GRAS Overview and Industry Perspectives

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International Food Additives Council
The International Food Additives Council (IFAC)

IFAC is an international association, representing companies who produce high quality substances used worldwide as food ingredients.

www.foodadditives.org
IFAC Strives to:

- Promote science-based regulation worldwide.

  - Increase IFAC’s involvement in international regulatory processes.
  
  - Further establish IFAC as a source of credible scientific information on food ingredients.

  - Organize and sponsor pertinent scientific research on food ingredients.
Key IFAC Global Issues

- **Global Harmonization of Food Ingredient Specifications**
  - Specifications for food ingredients exist in the US Code of Federal Regulations (CFR), the Codex Alimentarius (JECFA), the Food Chemicals Codex (FCC) and other national regulations
  - Concern for international trade when specifications do not coincide
  - IFAC members work very hard to ensure global harmonization of specifications through our work at the Codex Committee on Food Additives (CCFA)

- **Codex Alimentarius**
  - IFAC holds NGO status before Codex Alimentarius
  - IFAC actively participates in the CCFA meetings as well as electronic physical working groups
  - IFAC provides comments to other Codex Committees, as appropriate
Safety Evaluation of Food Additives in the US

• According to the US FDA, the term “safe” means that there is reasonable certainty in the minds of competent scientists that a substance is not harmful under intended conditions of use.

• According to the US FDA, the term “food additive” is any substance that the intended use of which results or may reasonably be expected to result -- directly or indirectly -- in its becoming a component or otherwise affecting the characteristics of any food.
Substances Added to Food in US

Food Additive Petition

OR

Generally Recognized As Safe (GRAS)

GRAS Notification

Independently-Determined GRAS
Generally Recognized As Safe (GRAS)

General recognition of safety based upon scientific procedures calls for the same quantity and quality of scientific evidence as would be required to obtain a food additive regulation for a substance by the US FDA.
Food Additive Petition Process

- For substances not generally recognized as safe or with a history of safe use
- Public Process
- Petitioner submits a food additive petition with supporting toxicological data to FDA for premarket approval
- After US FDA’s review, a notice appears in the *Federal Register* for public comment; the notice prescribes the conditions under which the food additive may be safely used
- Once approved, food additives will appear in the *Code of Federal Regulations* (CFR Part 172), as a direct food additive
- Slow Process: take years
GRAS Notification

• Manufacturer informs US FDA of GRAS action without the need for rulemaking
• More Timely and Less Burdensome
• Manufacturers who notify can show customers US FDA’s no objection letter.
• The US FDA has GRAS Notice Inventory of substances that have undergone a notification since 1998; some GRAS substances are listed in the CFR in Part 184
Independently Determined GRAS

- Same level of scientific support is required for Independently Determined GRAS as for GRAS Notification or Food Additive Petition approval; US FDA expects supporting documentation to be available upon request
- Data is required to be publicly available
- IFAC member companies typically use an expert panel for safety determination
Independently-Determined GRAS

- GRAS determinations “may be based only on the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food.” (21 CFR 170.30)

- FDA has provided guidelines on how to submit GRAS notices, which apply to Independently-Determined GRAS.

- Process works well for industry and US FDA; not aware of any safety concerns that have arisen from this process.
## Comparison of Food Additive Petition Vs. GRAS Process in the US

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<tbody>
<tr>
<td>Food Additive Petition</td>
<td>Same</td>
<td>Not Required</td>
<td>Yes</td>
<td>US FDA</td>
<td>Years</td>
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<tr>
<td>GRAS Notification</td>
<td>Same</td>
<td>Required</td>
<td>No</td>
<td>Submitter of Notification Uses Experts; FDA Issues No Objection Letter</td>
<td>Months to Get FDA’s No Objection Letter</td>
</tr>
<tr>
<td>Independently-Determined GRAS</td>
<td>Same</td>
<td>Required</td>
<td>No</td>
<td>Manufacturer uses Experts or Expert Panel</td>
<td>Days to Months</td>
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Value of the GRAS Process

- **Targeted use of limited FDA resources**
  - Market driven innovation spurs demand for substances with functional/health benefits and/or desired technological functionality

**1958**: FD& C Act → “Food Additive” definition

**Early 1970s**: FDA establishes formal GRAS-affirmation petition process, partly in response to industry requests

**1996**: Backlog of 290 Food additive petitions & 80 GRAS affirmation petitions led to calls for reform by President Clinton and the industry

**December 31, 2012**: FDA filed a total of 451 GRAS notices (averaging 30 notices/year)

**FDA Responses (as of December 31, 2012)**
- 79% FDA has no questions
- 4% Insufficient basis
- 17% Notifier stops process

Reference: Dr Mattia's (OFAS, CFSAN, FDA) Presentation on the GRAS notification program @ FDLI, Feb 2013
Value of the GRAS Process

- **Supports innovation and product development**
  - Shorter review times
  - Faster market introduction of new & innovative products to meet consumer demand for convenient & ‘healthy for you’ options

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<th>Average time for market clearance (excludes dossier preparation time)</th>
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<tr>
<td>Food additive petition</td>
<td>14-18 months (expedited i.e. enhances food safety) &gt;18 months</td>
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<tr>
<td>GRAS notification</td>
<td>~ 180 days (6 months)</td>
</tr>
<tr>
<td>GRAS expert panel</td>
<td>~ 1 month</td>
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“The Making of a GRAS substance”
- Ensuring a robust GRAS process

- Identity and characterization of the substance
  - Manufacturing process
    - Unit operations
    - Raw materials
  - Chemically defined vs Natural complexes
    - Challenges of ‘Clean label’ trend
    - “Fully” characterize
  - Stability
    - Reaction within food matrix
    - Breakdown products
“The Making of a GRAS substance”
- Ensuring a robust GRAS process

- **Data to assess safety & support GRAS claim**
  - Determining safe levels of intake
    - Literature search for all relevant information
      - Fair & balanced
      - Scope
    - Post launch product stewardship
      - Monitor & re-evaluate
  - Estimating daily intake/exposure
    - Market intelligence – similar competitive products
      - Existing history of use & use levels
    - Background levels from natural sources
“The Making of a GRAS substance”
- Ensuring a robust GRAS process

- **Expert panel**
  - Training and experience qualification standard

  “FDA would normally look for such qualifications as training and experience in the relevant scientific disciplines, professional positions held, name recognition by fellow members of the scientific community and publications in respected journals in the field.”


- **Independent**
  - Advisor vs expert panel member
  - Conflict of interest assessment SOP
Concluding remarks

- The GRAS process brings value and works well
- All stakeholders have vested interest in ensuring a robust and well accepted GRAS process
- The food ingredient industry has been and must continue to be diligent in shouldering their responsibility in ensuring that their products are safe, though the application of appropriate best practices and sound scientific principles.
- The food ingredient industry embraces initiatives to strengthen food safety that are based upon sound science and desires to contribute to the discussion by sharing industry specific expert knowledge and concerns.
Thank you.

Any Questions??