Feed Ingredient Utility

Mika Alewynse

Division of Animal Feeds

Center for Veterinary Medicine

FDA

AAFCO Definition Process

- Proposed definition
- Description/ purpose of the ingredient
  – Rationale for request
- Use limitations
- Literature information
- Feeding trials/ controlled observations

What Does the Substance Do?

- **Information sources**
  - Other uses
- **Scientific literature**
  - Books
  - Internet databases (AGRICOLA)
  - Libraries
- **Traditional research studies**
- **Behavior of related substances**

What Do You Want to Say About Substance X?

- **Technical effect on feed**
  - **Preservative**
  - **Emulsifier**
  - **Pelleting aid**
- **Source of something for the animal**

Types of Substances Intended for the Animal

- **Nutrient**
  - **Essential nutrients (amino acids, fatty acids, vitamins, minerals, water, and in some cases, fiber)**
- **Flavor (taste)**
- **Aroma (smell)**
- **Coloring – regulated process**
- **New substance**
  - **Feed components have effects beyond supplying essential nutrients**
    - **enzyme**

Caveats about What You Say

- **DSHEA does not apply to animal feed**
  - **Federal Register 61:17706**
- **Substance could be both a food and a drug, based on claims made for product**
  - **CVM Program Policy and Procedures Manual - Guide 1240.3605**
  - **Some structure/function claims could be acceptable if related to "food" properties**

How to Show Substance X Works (Utility)

- **Prior approval or acceptance?**
  - **Substance listed in CFR**
    - **approved Food Additives for feed - 21 CFR 573**
    - **partial List of Generally Recognized as Safe (GRAS) Substances – 21 CFR 582**
  - **Feed ingredient definition published in Official Publication of AAFCO**
- **If approved or listed for the intended use, no problem**
- **Remember intended use includes target species, may need to address this issue**

Showing Substance X Works (cont.)

- **Recognized by an authoritative organization**
  - **National Research Council**
    - **taurine for cats**
  - **Flavor & Extract Manufacturers Assn (FEMA)**
    - **Is the intended use the same?**
- **Demonstrate that Substance X has "food" properties**
  - **Therapeutic effect = animal drug**

What You Need to Show

- **Dependent on identity and properties of Substance X**
- **What is the possible mode of action?**
  - **Scientific literature**
  - **Non-therapeutic physiological effect**
  - **Effects of related compounds**
- **Number of needed studies varies**

Substance X is Nutrient

- **Look in the literature first**
- **Use the appropriate animal model**
  - Avoid chicks if intended use is cattle
- **Lots of different traditional study designs**
  - Deficiency/supplementation studies
- **Use a known comparator**
- **Account for bioavailability**

Substance X is Flavor/Aroma

- **Primarily pet food, but young animals, too**
- **Use the appropriate animal model**
  - Cats and dogs are very different
- **Be sure to use sufficient animals and choices**
  - Subjects need multiple bowls/feeders
- **If using older subjects, be aware of**
  - Prior exposure
  - Predispositions/conditioning
- **Consult with experts as palatability/food choice studies are tricky**

New Substance

- **What is the intended use?**
  - Many of these substances fall in a gray area
  - See CVM Program Policy and Procedures Manual - Guide 1240.3605
    - Improved productivity = drug
    - Disease prevention/treatment/mitigation = drug
- **Use appropriate measures for feed ingredient**

Designing the Study

- **You need statistics!**
- **Foreign locations can be used if conditions are like those in US**
- **Sound study design**
  - **Use sufficient experimental numbers (power of test)**
  - **Focus on effect of Substance X**
    - **studies often include too many additional factors**

Study Design (cont)

- **Mimic proposed conditions of use**
  - Target species
    - cattle versus chickens
    - "animal class"
      - Purpose statement in AAFCO Reg. 3
  - Test proposed use rate!
    - if test down to 500 mg/ lb, label use rate cannot be 250 mg/ lb
    - if test up to 4000 ppm, label use cannot be for 5000 ppm

Study Design (cont)

- – Pelleted versus mash diets
- – Free choice versus limit feeding
- Data must support claim
  - – Measuring fecal Ca levels does not support claims for improved bone density
  - – Animal production or disease prevention/treatment data can mean Substance X is an animal drug!

Study Conduct

- **Analyze feed for Substance X**
  - Do not assume it is there
  - Clearly explain how activity relates to amount added to feed
- **Account for:**
  - Bioavailability
  - Storage/ dietary stability
- **When study protocol is not followed, explain the changes**
  - Don't make us guess

Study Results

- **Appropriate statistical analysis**
  - **Use the CORRECT experimental unit**
    - **often the pen, not individual animal**
  - **Make sure you can compare treatments**
    - **lowest level which shows statistical improvement over negative control**
    - **contrast of control vs. all levels of substance X unlikely to be beneficial**

General Points

- **Submit complete study reports**
  - Raw data (sometimes)
  - Statistical printouts
- **Be sure submitted data support claim**
  - Substance X had a significant effect as expected
  - Data can be pooled over studies if appropriate
- **Submit all information and explain any conflicting studies**
  - Not good when we find conflicting studies that are not mentioned