Pet Food Institute Public Comments on Pre-Market Animal Food Ingredient Review Programs

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Food and Drug Administration
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The Pet Food Institute (PFI) appreciates the opportunity to provide comments regarding the Food and Drug Administration's (FDA or the agency) August 9 request for public input concerning the Food Additive Petition and Generally Recognized as Safe (GRAS) Notification programs to better determine if changes are needed to promote their efficiency. [FDA-2024-N-2979].

Established in 1958, PFI is the trade association and the voice of U.S. cat and dog food manufacturers. Our members account for the vast majority of the pet food and treats made in the United States, with more than $64 billion in domestic annual dog and cat food and treats sales and annual exports of more than $2.4 billion. PFI's members collectively contribute to rural communities' vibrancy by employing over 35,000 people in 34 states. Our membership also includes companies that supply ingredients, equipment, and services to dog and cat food makers. Our members are proud to be providing food for dogs and cats in over 82 million U.S. households.

PFI members appreciate the steps the agency is taking towards creating a stronger and more predictable U.S. regulatory framework, including this effort to find and implement efficiency improvements in the established ingredient review processes. This is a productive step towards a more definitive and predictable regulatory structure for the formulation and production of pet food.

The agency's stated purpose in seeking this input is to determine if changes are needed to improve efficiency in the two named ingredient review pathways. PFI members strongly believe that certain changes are needed. To best explain the rationale for PFI's recommended changes, we respond below to specific questions and information included in the notice to help guide stakeholder feedback.

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As CVM considers making changes to ingredient review processes, we know that pet safety will continue to be the FDA's highest priority. While the comments below suggest changes to improve processes, we also strongly believe that any changes should be implemented in a way that maintains the rigor needed to provide confidence in the safety of the animal food supply.

What do you perceive as barriers and/or benefits to pursuing a Food Additive Petition or GRAS Notification?

Benefits:

Both the Food Additive Petition (FAP) and GRAS Notification processes are legally recognized regulatory pathways to gain agency recognition of ingredients for general use in the manufacture of pet food. State, federal, and international governments readily accept the regulatory validity of the reviews, which clearly conveys the benefit to pursuing either of these pathways. These processes are well-understood around the world and demonstrate FDA agreement to ingredient safety and regulatory compliance, which in turn is accepted in other countries given that FDA is recognized as the competent authority by other countries. Since both pathways (FAP and GRAS) are included in U.S. law and regulation, they provide a level of regulatory permanence upon completion, absent new data that calls into question any prior decisions.

Additionally, the Food Additive Petition and GRAS Notification processes each require well-justified and explained rationales and scientifically rigorous studies for establishing the safety of food ingredients. Such requirements allow the FDA Center for Veterinary Medicine (CVM) to accomplish a safety review based on scientific merit. Should a company decide to make a self-determination of GRAS status without submitting a GRAS Notification, which is permitted under the law, the company must adhere to the same scientific standards in reaching the GRAS determination.

Barriers:

One major barrier to pursuing a FAP or GRAS Notification is the uncertainty associated with the agency review time. For example, despite the stated 180-day review period, PFI members have reported that every touch point with the agency would "reset" the timing for the 180-day period. This creates a lack of predictability that disrupts a firm's business plans.

The industry also lacks clarity in understanding how CVM determines the level of risk associated with an ingredient compared to derivatives. This is particularly true for ingredients that are a derivative or fraction of a previously reviewed whole ingredient. This leads to confusion of which pathway (FAP or GRAS) would be most efficient or

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appropriate to pursue. In simplest terms, our understanding is that a fractionated ingredient that is not common should follow the FAP route while more common fractionated ingredient may use GRAS.

Another concern PFI members have involves the protection of confidential business information during the process. While some redaction of information is possible in certain circumstances; overall, the information requirements and disclosure of such information provide insufficient protection for pet food formulations containing these novel ingredients, manufacturing processes, supply chain ingredient specifications, and partnerships between pet food makers and ingredient suppliers and do not provide confidentiality during the review process. This presents challenges for businesses trying to maintain a competitive edge and spur innovation.

Are there changes that could make the Food Additive Petition and GRAS Notification programs more feasible, such as regulatory changes, changes to guidance, or changes to FDA policy or processes?

PFI believes there are several process changes that would foster more utilization by industry stakeholders, and we appreciate CVM's interest in considering these. We recognize that this inquiry aligns with CVM's recent investments to improve existing processes. CVM has hired more reviewers and has taken helpful steps, such as encouraging pre-submission meetings, to facilitate a more efficient turnaround. Industry has realized the benefits of these changes and is encouraged by CVM's commitment to continuous improvement.

Innovation is part of pet food culture, and we would like to see changes to the current programs to help improve responsiveness and success of submissions. We encourage CVM to continue pre-submission consultation meetings with industry. It would be particularly helpful to use the consultations to discuss appropriate research study design to demonstrate safety and how such studies could be customized based on need and intended use.

If pre-submission consultations are utilized, there could be improvements to the timeline for FDA review, perhaps a reduction from 180 days to 90 days. As pre-submission consultations continue, it would be helpful for CVM to consider further adoption of some procedures used on the drug side for Pre-New Animal Drug Application meetings such as sharing of meeting notes and use of reference numbers that can be used for future submissions.

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We encourage CVM to consider the potential benefits of additional flexibility for the evidence required for some review packages. Considerations include:

- Allowance for greater extrapolation of studies that were conducted on other species when a justifiable basis is specified.
- Acceptance of well-designed non-published scientific studies based on the significance of evidence and scientific merit for GRAS reviews instead of a requirement to limit only to peer-reviewed journal publications.
- Utilization of streamlined reviews which may include factoring in historical safe use in other markets.
- Environmental assessment requirements for ingredients for which other characteristics help to establish low risk.

We encourage CVM to consider transparency to help us understand which process suits which ingredient depending on its complexity. It is particularly important considering the proposal of Animal Food Ingredient Consultations (AFIC), which describes a process that could help to identify which review pathway to follow. We believe AFIC could be a pathway for simple ingredients of low risk, to be reviewed following a more streamlined approach. A simple ingredient may be one that is a by-product of ingredients that are already reviewed without significant processing.

PFI has noted that animal food ingredients often are held to a higher standard than human food ingredients, particularly regarding the documentation burdens associated with the safety of an ingredient. We encourage CVM to utilize principles followed by the Human Foods Program (HFP) to simplify the process. We understand that the HFP process is currently working well.

As CVM moves forward with any changes, it would be helpful to clearly articulate the timelines, processes, and appropriate regulatory pathway for each ingredient under review.

Is there information that is currently required to be submitted in a Food Additive Petition or GRAS Notification that you do not think is necessary for evaluating the ingredient?

PFI members believe U.S. pets deserve a robust and efficient review process that supports safety and innovation for the ingredients going into their food. We also feel there are some process requirements that do not positively support these needs. We appreciate the agency's interest in reducing the collection of unnecessary information for this effort.

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Animal safety is the main purpose for ingredient review both for pet food makers and CVM and should be the main criteria regarding what data is needed for submission.

One area that we believe may benefit from revisions is related to efficacy of some ingredients. We understand in some instances, FDA staff have asked for information related to ingredients that are geared towards establishing physiological effects rather than focusing on such ingredients' basic safety. We believe that it will be clearer for all stakeholders if the review process for ingredients is focused primarily on ingredient safety.

We would like to ensure there is clarity in the terms used in context. Specifically, the term "intended use." This term has ambiguity between the intended use of the raw material related to nutritional purpose and the finished product marketing claims. This ambiguity resulted in a request for physiological effect beyond the safety assessment. The intended use of an ingredient should be established as the nutritional purpose and the level it can be fed safely to cats and dogs.

As an example, consider an ingredient supplier seeking authorization for a novel insect meal to provide protein for cat and dog food. The intended use is a macronutrient protein source, and the safety data should show it is appropriate for that use. However, a statement like "it is a high-quality or sustainable protein" is a marketing claim and should be substantiated by the firm making the marketing claim on their finished product and should not be relevant for the ingredient safety review.

Another area where we suggest efficiency improvements is in the request for published data. While we agree that the science supporting ingredient safety and stability is critical, we believe the limitation to only include peer-reviewed and published data is not practical. PFI members have noted a lack of interest by publishers of scientific journals to circulate data that shows nothing of significance outside of a niche marketplace. Because CVM is actively considering the data as part of all submissions, CVM should consider itself the competent peer reviewer to eliminate the current hurdle.

CVM currently requires extensive shelf-life testing to address ingredient stability. We agree that ingredient stability is critical, but we believe that added flexibility for accelerated shelf-life testing would provide a similar level of confidence in the stability of the ingredient while reducing the time to market for innovative products.

Ingredient shelf-life information is important for the assessment of an ingredient, the stability of an ingredient in pet food has limited utility for an ingredient approval

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process. The reason is that ingredient stability in finished pet food is highly dependent on factors (packaging, preservation, formulation) that are specific to one manufacturer. Since the approval process is not only an approval for that manufacturer to utilize the ingredient, this dataset provides very limited information about how the ingredient will be used across the broad industry following approval.

Is there information that is not currently required to be submitted in a Food Additive Petition or GRAS Notification, but should be to better enable CVM's evaluation?

This question is difficult to answer because there is a significant exchange between CVM and the ingredient supplier during the review of the submitted dossier. After a time, it becomes challenging to understand what is needed for a submission to be considered complete. Clearer guidance from the agency at the outset may help to eliminate this concern.

PFI also recommends that CVM considers a history of safe use of the ingredient in a global view rather than just domestic. Although PFI believes FDA should continue to hold to a science-based approach only, often the history of safe use exists in other markets for an ingredient or component. CVM should consider this as part of an ingredient safety review.

FDA should note that some foreign authorities and overseas trading partners use the American Association of Feed Control Officials' Official Publication (AAFCO OP) as a reference document. CVM should consider a plan to reach out to key trading partners, in and outside the U.S., to clearly state that FDA is the recognized competent authority for safe ingredients in pet food to minimize any confusion. A two-tiered regulatory (and ingredient review) system creates the potential for confusion and CVM needs to be prepared to proactively communicate its regulatory authority with trading partners.

What review process for proposed animal food ingredients would best enable FDA to review their safety?

Like the approach found in the Food Safety Modernization Act, CVM should consider a risk-based approach to ingredient reviews.

Ingredient reviews of new or modified uses of relatively well-known, low-risk ingredients should require less time (e.g., 90 days) for review, also allowing for a more streamlined review package when possible. An example of this class of ingredients might be a whole ingredient or a fraction of a whole ingredient that has a safe history

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of use as a pet food ingredient, and a sub-component of it is proposed for use. Novel ingredients could be expected to need a more substantive review process.

Should CVM decide that an additional category (based on risk assessment) of ingredient review is useful, PFI encourages CVM to support a statutory amendment to authorize the use of a consultation process and the resulting ingredient authorization. To this point, PFI would support AFIC as a permanent pathway but desires that the resulting ingredient authorization have a similar status to FAP and GRAS.

Finally, all regulatory pathways to spur innovation should be both efficient and protect sensitive business information, including confidentiality during the initial review process.

If you have submitted a request for an ingredient definition through the AAFCO ingredient definition process, what was your reason for doing so instead of filing a Food Additive Petition or submitting a GRAS Notification with FDA?

Historically, the AAFCO process was often used to enable ingredients that had already been safely used in animal food, in some cases for many years, to receive a definition based on a company's GRAS self-determination. If the ingredient was not clearly common or usual to a state label reviewer or a specific state did not recognize federal allowed GRAS self-determinations, companies pursued the AAFCO ingredient definition process to get the ingredient published in the AAFCO OP.

It is our understanding that pet food makers and ingredient suppliers have pursued the AAFCO ingredient definition process in the past for a variety of reasons. Some of these are described below.

Unlike the GRAS process, the AAFCO ingredient definition process does not require published data. As we shared previously, it is often exceedingly difficult or impossible to have all the relevant safety data meet this condition. AAFCO data requirements considered all available data on the ingredient of interest, regardless of publication status. Again, since GRAS dossiers are peer reviewed externally and are publicly available on FDA's GRAS notice database, we believe these documents should be considered peer reviewed and published for the purpose of the GRAS review process.

Submitters had received guidance from CVM staff that the AAFCO ingredient definition process would be the most appropriate pathway to seek review. PFI

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members found this to be a convenient pathway for ingredients that were a component or derivative of a whole ingredient that are already reviewed.

As companies in the past considered the three possible pathways (FAP, GRAS or AAFCO), some struggled to understand the data requirements especially for relatively simple ingredients. Many used the AAFCO ingredient definition process to assess whether the submission met an appropriate data standard. PFI believes there is an opportunity for CVM, while it considers efficiency improvements to the FAP and GRAS processes, to provide industry with clear expectations for data requirements across all statutory pathways. This will provide additional guidance to animal food makers in selecting the most appropriate review pathway for an ingredient.

On behalf of PFI members, whose more than 35,000 employees in 34 states provide safe food for dogs and cats across the United States, we appreciate the opportunity to share our views and look forward to working with the agency towards an outcome from this guidance that will continue to allow for the safe use of federally defined ingredients in food for U.S. pets.

Sincerely,

Dana Brooks
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