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FDA'S food ingredient approval process ☆ Safety assurance based on scientific assessment

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ABSTRACT

Fifty years ago, the Food and Drug Administration (FDA) began implementing new provisions of the Federal Food, Drug, and Cosmetic Act aimed at assuring the safety of new food additives before they enter the marketplace. Today, the agency's procedures for premarket evaluation of food additive safety have evolved into a scientifically rigorous, sound and dependable system whose objective and independent evaluations by FDA scientists assure that new food additives are safe for their intended uses before they arrive on the consumer's plate. Although controversy often surrounds food additives in the popular media and culture, and science-based challenges to FDA's decisions do arise, the agency's original safety judgments successfully withstand these challenges time and again. This article reviews the basic components of the FDA's decision-making process for evaluating the safety of new food additives, and identifies characteristics of this process that are central to assuring that FDA's decisions are marked by scientific rigor and high integrity, and can continue to be relied on by consumers.

1. Introduction

In the United States a range of government agencies have responsibility to ensure the safety and security of goods that American consumers purchase in the marketplace. Administering these responsibilities often requires specialized knowledge and the evaluation of information well beyond the scope or depth of an ordinary citizen's capabilities or interest. Typical consumers of food products certainly do not have the time or capacity to evaluate biochemical and safety data on every substance they encounter, or to assess for themselves on a daily basis the chemical components of every product they might consider purchasing. In the case of food, Congress has entrusted the Food and Drug Administration (FDA) with the responsibility to oversee the safety of food ingredients, including the premarket safety evaluation of new food additives destined for our foods. In this way consumers are freed from having to make their own personal judgments on a product-by-product basis about food ingredient safety issues each time they wish to make a purchase. Consumers, of course, still make personal decisions about the products they select based on information provided on the food label and their own preferences, but they do not have to review the laboratory data from the animal feeding studies and other safety studies just to decide whether to purchase a food item in the supermarket. This paper outlines major features of the system currently used by the FDA in performing its food additive safety evaluation responsibilities on behalf of the American consumer. This system began *de novo* in 1958 when Congress passed, and President Eisenhower signed into law, the Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act (FD&C Act, or the Act).[3,4]

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[3] The Food Additives Amendment of 1958 to the Federal Food, Drug, and Cosmetic Act, Pub. L. 85-929, 72 Stat. 1784 (codified as amended in 21 U.S.C. 348). Two years later, in 1960, Congress passed the Color Additive Amendments to the Act which established a similar regulatory regime for color additives. In the context of food, both food additives and color additives are often dealt with together because many of the statutory and regulatory requirements are similar, despite the fact that they are defined separately in the FD & C Act (Section 201(s) for food additives and Section 201(t) for color additives, respectively) and color additives are explicitly excluded from the food additive definition, along with pesticides, prior sanctioned food ingredients, dietary supplements and new animal drugs. Although many of the statutory and regulatory standards and procedures for food additives apply as well to color additives, there are some notable differences between these two classes of regulated entities. For example, the effective date of color additive regulations and the post-approval regulatory procedures differ somewhat from those for food additives. Color additives may be used not only in foods, but also in cosmetics, drugs and medical devices. Therefore, although we often refer in this paper to

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2. Food ingredient ABC's

Throughout history, there are innumerable references to the use of food ingredients (such as salt, seasonings and a host of other substances added to food that perform important technical functions in food) as well as techniques (such as culturing and fermentation) used in the preservation and processing of foods. During the mid-20th Century, however, and prior to the passage of the 1958 Food Additives Amendment, the United States was still largely an agrarian society where food was often locally grown, distributed and consumed, and the massive food production and processing system we have today serving large urban population centers did not yet exist. After mid-century, however, as more Americans began to concentrate in cities, it became more important to rely on sophisticated food processing and preservation technologies, including the use of specific food ingredients, to provide consumers with the wide range of appealing, safe, affordable and convenient foods they were seeking.

Food ingredients, as outlined in a brochure produced jointly by the FDA in collaboration with the International Food Information Council[5], provide a range of technical functions in food. We have adapted several basic points from this brochure below:

1. *To improve or maintain safety and freshness:* Preservatives slow product spoilage caused by mold, air, bacteria, fungi or yeast. In addition to maintaining the quality of the food, they help control contamination that can cause foodborne illness, including life-threatening botulism. One group of preservatives—antioxidants—prevents fats and oils (and the foods containing them) from becoming rancid or developing an off-flavor. They can also help prevent fresh cut fruits, such as apples, from turning brown when exposed to air.
2. *To improve or maintain nutritional value:* Vitamins, minerals and other components such as fiber are added to many foods to make up for those that might be lacking in a person's diet, that may be lost in processing, or to enhance the nutritional quality of a food. Others ingredients are used to help lower the calorie or fat content of foods. Such fortification and enrichment has helped reduce malnutrition in the U.S. and worldwide. All products containing added nutrients must be appropriately labeled.
3. *Improve taste, texture and appearance: Spices, flavors, and sweeteners are* added to enhance the taste of food. Food colors maintain or improve appearance. Emulsifiers, stabilizers and thickeners give foods texture and consistency. Leavening agents allow baked goods to rise during baking. Some ingredients help control the acidity and alkalinity of foods, while others help maintain the taste and appeal of foods with reduced fat content.

Furthermore, implicit in the use of any additive is that the use accomplishes a specific technical effect in the food. Title 21 of the Code of Federal Regulations (21 CFR Section 170.3(o)) contains a listing of definitions of physical and technical effects of food additives that help give insight into the various purposes for which additives can be used. In addition, "Good Manufacturing Practices," which apply to the production of any food or use of a food ingredient, dictate that the amount of an ingredient used does not exceed that which is required to achieve the desired technical effect. Overall, however, it is worth incorporating ingredients in food for the purposes outlined above only if these ingredients themselves have been demonstrated to be safe for their intended uses. FDA's food ingredient oversight and new food additive premarket review processes are designed to assure such safety.

3. What does the law require before a new food additive can be marketed?

- The Food Additive Definition and the "GRAS Exemption"

Section 201(s) of the FD&C Act defines a "food additive" as "...any substance, the intended use of which results or may be expected to result, directly or indirectly, in its becoming a *component* or otherwise affecting the characteristics of any food....if such substance is not *generally recognized* among experts qualified by scientific training and experience...to be safe under the conditions of intended use." [6] (*Emphasis added*) Because of its all-encompassing breadth, the first phrase, the so-called "component part" of the food additive definition, would seemingly include an infinitely large set of potential substances as food additives. Congress in its wisdom realized that such an inclusive definition, while correctly drawing a large universe of materials and their uses within its sweep, would, unless limited in some sensible way, also require many ostensibly safe food ingredients, some already in common use for years or millennia, to undergo premarket approval from the FDA. Spending public resources for this purpose would neither protect public health effectively nor make good public policy. Congress' solution was to add the latter clause, the so-called "GRAS exemption" to the food additive definition, where the acronym "GRAS" refers to the terminology "Generally Recognized as Safe."[7] We discuss the GRAS concept and FDA's administration of it later in this paper.

- The Meaning of "Safe"

The 1958 Food Additives Amendment placed new food additives under a strict premarket approval regimen and safety standard. Prior to marketing, new food additives are presumed to be *unsafe* for their intended uses unless and until they are proven "safe" on the basis of scientific data and information. The burden of proof of safety lies with the petitioner. The petitioner must assemble and present to the agency in the form of a petition, all relevant safety data (both that which supports safety and that

"food and color" additives where appropriate, we focus our regulatory discussion primarily on food additives, taking up issues relative to color additives only in certain examples where it is instructive.

[4] Note that meat and poultry products (and processed egg products) are covered separately from other foods by the Federal Meat Inspection Act of 1906, the Poultry Products Inspection Act of 1957, and the Egg Products Inspection Act of 1970, as currently amended. These federal laws, however, defer to the FD & C Act for the establishment of safety standards for additives and ingredients used in meat and poultry products, and the FDA reviews the safety of additives and other ingredients used in these products as well. See: http://www.nationalaglawcenter.org/assets/crs/RS22600.pdf.

[5] See IFIC Brochure: http://www.cfsan.fda.gov/~dms/foodic.html.

[6] The food additive definition in Section 201(s) also includes the so-called "indirect" food additives, or those substances whose use brings them into contact with food (for example, through food packaging) where their food additive status derives from their intentional use in contact with food and the inevitable migration of various components unintentionally into food. From 1958 on, the FD & C Act treated these materials as food additives themselves even though they were commonly called "indirect food additives." As such they required the full-blown filing, review and approval of a food additive petition in order to be lawfully used in the United States. After the passage of the FDA Modernization Act of 1997 (FDAMA) and the allocation in fiscal year 2000 by Congress of adequate funding to implement the new statutory changes, FDA instituted a premarket notification program for such "food contact substances" that obviated the need for a full-blown premarket petition review prior to marketing. In this new system, a company may notify the FDA 120 days prior to marketing and—if there is no FDA objection—go to market. FDA still requires that premarket notifications for food contact material uses contain the same quality and quantity of information previously applicable to indirect additive petitions, but the whole process is now greatly streamlined. In this paper we will not discuss this class of materials further.

[7] See: FD & C Act section 201(s). We discuss the GRAS exemption in more depth in a later section of this paper and include there a discussion of the specific GRAS regulations in 21 CFR 170.30 and 170.35 as well as the April 19, 2007, GRAS reform proposal.