Animal Feed GRAS Notifications

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GRAS Notification

What is GRAS?!?

What is GRAS?

- GRAS – Generally Recognized As Safe
- 1958 Food Additives Amendment to Federal Food, Drug and Cosmetic Act
  - Defined “food additive”
  - Required premarket approval of food additives
  - Established standards for safety and review
  - Created exemption to food additive definition
    - GRAS status for a specific use of substance

GRAS Exemption

- Any substance intentionally added to an animal feed must be used in accordance with a food additive regulation for that use unless

  the substance is GRAS among experts qualified by scientific training and experience to evaluate its safety under the conditions of its intended use

GRAS Exemption (cont.)

- What does this mean in practical terms?
  - General recognition of safety is for a substance for an intended use
- Two points
  - Substances are not GRAS, it is a particular use of a substance that is GRAS
  - Feed use of substances varies with the animal species, thus
- Feed GRAS determinations must address intended use in the intended animal species

GRAS Status

- There are two parts to establish that a use of a substance is GRAS
  - Safety - Defined in 21 CFR 570.3(i)
  - General recognition - Addressed in 21 CFR 570.30
- Fair evaluation of the data...
  - Need to address all data and information
    - Cannot ignore the “inconvenient” or contradictory

GRAS Status (cont.)

- Safety – same as food additive

  Reasonable certainty of no harm

  - 21 CFR 570.3(i) lists factors to be considered
    - Consumption
    - Cumulative effect\exposure
    - Appropriate safety factors
  - For food animal species, need to consider possibility of tissue residues

GRAS Status (cont.)

- General Recognition
  - Information needed for GRAS determination
    - Must be generally available
    - Must be generally accepted by qualified experts
  - Information needed to establish GRAS status of an intended use of substance cannot be confidential

Information

- Generally available data and information
  - Usually means published studies
  - Can include information in text books
- Availability allows review by any experts qualified by scientific experience and training to evaluate the safety of substances added to food
- Consensus among experts about these data and information establishes GRAS status of intended use of substance

Basis for GRAS Determinations

Experts may base safety conclusions on:

1) Experience based on common use in animal food before 1958
   - Data and information must be generally available
   - Need to show common use

OR

Basis for GRAS (cont.)

2) Scientific procedures
   - Most frequently used
   - Requires same quantity and quality of scientific evidence as required to obtain approval of a food additive regulation
   - Scientific evidence must be generally available

GRAS status is more difficult to establish than a food additive regulation due to requirement for general recognition

Safety Evaluations

- Addressing animal safety is complex
  - Difficult to do cross-species comparisons of toxicity data
  - Recent NRC report found insufficient data to support extrapolation across species
- Animal safety studies in the individual target species are often necessary
- Human food safety may also need to be addressed, dependent on intended use

GRAS Notification

- Proposed rule published in 1997
  - Changing from petition to notification process
- Publication date of final rule is unclear
- CVM implementing pilot program
  - Resources are still an issue
  - Will be announced in the Federal Register
  - Anticipated start date
    - Early 2010

GRAS Notification (cont.)

- Pilot program based on 1997 proposal
- Voluntary
  - Firms can conduct a GRAS determination without notifying FDA
- Notice informs FDA of notifier's determination that a use of a substance is GRAS
  - Notifier's determination and responsibility
  - Summary document, not raw data/complete reports
- FDA responds by letter
  - Notifier can withdraw notice at any time, stops FDA review

Types of FDA Response

- No questions
  - Based on the information provided by [notifier], ... the agency has no questions at this time regarding [notifier's conclusion that [substance] is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding ... GRAS status
- No basis
  - FDA has evaluated the information in [the GRAS Notice]...as well as other available data and information. Your notice does not provide a sufficient basis for a determination that [substance] is GRAS under the conditions of its intended use.

GRAS Notification (cont.)

- Inventory of GRAS notices and FDA responses on the Internet
- Notices available under Freedom of Information Act (FOIA)
  - May also be posted on Internet
  - General recognition means information that establishes safety cannot be confidential
- CVM's process will be similar to CFSAN's on-going pilot program
  - Information about CFSAN pilot program at

http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/default.htm.

Thank You

Center for Veterinary Medicine