness by design or analysis.

HOW DO YOU BEST CONVEY THAT?

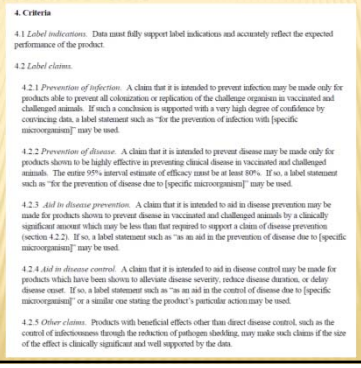
Efficacy

Labeling

LABELING IS REQUIRED TO:

- Provide full instructions on the proper use of the product including:
  - Vaccination schedules
  - Warning/caution statements
  - Etc.
- 4-tier approach to conveying efficacy information

VS MEMO 800.202



4. Criteria

4.1 *Label indications.* Data must fully support label indications and accurately reflect the expected performance of the product.

4.2 *Label claims.*

4.2.1 *Prevention of infection.* A claim that it is intended to prevent infection may be made only for products able to prevent all colonization or replication of the challenge organism in vaccinated and challenged animals. If such a conclusion is supported with a very high degree of confidence by convincing data, a label statement such as "for the prevention of infection with [specific microorganism]" may be used.

4.2.2 *Prevention of disease.* A claim that it is intended to prevent disease may be made only for products shown to be highly effective in preventing clinical disease in vaccinated and challenged animals. The entire 95% interval estimate of efficacy must be at least 80%. If so, a label statement such as "for the prevention of disease due to [specific microorganism]" may be used.

4.2.3 *Aid in disease prevention.* A claim that it is intended to aid in disease prevention may be made for products shown to prevent disease in vaccinated and challenged animals by a clinically significant amount which may be less than that required to support a claim of disease prevention (section 4.2.2). If so, a label statement such as "as an aid in the prevention of disease due to [specific microorganism]" may be used.

4.2.4 *Aid in disease control.* A claim that it is intended to aid in disease control may be made for products which have been shown to alleviate disease severity, reduce disease duration, or delay disease onset. If so, a label statement such as "as an aid in the control of disease due to [specific microorganism]" or a similar one stating the product's particular action may be used.

4.2.5 *Other claims.* Products with beneficial effects other than direct disease control, such as the control of infectiousness through the reduction of pathogen shedding, may make such claims if the size of the effect is clinically significant and well supported by the data.

THESE TIERS CREATE SOME ISSUES

- How well are they really understood?
- They often get used as marketing tools
- Efficacy and reference studies need to target individual tiers
- Differing levels of efficacy for multi-fraction products
- The agency expends resources determining where each study (not product) falls

PROPOSAL

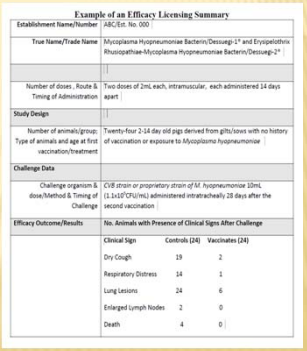
- Replace the multi-tier concept with a single claim/indication statement:

  For the vaccination of healthy (animal) against the (system) form of disease caused by (microorganism).

  (Minimum age, schedule, and revaccination recommendations to follow)

THE OTHER HALF OF THE EQUATION:

Information available on a public web-site



Example of an Efficacy Licensing Summary

Establishment Name/Number	ABC/Est. No. 000
True Name/Trade Name	Mycoplasma Hyopneumoniae Bacterin/Dessuegi-1[a] and Erysipelothrix Rhusiopathiae-Mycoplasma Hyopneumoniae Bacterin/Dessuegi-2[a]
Number of doses , Route & Timing of Administration	Two doses of 2mL each, intramuscular, each administered 14 days apart
Study Design	
Number of animals/group; Type of animals and age at first vaccination/treatment	Twenty-four 2-14 day old pigs derived from gilts/sows with no history of vaccination or exposure to *Mycoplasma hyopneumoniae*
Challenge Data	
Challenge organism & dose/Method & Timing of Challenge	*CVB strain or proprietary strain of M. hyopneumoniae* 10mL ($1.1x10^{9}$CFU/mL) administered intratracheally 28 days after the second vaccination
Efficacy Outcome/Results	No. Animals with Presence of Clinical Signs After Challenge

Clinical Sign	Controls (24)	Vaccinates (24)
Dry Cough	19	2
Respiratory Distress	14	1
Lung Lesions	24	6
Enlarged Lymph Nodes	2	0
Death	4	0

WHAT DO YOU THINK?

- Concept paper
- Q&A's
- Open forum
- Additional meetings as required
- Proposed rule (designated Tier 1 rule)
  - Target is Oct/Nov 2011
  - Address the comments
  - Final rule targeted for Oct. 2012
- At this point, nothing is finalized
- Please share your thoughts

ADDITIONAL QUESTIONS???

- How will we implement this rule?
  - New products vs. Old products
- How will we handle conditionally licensed products?
- How does this rule impact other classes of products?
  - Diagnostic test kits
  - Allergenic extracts
  - Antibody products

ADDITIONAL QUESTIONS (CON'T) ???

- How much safety data, if any, should we include in this proposal?
- How much specific information should be included for challenge strains?
  - Homologous vs. heterologous, etc.
- Does CVB or the manufacturer generate the Product Licensing Summary?
- Will this rule impact information that is currently included in product circulars?

ADDITIONAL QUESTIONS (CON'T.) ???

- Does this rule create any unexpected issues with products sold internationally?
- How will the rule accommodate beneficial products that do not have a direct role in disease control (i.e. for colonization/shedding)?