

GRAS Notices for Human Food Ingredients Produced Using Genetically Engineered Microbes

The Future of Microbial Biotechnology Workshop

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Overview

Who We Are & What We Do

- Organization
- Mission

Food, Drug & Cosmetic Act

- Definition of GRAS
- Requirements for GRAS Status

GRAS Notices Describing Uses of GE Microbe-Produced Ingredients

- Overview of Safety Considerations
- Examples

Conclusion

- Summary
- Where to Get More Information

Who We Are & What We Do



U.S. Food and Drug Administration (FDA)



Center for Food Safety and Applied Nutrition (CFSAN)



Office of Food Additive Safety (OFAS)

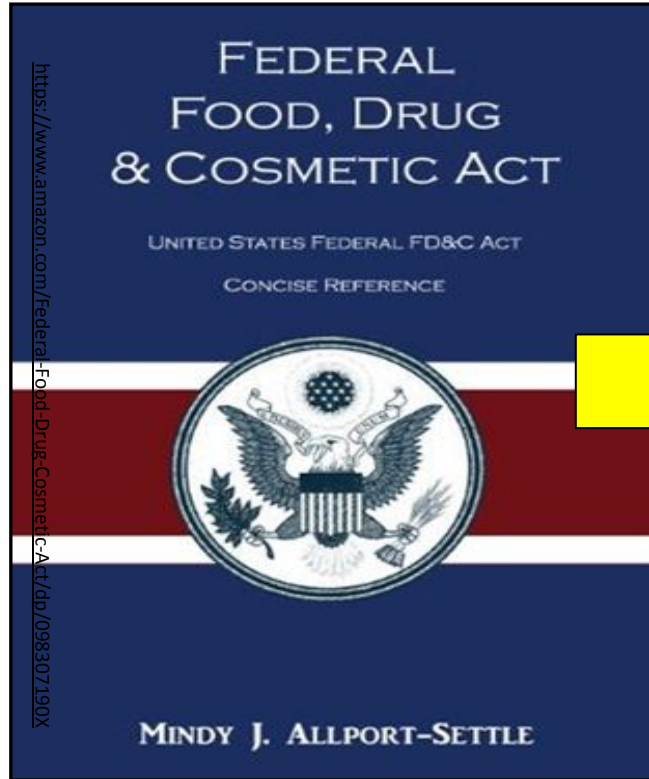


Division of Food Ingredients (DFI)



Ensures the **SAFETY** of substances added to food

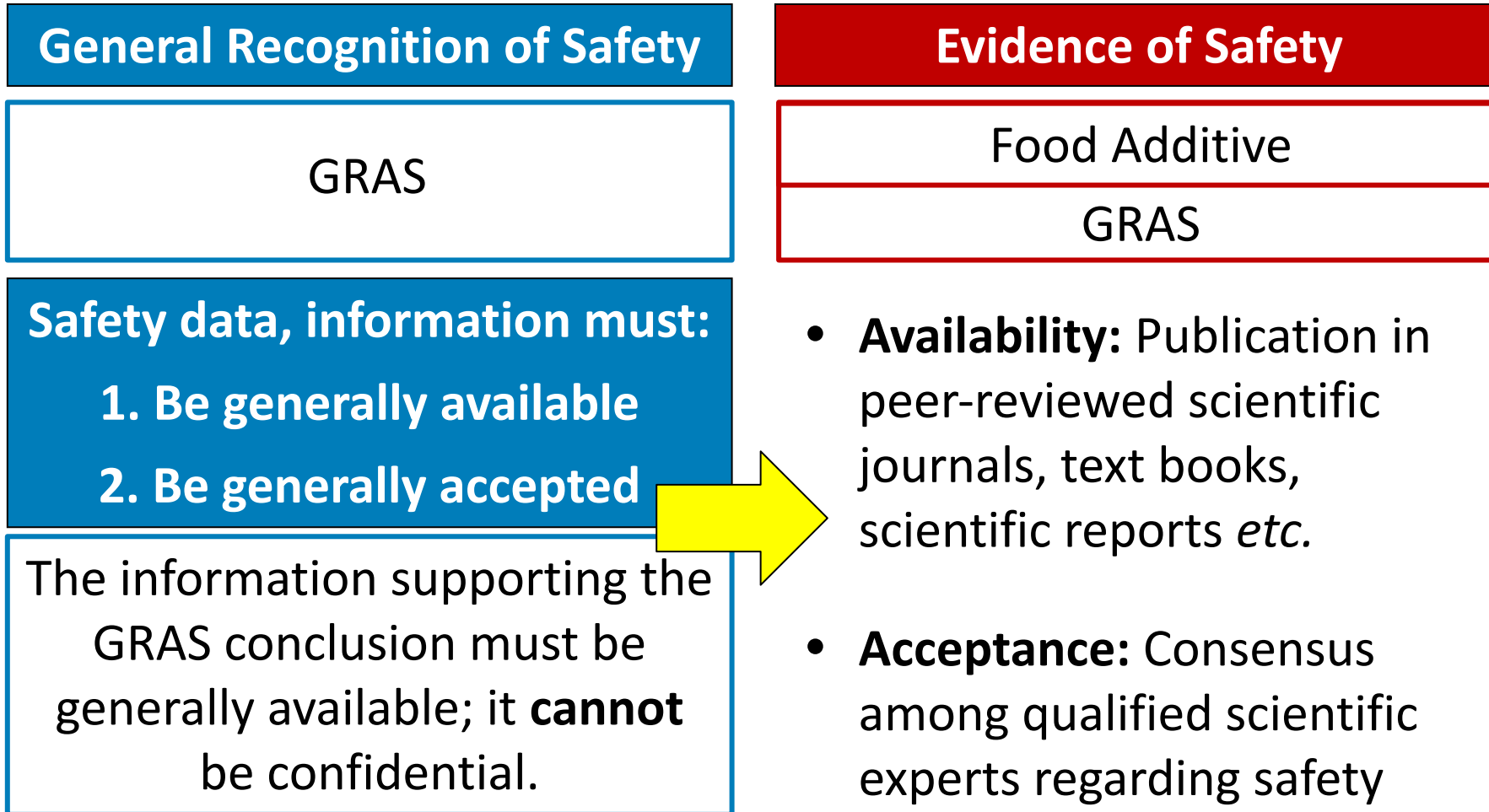
Federal Food, Drug & Cosmetic Act



The Law

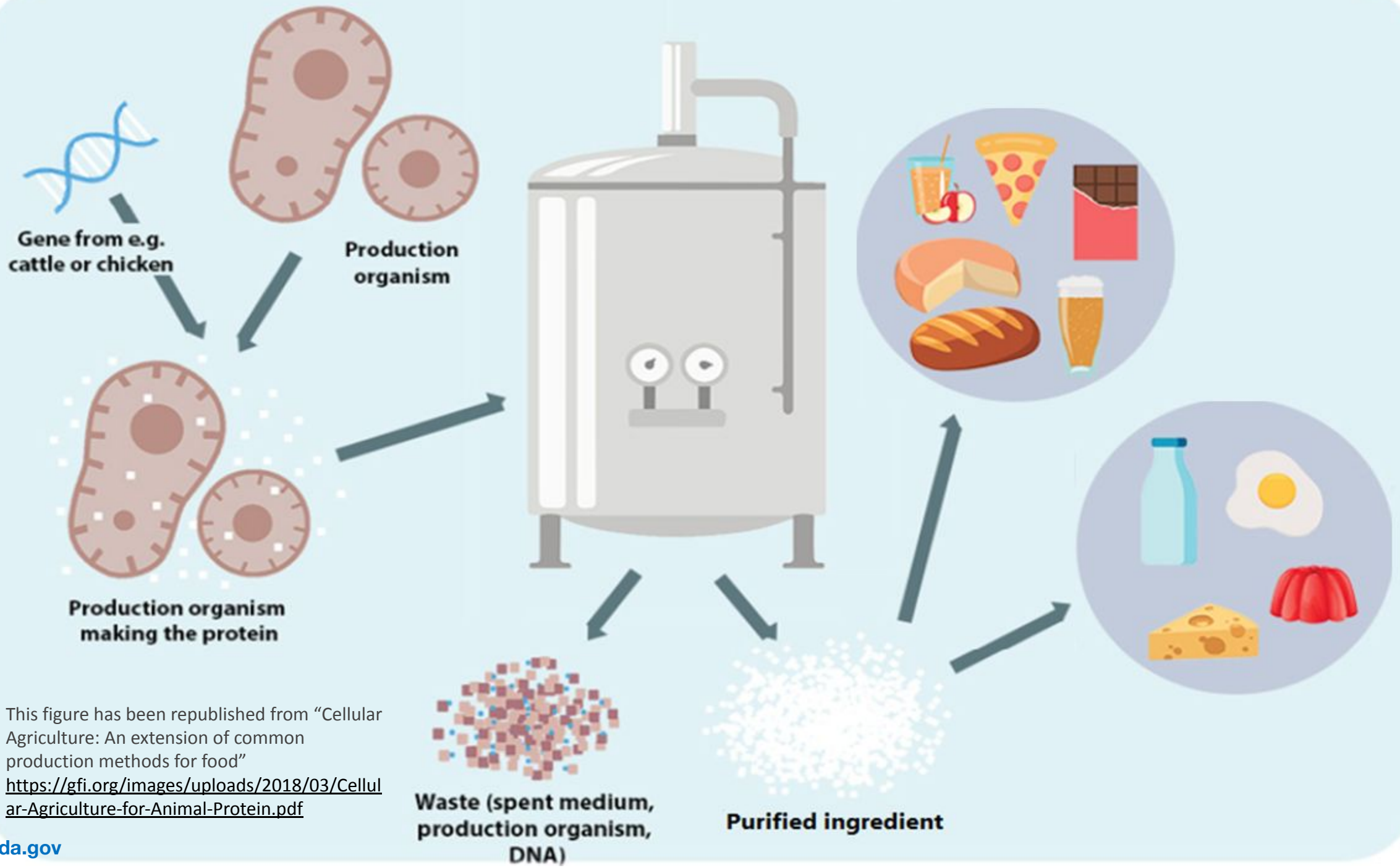
**Foods, Food Ingredients,
Drugs & Cosmetics**

Two Components of GRAS



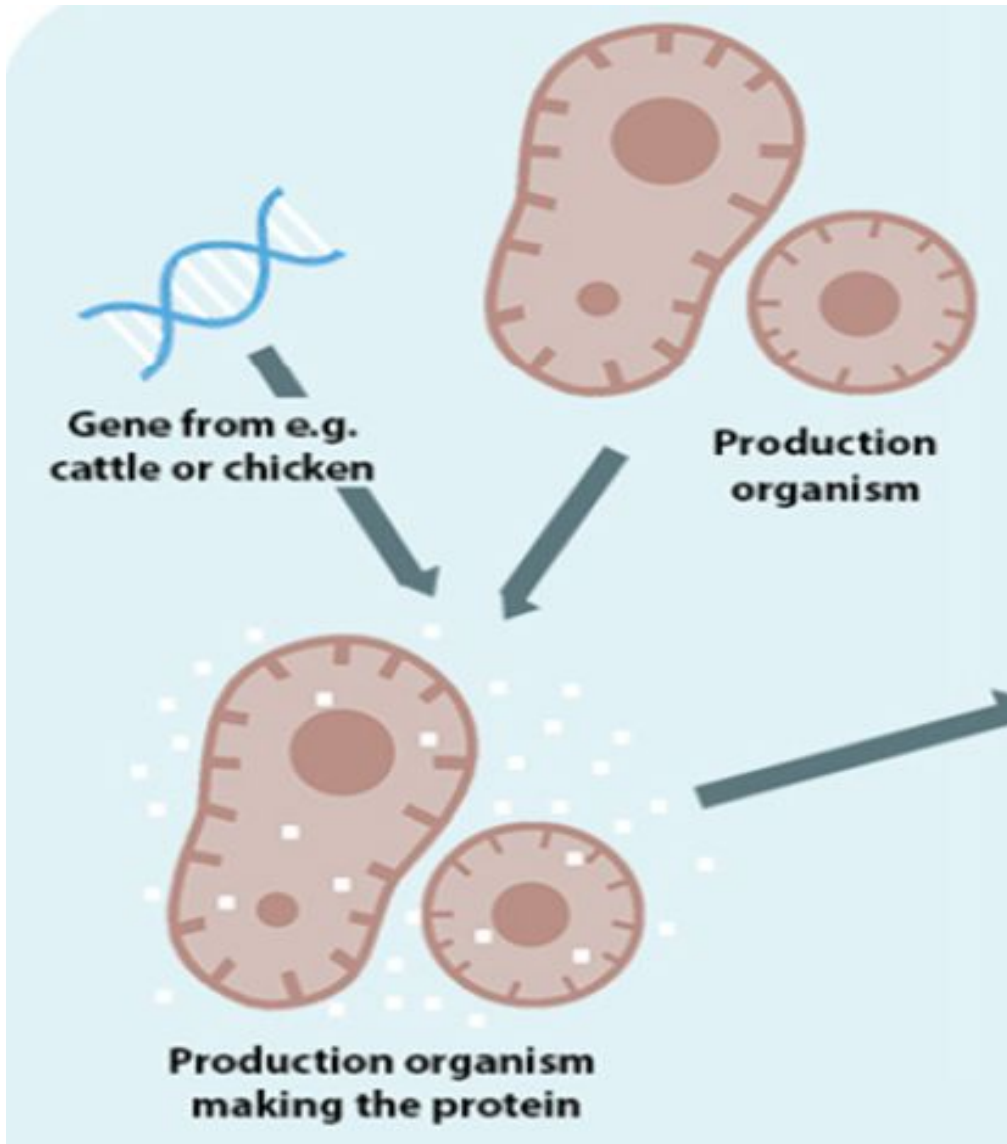


Safety Considerations for GRAS Notices Describing Uses of GE Microbe-Produced Ingredients



This figure has been republished from “Cellular Agriculture: An extension of common production methods for food”
<https://gfi.org/images/uploads/2018/03/Cellular-Agriculture-for-Animal-Protein.pdf>

Safety Considerations



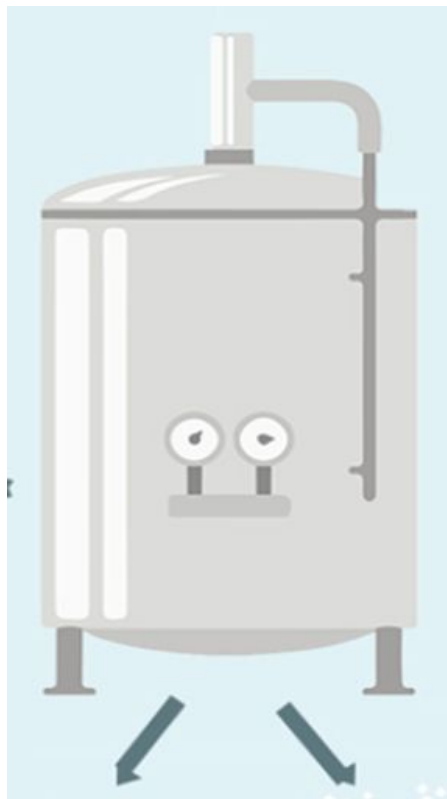
- Identification of production strain
 - Safe strain lineage
 - Pathogenicity of host strain
 - Whether the host strain is toxic (e.g., production of any toxigenic metabolites)
 - Antibiotic resistance profile
- Deposit designation (strongly recommended), or how the identity was confirmed
- Modifications made to production strain
 - How the strain was genetically engineered (e.g., construction of the production strain)

Safety Considerations, cont'd.

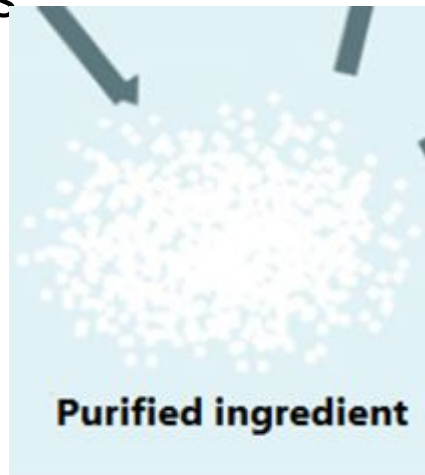


- Identification and function of inserted genetic sequences
 - Explicitly state what genetic material was inserted, and any extraneous DNA left behind
 - Introduction of new traits (genes) that yield additional by-products or impurities
 - Identification of any possible proteins produced, including a 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

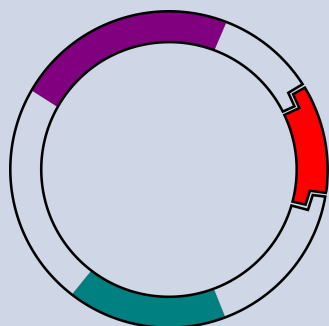




Examples

Enzymes

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



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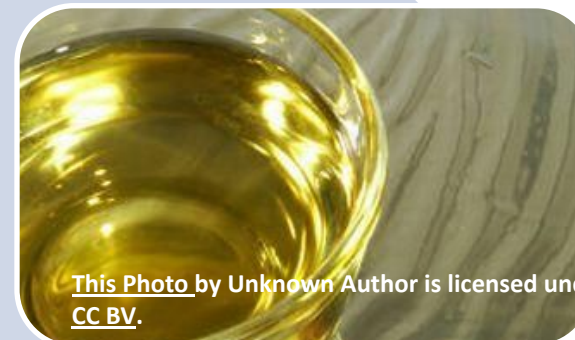
- Safety of: donor DNA, parent and production strains, fermentation product(s), manufacturing, and the enzyme itself



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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



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- 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 Premarkt@fda.hhs.gov.

U.S. Department of Health & Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

GRAS Notices

◉ FDA Home ◉ Generally Recognized as Safe ◉ Food Ingredient & Packaging Inventories ◉ GRAS Notices

The inventory of GRAS notices provides information about GRAS notices filed since 1998, when FDA received its first GRAS notice. As of October 17, 2016, the GRAS final rule (81 FR 54960; August 17, 2016) requires a specific format for a GRAS notice. Prior to that date, FDA processed GRAS notices under the framework of the GRAS proposed rule (62 FR 18938; April 17, 1997). Notices received prior to the effective date of the GRAS final rule provide examples for potential notifiers for the types of information that may support a GRAS conclusion. In the inventory, notices follow the requirements for the format and content of a GRAS notice as of the effective date of the GRAS final rule.

We will update this information approximately monthly. More information about this inventory is available on the [GRAS Notice Inventory Introduction page](#).

Search and display hints:

- Select the specific GRN number below to view additional details about any GRAS Notice.
- To sort by a specific field, click on the column header for that field.
- To browse the records, use the Show All, First/Previous/Next/Last, and Jump To options at the bottom of the data table.
- To search for a specific substance/term, enter the term in the Search box and select Show Items to display only those records that contain the selected term. (The search results also includes terms not shown on this page, but included in the full record on the detail page.)
- The search results will return hits of records containing words that include the search term. For example, a search for the color *red* will return results that include terms such as *reduce*, *ingredient*, and *cultured*. To limit results to only the searched term, place a space before and after the word in the basic search or in the advanced search "this exact phrase" field.

Download data from this searchable database in Excel format. If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).

Basic Search **Advanced Search** Field Search

Search: Show Items Clear

Records Found: 1017 Show All Page 1 of 21

GRN No. (sorted Z-A)	Substance	Date of closure	FDA's Letter
1017	Lacto-N-tetraose		Pending
1016	6'-sialyllactose sodium salt		Pending
1015	3'-sialyllactose sodium salt		Pending
1014	2'-fucosyllactose		Pending
1013	<i>Lactobacillus rhamnosus</i> DSM 33156		Pending
1012	Powdered sap from <i>Angelica keiskei</i> (ashitaba) containing 8% chalcones (ashitaba sap)		Pending
1011	Alpha-amylase enzyme preparation produced by <i>Bacillus subtilis</i> strain AR-651 expressing the gene encoding alpha-amylase from <i>Thermoactinomyces vulgaris</i>		Pending





Thank you!