

FDA Issues Draft Guidance On Best Practices for Convening a GRAS Panel

November 17, 2017

Food, Beverage, and Dietary Supplements

Earlier this week, FDA issued a long-anticipated [draft guidance](#) on best practices to follow when convening an expert panel to evaluate whether a substance is “generally recognized as safe,” or GRAS, under the conditions of its intended use in food. The draft guidance is meant to address one of the areas of concern raised by critics of the GRAS process--namely, the GRAS panel and its inherent potential for conflict of interest. For more information on the GRAS voluntary notification process, please refer to [Covington's client alert](#) on FDA's August 2016 final rule.

The draft guidance recommends best practices for convening a GRAS panel, including:

- identify GRAS panel members with appropriate and balanced expertise;
- take steps to reduce the risk that bias will affect the credibility of the GRAS panel's output (e.g., conflict of interest); and
- limit the data and information provided to a GRAS panel to public information (e.g., not trade secret information).

Background

A GRAS panel is a panel of qualified experts who independently evaluate whether the available scientific data, information, and methods establish that a substance is safe under the conditions of its intended use in food. The panel's determination is part of an evaluation of whether adding that substance to food is lawful under the GRAS provision of the Federal Food, Drug, and Cosmetic Act (FDCA).¹ A GRAS panel is one mechanism that food manufacturers have used to

¹ Section 201(s) of the FDCA describes a GRAS substance as one that is:

generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use.

21 U.S.C. § 321(s).

show that the safety of a substance under the conditions of its intended use is generally recognized by qualified experts.

In August 2016, FDA issued a [final rule](#) regarding the voluntary GRAS notification procedure, or “GRAS notice,” completing the rulemaking that began in 1997 and effectively codifying the agency’s interim process that industry had been following for almost 20 years. Some consumer, health, and food safety groups have long challenged the voluntary GRAS system on the grounds that there is an inherent conflict of interest in allowing manufacturers to decide for and by themselves whether a substance is safe to be added to food. To that end, the draft guidance is intended to provide industry with best practices for convening a GRAS panel, including best practices for reducing the risk that bias will affect the credibility of the GRAS panel’s conclusions.

A written GRAS panel policy

The draft guidance recommends that GRAS panel best practices be memorialized in a written GRAS panel policy. The draft guidance does not appear to specifically address who would be responsible for the written policy, when for example, a company engages a consulting firm who then engages the GRAS panel. This is a common practice of many companies who obtain GRAS determinations from GRAS panels. In such a case, as a practical matter, it would seem that the consultancy should have the written policy, but the draft guidance does not appear to address this expressly.

Selecting Members for a GRAS Panel

A GRAS panel acts as “a proxy for the larger scientific community of qualified experts.” The draft guidance provides recommendations on how to reduce the risk of bias that could affect the credibility of a GRAS panel report. These recommendations include:

- Assess and balance the knowledge, experience, and perspectives of potential GRAS panel members in terms of the subtleties and complexities of the particular scientific and technical issues applicable to the food substance and its intended use;
- Consider and take steps to address procedural issues associated with the organization and deliberation of the GRAS panel;
- Consider and take steps to assess potential GRAS panel members for conflicts of interest and appearance issues;
- Document how the proponent or organizer applied the written GRAS panel policy to the selection and vetting of each panel member; and
- Take steps to provide transparency and clarity regarding the selection and vetting of each member of the GRAS panel.

Appropriate and Balanced Expertise in a GRAS Panel

The draft guidance recommends that the GRAS panel be composed of individuals with expertise reflecting the physical, chemical, and biological properties of the food substance and the scientific questions that arise in relation to the conditions of its intended use. At a minimum,

a GRAS panel should include members with expertise in chemistry or biochemistry, toxicology, and exposure assessment. The draft guidance provides a chart with examples of recommended expertise on a GRAS panel based on the food substance or conditions of its intended use. For example, a GRAS panel convened to evaluate a food substance for use infant formula should include an individual with expertise in pediatric nutrition.

The draft guidance recommends that the number of GRAS panel members be determined based on the substance, the complexity of the scientific issues associated with the conditions of its intended use, and the available data and information about the substance. For example, a single representative of each applicable area of expertise could suffice when the available data and information relevant to the intended conditions of use of the substance do not raise any safety questions for experts to interpret and resolve. On the other hand, when the available data and scientific information relevant to the substance's intended use involve complex scientific issues that experts must interpret and resolve, the panel's proponent or organizer should consider having multiple representatives with expertise applicable to those scientific issues.

Managing Procedural Issues Associated with the Organization and Deliberations of a GRAS Panel

The draft guidance recommends that a written GRAS panel policy address the potential for bias that could occur through procedures associated with the organization and deliberation of a GRAS panel. Specific recommendations include: (1) establish clear roles and responsibilities for each panel member; (2) establish clear decision-making procedures for the panel to follow; (3) specify whether the panel should be informed about the potential for bias; and (4) consider factors such as seniority or perceived status among panel members and the leadership skills of an individual who would be the formal leader of the panel.

Managing Conflict of Interest and Appearance Issues

The draft guidance recommends that a written GRAS panel policy assess the potential for conflict of interest and appearance issues during the selection and vetting of GRAS panel members by including the following factors: (1) the process for identifying conflict of interest and appearance issues; (2) criteria for evaluating identified conflicts of interest and appearance issues; and (3) documentation of conflicts of interest, appearance issues, and rationales for waivers.

Identifying conflict of interest and appearance issues

The draft guidance recommends that a written GRAS policy include a process for identifying competing interests and appearance issues. For purposes of the draft guidance, conflicts of interest include "financial interests that can be directly and predictably affected by the work of the GRAS panel," whereas appearance issues include "a broader and more complex set of interests and relationships that could cause a reasonable person to question impartiality."

Examples of sources of conflict of interest include:

- Ownership of any equity of an affected entity

- Compensation for services, such as management or consulting services to an affected entity (excluding honoraria for service on the GRAS panel)
- A role as director, officer, trustee, general partner, or employee of an affected entity

Examples of appearance issues include:

- Direct and predictable effect on the current financial interest of a household member
- Having or seeking a business, contractual, or other financial relationship with an affected entity
- Having a household member or relative with a close personal relationship who is an affected entity
- Consistently and strongly advocating specific views or positions on a specific issue relevant to safety assessment

Criteria for evaluating and strategies for managing identified conflicts of interest and appearance issues

The draft guidance suggests including in a written GRAS policy the following strategies for managing conflicts and appearance issues:

- Establish pre-existing criteria for excluding an individual from a GRAS panel based on conflict of issue or appearance issue of sufficient significance;
- Establish pre-existing criteria for waiving an exclusion triggered by a conflict of interest or appearance issue;
- Include “balancing” viewpoints on a particular issue where one or more participants is strongly associated with a particular viewpoint;
- Disclose conflicts and appearance issues to all panel participants to allow them to weigh this information in their assessments; and
- Include some panel members who have a conflict of interest or an appearance issue as non-voting members.

Notably, the draft guidance acknowledges that due to the “finite number of qualified experts [] available to serve on a GRAS panel . . . [,] [t]here may be circumstances in which the need for the individual’s services outweighs the potential for a conflict of interest or appearance issue in order to provide the GRAS panel essential expertise.”

Documentation of conflicts of interest, appearance issues, and rationales for waivers

The draft guidance recommends that a written GRAS policy describe how to document that a particular GRAS panel used the process to identify and manage conflicts of issues and appearance issues. In addition, the draft guidance recommends that the policy should require documentation of all conflicts of interest and appearance issues and how these issues were managed (e.g., waivers).

Other Recommendations in the Draft Guidance

- *Information provided to a GRAS panel.* The draft guidance recommends that the panel's proponent or organizer minimize the amount of non-public information provided to a GRAS panel, with the exception of data and information that could raise a question about the safety of the substance under the conditions of its intended use. The draft guidance recommends that the data and information provided to a GRAS panel include a description of all data and information that could raise such a safety question, regardless of whether those data and information are publicly available.
- *Documenting a GRAS panel's deliberations and conclusions.* The draft guidance recommends that the proponent or organizer consider how to document the GRAS panel's deliberations and conclusions. Specifically, the draft guidance recommends clear and explicit documentation of: (1) the available data and information that the GRAS panel reviewed; (2) how the GRAS panel handled its deliberations; and (3) the basis for the GRAS panel's conclusions.
- *Considerations when a GRAS Notice is or is not submitted to FDA.* The draft guidance provides recommendations on the submission to FDA of a GRAS notice, including the certification statement and accompanying narrative. Importantly, the draft guidance also explains that the GRAS criteria apply regardless of whether a conclusion of GRAS status is submitted to FDA as a GRAS notice, or whether it is an independent conclusion of GRAS status that remains with the proponent.

Conclusion

The draft guidance reflects FDA's current thinking on best practices for convening a GRAS panel, including assembling an appropriate and balanced panel and taking steps to address conflicts of interest, to help ensure that the GRAS panel effectively acts as a sufficient proxy for the larger scientific community. Companies who engage GRAS panels may want to examine the draft guidance closely and determine whether to submit comments. The formal comment period ends May 15, 2018.

If you have any questions about this client alert or need any assistance further assessing the impact of the draft guidance or drafting and submitting comments to FDA, please feel free to contact any of the following members of our Food & Beverage practice:

<u>Miriam Guggenheim</u>	+1 202 662 5235	<u>mguggenheim@cov.com</u>
<u>Jeannie Perron</u>	+1 202 662 5687	<u>jperron@cov.com</u>
<u>Jessica O'Connell</u>	+1 202 662 5180	<u>jpoconnell@cov.com</u>
<u>MaryJoy Ballantyne</u>	+1 202 662 5933	<u>mballantyne@cov.com</u>
<u>Matt Hegreness</u>	+1 202 662 5418	<u>mhegreness@cov.com</u>
<u>Stephanie Resnik</u>	+1 202 662 5945	<u>sresnik@cov.com</u>

This information is not intended as legal advice. Readers should seek specific legal advice before acting with regard to the subjects mentioned herein.

Covington & Burling LLP, an international law firm, provides corporate, litigation and regulatory expertise to enable clients to achieve their goals. This communication is intended to bring relevant developments to

Food, Beverage, and Dietary Supplements

our clients and other interested colleagues. Please send an email to unsubscribe@cov.com if you do not wish to receive future emails or electronic alerts.