SRIS SCIENTIFIC REVIEW OF INGREDIENT SUBMISSIONS

AAFCO Association of American Feed Control Officials | K-STATE OLATHE

A Guide to Submitting New or Modified Ingredient Definitions to AAFCO

Section Editor – FASS

The following guide is to assist in development of new or modified feed ingredient definitions within the AAFCO Definition Process that are concluded to be Generally Recognized as Safe (GRAS - 21 CFR 570.30 (b)) for its intended use in animal food. The roles of each party are described below. The definitions should be non-proprietary as not to favor one ingredient producer over another. The defined ingredient should be a single ingredient and not a combination of ingredients. The intended use should not be to mitigate, treat, or diagnose a disease **(other than prevent a nutritional deficiency)**, but rather to provide nutrition, flavor, aroma for the animal or provide a technical effect in the feed. It is the manufacturer's responsibility to produce a safe ingredient for its intended purpose in the intended species.

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The Submitter

Prior to submitting a request for a new or modified definition, the submitter should consider the current ingredient definitions and develop a draft definition that includes the intended use. The submitter should then contact the appropriate AAFCO investigator (see the AAFCO *Official Publication (OP)* or website for current listing) by email to definitions@aafco.org to discuss the draft definition. Following the initial discussion, a submitter should then submit a data packet to the investigator in writing that contains the information described below, if pertinent, so there is sufficient information to present to an expert panel. Confidentiality cannot be claimed for any of the information submitted in this packet.

Part One – Signed Statements & Certification

In Part One of your submission packet, you will:

1. Provide a statement that the filing meets the definition of GRAS. Inform AAFCO that you are submitting a Generally Recognized as Safe (GRAS) conclusion in accordance with 21 CFR 570 Subpart E;
2. Provide the name and address of your organization.
3. Provide the common name of the substance, using an appropriately descriptive term.
4. Describe the intended conditions of use of the substance, including stating whether the substance will be added to food and/or drinking water for animals, identifying the foods to which it will be added, the levels of use in such foods, and the animal species for which these foods are intended (including, when appropriate, a description of a subpopulation expected to consume the substance); and the purposes for which the substance will be used;
5. Provide a Proposed AAFCO OP Chapter 6 Ingredient Definition;
6. State your view that the substance is not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on your conclusion that the substance is GRAS under the conditions of its intended use;
7. Provide the full data package, as well as copies of all the published data to be relied on;
8. Certify, to the best of your knowledge, the submission packet is a complete, representative, and balanced submission that includes unfavorable information, as well as favorable information, known to you and pertinent to the evaluation of the use of the substance;
9. State the name, title, and contact information of the person responsible for submitting the AAFCO ingredient definition. It must be signed by a responsible official of your organization, or by your attorney or agent.

Part Two – Identity, method of manufacture, specifications, and physical or technical effect

In Part Two of your submission packet, you must include:

1. Scientific data and information that identifies the substance.
    a. Examples of appropriate data and information include the chemical name, applicable registry numbers (such as a Chemical Abstracts Service (CAS) registry number or an Enzyme Commission (EC) number), empirical formula, structural formula, quantitative composition, and characteristic properties.
    b. When the source of a substance is a biological material, you must include data and information sufficient to identify:
        i. The taxonomic source (*e.g.*, genus, species), including as applicable data and information at the sub-species level (*e.g.*, variety, strain);
        ii. The part of any plant or animal used as the source; and
        iii. Any known toxicants that could be in the source.
2. A description of the method of manufacture of the substance in sufficient detail to evaluate the safety of the substance as manufactured;
3. Specifications for material that is of appropriate grade for use in animal food supported by 3 to 5 batch analysis;
4. Summary statement to support stability of ingredient;
5. Summary statement that validated analytical methods and/or citation of published methods were used to support testing;
6. Utility data is only required when the intended use of the ingredient has an impact on the safety of the feed.

Part Three – Target animal & human exposures

In Part Three of your submission packet, you must provide data and information about exposure to the target animal and, if applicable, to humans consuming human food derived from food- producing animals.

1. Target Animal Exposure

    For exposure to the target animal, you must provide:

    a. The amount of the substance that different target animal species are likely to consume in the animal food (including drinking water) as part of the animal's total diet, including the intended use and all other sources in the total diet; and
    b. When applicable, the amount of any other substance that is expected to be formed in or on food because of the use of the substance (*e.g.*, hydrolytic products or reaction products);
    c. When applicable, the amount of any other substance that is present with the substance either naturally or due to its manufacture (*e.g.*, contaminants or by-products);

d. The data and information you rely on to establish the amount of the substance and the amounts of any other substance in accordance with paragraphs a-c of this section that different target animal species are likely to consume in the animal food (including drinking water) as part of the animal's total diet.

2. Potential for Human Food Exposure

When the intended use is in food for food-producing animals, you must provide:

a. The potential quantities of any residues that humans may be exposed to in edible animal tissues, including:
   i. Residues of the substance;
   ii. Residues of any other substance that is expected to be formed in or on the animal food from the use of the substance; and
   iii. Residues from any other substance that is present with the substance whether naturally, due to its manufacture (*e.g.*, contaminants or by-products), or produced as a metabolite in edible tissues when the substance is consumed by a food-producing animal; and

b. The data and information you rely on to establish, in accordance with paragraph (a) of this section, the potential quantities of any residues that humans may be exposed to in edible animal tissues.

Part Four – Self-limiting levels of use

In Part Four of your submission packet, you must include data and information on self-limiting levels of use in circumstances where the amount of the substance that can be added to animal food is limited because animal food containing levels of the substance above a particular level would become unpalatable or technologically impractical.

Part Five – Narrative

In Part Five of your submission packet, you must include a narrative that provides the basis for your conclusion of safety, in which:

1. You must explain why the data and information in your submission provide a basis for your view that the substance is safe under the conditions of its intended use for both the target animal and, if applicable, for humans consuming human food derived from food-producing animals. In your explanation, you must address the safety of the substance, considering all animal food (including drinking water) as part of the animal's total diet, taking into account any chemically or pharmacologically related substances in such diet. In your explanation, you must also address the safety of the substance in regard to human exposure, considering all dietary sources and taking into account any chemically or pharmacologically related substances;

    a. In your explanation, you must identify what specific data and information that you discuss in accordance with paragraph 1 of this part are generally available, and what specific data and information that you discuss in accordance with paragraph 1. of this part are not generally available, by providing citations to the list of data and information that you include in Part Six of your submission.
2. You must explain the generally available data and information that you rely on to establish safety in accordance with paragraph 1 of this part and provide a basis for your conclusion that the substance is generally recognized, among qualified experts, to be safe under the conditions of its intended use for both the target animal and, if applicable, for humans consuming food derived from food-producing animals;
3. You must either:
    a. Identify, discuss, and place in context, data and information that are, or may appear to be, inconsistent with your conclusion of safety, regardless of whether those data and information are generally available; or
    b. State that you have reviewed the available data and information and are not aware of any data and information that are, or may appear to be, inconsistent with your conclusion of safety;
4. For non-public, safety-related data and information (corroborative data) considered in reaching a conclusion of safety, you must explain how there could be a basis for a general conclusion of safety if qualified experts do not have access to such data and information.

Part Six – List of supporting data and information in your submission

1. In Part Six of your submission packet, you must include a list of all of the data and information that you discuss to provide the basis for your review that the substance is safe under the conditions of its intended use in Part Five (1)(a);
2. You must specify which data and information that you list in accordance with paragraph 1 of this part are generally available, and which data and information are not generally available.

Resources

FDA and others (International Cooperation for the Convergence of Technical Requirements for the Assessment of Feed Ingredients) have published guidance describing the information that may be considered when drafting GRAS conclusions. FDA Guidance For Industry 221 provides some guidance and hyperlinks to other potentially useful guidance documents.

[FDA: Guidance Document on CVM GFI #221] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-221-recommendations-preparation-and-submission-animal-food-additive-petitions

[ICFF: Guidance Documents Library] https://iccffeed.org/guidance/

The Investigator

The AAFCO investigator will conduct the initial review of the request for a new definition or modified definition. One of the goals of the investigator is to develop official feed definitions that are just and equitable in cooperation with the members of the industry producing the ingredient. A second goal is to ensure that the production, sale, and use of ingredients will result in safe and effective feeds. The ingredient definitions should be non-proprietary, meaning they do not include a trade name that would favor one producer over another.

Upon receipt of the request for a new AAFCO ingredient definition or request for modification of an existing ingredient definition, the investigator will:

1. Work with the KSO program manager to assure the request is complete.
2. Determine if the proposed ingredient definition fits in the requested section of the AAFCO OP. If not, the request will be referred to the appropriate investigator or to the chair of the Ingredient Definitions Committee with the requesting party notified of the referral.
3. Confirm that the proposed ingredient does not fall within the scope of an existing definition.
4. Confirm that the proposed revision to an existing ingredient definition will not cause it to be moved to a different section of the OP or fall within the scope of another existing ingredient definition.
5. Confirm that the ingredient definition request is complete and contains all the information needed from the submitter listed in Parts 1 through 6 above.

If the submission is considered complete the investigator will provide the full submission to the Kansas State Olathe (KSO) program manager for evaluation.

Upon receiving a request for a new or modified AAFCO ingredient definition, the expected administrative review time for the AAFCO investigator is 30 calendar days. If the investigator expects their review to take longer than 30 days, he/she may request an extension from the chair of the Ingredient Definitions Committee (IDC) or request the chair of the Ingredient Definitions Committee assign the definition to another investigator.

The investigator may initiate a modification of an ingredient definition based upon their knowledge of the affected industry and not on a specific request from an external

submitter. It is the responsibility of the investigator to amass sufficient documentation to support their submission, just as it is industry's responsibility to provide sufficient documentation to support their request.

After the KSO Expert Review Panel report is provided to the investigator, the investigator will submit the recommendation for the new or revised AAFCO ingredient definition to the IDC chair.

Kansas State Olathe

Kansas State Olathe (KSO) administers the expert review panel for the scientific reviews of AAFCO ingredient definition submissions and provides recommendations to the investigator for new and amended ingredient definitions. It typically takes 60 to 90 days to review a new or modified ingredient definition, depending on the complexity of the request and discussions that may occur between the panelists and the submitter.

The KSO Expert Review Panel is a scientific review panel proposed to consist of 1-5 subject matter experts (SMEs) with expertise in ingredients, processing, and nutrition for species of interest and/or relevant to the proposed new ingredient definition. Experts asked to serve on this panel will be drawn from a larger pool based on their expertise pertinent to the proposed ingredient definition request. In selecting the members of the Expert Review Panel, KSO will take steps to avoid bias, include balance of expertise, and maintain independence. The SMEs will be recruited from KSO, other universities in the US, independent consultants, and other relevant experts.

A program manager will work directly with the AAFCO Investigators to review the AAFCO ingredient definition request submissions. The manager will ensure that the data package contains all the necessary information for the scientific review panel.

Upon receipt of the request for a new AAFCO ingredient definition or request for modification of an existing ingredient definition, KSO will:

1. Manage the entire process for the scientific review of the submission including:
    a. Providing SMEs materials and templates for pre-evaluation notes/comments;
    b. Communication with the SMEs;
    c. Scheduling deliberation meeting(s) for discussions and voting;
    d. Taking meeting minutes and other responsibilities as identified.
2. Develop draft expert review panel report and submit draft to panelists for review prior to finalization of the report; and
3. Submit final expert review panel report with recommendation to the AAFCO Ingredient Definitions Committee investigator.

AAFCO anticipates that each review will require some level of back and forth to answer questions the panelists may have. All questions should be addressed by the submitter or agent in as timely a manner as possible to ensure the review time remains expeditious. However, if during the course of the review questions arise where additional data is needed, AAFCO and KSO will work to temporarily pause the review and allow the submitter to gather the data needed. Requests for additional time will be considered based on the complexity of the question(s) and data needed.

AAFCO also acknowledges that there may be some cases where time is needed to conduct additional research to address questions or support a conclusion. AAFCO will work with submitters if this situation arises to avoid incurring a separate cost; however, this may not always be feasible.

The Association

Once reviewed by the investigator and the KSO Expert Review Panel, the proposed AAFCO ingredient definition is submitted by the investigator to the chair of the Ingredient Definitions Committee. The IDC is the clearing house for all new or modified definitions by acting as a review panel to assure that definitions are acceptable and consistent with AAFCO policies and existing definitions. Membership of the committee is drawn from the ranks of AAFCO members. The submission deadline to the IDC chair is 30 business days before the next IDC meeting to allow ample time for committee review and corresponding with the investigator.

Once a new or modified ingredient definition is approved by the Ingredient Definitions Committee, the chair will forward a recommendation to the AAFCO Board to place the definition in the Official Publication in official status. The Board will vote for or against this recommendation before the next membership meeting so members can vote on the recommendation during the Annual or Midyear meetings. Once approved by membership, the official ingredient definition will be published in the Official Publication.

If deletion of an ingredient from the Official Publication is proposed, the investigator will follow the same dateline as if proposing any other ingredient definition change. This will allow the IDC the opportunity to review and discuss the proposed deletion.