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A MATTER OF SCIENCE + FOOD

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Regulatory Paths for Animal Feed Ingredients: Differentiating Between GRAS, Food Additive and Drug

Why Regulation of Food is So Important: Farm Animals

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Why Regulation of Food is So Important: Our Pets

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What is in Animal Food?

- **The use of food products is governed by the provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA), and the regulations issued under its authority. These regulations are published in the Code of Federal Regulations (CFR).**
- **The FFDCA defines food as "articles used for food or drink for man or other animals..."**
  - Therefore, any article that is intended to be used as an animal feed ingredient, to become part of an ingredient or feed, or added to an animal's drinking water is considered a "food" and thus, is subject to regulation.
- **FFDCA sets forth requirements for "foods".**
  - Failure to meet these requirements can result in a product being deemed adulterated or misbranded. Adulteration includes food packaged or held under unsanitary conditions, food or ingredients that are filthy or decomposed, and food that contains any poisonous or deleterious substance. A food may be considered misbranded if its labeling is false or misleading in any way or fails to include required information.

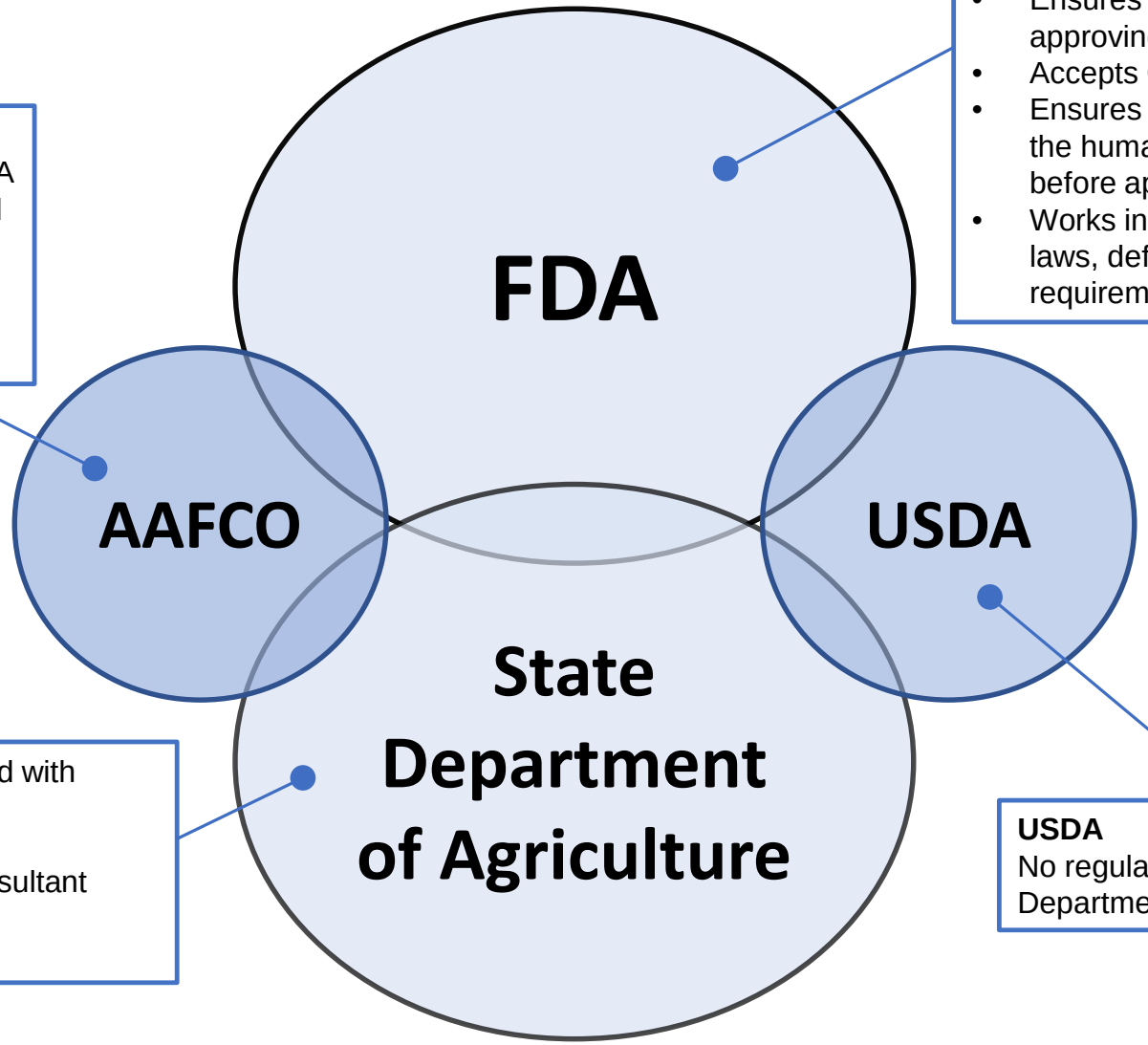
Who Regulates Animal Food?

FDA (CVM): Regulatory authority for animal food charged with enforcing federal laws:

- Ensures food is safe and properly labeled;
- Ensures a food additive is safe and effective before approving it;
- Accepts GRAS Notifications;
- Ensures an animal drug is safe (for the animal and the human (for a food-producing animal) and effective before approving it.
- Works in cooperation with AAFCO developing state laws, defining ingredients, establishing nutritional requirements (extended to 10-1-19).

AAFCO – No regulatory authority. Members from State Department of Agriculture and FDA

- Write Model Bills which may be accepted as state law
- Establish legal definition of ingredients
- Labelling requirements of pet food
- Nutritional requirements of pet food



State Department of Agriculture: Charged with enforcing state laws. Duties include

- Inspections
- Investigations based on veterinary/consultant complaints
- Random testing

USDA
No regulatory authority over pet food; assists State Department of Agriculture and FDA in investigations

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Center for Veterinary Medicine

- **FDA's Center for Veterinary Medicine (CVM)**
  - Mission statement: “Protecting Human and Animal Health”
  - Responsible for approving drugs and food additives and monitoring the safety and effectiveness of these products for animals

Regulatory Pathways for Ingredients

- **Approved Food Additive permitted in feed and drinking water of animals, listed in 21 CFR 573**
- **Substance Generally Recognized As Safe (GRAS) for a use**
  - Partial list in 21 CFR 582 and 584
  - Notified substances to CVM GRAS Program (not required)

    http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/GenerallyRecognizedasSafeGRASNotifications/default.htm
  - Self-determination by qualified experts
- **Approved Color Additive, 21 CFR 73**

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Regulatory Pathways (cont.)

- **Dietary supplement**
  - Regulatory class established by (DSHEA) Dietary Supplement Health and Education Act.
  - 1996 Federal Register Notice 61:17706 – **Does NOT apply to animal food.**
  - Many supplements are animal drugs based on their intended use:
    - Under the FFDCA, expressed or implied claims that establish the intended use to cure, treat, prevent or mitigate disease, or affect the structure/function of the body in a manner other than food (nutrition, aroma, or taste), may identify an intent to offer the product as a "new animal drug." Unless the "new animal drug" product has been shown to be safe and effective for its intended use via approval of a New Animal Drug Application (NADA), it could be subject to regulatory action as an adulterated drug.
    - For example, probiotics for gastrointestinal health are drugs but microorganisms that provide nutritional benefit through SCFA may be GRAS or food additive.

Food Additive Approval

- **Used when a regulation is needed to ensure safe use of the substance**
  - Regulation established via the food additive petition process
  - Must be approved prior to marketing
  - When petition is approved, a food additive regulation is published and added to 21 CFR 573
- **Procedure is described in 21 CFR 571**
- **Regulatory definitions are in 21 CFR 570**

Food Additive Petition

- **Identity and composition of the substance**
  - Chemistry, manufacturing, and controls
- **Intended use, use level, and labeling**
- **Data establishing intended effect**
  - Nutritional, physical, or other technical effect
- **Analytical methods to determine strength, purity, and quality**
  - Must be validated – either accepted by AOAC, FCC, USP or validation data included in the petition

Food Additive Petition (cont.)

- **Safety evaluation**
  - Target animal
  - Human food, if substance is to be fed to food producing animals, including tolerance for residues if needed
- **Proposed regulation**
- **Environmental assessment**
  - Potential environment impacts of additive manufacture, use and disposal, positive or negative, must be addressed – 21 CFR 25

Generally Recognized As Safe (GRAS)

- **Any substance intentionally added to an animal food must be used in accordance with a food additive regulation for that use <u>unless</u>**
  - The substance is GRAS among experts qualified by scientific training and experience to evaluate its safety under the conditions of its intended use
  - General recognition of safety is an exemption in legal definition of food additive

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GRAS and Substances

- **General recognition of safety is for a substance for an intended use**
- **Two important concepts**
  - Substances are not GRAS, it is the particular use of a substance that is GRAS
  - Animal food use of substances varies with the animal species, thus
- **Animal food GRAS determinations must address the intended use in the intended animal species**

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What Uses Cannot be GRAS

- **The uses of the substances listed below cannot be GRAS**
  - Pesticides
  - Color additives
    - Approved under another FDA premarket process
  - Drugs and new animal drugs

GRAS and Substances

- **Two parts to establish that an use of a substance is GRAS**
  - "Safety" as defined in 21 CFR 570.3(i)
    - Standard is same as food additive – "Reasonable certainty of no harm"
    - Factors to be considered
      - Consumption
      - Cumulative effect/exposure
      - Appropriate safety factors
      - For food producing animal species, possibility of residues

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GRAS and Substances

- **Two parts to establish that an use of a substance is GRAS**
  - "General recognition" as stated in 21 CFR 570.30
    - Information needed for a GRAS determination
      - Must be generally available
      - Must be generally accepted by qualified experts
      - Cannot be confidential
    - Generally available data and information
      - Usually means published studies in peer-reviewed scientific journals
      - Information in text books

Basis for GRAS Determination

- **Experts may draw safety conclusions based on:**
  - Experience from common use in animal food prior to 1958
    - Data and information must be generally available
    - Need to show common use

    OR

  - Scientific procedures
    - Most frequently used
    - Requires same quantity and quality of scientific evidence as required to obtain approval of food additive
    - Scientific evidence must be generally available
- **GRAS status is more difficult to establish than a food additive regulation due to requirement for general recognition**

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Animal Drugs

- **The FD&C Act defines "drug" to include, among other things, "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals."**
  - When a company sells bottled water for people to drink as a beverage, the water is not a drug. But if the company sells those same bottles of water as a cure for cancer in dogs, then the water is a drug under the FD&C Act because the intended use is to cure a disease (cancer) in dogs.
  - When a company sells a product claiming it makes cows ovulate at the same time, the product is a drug. Although it's not treating or preventing a disease in the cows, the product's intended use is to change how their bodies function, which makes it a drug under the FD&C Act.

New Animal Drugs

- **The FD&C Act defines “new animal drug” as a drug intended for use in animals that is not Generally Safe and Effective (GRASE) by qualified experts for the uses listed on the label.**
  - If a drug is GRASE, then it's not a new animal drug under the FD&C Act. For an animal drug to be GRASE, the experts must generally agree that, based on published studies, the drug is safe and effective for its intended uses.
  - FDA thinks it's very unlikely that any currently marketed animal drug would be considered GRASE and so if a drug is intended for use in animals, it's almost certain to be a new animal drug.

New Animal Drugs: Three Pathways to Legal Marketing Status

- New Animal Drug Application (NADA) process.
- For an approved generic animal drug, the Abbreviated New Animal Drug Application (ANADA) process.
- Conditional approval is only available for drugs for minor species or minor uses in a major species. A conditionally approved animal drug has gone through FDA's drug approval process except the drug has not yet met the effectiveness standard for full approval and is valid for one year.

Association of American Feed Control Officials (AAFCO)

- **Who and what is AAFCO?**
  - Association of American Feed Control Officials
  - Established in 1909
  - Members are regulatory officials from federal, state, and international agencies
  - One of its functions is “to provide a mechanism for developing and implementing uniform and equitable laws, regulations, standards, definitions, and enforcement policies for regulating safe, effective and useful feeds.”
  - FDA recognizes AAFCO as a standard setting body – 21 CFR 10.95

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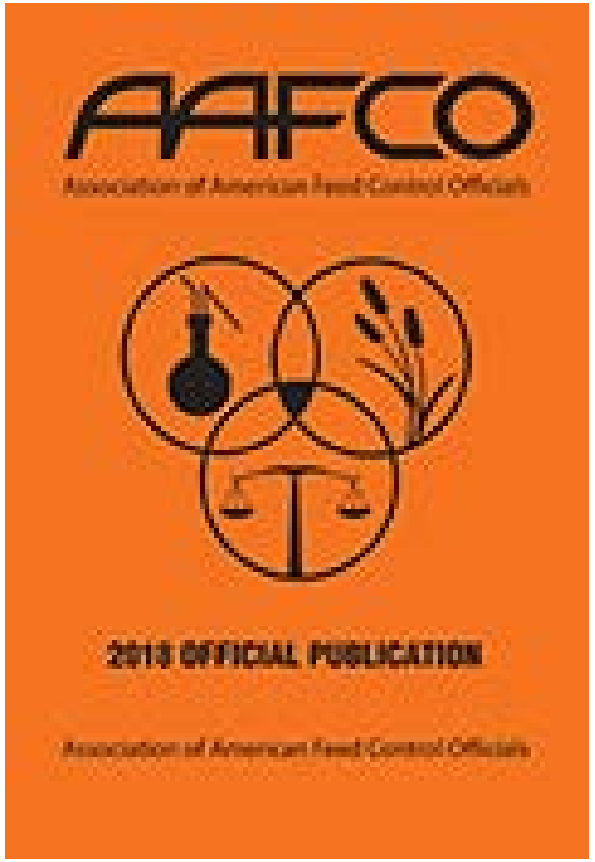
Association of American Feed Control Officials (AAFCO)

https://petfood.aafco.org/Marketing-Romance-Claims Accessed June 14, 2018

- No direct regulatory authority (non-governmental body, but all members must be regulators)
- Does not regulate, test, approve or certify animal foods in any way
- Provides “model” bills and regulations for state adoption
- More extensive and specific feed and pet food nutritional standards and labeling regulations, ingredient definitions
- State officials ensure compliance of laws and rules for the protection of companion animals



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AAFCO Ingredient Definitions

- **Ingredient definitions**
  - AAFCO Official Publication contains the most comprehensive list of substances accepted in the U.S. for use in animal food
  - FDA recognizes AAFCO feed ingredient definitions as establishing common or usual name of ingredients
- **Ingredient definition process**
  - Used for substances that present no apparent safety concerns for intended use to
    - Target animal
    - Human food
    - Environment
  - Outlined in AAFCO Official Publication
  - AAFCO section investigator is the contact for submission of definition request, not CVM

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AAFCO Ingredient Definitions

- **Request for new definitions must include**
  - Firm and contact person
  - Summary
    - Ingredient name, intended use, and rationale for request
  - Proposed definition and description of ingredient
  - Prior sanctioned use
    - Common use in United States pre 1958 and/or
    - Historical regulation of ingredient
  - General description of the manufacturing processes
  - Purpose of ingredient
  - Use limitations, if any
  - Data and observations to support intended use
  - Summary of safety assessment
  - List of cited literature

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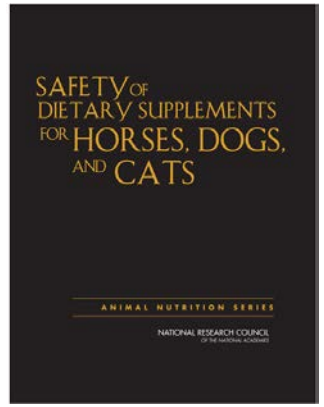
AAFCO Ingredient Definitions

- **AAFCO section investigator**
  - Reviews definition request for completeness
  - Sends to CVM for concurrence – CVM serves as scientific advisor to AAFCO
- **Proposed definition reviewed and voted on by state feed control officials**
- **Final definition is published in AAFCO Official Publication**

National Animal Supplement Council



- **No regulatory authority but engages regulatory agencies for consistent, transparent policies.**
- **To earn the NASC Quality Seal, members must follow standards for good manufacturing practices, participate in the NASC Adverse Event Reporting System, and follow labeling and claims guidelines. Companies that earn the NASC Quality Seal must pass an audit by the NASC every two years.**
- **DSHEA (1994): the agency's assessment of the law is that it was not intended and does not apply to animal feed, including pet food. Products marketed as dietary supplements or "feed supplements" for animals still fall under the FFDCA prior to DSHEA, i.e., they are considered "foods" or "new animal drugs" depending on the intended use. ***

*FDA **does not** enforce all laws they are required to enforce with pet food/animal feed; through FDA policy the agency allows pet food to violate some federal laws. State Department of Agriculture **does not** enforce all laws they are required to enforce with pet food/animal feed; follow FDA's lead in lack of enforcement of some pet food laws.

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Key Takeaways

- Any article that is intended to be used as an animal feed ingredient is considered a “food” and thus, is subject to regulation under the Federal Food, Drug, and Cosmetic Act (FFDCA).
- FDA (Center for Veterinary Medicine) is the regulatory authority for animal food charged with enforcing federal laws; the State Department of Agriculture is charged with enforcing state laws.
- FDA recognizes only approved Food Additives and substances Generally Recognized As Safe (GRAS) for feed and drinking water of animals; the agency's assessment of DHSEA is that it was not intended for and does not apply to animal feed, including pet food (FDA policy allows the agency to violate some federal laws for pet food).
- Expressed or implied claims that establish the intended use to cure, treat, prevent or mitigate disease, or affect the structure/function of the body in a manner other than food (nutrition, aroma, or taste), may identify an intent to offer the product as a “new animal drug” requiring a New Animal Drug Application.

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