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How Food Ingredients Are Approved

In the U.S., food ingredients may either be FDA-approved food additives or generally recognized as safe. Here's a look at how the regulatory process works.

Food additives were first subjected to regulation in the United States under the Food and Drug Act of 1906. The act states that a food shall be deemed adulterated: "If it bears or contains any poisonous or deleterious substance, which may render it injurious to health; but in case the substance is not an added substance, such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health" (Food and Drug Act, 1906).

"Added" is not defined but is generally understood to mean a substance not present in a food in its natural state. The intent of this section is to prohibit any level of added food substance inconsistent with public health. The Federal Food, Drug, and Cosmetic Act of 1938 contains food safety provisions similar to those in the 1906 Act.

The basic Food, Drug, and Cosmetic Act was last updated in 1958 and defines a "food additive" as: "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 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 any such use) (FFDCA Section 201(s), 1958).

Congress passed the Food Additives Amendment, Section 409 of the Food, Drug, and Cosmetic Act, in 1958, as well. This amendment exempts two important groups of substances from the food additive definition. Those are: (a) substances generally recognized as safe (GRAS) among experts qualified by scientific training and experience to evaluate safety; and (b) substances that either FDA or the U.S. Dept. of Agriculture (USDA) had sanctioned for use in food prior to 1958 (so-called "prior sanction" substances). The amendment does not pertain to pesticides in or on raw agricultural commodities.

The 1958 Food Additives Amendment forbids the use of any food additive not approved by FDA, and the agency may only approve additives shown to be "safe." The act outlines the requirements for requesting approval for a food additive (i.e., "Petition to establish safety") and details the action to be taken by FDA in dealing with such a petition.

Approval and Guidance for Petitioners

A petitioner, requesting the issuance of a food additive regulation, must provide, in addition to any explanatory or supporting data: "(A) the name and all pertinent information concerning such food additive, including, where available, its chemical identity and composition; (B) a statement of the conditions of proposed use of such additive, including all directions, recommendations, and suggestions proposed for the

use of such additive, and including samples of its proposed labeling; (C) all relevant data bearing on the physical or other technical effect such additive is intended to produce, and the quantity of the additive required to produce such effect; (D) a description of practicable methods of determining the quantity of such additive in or on food, and any substance formed in or on food, because of its use; and (E) full reports of investigations made with respect to the safety of such additive, including full information as to the methods and controls used in conducting such investigations (FFDCA Section 409(b)(2), 1958).

The Federal Food, Drug, and Cosmetic Act does not describe the safety investigations to be conducted on the proposed food additive. The FDA, therefore, issued a guidance document entitled, "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food" (referred to as the "Redbook") in 1982 (Federal Register, 1982). Redbook II was issued in 1993 and is periodically updated on the FDA Web site. It is intended to provide guidance on criteria used for the safety assessment of food and color additives used in food and to assist petitioners in developing and submitting toxicological safety data for FDA review. Although the Redbook is not legally binding and FDA states that a petitioner may follow the guidelines and protocols in Redbook II or choose to use alternative procedures, the agency notes that alternative procedures should be discussed informally with the agency "to prevent expenditure of money and effort on activities that may later be determined to be unacceptable to the FDA" (FDA, 1993).

Generally Recognized as Safe Process

●**GRAS Affirmation.** According to current federal law and regulations, any substance that is "Generally Recognized As Safe" (GRAS) for a particular use may be used in food for that purpose without pre-market approval from FDA. General recognition of safety (i.e., a GRAS determination) must reflect the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. Those expert views must be based on "scientific procedures," supplemented in the case of substances used in food prior to 1958 by experience based on common use in food. According to the Code of Federal Regulations, 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 (CFR, 2007).

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. Scientific procedures include human, animal, analytical, and other studies, whether published or unpublished, appropriate to establish the safety of a substance. General recognition of safety through scientific procedures is usually based on published studies, although those studies can be bolstered by unpublished evidence.

Under current law, when general recognition of safety is based on experience from common use in food before January 1, 1958, the determination may be made without the quantity or quality of scientific procedures required for a food additive approval. Common use means a substantial history of consumption by a significant number of people before January 1, 1958 (FFDCA, Section 201(s), 1958). General recognition of

the safety from common use in food should be based upon generally available data (usually published data) and information and can include well-documented use in foreign countries.

Any interested person may make a determination that a substance is GRAS for a particular use(s) (i.e., GRAS self-determination) using the criteria as outlined above. Current regulations acknowledge that current GRAS lists do not include all GRAS substances and are not expected to include pre-1958 natural, nutritional substances. The regulations therefore provide for any interested party to petition FDA to affirm that a substance is GRAS.

A determination of GRAS, with or without a petition to FDA, does not require FDA action. For instance, if a petition is submitted requesting GRAS affirmation, once the petition is accepted for filing, the substance may be legally used for the petitioned purposes while FDA affirmation action is awaited.

●**GRAS Notification.** In April 1997, FDA proposed a replacement for the system under which manufacturers may get affirmation from FDA that a food substance is generally recognized as safe (GRAS) (Federal Register, 1997). Under this “GRAS notification system,” manufacturers may still make a self-determined GRAS declaration, claiming exemption from the premarket or food additive approval requirements. Instead of petitioning FDA for affirmation, manufacturers would notify FDA of their GRAS determination and provide evidence supporting their decision. After evaluating the notification, FDA is to respond to the manufacturer, conveying the agency’s disposition within 90 days. A response that does not identify a problem is *not* equivalent to an affirmation of GRAS status. The proposal allows for a notification to be revisited if new information indicates a reason for concern.

The notification procedure is designed to inform FDA of GRAS actions without the need for rulemaking. Under the proposal, any GRAS affirmation petition pending for a given substance when the notification rule is finalized would be converted or dropped from review. Since the substantive requirements of an acceptable GRAS notification differ from those for a GRAS affirmation petition, any pending petition would have to be amended. For example, a GRAS exemption claim, signed by the notifier and explicitly accepting full responsibility for the GRAS determination, would be necessary. In lieu of this, the GRAS affirmation petitioner could petition for food additive approval, cross-referencing information in the GRAS petition, or submit a complete GRAS notification.

In notifying FDA of their GRAS determination, manufacturers must provide evidence supporting their decisions. Such data includes generally available and accepted scientific data, information, methods, or principles. Under certain circumstances, other scientific data, as well as analytical methods, methods of manufacture, and/or accepted scientific principles could be relied upon as part of the technical information. FDA notes that the quantity and quality of scientific evidence required to demonstrate safety may vary depending on the estimated dietary exposure and the chemical, physical, and physiological properties of the substance. The notice summary must consider the totality of the publicly available information and evidence about the safety of the substance for its intended use, including favorable and potentially unfavorable information.

Although the proposed procedure facilitates a prompt response to self GRAS affirmations, FDA is not required to provide its affirmation. FDA would affirm GRAS status only when the agency of its own volition wants to so affirm a substance.

Until the GRAS notification proposal is finalized, FDA has invited interested parties to use the proposed GRAS notification procedure. This invitation includes those who wish to convert pending GRAS affirmation petitions to GRAS notification. FDA will acknowledge receipt and make a "Good Faith" effort to meet the 90-day time frame but is not required to do so. Approximately 150 GRAS notifications have been reviewed and so acted upon by the agency since 1998.

Both the new and old procedures of GRAS self-affirmation allow ingredients to be used in the U.S. food supply without a published FDA GRAS or food additive regulation. The GRAS notification procedure, however, has essentially replaced GRAS affirmation, even though regulations for GRAS notification have not been finalized.

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