



# FDA's Food Ingredient Regulatory Programs

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# Outline

- History of Food Ingredient Regulation in the US
- Defining Ingredients, Additives, and GRAS Substances
- FDA Review of Food Ingredients
  - Food Additive Petitions
  - Color Additive Petitions
  - GRAS Notification Program

# History of US Food Additive Regulation

- 1906: Pure Food & Drug Act
- 1938: Federal Food, Drug, and Cosmetic (FD&C) Act
- 1958: Food Additives Amendment
  - Defined food additive with a provision for generally recognized as safe (GRAS) substances
  - Required pre-market approval of new uses of food additives
  - Established standard of safety, standard of review, and formal rulemaking procedures
- 1960: Color Additive Amendment

**STATUTE:  
FD&C Act**

- Enacted by Congress
- Establishes legal framework within which FDA operates
- Can be found in the United States Code

**REGULATION:  
Code of Federal  
Regulations**

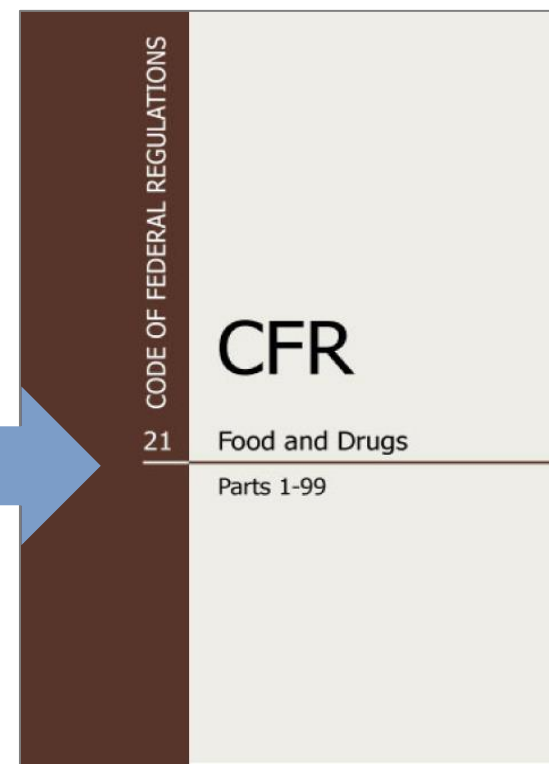
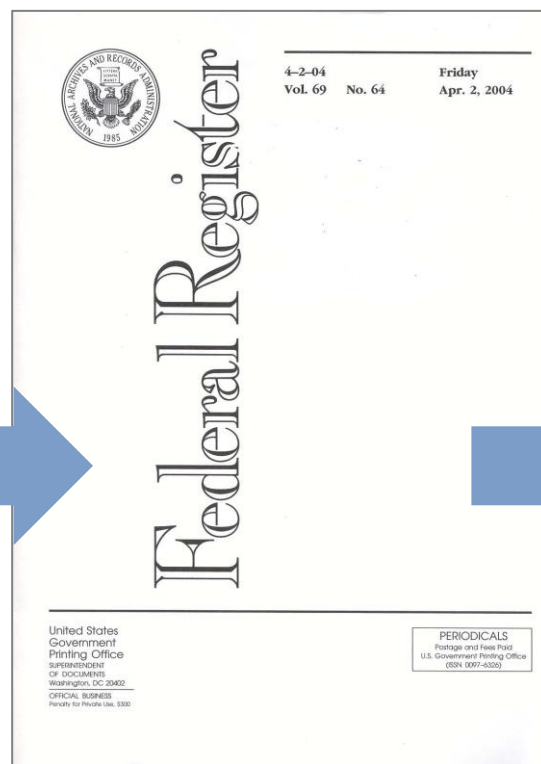
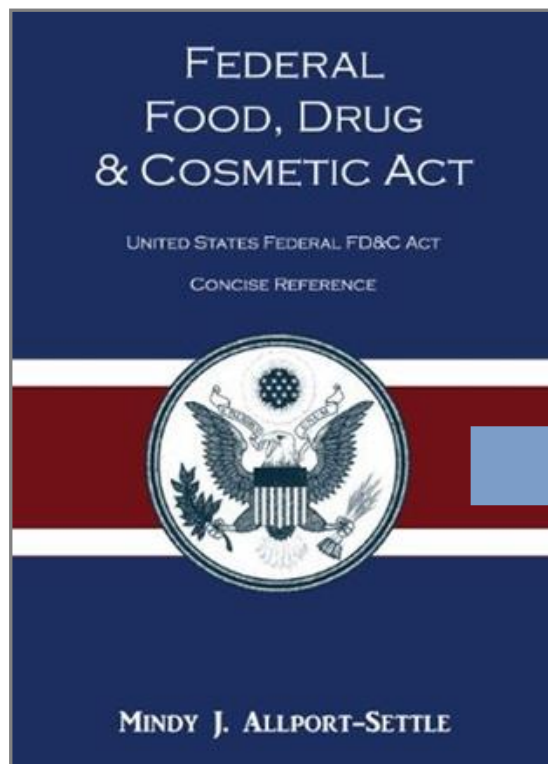
- FDA publishes rules that implement the law
- FDA publishes rules for food or color additives

**GUIDANCE:  
FDA Guidance  
Documents**

- FDA follows “Good Guidance Practice” regulation to issue guidance
- Describes agency’s thinking on a regulatory issue
- Not legally binding on the public or FDA
- Found on FDA website



# The Act and the CFR



[Regulations.gov](http://www.Regulations.gov)

[www.ecfr.gov](http://www.ecfr.gov)

# Navigating the CFR

- Can be accessed online at [www.ecfr.gov](http://www.ecfr.gov)



**Title 21** Food & Drugs  
**Subchapter B** Food for Human Consumption  
**Part 182** Substances Generally Recognized as Safe  
**Section 10** Spices and Other Natural Seasonings  
 and Flavors

**TITLE**

**PART/ SECTION**

**21 CFR § 182.10**



# Statutory Definitions

# Food Additive

- Per section 201(s) of the FD&C Act:
  - “... any substance 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 a food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), ...”



# Direct & Indirect Additives

- **Direct Food Additives (21 CFR Part 172):**
  - Substances added to food for a specific purpose (e.g., technical effect) in that food. Most direct food additives are identified on the ingredient label of foods.
  
- **Secondary Food Additives (21 CFR Part 173):**
  - Substances added during manufacturing or processing. Not intended to remain in the food after its technical effect has been accomplished.
  
- **Indirect Food Additives (21 CFR Parts 174-178):**
  - Substances that become part of the food in trace amounts due to its packaging, storage or other handling.

# Food Additive Exceptions

- Color additives
- Pesticides (EPA)
- Animal drugs (that may remain in food)
- Dietary ingredients in dietary supplements
- Prior sanctioned ingredients

# Prior Sanctioned Ingredients

- Found in 21 CFR 181
  - Specific to the use of the substance, including the specified levels, conditions, and products for which there was explicit approval by the FDA or USDA prior to September 6, 1958
  - List available in CFR is subject to amendment if any use is shown to be injurious to health based on scientific data

# Generally Recognized as Safe (GRAS)

- Discussed in 21 CFR 182
  - Excepted from the definition of a food additive if a substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use
  - Use of an ingredient may be GRAS either through scientific procedures or, for a substance used in food before 1958, through experience based on common use in food



# Food Additive and Color Additive Approval in the US

# Food Additive Petitions

To market a new food additive, or before using an approved additive for a new intended use, a manufacturer must submit a petition proposing:

- A regulation prescribing the conditions under which a food additive may be safely used

OR

- An amendment of an existing food additive regulation
  - Petition must include an assertion of facts, supported by data, showing that new information exists with respect to the food additive; or, that new uses have been developed or old uses abandoned

# Food Additive Petitions

- Food additive petitions submitted to FDA must provide evidence that the substance is safe for its intended use(s)
- Specific requirements, language is prescribed in 21 CFR 171.1:
  - Identity and composition
  - Proposed use in food
  - Amount to be added to food
  - Data establishing its intended effect
  - Analytical methodology
  - Full reports of safety studies
  - Proposed tolerances, if needed
  - Environmental information

# Color Additives

- 1960 Color Additives Amendment of the FD&C Act:
  - Established pre-market approval requirement for color additives and a process for submitting color additive petitions (section 721)
- Per section 201(t) of the FD&C Act:
  - “... a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction to another substance) of imparting color thereto ...”



# Is it a color additive?

## 21 CFR 70.3(f)

Food ingredients such as cherries, green or red peppers, chocolate, and orange juice **which contribute their own natural color** when mixed with other foods are not regarded as color additives; but where a food substance such as beet juice is deliberately used as a color, as in pink lemonade, it is a color additive.

## 21 CFR 70.3(g)

For a material otherwise meeting the definition of color additive to be exempt from section 721 of the Act, on the basis that it is used (or intended to be used) **solely for a purpose or purposes other than coloring**, the material must be used in a way that any color imparted is **clearly unimportant** insofar as the appearance, value, marketability, or consumer acceptability is concerned.



# GRAS Ingredients and GRAS Notices

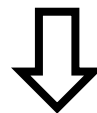
# Food Additives vs GRAS Substances

**Food Additive**



**Evidence of Safety**

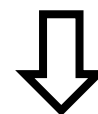
**GRAS Substance**



**Evidence of Safety**

**&**

**General Recognition of Safety**



**General Availability of Safety Data and Information**

**&**

**General Acceptance of Safety**

Both must meet the same FDA safety standard (21 CFR 170.3(i)): “...there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use...”

# Food Additive v. GRAS

- Food Additives:
  - Subject to **pre-market** review & approval by FDA
  - Successful food additive petitions result in a regulation number
- GRAS Substances
  - Not subject to pre-market **review** requirements of the Act, **BUT** still subject to the same safety standard as food additives
  - Some GRAS substances listed in Parts 182, 184, 186
  - No regulation number for GRAS notices

# Two Components of GRAS

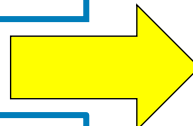
## General Recognition of Safety

GRAS

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.



## Evidence of Safety

Food Additive

GRAS

- **Availability:** Publication in peer-reviewed scientific journals, textbooks, scientific reports *etc.*
- **Acceptance:** Consensus among qualified scientific experts regarding safety

# Two pathways to GRAS

- Scientific procedures
  - 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.
  
- Experience based on common use in food
  - Requires a substantial history of consumption for food use by a significant number of consumers
  - Rare

# Important Caveats for GRAS Ingredients

- Specific to use
  - An ingredient on its own cannot be GRAS
- GRAS notices are not mandatory
  - Companies may maintain self-GRAS conclusions
- FDA response to a GRAS notice is NOT a regulation or approval
  - Represents an opinion
- Color additives cannot be GRAS

# Evaluation of GRAS Notices

**No  
questions\***

**FDA does not question the  
basis for the notifier's GRAS  
conclusion**

**Insufficient  
basis**

**FDA concludes that the notice  
does not provide a sufficient  
basis for a GRAS conclusion**

**Cease to  
evaluate**

**Notifier requests that FDA  
cease evaluation of the notice**

\*If applicable, letters may include a statement that some uses may require a color additive listing.





# Resources & Regulations



# Regulations

Regulation	Topic
21 CFR 73	Listing of Color Additives Exempt from Certification
21 CFR 74	Listing of Color Additives Subject to Certification
21 CFR 172	Food Additives Permitted for Direct Addition to Food for Human Consumption
21 CFR 173	Secondary Direct Food Additives Permitted in Food for Human Consumption
21 CFR 175	Indirect Food Additives: Adhesives and Components of Coatings
21 CFR 176	Indirect Food Additives: Paper and Paperboard Components
21 CFR 177	Indirect Food Additives: Polymers
21 CFR 178	Indirect Food Additives: Adjuvants, Production Aids, and Sanitizers
21 CFR 180	Food Additives Permitted in Food or in Contact with Food on an Interim Basis Pending Additional Study
21 CFR 181	Prior-Sanctioned Food Ingredients
21 CFR 182	Substances Generally Recognized as Safe
21 CFR 184	Direct Food Substances Affirmed as Generally Recognized as Safe
21 CFR 186	Indirect Food Substances Affirmed as Generally Recognized as Safe
21 CFR 189	Substances Prohibited From Use in Human Food

# Resources

- eCFR: <https://www.ecfr.gov/>
- GRAS Inventory:  
<https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices>
- SCOGS Database:  
<https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=SCOGS>
- Food & Color Additive Petitions Under Review Or Held In Abeyance:  
<https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=FAP-CAP>
- Substances Added to Food Inventory:  
<https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=FoodSubstances>
- Food Additive Status List: <https://www.fda.gov/food/food-additives-petitions/food-additive-status-list>
- Color Additive Status List: <https://www.fda.gov/industry/color-additive-inventories/color-additive-status-list>
- Import Alerts: <https://www.fda.gov/industry/import-alerts/search-import-alerts>
- Warning letters: <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters>

# Contacts

- FDA's Food and Cosmetics Information Center: 1-888-SAFEFOOD (1-888-723-3366) or <https://cfsan.secure.force.com/InquiryPage>
- General questions, including about food additives, GRAS substances, and food contact substances: [premarkt@fda.hhs.gov](mailto:premarkt@fda.hhs.gov)
- Dietary supplements, Office of Dietary Supplement Programs: [ODSP@fda.hhs.gov](mailto:ODSP@fda.hhs.gov)



# Thank You

For questions about the regulation of food additives, please reach out to [premarkt@fda.hhs.gov](mailto:premarkt@fda.hhs.gov)