



ENZYME TECHNICAL ASSOCIATION

1800 Massachusetts Avenue, NW, 2nd Floor
Washington, DC 20036-1800

Telephone (202) 778-9335
Fax (202) 778-9100
www.enzymetechnicalassoc.org

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2003N-0312, Submission of Comments on Animal Feed Safety System Proposing Need for CVM Adoption of GRAS Notification Process

Dear Sir or Madam:

On behalf of the Enzyme Technical Association ("ETA"), we submit these comments in response to the U.S. Food and Drug Administration's ("FDA") notice of public meeting for the Animal Feed Safety System ("AFSS") (Docket No. 2003N-0312).¹ In particular, we submit comments regarding the first component comprising the AFSS, which the agency refers to as "Ingredients and the approval process."

In response to FDA's request for comments regarding the approval process of ingredients (AFSS Component 1), we write to notify the agency of the need for the Center for Veterinary Medicine ("CVM") to adopt the GRAS notification process promulgated in the Proposed Rule for Substances Generally Recognized as Safe (62 Fed. Reg. 18,938 (April 17, 1997)). For the reasons discussed below, we believe that CVM's adoption of the GRAS notification process would benefit both the American public and the agency, as well as remediate the shortcomings of the current GRAS affirmation process.

Problems with Prior GRAS Systems

The agency considers a substance that becomes a component of food or otherwise affects the characteristics of any food to be a food additive and therefore requires a food additive regulation for the substance to be lawfully marketed, unless the substance is exempted because it is generally recognized as safe ("GRAS"). See 21 U.S.C. § 321(s); *cf.* 62 Fed. Reg. 18,938, 18,939 (April 17, 1997). *Cf. also* 21 C.F.R. § 570.35 (affirmation of generally recognized as safe (GRAS) status).

¹ See 70 Fed. Reg. 6,448 (February 7, 2005).

Historically, FDA determined the GRAS status of a substance either by opinion letters issued by the agency's corresponding directly with the manufacturer of the substance² or by the affirmation process detailed in 21 C.F.R. §§ 170.35 and 570.35 (for human food and animal feed, respectively).

However, the shortcomings of these processes did not allow for the most efficacious review of the GRAS status of these substances. With regard to a determination of GRAS status by opinion letters, this process did not provide for a public dissemination of the agency's determination as to the GRAS status of a particular substance because such opinion letters were often available only to the requestor of the opinion letter. Thus, while the manufacturer seeking the agency's input could determine FDA's position as to a particular substance, no other firm was privy to the GRAS status of the substance discussed in correspondence with the agency. Furthermore, these opinion letters were not binding on the agency at the time they were issued and were in fact formally revoked in 1970. *Cf.* 62 Fed. Reg. 18,938, 18,939 (April 17, 1997).

With regard to the affirmation process for GRAS status, this process involves the resource-intensive rulemaking process, which includes: (1) publishing a filing notice in the Federal Register; (2) requesting comments on the petitioned request; (3) conducting a comprehensive review of the petition's data and information and comments received; (4) drafting a detailed explanation of why the use is GRAS; and (5) publishing that explanation in the Federal Register. *Cf.* 62 Fed. Reg. 18,938, 18,941 (April 17, 1997).

The agency thus proposed the rule for determining GRAS status by notification precisely because the current affirmation process is not the most efficient use of the agency's scarce resources. *See* 62 Fed. Reg. 18,938, 18,941 (April 17, 1997). In fact, we note that the CVM has rarely used the affirmation process, presumably because the GRAS affirmation process would not be the best utilization of the CVM's limited resources.

The GRAS Notification Procedure

In the GRAS notification procedure, which would replace the current GRAS affirmation petition process,³ any person may notify FDA of a determination that a particular use of a substance is GRAS. The submitted notice would include a "GRAS exemption claim" that would provide specific information about a GRAS determination, and this notification process would place the burden on the sponsor to make the GRAS determination.

FDA would then evaluate whether the notice provides a sufficient basis for a GRAS determination and respond to the notifier within 90 days in writing. *See* 62 Fed. Reg.

² Prior to 1973.

³ *See* 62 Fed. Reg. 18,938, 18,941 (April 17, 1997).

18,938, 18,941 (April 17, 1997). This 90-day response period would serve the double benefit of lower costs to the agency and greater certainty for the GRAS status of a substance (in addition to the time advantage of a faster response period). *Cf.* 62 Fed. Reg. 18,938, 18,958 (April 17, 1997).

Benefits of Adopting the GRAS Notification Process

Consistency across FDA Centers

This GRAS notification process has been shown to work by the FDA Center for Food Safety and Applied Nutrition's ("CFSAN") use of this process for over seven years now. Furthermore, we note that the provisions in 21 C.F.R. § 170.30 for human food and the provisions in 21 C.F.R. § 570.30 for animal feed implement the same statutory provisions. The agency's review process standards concerning GRAS substances must therefore be consistent with respect to substances used in human food and substances used in animal food or feeds. *See* 62 Fed. Reg. 18,938, 18,955 (April 17, 1997). Thus, to maintain consistency across Centers within the agency, the CVM should adopt the GRAS notification process.

Efficient Allocation of Scarce Resources

The benefits of the GRAS notification procedure are not limited merely to the maintenance of consistency across Centers. As noted above, the GRAS notification procedure would reduce FDA workload by allowing the agency to focus its resources. This notification procedure would reduce the amount of data submission because the notification would be based on an analysis of the data, while the data would still be available to the agency upon request. *See, e.g.,* 62 Fed. Reg. 18,938, 18,963 (April 17, 1997).

Encouragement of Agency-Industry Cooperation

We further note that the proposed notice is simpler than the GRAS affirmation petition process and thus conceivably provides an incentive for manufacturers to inform FDA of their GRAS determinations. This process would result in increased agency awareness of the composition of the nation's animal food and feed supply. *Cf.* 62 Fed. Reg. 18,938, 18,941 (April 17, 1997). In fact, such a notification process could encourage industry to consult with FDA early in the development of animal feed substances to identify the critical aspects of the safety determination that would need general recognition to qualify for a GRAS exemption. *Cf.* 62 Fed. Reg. 18,938, 18,945 (April 17, 1997). The GRAS notification process would also have the benefit of placing the burden on the sponsor to state and support the GRAS status of a substance.⁴

⁴ Furthermore, we note that the agency would be replacing one voluntary administrative process with a different voluntary administrative procedure. Under both the current and the proposed procedures, a manufacturer may market a substance that the

Public Access to GRAS Exemptions

Furthermore, this process would also create a readily available public format for submission by a sponsor and response by the agency as to GRAS exemptions, as well as a CVM GRAS notification file. In addition, such a notification process would facilitate the listing of ingredients in the Association of American Feed Control Officials (AAFCO) Handbook.

We note that CFSAN has currently made publicly available the GRAS notifications submitted to FDA.⁵ This information is on the CFSAN website, and correspondingly, the information is available not just to firms located in the United States but also to those located in other countries. We believe that making this information available publicly to the international community through the internet is having a positive worldwide impact in relation to the use of these substances in human foods. Likewise, the public could benefit from a compilation of GRAS notifications submitted to the CVM in relation to animal feed.

Policy Conformity with CVM Procedures and Timelines

Lastly, we note that the current CVM system is not currently the subject of specific regulatory policy, while the new GRAS notification process would subject GRAS exemption claims to CVM procedures and timelines. The proposed GRAS notification regulation would also revoke 21 C.F.R. § 570.35, which is rarely used by the CVM.

Thus, for the reasons outlined above, as the agency reviews the development of the AFSS, we note that the CVM should adopt the GRAS notification process as promulgated in the Proposed Rule for Substances Generally Recognized as Safe.

Sincerely,



Alice Caddow
Chair

manufacturer determines is GRAS without informing the agency. Thus, from a legal and regulatory perspective, this substitution is neutral. See 62 Fed. Reg. 18,938, 18,941-42 (April 17, 1997). We also note that the Commissioner of FDA may still affirm, on his/her own initiative, the GRAS status of substances. See 62 Fed. Reg. 18,938, 18,944 (April 17, 1997).

⁵ See, e.g., <http://www.cfsan.fda.gov/~rdb/opa-gras.html> (last accessed March 21, 2005) (listing a summary of all GRAS notices).