2025 NASC Annual Conference

April 22–24 | Columbus, OH | The Hilton Columbus at Easton

THE ENDING OF THE CVM/AAFCO MOU: NAVIGATING THE NEBULOUS REGULATORY LANDSCAPE FOR THE ANIMAL FOOD INDUSTRY

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History of Regulations AAFCO and CVM

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Thank you for the opportunity to speak to you today.

This material is presented by Dr. Erik Hedrick, Executive Vice President and Director of Toxicology at Burdock Group, Orlando, Florida.

If you would like receive additional information regarding Burdock Group's capabilities in human and animal feed safety and regulations, dietary supplements, personal care products and related areas, please contact Brian Mitchell at (Bmitchell@burdockgroup.com) or info@burdockgroup.com.

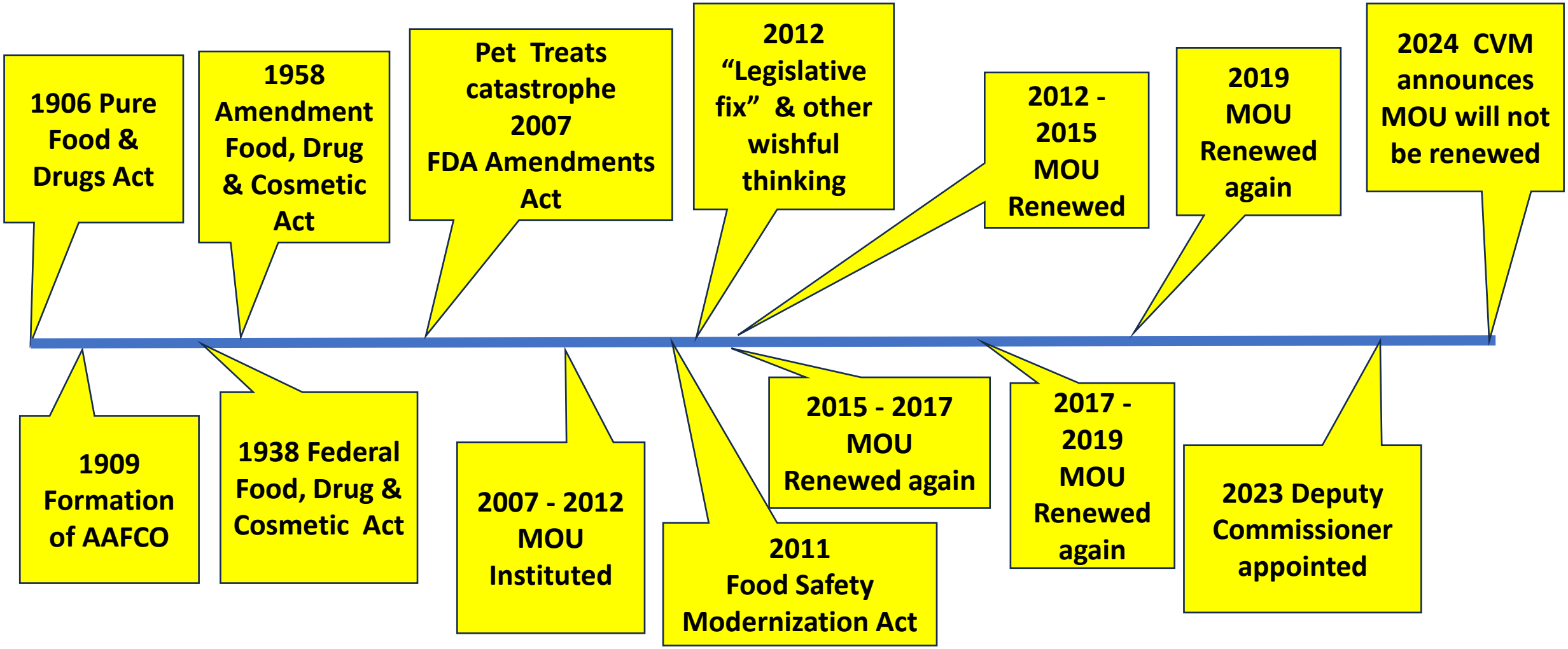
Disclaimer. Concepts and examples discussed in this lecture are for illustrative purposes only and do not constitute safety or regulatory advice specific to your situation. Please contact us for an analysis of your particular circumstance to determine the best pathway for your product and team.

Why do we need regulations?

Upton Sinclair – *The Jungle*

- Economic adulteration
  - Addition of sawdust to bread and bologna
  - Formaldehyde in milk, spent tea colored and re-sold
- Misrepresentation (misbranding)
  - False weights, deceptive packaging
  - Drug claims
- Safety
  - Unsafe (carcinogenic or neurotoxic) dyes added to food
  - Lead solder in cans, tin coated lead to seal wine bottles
  - Cobalt salts added to beer to stabilize beer foam were cardiotoxic
  - Safrole in sarsaparilla & coumarin in French vanilla flavor - both determined to be carcinogenic

CVM – AAFCO Timeline



1906 Pure Food & Drugs Act

1906 Federal laws governing human food & drugs

- Passage of the 1906 Pure Food and Drug Act
  - A very early federal law
  - Some food handling and limits “toxins” in food
  - Does not address animal feed
  - Eliminated “…filthy, putrid, or decomposed substance, or if it is otherwise unfit for food…”
- Passage of Meat Inspection Act of 1906
  - Addresses meat sanitation, standards and inspection of plants

1909 Formation of AAFCO

1909 Formation of AAFCO

- Federalism
  - States > federal government
  - Individual states had their own feed definitions
- AAFCO is formed – 1909
  - A private organization comprised of regulators from various states
  - AAFCO has no regulatory or enforcement power
- Goal of AAFCO
  - Harmonize the laws that govern the flow of animal feed and pet food between the states.
  - *model legislative bill*
  - *Official Publication*
- In practice – each state
  - May elect/chose not to to adopt the definition
  - tweak the definition

1938
Food, Drug & Cosmetic Act

1938 – Change is in the works, but misses the target

- 201(f) The term “food” means (1) articles used for food or drink for man or other animals.
- No requirement for pre-market demonstration of safety of “additives”
  - No definition of “food additive” (or GRAS) nor a requirement for evaluation of safety of drugs before introduction into commerce…
  - For foods: only standards of identity and “a reasonable standard of quality”
  - Foods may not contain any poisonous or deleterious substance which may ender it injurious to health…
- There was a provision for pre-market demonstration of safety of drugs, but not for human or animal food ingredients.

AAFCO and CVM and lead up to the MOU

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1958 Amendment Food, Drug & Cosmetic Act

1958 – A Pivotal Year in Food and Feed

- Definition of food carried over as being for “man and other animals”.
- Food additive defined as “any substance becoming a component of any food”
- Pre-market approval required as Food Additive or GRAS
    - Food additive – approval by FDA required
    - GRAS
        - “Scientific procedures”
        - History of use
- Substance must be safe “under the conditions of its intended use”
- CFSAN gets busy preparing lists of GRAS ingredients

1958 Amendment Food, Drug & Cosmetic Act

1958 – Early 1990's

- CFSAN actions
  - Original list of GRAS substances revised in 1970's
  - Entered into the Code of Federal Regulations (CFR)
    - 21CFR172 – Food additive
    - 21CFR182 – GRAS - 76 + flavors, spices, packaging migrants and pesticide adjuvants
    - 21CFR184 – GRAS affirmed - 213
    - 21CFR186 – GRAS affirmed - 15

- CVM actions
  - GRAS and GRAS affirmed
    - 21CFR 582 – GRAS – 234 + flavors, spices, trace minerals and pesticide adjuvants
    - 21CFR 584 – GRAS affirmed – 3
  - CVM passively recognizes AAFCO *OP*

1958 Amendment Food, Drug & Cosmetic Act

AAFCO *OP* Ingredients (A GRAS list in disguise? Federally compliant?)

- AAFCO adopts some Ingredients in 21 CFR 500-584 into *Official Publication*
- *Ingredient definitions* (~500)
  - not cited in 21 CFR 500-584
  - No federal compliance (GRAS & not food additives)
  - Ingredients had never been declared GRAS, but only listed in the *OP.*
    - Not listed as exempt via historical use
    - Not GRAS via scientific procedures
      - Safety in use never demonstrated
      - Persons approving entry into the OP never verified their bona fides as "experts by training and experience"
- Therefore, because substances in *OP* not compliant with FFDCA
  - Only legitimate within states where they are approved by state law
  - Could not enter interstate commerce as feed ingredients

1958 Amendment Food, Drug & Cosmetic Act

AAFCO *OP* Ingredients (A GRAS list in disguise? Federally compliant?)

- Flavor and Extract Manufacturers' Association (FEMA) GRAS list
  - Ingredients designated GRAS and published in Food Technology magazine
  - Criteria on which safety in use is based published in scientific journal and/or disclosed to FDA
  - Experts designating safety in use have credible *bona fides*
- Enzyme Technical Association (ETA)
  - FDA *via* GRAS Notification process
  - Safety-in-use concluded *via* algorithm designed by experts and approved by FDA
  - Disclosure of safety-in-use met *via* GRAS notification.
- AAFCO *OP* Ingredients
  - Ingredients had never been declared GRAS, but only listed in the *OP.*
    - Not GRAS via historical use (prior to January 1, 1958).
    - Not GRAS via scientific procedures
      - Safety in use never demonstrated
      - Persons approving entry into the OP never verified their bona fides as "experts by training and experience"

1958 Amendment Food, Drug & Cosmetic Act and beyond

CVM Actions?

- CVM refusing to acknowledge GRAS determinations
- Cooperation between CVM and AAFCO ramps up
  - CVM starts attending AAFCO meetings
- CVM passively recognizing AAFCO *OP* - not a good idea
  - Allows a private entity to set "metrics and standards" – a delegation of legislative power
  - Abandonment of due process
- CVM sees advantages to AAFCO
  - CVM resources conserved
  - In the absence of a complete positive list by CVM, *OP* recognized as the only (official?) list of US approved ingredients
  - International recognition of AAFCO list as USA list

The beginning and the end of the MOU

3

Pet Treats & 2007 FDA Amendments Act (FDAAA)

Finally, the stuff hits the fan
The FDA Amendments Act (FDAAA) of 2007

- FDAAA passed in response to pet deaths from melamine and cyanuric acid in pet treats
  - Among the requirements of the law: §1002(a)(1) [21 USC 2102] "…ingredient standards and definitions with respect to pet food".
  - A cue to stakeholders that regulation is coming.
- Memorandum of understanding (MOU) issued – 2007
  - Many overjoyed at the prospect of transparency in the process & CVM participation in ingredient definition review.
  - CVM initiates a GRAS notification program
  - Everyone seemed to miss the "effective period of performance" of September 1, 2012.

2010 GRAS Notification Pilot program

Events Following MOU – What to do with GRASes?

- CVM only recognizes GRASes via a notification process
- CVM GRAS notification process becomes very onerous
  - Review period too long/unfair; little/no contact from CVM for questions
  - Few "no objection" letters issued
- AAFCO response to GRAS
  - Even GRASes with no objection from FDA get short shrift in the *OP*
    - GRAS list not incorporated into *OP* as are CFR determinations, but in separate section
    - Manufacturers put on notice there may be additional scrutiny by the Ingredient Definition Committee
  - Self-GRASes
    - often refused with states
    - Not qualified/limited resources to evaluate GRASes

2011 Food Safety Modernization Act (FSMA)

Food Safety Modernization Act 2011 Signed into Law

Another blow to AAFCO's Standing

- Good Manufacturing Practice (GMP) instituted
- Non-federally compliant substances cannot be present in the feed preparation facility
  - Substances subject to immediate seizure

MOU
2007 - 2024

AAFCO Response to MOU

- Continued negotiations with CVM to extend MOU
  - 2007 – 2012
  - 2013 – 2015
  - 2015 – 2017
  - 2017 – 2019
  - 2019 – October 1, 2024
- Unacceptable measures taken by AAFCO
  - Congress lobbied for “legislative fix” – Letter to Senator Durbin
  - Pleading to Dr. Hamburg (Commissioner of FDA)

Plans for the future of regulatory compliance for feed

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2024
MOU not
renewed

Sept 2024 - MOU Expires

- CVM announces end of the MOU
  - CVM involvement until October 1, 2024
  - Interim guidances offered – neither offer much hope of going back to the old ways
  - CVM website – making the ruling crystal clear:

    "To be legally marketed, an ingredient used in animal food (including pet food) must be the subject of an FDA-approved animal food additive petition (FAP) or be generally recognized as safe (GRAS) for the intended use in animal food."
  - CVM released GFI 293 and 294 (AFIC)
- What about ~500 non-compliant ingredients defined in the *OP*?
  - Non-compliant ingredients could be seized.
  - Products containing non-compliant ingredients may be subject to recall.
  - Feed mills with non-compliant ingredients present could subject to shutdown and fines.

KSU Plan

KSU Plan for Scientific Panel for Ingredient Approval (January 2025)

SUBMISSION TIER	AMOUNT
Full Submission Package • Includes data to support approval for 3+ species of animals • Includes review by 3-5 Subject Matter Experts (SMEs) • (May require an additional 10-15 days of review time)	$50,000
Minor Submission Package • Includes data to support approval for 1-2 species of animals • Includes review by 2-3 SME's	$30,000
Basic Scientific Review • Needed for modification of an AAFCO definition that requires a scientific review from qualified SME's.	$15,000

KSU Plan

KSU Plan for Scientific Panel for Ingredient Approval

Major issues include the following:

- **Only forward looking**
  - no retroactive approach
  - Continued hope for use of regulatory discretion
- **Very little data to address safety**
  - GRAS or food additive petition (FAP) is all about safety
  - Need qualified experts (toxicology)
  - nutrition or benefit to the animal, environment, novelty or reduced time to market are secondary considerations.
- **Data requirements too broad: Shotgun approach for the data required, rather than a more surgical approach.**
  - An excessive data requirement is going to make application uneconomical; may set precedent for requirements for data for substances that clearly do not need so much testing.
  - This is a common problem, manufacturers, to be thorough, often test themselves out of a product.
- **Submission Tiers (full, minor and basic) make assumption one of the three classes of submissions will fit all imaginable combinations of applications.**
  - Basic Scientific Review indicates that to modify an existing definition is only $15K
  - To modify a GRAS, the substance must be GRAS in the first place.
- **Data/information needs to be published in the relevant scientific literature**
  - November 2017 Guidance)
  - accepted by the scientific community.
  - Daubert trilogy of decisions of several years ago

Industry revolution

If AAFCO Definitions are Not a "Legitimate Home", What Happens Now? - Industry Resolution -

Formation of industry *ad hoc* committees to share in the cost of legitimizing the status of feed ingredients according to Federal Law

Precedent

- Flavor and Extract Manufacturers Association (FEMA)
- Cosmetic Ingredient Review (CIR)
- Drug Excipients Council
- Certified Color Manufacturers Association
- And others

A Plan for Resolution

Form *ad hoc* Committees of Mutual Interest Ingredients
(costs shared on the basis of production)

↓

Consult with AAFCO
(Specifications and Specific State Needs)

↓

Seed money to perform feasibility study for each ingredient

↓

Determine which requirements are most cost effective to fulfill

↓

Produce standardized product for testing.
Conduct and publish animal studies and utility studies

↓

Generate GRAS dossier & Approval by Committee Members
Present to Expert Panel

↓

Share final product with Committee Members

Bottom Line

A Plan for Resolution: The Bottom Line for Compliance

- The GRAS dossier and Conclusion
  - Would only be shared with Committee Members (sponsors)
  - Those companies without a GRAS would be at the mercy of CVM
- The substance is still GRAS regardless of the actions of CVM *in re* GRAS or Food Additive regulation – substance is federally compliant
- AAFCO adoption and incorporation into OP likely

The time to act is now!

Plan for the future

- **Identify ingredients of interest out of the ~500 non-compliant ingredients in the *OP***
  - Create a survey of poundage produced
- **Prioritize ingredients on the basis of production**
  - Eliminate those with no production or interest
- **Identify exempt ingredients**
  - Exempt on the basis of historical use.
  - Exempt on the basis of having been food/forage.
- **Prioritize those ingredients remaining requiring "scientific procedures"**
  - Solicit funding for feasibility studies to determine cost for a GRAS.
  - Prepare reports based on feasibility studies for CVM on which must be FAPs.
  - Based on which may be GRAS or FAP and cost associated with either, solicit funds based on poundage produced.
  - Prepare and submit GRASes or FAPs

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