Food and Drug Law Institute: Introduction to Food Law and Regulation

March 19, 2024

Ingredient Preclearance and Intentional Components of Food

Nury Yoo, Faegre Drinker Biddle & Reath LLP

Nury Helena Yoo

Partner
San Francisco | Los Angeles
nury.yoo@faegredrinker.com
+1 415 591 7550 direct

Nury Yoo helps clients in the food and beverage, fresh produce, cosmetics, dietary supplement, OTC drug, personal care, medical device, restaurant, and alcohol beverage industries to navigate regulations, anticipate and manage litigation risk, and defend against challenges.

Her areas of focus include regulatory compliance and enforcement, labeling, claims and substantiation, marketing and advertising, food safety, product recalls, due diligence reviews for private investment, consumer and competitor challenges, and California's Proposition 65. She also advises clients on the complex federal and state issues in the use of cannabidiol (CBD) and related cannabinoids in consumer products.

Legal Disclaimer

- This presentation provides information about the law. Legal information is not the same as legal advice, which involves the application of law to an individual's specific circumstances. The interpretation and application of the law to an individual's specific circumstance depends on many factors. This presentation is not intended to provide legal advice.
- The information provided in this presentation is drawn entirely from publicly available information. The views expressed in this presentation are the presenter's alone.

Statutory Framework for Food Additives

- Federal Food, Drug & Cosmetics Act
- Food Additives Amendment (1958)

“Food Additives”

- Section 201(s) of the FD&C Act defines a “food additive” as:

  > [A]ny 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 any 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 such use); . . .

- Unless the substance 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” (GRAS);

. . .

“Food Additives” (cont’d)

Excludes:

- A prior-sanctioned ingredient – a substance “used in accordance with a sanction or approval granted prior to the enactment of” the FD&C Act as amended, or pursuant to the Poultry Products Inspection Act or Meat Inspection Act;
- Color additives (Color Additive Petitions and regulations);
- A pesticide chemical or residue (EPA);
- A new animal drug; and
- “Dietary” ingredient used in a dietary supplement.
- Exclusions above are not subject to GRAS.

Direct and Indirect Additives

- **Direct Food Additives** (21 CFR Part 172)
  - Substances intentionally added to food to serve a particular functional or technical effect in the food (typically declared on the ingredient statement)
- **Secondary Food Additives** (21 CFR Part 173)
  - Substances added during manufacturing or processing, that are generally not intended to remain in the food
- **Indirect Food Additives** (21 CFR Part 174-178)
  - Substances that migrate to or become part of the food in trace amounts due to packaging, manufacturing, storage, or other handling (subject to Food Contact Notification)

Food Additive Petitions

- To receive approval to market a new food additive, or use an approved food additive for a new intended use, a manufacturer must submit to FDA a food additive petition (FAP) proposing a new food additive regulation, or an amendment to an existing food additive regulation.
- A FAP should include:
  - A proposed tolerance for the additive, if required to ensure its safety;
  - The name of the proposed chemical, chemical identity, composition, conditions of use, labeling;
  - Physical effects data, technical effects (and levels) data, dietary exposures, methods of determining quantity in food after use, environmental information, and results of safety studies; and
  - Details about the manufacturing process, facilities and analytical controls used to establish that the additive is a substance of reproducible composition;
  - FDA must act upon a FAP in 180 days (90 days and one extension). If additional data must be submitted to resolve questions raised by FDA, it can easily take years before approval is granted.

GRAS (Generally Recognized as Safe)

- Excluded from the definition of “food additive”; thus, not subject to preclearance requirements that apply to food additives.
- Some uses of GRAS substances codified in 21 CFR Parts 182, 184, and 186.
- Subject to mandatory safety conclusion (whether through voluntary GRAS Notification Program, self-affirmed GRAS, etc.) prior to use in food.
- Notices, response letters (FDA and notifier) posted to public GRAS Notice Inventory (FDA website, at http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=grasListing)
- GRAS requires evidence of safety (like a FAP) but also requires general recognition of safety (general availability of safety data and information, and general acceptance of safety).
- Once a GRAS determination is reached for a substance, there is no requirement that FDA approval of GRAS status be sought before marketing the substance.

GRAS (cont'd)

GRAS notifications submitted to FDA are required to include the following seven parts:

1. Signed statements and certification, under 21 C.F.R. § 170.225);
2. Information on identity, method of manufacture, specifications, and physical or technical effect, under 21 C.F.R. § 170.230;
3. Estimation of dietary exposure, under 21 C.F.R. § 170.235;
4. Information on self-limiting levels of use, under 21 C.F.R. § 170.240;
5. Experience based on common use in food before 1958, under 21 C.F.R. § 170.245;
6. Narrative, under 21 C.F.R. § 170.250; and
7. List of supporting data and information, under 21 C.F.R. § 170.255.

Not all seven parts may be relevant to every GRAS Notice, but notifiers must include all seven parts in a submission.

81 Fed. Reg. 54960-55055 (Aug. 17, 2016), available at https://www.federalregister.gov/articles/2016/08/17/2016-19164/substances-generally-recognized-as-safe.

GRAS (cont'd)

FDA guidance and tips on GRAS Panels:

- 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 humans food or animal food as part of an evaluation of whether adding that substance to food is lawful under the GRAS provision of the FD&C Act."
- If published results in the primary scientific literature raise no ambiguities or questions that scientific experts need to interpret, a GRAS panel may not be necessary for a well-supported GRAS conclusion
- GRAS panel is one mechanism to provide evidence of general acceptance and to interpret scientific data if needed.

Safety

- The safety of a food additive must be demonstrated by properly conducted and evaluated scientific tests, but the additive need not be shown to be absolutely safe.
- Congress recognized the impossibility of proving the safety of an additive beyond any doubt and under any conditions of use.
- Reflecting the viewpoint of the various scientists who testified in support of a reasonable standard for the safety of an additive, the House of Representatives report on the Amendment indicated:
- “The concept of safety used in this legislation involves the question of whether a substance is hazardous to the health of man or animal. Safety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstances.” H. Rep. No. 2284, 85th Cong., 2d Sess. 1 (1958).
- FDA regulations governing the safety assessment of food additives have incorporated that language. Under 21 C.F.R. § 170.3(i), “safety” within the context of a food additive means that there is a reasonable certainty in the minds of competent scientists that a substance is not harmful under its intended conditions of use.

Safety (cont'd)

- The statute leaves the methods and criteria for interpreting safety data up to the discretion and expertise of the Agency. Congress did, however, direct FDA to consider the following three factors:

  (A) The probable consumption of the additive and of any substance formed in or on food because of the use of the additive;

  (B) The cumulative effect of such additive in the diet of man or animals, taking into account any chemical or pharmacologically related substance or substances in such diet; and

  (C) Safety factors which in the opinion of experts qualified by scientific training and experience to evaluate the safety of food additives are generally recognized as appropriate for the use of animal experimentation data.

FD&C Act § 409(c)(5), 21 U.S.C. § 348(c)(5).

Color Additives

- 1960 Color Additives Amendment of the FD&C Act (premarket approval requirement for color additives and framework for submitting petitions)
- 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 . . . ."
- Certified color additives require batch certification (representative samples of each batch sent to FDA for analysis and certified by number) - synthetic organic dyes, lakes, or pigments ("FD&C" colors on labels).
- Certain color additives "exempt" from certification (*e.g.*, derived from "natural" plant or mineral sources; do not require individual identification, other than carmine and cochineal extract due to allergenicity).
- Color Additives are outside of scope of GRAS.
- Contribution of own natural color v. purpose other than color v. colors added from "natural" sources.

Thank you!

Any questions?

Presented by:

Nury Helena Yoo
Partner
San Francisco | Los Angeles
nury.yoo@faegredrinker.com
+1 415 591 7550 direct