

January 5, 2011

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## Back to the Future! FDA Reopens Comment Period for 1997 GRAS Notification Proposed Rule

After cooling its heels for over ten years, the Food and Drug Administration (“FDA” or “Agency”) finally appears to be making some progress moving the proposed voluntary GRAS Notification regulation forward. The voluntary Notification procedure was originally proposed in the *Federal Register* in 1997<sup>1</sup> and was intended to replace the voluntary regulatory petition process at 21 C.F.R. 170.35 to affirm the generally recognized as safe (“GRAS”) status of a substance intended for use in food for humans or animals. While FDA has been accepting and reviewing GRAS Notifications since 1997, the proposed rule has never been finalized despite the unquestionable success of the program.

On December 28, 2010, FDA published a notice<sup>2</sup> reopening the comment period for the proposed rule published in the *Federal Register* of April 17, 1997. FDA is seeking updated comments to the docket (FDA-1997-N-0020, formerly 1997N-0103) on the entire 1997 proposed rule as well as issues specified in the December 28 *Federal Register* notice. The deadline to submit comments is March 28, 2011.

While general comments will be accepted, we have briefly summarized specific issues for which FDA is requesting comment. Clearly, these specific issues are matters the FDA feels it must address:

### Issue 1. Description of Common Knowledge Element and Related Definition of “Scientific Procedures”

FDA is considering whether to revise Sec. 170.30(b) of the proposed rule to require that general recognition of safety through scientific procedures be based upon the application of generally available and accepted scientific data, information, or methods, which ordinarily are published, as well as the application of scientific principles, and may be corroborated by the application of unpublished scientific data, information, or methods. FDA is also considering whether to revise the definition of scientific procedures to include the application of scientific data (including, as appropriate, data from human, animal, analytical, and other scientific studies), information, and methods, whether published or unpublished, as well as the application of scientific principles, appropriate to establish the safety of a substance.

<sup>1</sup> Proposed 21 C.F.R. 170.36; 62 Fed. Reg. 18,938 (April 17, 1997), available at <http://www.gpo.gov/fdsys/pkg/FR-1997-04-17/html/97-9706.htm>.

<sup>2</sup> 75 Fed. Reg. 81,536 (December 28, 2010), available at <http://www.gpo.gov/fdsys/pkg/FR-2010-12-28/pdf/2010-32344.pdf>.

## Issue 2. Terms

To clarify that the submission of a GRAS notice reflects the view of the notifier and may not necessarily provide an adequate basis for a GRAS determination, FDA has tentatively concluded that the terms “conclude” and “conclusion” in lieu of “determine” and “determination” would be more appropriate to describe the action of a person who informed FDA that the use of a food substance is GRAS under the Notification procedure.

## Issue 3. Definitions

FDA seeks comment on the following definitions:

- Amendment - any data or other information that is submitted regarding a filed GRAS notice before FDA responds to the notice.
- Supplement - any data or other information that is submitted regarding a filed GRAS notice after FDA responds to the notice.
- Notified substance - the substance that is the subject of a GRAS notice.
- Notifier - the person who is responsible for the GRAS notice, even if another person (such as an attorney, agent, or qualified expert) prepares or submits the notice or provides an opinion about the basis for a conclusion of GRAS status.
- Qualified expert - an individual who is qualified by scientific training and experience to evaluate the safety of substances added to food (consistent with Sec. 201(s) of the Federal Food, Drug, and Cosmetic Act (“FD&C Act”) (21 U.S.C. 321(s))).

## Issue 4. Incorporation by Reference

FDA seeks comment on whether to include a provision in the final rule to expressly permit the notifier to incorporate by reference either data and information that were previously submitted by the notifier, or public data and information submitted by another party, when such data and information remain in FDA’s files, such as data and information contained in a previous GRAS notice, a food additive petition, or a food master file.

## Issue 5. Request That FDA Cease to Evaluate a GRAS Notice

FDA seeks comment on whether the rule should explicitly state that a notifier may request in writing that FDA cease to evaluate the GRAS notice at any time during evaluation of the GRAS notice.

## Issue 6. Notifier’s Responsibility for a GRAS Conclusion

FDA seeks comment on how to best ensure that the identity and authority of the person who is signing the GRAS notice is made clear. For example, FDA is considering requiring that the GRAS notice state the name and the position or title of the person who signs it. FDA also seeks comment on whether to require a notifier to certify to this statement: “To the best of his knowledge, it [the GRAS affirmation petition] is a representative and balanced submission that includes unfavorable information, as well as favorable information, known to him and pertinent to the evaluation of the safety of the substance.”

## Issue 7. Appropriately Descriptive Term for the Notified Substance

The proposed GRAS Notification procedure is meant to focus on the safety of the food substance, not on how it is identified on the label. FDA seeks comment on whether to revise proposed Sec. 170.36(c)(1)(ii) to make more clear that a GRAS notice addresses Secs. 201(s) and 409 of the FD&C Act and does not address the labeling provisions of the FD&C Act or FDA’s corresponding regulations. For example, instead of requiring that the GRAS notice include the common or usual name of the notified substance, FDA is considering requiring that the GRAS notice include the name of the notified substance, using an appropriately descriptive term (which could also be what the notifier believes would be the common or usual name of the substance under 21 C.F.R. parts 102 (human food) and 502 (animal food)). This way, the focus of the GRAS review of the food substance by the notifier remains on the safety of the substance and not on how the substance is identified.

### Issue 8. Public Disclosure

FDA seeks comment on whether the final rule should explicitly require that the information submitted under proposed Sec. 170.36(c)(1) exclude non-public information.

### Issue 9. Including Confidential Information in a GRAS Notice

FDA seeks comment on whether proposed Sec. 170.36(c)(2) should stipulate that the method of manufacture exclude any trade secrets, as it was proposed. FDA seeks comment on whether to require that a notifier who identifies one or more trade secret(s), as defined in Sec. 20.61(a), or confidential commercial or financial information, as defined in Sec. 20.61(b), in the GRAS notice explain why it is trade secret, confidential commercial, or financial information and how qualified experts could conclude that the intended use of the notified substance is GRAS without access to such information.

### Issue 10. Describing the Identity of a Notified Substance

FDA seeks comment on what scientific information would be sufficient to identify the biological source when the notified substance is a biological material (e.g., a plant, animal, or microorganism) and whether it should require that information about the identity of the notified substance specify any known toxicants that could be in the source. In addition, FDA seeks comment on whether the final rule should address, as part of identity, particle size and other chemical and physical properties that may be used to characterize engineered materials.

### Issue 11. Dietary Exposure

FDA seeks comment on:

- Whether the rule should include more specific language about dietary exposure, for example, by requiring information about the amount of the notified substance that consumers are likely to eat or drink as part of a total diet;
- Whether it should require information about dietary exposure to contemporary consumers regardless of whether the determination of GRAS status is through scientific procedures or

through experience based on common use in food;

- Whether it is necessary to clarify that the GRAS Notification procedure is applicable to substances used in both food and drinking water of animals and, if so, whether it would be necessary to clarify this in the provisions of proposed Sec. 570.36;
- Whether it is necessary to clarify proposed Sec. 570.36(c)(1)(iii) to explicitly require submission of information about the animal species expected to consume the substance; and
- Whether it is necessary to clarify applicable sections of the proposed rule to explicitly require, for substances intended for use in the food of an animal used to produce human food, the submission of information about both target animal and human safety (information sufficient to show that the use of the substance is generally recognized among qualified experts to be safe for animals consuming food containing the substance as well as for humans consuming food derived from such animals under its intended conditions of use).

### Issue 12. Filing Decision

FDA seeks comment on whether it should make explicit the process by which FDA makes a filing decision, including the factors that should be used to determine whether to file a submission as a GRAS notice. Some potential factors could be the following:

- Whether the submission includes all required sections;
- Whether all required copies have been provided;
- Where information provided is identified as being confidential, whether there is an explanation of the basis for the conclusion of GRAS status;
- Whether FDA will retain as a record any data or information that is incorporated by reference; and

- Whether the subject of the submission is: (1) already authorized for use under FDA regulations, or (2) a mixture of substances that are already authorized for use under FDA regulations. For example, if FDA receives a submission about a mixture of substances, each of which is affirmed as GRAS under 21 C.F.R. part 184 for use as an antimicrobial in human food, and the intended use of the mixture is as an antimicrobial, FDA may treat the submission as general correspondence and inform the notifier that FDA does not devote resources to evaluating the use of such mixtures under the GRAS Notification procedure.

### **Issue 13. Substances Intended for Use in Products Subject to Regulation by the U.S. Department of Agriculture's Food Safety and Inspection Service ("FSIS")**

FDA seeks comment on whether to make its coordinated review process with FSIS explicit in the final rule. FDA also seeks comment on whether such a procedure should provide that a notifier who submits a GRAS notice for the use of a notified substance in products subject to regulation by FSIS provide an additional paper copy or an electronic copy of the GRAS notice that FDA could send to FSIS.

### **Issue 14. Timeframe for FDA's Evaluation of a GRAS Notice**

FDA requests comment on whether it should retain a set timeframe for FDA to respond to a GRAS notice, and, if so, whether it should be 90 days or another timeframe.

### **Issue 15. Conflict of Interest**

FDA seeks comment on whether companies would find it useful to have guidance on potential conflicts of interest of GRAS expert panelists. If such guidance would be useful, FDA seeks comment on what companies currently do to mitigate such a conflict. FDA also seeks comment on whether to require that GRAS notices include information regarding expert panelists' independence.

### **Issue 16. Additional Guidance on Documenting GRAS Conclusions**

FDA seeks comment on whether there is a need to clarify that its existing guidance (guidance in the preamble to the GRAS proposal and the guidance on its Web site that answers common questions about the food ingredients classified as GRAS in the form of frequently asked questions) also applies to a GRAS conclusion that is not submitted to FDA under the proposed Notification procedure and whether there is a need for FDA to develop further guidance on documenting such a GRAS conclusion.

### **Issue 17. Pending GRAS Affirmation Petitions**

FDA seeks comment on how to reduce the impact on affected petitioners while retaining the principle that FDA will not devote resources to "pending" GRAS affirmation petitions. FDA is interested as to whether an outcome of "withdrawal without prejudice" instead of "insufficient basis" would be more appropriate when an affected petitioner simply chooses not to have the pending petition considered under the GRAS Notification procedure. FDA also seeks comment on whether an affected petitioner could request that FDA incorporate by reference a withdrawn GRAS affirmation petition into a GRAS notice, and if so, if any requirements of the GRAS Notification procedure should be waived.

The complete *Federal Register* notice may be accessed at:

<http://edocket.access.gpo.gov/2010/2010-32344.htm>.

### **Conclusion**

Finalizing the 1997 proposed rule will be beneficial to the industry and FDA as the GRAS Notification program has been a very successful and efficient tool for both parties. However, the details of the program, such as the issues raised in the FDA's December 28, 2010 *Federal Register* notification, can be critical and bear analysis and comment. The Food and Drug Team at K&L Gates would be pleased to assist any interested parties with the preparation of comments.

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