GRAS Notices for Human Food Ingredients Produced Using Genetically Engineered Microbes

The Future of Microbial Biotechnology Workshop

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Ensures the safety of substances added to food
Federal Food, Drug & Cosmetic Act

The Law

Foods, Food Ingredients, Drugs & Cosmetics

# Two Components of GRAS

<table>
<thead>
<tr>
<th>General Recognition of Safety</th>
<th>Evidence of Safety</th>
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<tbody>
<tr>
<td>GRAS</td>
<td>Food Additive GRAS</td>
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**Safety data, information must:**

1. Be generally available
2. Be generally accepted

The information supporting the GRAS conclusion must be generally available; it **cannot** be confidential.

- **Availability:** Publication in peer-reviewed scientific journals, text books, scientific reports *etc.*

- **Acceptance:** Consensus among qualified scientific experts regarding safety
Safety Considerations for GRAS Notices
Describing Uses of GE Microbe-Produced Ingredients
This figure has been republished from “Cellular Agriculture: An extension of common production methods for food”
Safety Considerations

• Identification of production strain
  – Safe strain lineage
  – Pathogenicity of host strain
  – Whether the host strain is toxic (e.g., production of any toxigenic metabolites)
  – Antibiotic resistance profile

• Deposit designation (strongly recommended), or how the identity was confirmed

• Modifications made to production strain
  – How the strain was genetically engineered (e.g., construction of the production strain)
Safety Considerations, cont’d.

• Identification and function of inserted genetic sequences
  - Explicitly state what genetic material was inserted, and any extraneous DNA left behind
  - Introduction of new traits (genes) that yield additional by-products or impurities
  - Identification of any possible proteins produced, including a discussion on allergenicity
  - Stability of the introduced genetic sequences; including potential for transmission of genetic sequences
  - Confirmation of the identity of the inserted genetic sequences
Safety Considerations, cont’d.

- Whether any of the raw materials used in the fermentation media are major allergens or are derived from major allergens
- Composition and purity of the final food ingredient, including presence/absence of production
- Intended target foods and use levels
Examples
Enzymes

• Enzyme genes expressed by various production microorganisms during fermentation and recovered and purified

• Safety of: donor DNA, parent and production strains, fermentation product(s), manufacturing, and the enzyme itself
Algal Oils

• Microalgae that produce oils enriched in unsaturated fatty acids

• Safety of: parent and production strains, microbial inactivation and product purification, and the product oil itself
Yeast

• Hops flavor biosynthetic enzyme genes from mint and basil plants expressed by yeast during fermentation of beer

• Safety of: donor DNA, parent and production strains, manufacturing, and the hops flavor molecules produced
Conclusions

• DFI ensures that food ingredients are safe for their intended uses.

• FDA’s GRAS Notification Program is transparent.

• We strongly encourage pre-submission meetings; request one at Premarket@fda.hhs.gov.
Thank you!