Regulatory Report on Irradiation of Food Packaging Materials

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The U.S. Food and Drug Administration (FDA) allows the use of irradiation as a means for improving food safety and extending the shelf life of certain foods. Although not yet widely used, irradiation can kill the bacteria responsible for foodborne illness and food spoilage, as well as insects and parasites that may be present on food. Additionally, in certain fruits and vegetables irradiation can inhibit sprouting and delay ripening. For example, irradiated strawberries stay unspoiled up to three weeks, versus three to five days for untreated berries. Foods are typically packaged in final form prior to being irradiated, thus reducing the likelihood that new pathogens will be introduced after the irradiation step. This means that the packaging materials are being exposed to the same irradiation source as the food itself. In an effort to ensure the safety of the food, one must be certain that an otherwise safe packaging material is not being altered in a fashion that causes a chemical in the packaging to be added indirectly to the food.

Over the years many food packaging materials have been approved for irradiation. Likewise, new food packaging products, such as oxygen barrier materials, have also been introduced. The safety assessment of such complex materials has presented new challenges to FDA and the food industry. This article describes FDA regulations pertaining to packaging materials that are in contact with food during irradiation, the effects of irradiation on new food packaging materials, and the premarket safety assessments of these materials.

Regulatory Requirements

Provisions to ensure the safety of food packaging materials exposed to irradiation are found in a number of parts of the Federal, Food, Drug, and Cosmetic Act (the Act). Section 201(s) of the Act, 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 source of radiation intended for such use…". Under Section 409(a) of the Act, a food is deemed adulterated, and thus prohibited from interstate commerce if it has been intentionally irradiated, unless the irradiation is carried out in compliance with an applicable food additive regulation under the prescribed conditions of use specified in the regulation. The primary regulation covering the use of irradiation in the production, processing, and handling of food is 21 *Code of Federal Regulations (CFR)* 179. This

regulation explains the general provisions for food irradiation, lists approvals FDA has granted to food additive petitions pertaining to irradiation, and describes radiation and radiation sources, including ionizing, radiofrequency, ultraviolet and pulsed light radiation.

Most significantly, 21 *CFR* 179 specifies that the irradiation of both food and packaging materials in contact with food is subject to premarket approval before introduction of the food into interstate commerce. It further specifies that the current good manufacturing practice for irradiated foods includes three things. First, manufacturers must comply with the general requirements of the current good manufacturing practice for manufacturing, packaging or holding human food, found in 21 *CFR* 110. Second, manufacturers must ensure that the radiation dose used is the minimum dose required to achieve the intended technical effect and does not exceed the level specified in the regulations. Third, the packaging materials used during the irradiation treatment must comply with the requirements found in 21 *CFR* 179.45, the specifications for an effective food contact notification, or a threshold of regulation (TOR) exemption. Foods currently permitted to be irradiated are listed in 21 *CFR* 179.26(b) [Table 1]. Finally, the irradiated food must be properly labeled.

Table 1. Foods permitted to be irradiated under 21 CFR 179.26(b) as of October 2007.

Food	**Purpose**	**Dose**
Fresh, non-heated processed pork	Control of *Trichinella spiralis*	0.3 kGy min. to 1 kGy max.
Fresh foods	Growth and maturation inhibition	1 kGy max.
All foods	Arthropod disinfestation	1 kGy max.
Dry or dehydrated enzyme preparations	Microbial disinfection	10 kGy max.
Dry or dehydrated spices/seasonings	Microbial disinfection	30 kGy max.
Fresh or frozen, uncooked poultry products	Pathogen control	3 kGy max.
Frozen packaged meats (solely NASA)	Sterilization	44 kGy min.
Refrigerated, uncooked meat products	Pathogen control	4.5 kGy max.
Frozen uncooked meat products	Pathogen control	7 kGy max.
Fresh shell eggs	Control of *Salmonella*	3.0 kGy max.
Seeds for sprouting	Control of microbial pathogens	8.0 kGy max.
Fresh or frozen molluscan shellfish	Control of *Vibrio* species and other foodborne pathogens	5.5 kGy max.

Although many packaging materials and their components are available for non-irradiation uses, their utilization during the irradiation of prepackaged food is considered a new use and they must pass a premarket safety evaluation before they can be legally used in direct contact with food during irradiation. Table 2 lists the packaging materials and maximum dose levels currently authorized under 21 *CFR* 179. Originally, most of these authorizations were only for gamma-irradiation treatment. However, in response to a food additive petition, FDA evaluated the safety of the materials listed in 21 *CFR* 179.45(b) for doses up to 10 kGy from other types of irradiation. FDA concluded that gamma, e-beam and X-ray sources are equivalent in terms of the types and levels of radiolytic products generated in the packaging materials under the conditions for which prepackaged foods are irradiated. [1] As a result FDA amended, 21 *CFR* 179.45(b) to allow most of the materials to be subjected up to 10 kGy of radiation.

Table 2. Packaging Materials Listed in 21 CFR 179.45 for Use During Irradiation of Prepackaged Foods.

Section	Packaging Materials	Max Dose [kGy]
179.45(b)	Nitrocellulose-coated cellophane	10
	Glassine paper	10
	Wax-coated paperboard	10
	Polyolefin film	10
	Kraft paper	0.5
	Polyethylene terephthalate film	10
	Polystyrene film	10
	Rubber hydrochloride film	10
	Vinylidene chloride-vinyl chloride copolymer film	10
	Nylon 11 [polyamide-11]	10
179.45(c)	Ethylene-vinyl acetate copolymer	30
179.45(d)	Vegetable parchment	60
	Polyethylene film	60
	Polyethylene terephthalate film	60
	Nylon 6 [polyamide-6]	60
	Vinyl chloride-vinyl acetate copolymer film	60

At one time authorizations for the irradiation of packaging materials in contact with food could be obtained solely by the submission of a food additive petition. However, in 1999 the food contact notification (FCN) process was established and became another acceptable mechanism to obtain FDA approval. At present there are no effective food contact notifications for the irradiation of packaging materials, though a number of recent authorizations have been approved via the Threshold of Regulation (TOR) exemption process described in 21 *CFR* 170.39. The recent TOR exemptions all involve packaging constructions and proposed use conditions under which the prepackaged food is irradiated in an inert atmosphere and/or frozen and under vacuum conditions where the levels of radiolytic products would be essentially zero.

Of recent significance, a new TOR exemption permits all food contact articles and their components (i.e., food contact substances) currently authorized for non-irradiated uses to be used during the irradiation of prepackaged food. To qualify for this exemption, the radiation processing must be performed in compliance with 21 *CFR* Part 179, the packaging materials may not be subjected to radiation doses higher than 3 kGy, and the packaged food must be irradiated either in a verifiably oxygen-free environment or while frozen and contained under vacuum. This TOR exemption applies to all substances listed in 21 *CFR* Parts 174 through 186, the inventory of effective food contact notifications, and the inventory of TOR exemptions issued under 21 *CFR* 170.39 that are otherwise permitted for the equivalent non-irradiated uses. This effectively increases the number of base polymers and adjuvants authorized for irradiation of prepackaged food. However, packaging materials authorized for non-irradiated uses but intended for the irradiation of prepackaged food at higher dose levels or in the presence of oxygen, must still undergo premarket approval. Of course, those packaging materials currently not authorized for food contact uses are subject to premarket approval regardless of intended use.

Effects of Irradiation

Irradiation can cause changes to a packaging material that might affect its integrity and functionality as a barrier to chemical or microbial contamination. Radiation does not generally affect all properties of a polymer or adjuvant to the same degree. Two concepts are important here. First, most food packaging materials are composed of polymers that may be susceptible to chemical changes induced by ionizing radiation that are the result of two competing reactions, cross-linking (polymerization) and chain scission (degradation). Radiation-induced cross-linking of polymers dominates under vacuum or an inert atmosphere. Chain scission dominates during irradiation of polymers in the presence of oxygen or air. Both reactions are random, generally proportional to dose, and depend on dose rate and the oxygen content of the atmosphere in which the polymer is irradiated. The idea of cross-linking predominating under vacuum or in an inert atmosphere is important because it served as the basis for granting recent exemption requests under 21 *CFR* 170.39 for packaging materials irradiated in contact with food either in a verifiably oxygen-free environment or while frozen and contained under vacuum.

Second, in the presence of an oxygen atmosphere, radiation-induced degradation of both the base polymer and adjuvants, such as antioxidants or stabilizers, is likely to occur and result in the formation of radiolytic products. The radiolytic products formed upon irradiation may be present at significant levels such that they could migrate into food and affect the odor, taste, or safety of the irradiated food. For example, it is well known that certain adjuvants are prone to degradation during polymer processing. During irradiation they would be expected to degrade preferentially over the polymer and result in the formation of radiolytic products in the polymer that could potentially migrate into food. Therefore, the migration of both base polymers and adjuvants, as well as migration of their radiolytic products, must be evaluated in the premarket safety assessment of new packaging materials prior to their use, especially at high dose levels and in the presence of oxygen.

Irradiating New Materials

As discussed in detail by Twaroski, et al (2007), FDA's safety assessment relies on evaluating probable consumer exposure to a food contact substance, including all constituents or impurities as a result of the proposed use and on the available toxicological information.[2] It is important to understand that the safety assessment focuses on those substances that would be expected to become components of food as a result of the proposed use of the food contact substance. The safety information required in a new submission to the Center for Food Safety and Applied Nutrition's Office of Food Additive Safety generally includes chemical, toxicological and environmental components. The chemistry data, include the identity and amounts of migrants, as well as other data to allow the calculation of dietary exposures for the migrants under the intended conditions of use. FDA's toxicological assessment is based on a tiered approach and, therefore, the recommended toxicological data depend on the exposure estimates for the radiolytic products and other migrants from the proposed use. FDA recommends that all data and information be generated in accordance with the available guidance documents.[3] The identities, residue and migration levels, and consumer exposures to the radiolytic products that are generated in the packaging materials may be of concern depending on the regulatory status of the substances, as well as the presence or absence of oxygen.

Many previous studies in the literature describe the effects of ionizing radiation on various food packaging polymers, which include homopolymers, copolymers, and multilayer structures, as well as adjuvants.[4,5] The results from these studies showed that the formation of radiolytic products depended on irradiation conditions which include the absorbed dose, dose rate, the amount of oxygen in the atmosphere, temperature, time after irradiation, and food simulant. To evaluate the fate of the components of irradiated new packaging materials in comparison to non-irradiated materials, one can develop an appropriate testing protocol that might involve an irradiation experiment designed to simulate the actual application conditions for determining the effects of irradiation on the packaging materials. After irradiation, the test materials can be analyzed for radiolytic products or other migrants, as applicable, using methods and techniques

that may require various analytical instruments. Any analytical methods used in the analysis for radiolytic products in an irradiated test specimen should give some consideration to identification and quantification of an unknown migrant.

In performing a safety assessment, the dietary exposure to radiolytic products and other migrants must be paired with the evaluation of the toxicological information on these substances. The identities of radiolytic products are generally unknown, but may be deduced from the structure of the polymer or adjuvant. This, in turn, might allow chemically similar radiolytic products, such as low molecular weight carboxylic acids, to be grouped and evaluated as a structural class rather than individually. Bailey, et al recently reported on the use of structure-activity relationship (SAR) analysis in the FCN program to determine the toxicity of components of food packaging materials according to their structural similarities with many industrial chemicals that have been analyzed for toxicological concern.[6] SAR analysis has been shown to be a useful tool in the FCN program and has the potential to be useful in the safety assessment of structurally classified radiolytic products from the irradiation of packaging materials in contact with food. However, one should keep in mind that this approach is more appropriate for low exposures. Although FDA does not have a set exposure "cut-off" for the identification of a migrant, FDA generally recommends toxicity testing of migrants at dietary concentrations > 0.5 parts per billion (ppb).

Conclusion

Improved microbiological safety of food may be attained by using irradiation in the production of several types of raw or minimally processed foods such as poultry, meat and meat products, fish, seafood, fruits, and vegetables.[7] In fact, following the recent outbreaks of foodborne pathogens in fresh produce, there has been increased interest in using irradiation for improving the safety of fresh produce. However, food manufacturers must ensure that both the irradiated food and packaging materials used during the irradiation process are authorized for the proposed use.

Currently the packaging materials that comply with the provisions of 21 *CFR* 179.45, the specifications of an effective food FCN or a TOR exemption may be used in direct contact with food during irradiation. Materials that do not fall under one of these umbrellas require a premarket safety assessment before being used in foods. In instances where food packages contain oxygen, such as in modified atmosphere packaging to maintain the quality of fresh produce, the safety assessments can be quite complex. FDA's safety assessments hinge on the likely consumer exposure to radiolytic products and other migrants resulting from the intended use and on evaluation of the available toxicological information on the radiolytic products and other migrants. Given that the identities of radiolytic products are generally unknown, but may often be grouped into structural classes of substances, SAR analysis may be useful in evaluating

the safety associated with dietary exposure to such migrants. FDA encourages individuals to discuss proposed studies with FDA prior to the submitting a petition or notification to ensure that the studies will address FDA's safety concerns, and provide adequate data.

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