FDA Regulatory Aspects of Food Irradiation

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ABSTRACT

The Federal Food, Drug, and Cosmetic Act requires that a food that has been irradiated may not be sold in the United States unless the Department of Health and Human Services finds that the food is safe and issues a regulation specifying safe conditions of irradiation. This presentation briefly outlines the types of information needed to issue an authorizing regulation, describes the conditions under which food may currently be irradiated, and discusses the basis for current regulations.

Key words: Food irradiation, food safety, FDA

The role of the Food and Drug Administration (FDA) in determining whether foods may be irradiated in this country stems from the passage in 1958 of the Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act in that legislation; Congress explicitly included a source of radiation under the food additive provisions of the law. The Food Additives Amendment provides that a food is adulterated (that is, it cannot be marketed legally) if it has been intentionally irradiated, unless the irradiation is carried out in conformity with a regulation prescribing safe conditions of use. The FD&C Act and FDA's regulations describe the kinds of information and data that are required to be reviewed by the FDA before a food additive regulation can be issued. In this article, we will briefly outline these requirements, focusing on some areas of special relevance to food irradiation regulations, and summarizing major features in the current regulations.

Petitions for an authorizing regulation

In general, the food additive regulations may be amended in one of two ways. In the first, FDA proposes a regulation on its own initiative. The public is given an opportunity to comment on the proposal, and all substantive comments are considered. This procedure is used relatively infrequently and usually only in special circumstances. (In fact, FDA did use this procedure in the mid-1980s to amend the food additive regulations regarding food irradiation; however, it is unlikely that FDA will undertake on its own initiative to amend these regulations again in the near future.)

Far more commonly, the food additive regulations are amended in response to petitions filed by proponents of an additive's use. In this case, the sponsor petitioning for a regulation authorizing a new use of an additive bears the entire burden of demonstrating that the requested use is safe. The petitioner is responsible for assembling the data and information necessary for the agency to reach a safety decision.

The petition is a scientific and legal document that forms the basis of the administrative record underpinning the agency's decision. That decision must be based on a record that is explicit, complete (showing, for example, that all reasonable safety questions have been addressed), and unassailable (if a regulation is challenged, it is the agency that will go to court to defend it).

Furthermore, a petition must contain information adequate to demonstrate that the additive is safe under all conditions of use to be permitted. When FDA issues an authorizing regulation, that regulation is all that is needed for anyone, not only the petitioner, to use the additive in conformance with the specified conditions of use. That is, authorization is granted generically; FDA does not approve particular products or companies, and there are no further licensing or other requirements. Therefore, the agency must establish any limitations necessary to assure safe use before authorization is granted.

Data requirements

Section 409 of the FD&C Act lists the information that must be reviewed by the agency before a food additive regulation can be issued. These requirements are described in greater detail in FDA's regulations in Title 21, Part 171, of the Code of Federal Regulations (CFR). These data include the identity of the food additive, conditions of proposed use, the intended technical effect, a method for determining the quantity of the additive, an assessment of the effect on the environment, and, of course, information to establish safety.

In the specific context of food irradiation, then, what kind of information is needed in each of these areas?

Identity of the food additive. A petition should specify the sources of radiation that are proposed to be used. A number of sources are currently authorized in FDA regulations in Section 179.26 of Title 21 of the CFR (21 CFR 179.26). The authorized sources include gamma rays from sealed units of cobalt 60 or cesium 137, electrons generated from machine sources at energies not to exceed 10 million electron volts, and x-rays generated from machine sources at energies not to exceed 5 million electron volts.

Conditions of proposed use. Required data concerning conditions of proposed use would include information such
as foods to be irradiated, dose limits proposed, and specific processing conditions (e.g., if the food is to be irradiated fresh or frozen, cooked or uncooked, etc.). Where particular conditions of use are necessary to ensure safety, the petition should be as explicit and specific as possible because, as noted earlier, the data in the petition must be adequate to support safety of an additive under all conditions of use to be permitted.

**Intended technical effect.** A petition should clearly lay out what it is that irradiation will accomplish, and how much radiation it will take to do it. Again, the petition should be specific and explicit.

**Method for determining the quantity of the additive.** A petition should discuss methods to be used to ensure that the food receives the intended dose (i.e., dosimetry).

**Assessment of the effect on the environment.** This requirement is not mandated by the FD&C Act; rather it is required to assure compliance with the National Environmental Policy Act (NEPA). Like all government agencies, FDA must consider the effect on the environment of its actions, including the issuance of a food additive regulation. Therefore, a food additive petition must include an environmental assessment that contains data that must be evaluated by the agency to determine whether a finding of no significant impact on the environment can be supported.

In the context of irradiation, examples of data needed in an environmental assessment might include information relating to the disposal of used dosimeter materials and evidence of compliance with pertinent standards of other regulatory agencies, such as the Nuclear Regulatory Commission. An environmental assessment must be prepared as a self-contained, stand-alone document that contains the information necessary to show that there is no reasonable potential for an adverse impact on the environment.

**Information to establish safety**

The issuance of an authorizing regulation also requires, of course, information to establish the safety of the petitioned use. In the case of irradiated food, consideration of wholesomeness (that is, safety for human consumption) requires that four broad areas be addressed: radiological safety, toxicological safety, microbiological safety, and nutritional adequacy.

In the remainder of this article, we want to very briefly pose some questions that each of these areas raises and that must be adequately addressed for the proposed conditions of use of irradiation.

**Radiological safety.** Here, the question is, will radioactivity be induced in the food?

In early work on food irradiation, sources of sufficiently high energies to induce radioactivity in foods were sometimes used. As research continued, sources whose energies are too low to induce radioactivity were adopted by the international community. Therefore, this issue is of no concern when currently approved sources of radiation are used, but must be addressed if other sources are being considered.

**Toxicological safety.** Among the questions that have been raised in attempting to establish the toxicological safety of irradiated food are: (1) Is there evidence of adverse toxicological effects that can be attributed to toxic substances produced by irradiating the food? (2) What should be tested? (3) What tests provide useful information?

Answering these questions has, over the years, proven difficult, as the toxicological evaluation of irradiated foods has presented special challenges. Toxicological safety of typical food additives has traditionally been assessed by using animal feeding studies. Such studies typically involve determination of the highest dose of a tested substance that causes no toxic effects and application of "safety factors" (usually 100-fold) to account for individual variability and for uncertainty in extrapolating from animals to humans. For substances like irradiated whole foods, which may become a large proportion of a diet, application of a 100-fold safety factor is impossible; attempts to exaggerate the amount of irradiated food in the diet have produced adverse nutritional effects that have confounded the results of many feeding studies.

Over time, however, our knowledge of the changes caused in food by radiation has grown. This has provided a basis for estimates of the amounts, types, and potential toxicity of the compounds formed upon irradiation (so-called radiolytic products). A little more than a decade ago, FDA established a committee (the Bureau of Foods Irradiated Food Committee, BFIFC) to, among other things, recommend toxicological testing requirements appropriate for assessing the safety of irradiated foods. The Committee considered the characteristics and quantities of radiolytic products, estimates of projected levels of human exposure, and sensitivity of state-of-the-art toxicity testing, and made several recommendations that have guided subsequent agency decisions.

Specifically, BFIFC recommended that foods irradiated at doses of less than 1 kilogray (kGy), or foods representing a very small fraction of the diet, should be exempt from requirements for toxicological testing. For other irradiated foods, the Committee recommended testing consisting of a battery of short-term mutagenicity tests conducted under conditions that maximize the concentration of radiolytic products and 90-day feeding studies in two species (one rodent and one non-rodent). Further testing could be required to clarify any inconclusive findings in the basic battery of tests.

Following the issuance of the BFIFC report, the agency established a Task Group to review the available animal feeding and mutagenicity studies. The Task Group found that the studies did not appear to show any toxicological effects of irradiated food. The Task Group concurred with the BFIFC recommendation that toxic effects would not be expected from foods irradiated at doses below 1 kGy, and that such foods did not require further toxicological testing. Thus, toxicology data would not be required in a petition for irradiation of food under conditions of use in which the maximum dose would not exceed 1 kGy.

Because many of the studies reviewed by the Task Group were incompletely reported or inadequately designed, the Task Group concluded that the available data were not adequate to evaluate the safety of irradiation of all foods at doses greater than 1 kGy. The Task Group recommended that the agency consider requests for authorization of irra-
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Microbiological safety. In general, the issue of microbiological safety of irradiated foods has raised two questions: (1) Can irradiation mutate microorganisms, producing more virulent pathogens? (2) Will irradiation reduce the numbers of spoilage organisms, allowing pathogens to grow undetected without competition?

The first question is generally not an area of concern. There is no evidence that mutants that may be produced by irradiation are any more virulent than the parent microorganism; in fact, the opposite is more likely to be the case. It is the second question that is of special relevance to most of the applications of irradiation of interest that have not been already authorized by FDA, i.e., irradiation at doses that do not sterilize the food, but that are high enough to appreciably reduce the number of spoilage organisms and to alter the makeup of the residual microbial population.

In these instances, the petition must contain evidence that the proposed conditions of use (dose and temperature of irradiation, for example) are adequate to achieve the intended microbiological technical effect and, most particularly, to ensure that irradiated food is not potentially less safe than nonirradiated food because of the possibility of undetected pathogen outgrowth or toxin production before spoilage is evident. This safety must be demonstrated under all realistic scenarios that may occur in commercial practice, even conditions of temperature abuse or of high initial pathogen loads. The organism that has been of greatest interest in this regard is Clostridium botulinum, both because of its public health significance, and because the spores of this organism are among the most resistant to radiation. Other relatively radiation-resistant pathogens may also be relevant, depending on the particular food and specific proposed conditions of use.

Nutritional adequacy. With regard to nutritional issues, the agency’s concern is for nutritional effects of dietary significance. Two questions are relevant: (1) Does irradiation under the proposed conditions of use result in a significant loss of any nutrient in the food? (2) Is this food an important dietary source of the affected nutrient?

In general, nutrient loss depends on many factors, such as radiation dose, temperature of irradiation, food composition, and the presence or absence of oxygen. At the doses relevant to irradiation of food, losses of micronutrients, particularly vitamins, may be of concern. A petition should address the issue of possible vitamin loss under the specific proposed conditions of use. If there is evidence that any vitamin level is affected significantly under the proposed conditions, data to show that these losses are not significant with respect to the overall diet will be needed.

Current regulations

Based on the considerations above, the FDA has found irradiation of food to be safe under several conditions. Authorizing regulations have been issued both in response to petitions and at the FDA’s initiative. In sum, the FDA has issued broad approvals for irradiation: of food at doses not to exceed 1 kGy to control insects and other arthropods and to inhibit maturation (e.g., ripening or sprouting) of fresh foods; of pork at doses between 0.3 and 1 kGy to control Trichinella spiralis; of poultry at doses not to exceed 3 kGy to control food-borne pathogens; of dry or dehydrated enzymes at doses not to exceed 10 kGy to control microorganisms; and of dry or dehydrated aromatic vegetable substances (e.g., spices and seasonings) at doses not to exceed 30 kGy to control microorganisms. These foods either are minor ingredients in the diet or are irradiated at doses below 1 kGy, except for poultry. The poultry regulation was supported by animal feeding studies. The regulations prescribe irradiation conditions where the microbiological impact is small, where the foods are too dry to support microbiological growth or where microbiological data show that temperature abuse would lead to organoleptic spoilage before development of botulinum toxin.

Labeling

Because irradiation, like other forms of processing, can affect the characteristics of food, the FDA has found it necessary to inform the consumer that an irradiated food has been processed. For situations where the processing is not obvious, such as whole foods that have been irradiated, FDA requires that the label bear the radura symbol and the phrase “treated with radiation” or “treated by irradiation.” If irradiated ingredients are added to foods that have not been irradiated, no special labeling is required on retail packages because it is obvious that such foods have been processed. Special labeling is required for foods that will undergo further processing, however, to ensure that foods are not irradiated multiple times.

Packaging

Irradiation can cause chemical change in packaging, as well as in food, and this can affect migration of the package components to food. Irradiation can cause cross-linking, which would likely reduce migration, but it also can cause decomposition to lower molecular-weight entities, with increased migration characteristics. Sometimes, irradiation has been used in the manufacture (or sterilization) of packaging. The FDA considers this use to be the same as any other manufacturing process, namely, the final irradiated packaging must comply with the appropriate regulations and must not otherwise adulterate food, e.g., by releasing decomposition products that may render the food injurious. The FDA believes that, as part of good manufacturing practice, manufacturers must always consider the effects of changes in their manufacturing processes.

Irradiation of food in a package is a special case, however, because any volatile decomposition products that might be released during irradiation would migrate directly into food. This is different from irradiation during the manufacture of the packaging material because, in that case, a volatile decomposition product may not be present when the food is put into the package. Therefore, the FDA requires that packaging that holds food during irradiation comply with regulations (21 CFR 179.45) based on appropriate testing. It is important to note, however, that these regulations have been amended only once in recent years. The FDA urges packaging manufacturers and others interested in using a packaging material for holding food during irradiation to check these regulations early in their planning for
commercial development, either to ensure that the proposed packaging has been listed in the regulations for packaging to be used during irradiation or to submit a petition for approval of additional packaging materials. In brief, a petition to permit irradiation of packaging material otherwise approved for food use must show that migration from the irradiated material does not raise new issues not considered in the earlier approval. The FDA would be happy to provide guidance to anyone interested in submitting such a petition.

In summary, petitions for a food additive regulation authorizing irradiation of food must include data and information adequate to demonstrate safety. The information needed would be that required to show that irradiation under the proposed conditions of use will not cause adverse toxicological, microbiological, nutritional, or environmental effects. Proposed conditions of use of irradiation at doses exceeding 1 kGy are considered on a case-by-case basis; the type of data necessary would be that described here, and could vary in detail, depending on the specific authorization requested. Therefore, any potential petitioner might find it helpful to consult with the FDA early in the process of preparing a submission. A food that has been irradiated must be so labeled. Finally, packaging used to hold food during irradiation must have been tested and a regulation issued for that use.