§ 3550.61 Insurance (loans only).

(a) Borrower responsibility. Any borrower with a secured indebtedness in excess of $15,000 at the time of loan approval must furnish and continually maintain hazard insurance on the security property, with companies, in amounts, and on terms and conditions acceptable to RHS including a ''loss payable clause'' payable to RHS to protect the Government's interest.

(b) Amount. The borrower is required to insure the dwelling and any other essential buildings in an amount equal to the insurable value of the dwelling and other essential buildings. However, in cases where the borrower's outstanding secured indebtedness is less than the insurable value of the dwelling and other essential buildings, the borrower may elect a lower coverage provided it is not less than the outstanding secured indebtedness. If the borrower fails, or is unable, to insure the secured property, RHS will force place insurance and charge the cost to the borrower's account. Force place insurance only provides insurance coverage to the Agency and does not provide any direct coverage or benefit to the borrower. The amount of the lender-placed coverage will generally be the property's last known insured value.

* * * * *

(d) * * *

(1) Loss deductible clauses for required insurance coverage may not exceed the generally accepted minimums based on current industry standards and local market conditions.

* * * * *

■ 4. Section 3550.64 is revised to read as follows:

§ 3550.64 Down payment.

Elderly families must use any net family assets in excess of $20,000 towards a down payment on the property. Non-elderly families must use net family assets in excess of $15,000 towards a down payment on the property. Applicants may contribute assets in addition to the required down payment to further reduce the amount to be financed.

Subpart C—Section 504 Origination and Section 306C Water and Waste Disposal Grants

■ 6. Section 3550.103 is amended by revising paragraph (e) to read as follows:

§ 3550.103 Eligibility requirements.

* * * * *

(e) *Need and use of personal resources.* Applicants must be unable to obtain financial assistance at reasonable terms and conditions from non-RHS credit or grant sources and lack the personal resources to meet their needs. In cases where the household is experiencing medical expenses in excess of three percent of the household's income, this requirement may be waived or modified. Elderly families must use any net family assets in excess of $20,000 to reduce their section 504 request. Non-elderly families must use any net family assets in excess of $15,000 to reduce their section 504 request. Applicants may contribute assets in excess of the aforementioned amounts to further reduce their request for assistance. The definition of assets for this purpose is net family assets as described in § 3550.54 of subpart B of this part, less the value of the dwelling and a minimum adequate site.

* * * * *

■ 7. Section 3550.110 is amended by revising paragraphs (a), (b) and (d)(1) to read as follows:

§ 3550.110 Insurance (loans only).

(a) Borrower responsibility. Any borrower with a secured indebtedness in excess of $15,000 at the time of loan approval must furnish and continually maintain hazard insurance on the security property, with companies, in amounts, and on terms and conditions acceptable to RHS including a ''loss payable clause'' payable to RHS to protect the Government's interest.

(b) Amount. The borrower is required to insure the dwelling and any other essential buildings in an amount equal to the insurable value of the dwelling and other essential buildings. However, in cases where the borrower's outstanding secured indebtedness is less than the insurable value of the dwelling and other essential buildings, the borrower may elect a lower coverage provided it is not less than the outstanding secured indebtedness. If the borrower fails, or is unable to insure the secured property, RHS will force place insurance and charge the cost to the borrower's account. Force place insurance only provides insurance coverage to the Agency and does not provide any direct coverage or benefit to the borrower. The amount of the lender-placed coverage generally will be the property's last known insured value.

* * * * *

(d) * * *

(1) Loss deductible clauses for required insurance coverage may not exceed the generally accepted minimums based on current and local market conditions.

* * * * *

Dated: July 28, 2008.

Russell T. Davis,

Administrator, Rural Housing Service.

[FR Doc. E8–19350 Filed 8–21–08; 8:45 am]

BILLING CODE 3410–XV–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 179

[Docket No. FDA–1999–F–2405] (formerly 1999F–5522)

Irradiation in the Production, Processing and Handling of Food

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of ionizing radiation for control of food-borne pathogens, and extension of shelf-life, in fresh iceberg lettuce and fresh spinach (hereinafter referred to in this document as ''iceberg lettuce and spinach'') at a dose up to 4.0 kiloGray (kGy). This action is in partial response to a petition filed by The National Food Processors Association on behalf of The Food Irradiation Coalition.

DATES: This rule is effective August 22, 2008. Submit written or electronic objections and requests for a hearing by September 22, 2008. See section VI of this document for information on the filing of objections.

ADDRESSES: You may submit written or electronic objections and requests for a hearing identified by Docket No. FDA–1999–F–2405] (formerly 1999F–5522, by any of the following methods:

Electronic Submissions

Submit electronic objections in the following way:

• Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.

Written Submissions

Submit written objections in the following ways:

• FAX: 301–827–6870.

• Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]: Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of objections, FDA is no longer accepting objections submitted to the agency by e-mail. FDA encourages you to continue

to submit electronic objections by using the Federal eRulemaking Portal, as described in the *Electronic Submissions* portion of this paragraph.

Instructions: All submissions received must include the agency name and docket number for this rulemaking. All objections received will be posted without change to *http://www.regulations.gov*, including any personal information provided. For detailed instructions on submitting objections, see the ''Objections'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or objections received, go to *http://www.regulations.gov* and insert the docket number(s), found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Lane A. Highbarger, Center for Food Safety and Applied Nutrition (HFS–255), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, 301–436–1204.

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I. Background

In a notice published in the **Federal Register** of January 5, 2000 (65 FR 493), and amended May 10, 2001 (66 FR 23943), FDA announced that a food additive petition (FAP 9M4697) had been filed by The National Food Processors Association on behalf of The Food Irradiation Coalition, 1350 I St. NW., suite 300, Washington, DC 20005. The petition proposed that the food additive regulations in part 179, *Irradiation in the Production, Processing, and Handling of Food* (21 CFR part 179), be amended to provide for the safe use of ionizing radiation for control of food-borne pathogens, and extension of shelf-life, in a variety of human foods up to a maximum irradiation dosage of 4.5 kGy for non-frozen and non-dry products, and 10.0 kGy for frozen or dry products, including: (1) Pre-processed meat and poultry; (2) both raw and pre-processed vegetables, fruits, and other agricultural products of plant origin; (3) certain multi-ingredient food products containing cooked or uncooked meat or poultry. Subsequently, in a letter dated December 4, 2007, the petitioner amended the petition to request a response to part of the original request while the remainder of the request would remain under review. Specifically, the petitioner requested a response regarding amending the food additive regulations to provide for the safe use of ionizing radiation for control of food-borne pathogens, and extension of shelf-life, in iceberg lettuce and spinach up to a maximum dose of 4.0 kGy. This final rule is a partial response to the petition and addresses only the use of ionizing radiation on iceberg lettuce and spinach. The use of ionizing radiation on the remaining foods included in the petition remains under review.

II. Safety Evaluation

Under section 201(s) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(s)), a source of radiation used to treat food is defined as a food additive. The additive is not added to food literally, but is rather a source of radiation used to process or treat food such that, analogous to other food processing technologies, its use can affect the characteristics of the food. Importantly, the statute does not prescribe the safety tests to be performed but leaves that determination to the discretion and scientific expertise of FDA. Not all food additives require the same amount or type of testing. The testing and data required to establish the safety of an additive will vary depending on the particular additive and its intended use.

In evaluating the safety of a source of radiation to treat food intended for human consumption, the agency must identify the various effects that may result from irradiating the food and assess whether any of these effects pose a public health concern. In doing so, the following three general areas need to be addressed: (1) Potential toxicity, (2) nutritional adequacy, and (3) effects on the microbiological profile of the treated food. Each of these areas is discussed in this document. Because an understanding of radiation chemistry is fundamental in addressing these three areas, key aspects of radiation chemistry relevant to the evaluation of the request that is the subject of this rulemaking are also discussed. FDA has fully considered the data and studies submitted in the petition as well as other data and information relevant to safety.

A. Radiation Chemistry

The term ''radiation chemistry'' refers to the chemical reactions that occur as a result of the absorption of ionizing radiation. In the context of food irradiation, the reactants are the chemical constituents of the food and initial radiolysis products that may undergo further chemical reactions. The chemistry involved in the irradiation of foods has been the subject of numerous studies over the years and scientists have compiled a large body of data regarding the effects of ionizing radiation on different foods under various conditions of irradiation. The basic principles are well understood (Refs. 1 to 4) and provide the basis for extrapolation and generalization from data obtained in specific foods irradiated under specific conditions to draw conclusions regarding foods of a similar type irradiated under different, yet related, conditions. The types and amounts of products generated by radiation-induced chemical reactions (''radiolysis products'') depend on both the chemical constituents of the food and on the specific conditions of irradiation. The principles of radiation chemistry also govern the extent of change, if any, in both the nutrient levels and the microbial loads of irradiated foods.

In the next section, FDA will discuss important aspects of radiation chemistry and related topics as they apply specifically to iceberg lettuce, spinach, and foods of similar composition.

1. Factors Affecting the Radiation Chemistry of Foods

Apart from the chemical composition of the food itself, the specific conditions of irradiation that are most important in considering the radiation chemistry of a given food include the radiation dose, the physical state of the food (e.g., solid or frozen versus liquid or nonfrozen state, dried versus hydrated state), and the ambient atmosphere (e.g., air, reduced oxygen, and vacuum).[1]

The amounts of radiolysis products generated in a particular food are directly proportional to the radiation dose. Therefore, one can extrapolate from data obtained at high radiation

[1] The temperature at which irradiation is conducted can also be a factor, with more radiation-induced changes occuring with increasing temperature. Temperature is less important, however, than the physical state of the food.

doses to draw conclusions regarding the effects at lower doses.

The radiation chemistry of food is strongly influenced by the physical state of the food. If all other conditions, including dose and ambient atmosphere, are the same, the extent of chemical change that occurs in a particular food in the frozen state is less than the change that occurs in the non-frozen state. This is because of the reduced mobility, in the frozen state, of the initial radiolysis products, which will tend to recombine rather than diffuse and react with other food components. Likewise, and for similar reasons, if all other conditions are the same, the extent of chemical change that occurs in the dehydrated state is less than the change that occurs in the fully hydrated state.

The formation of radiolysis products in a given food also is affected by the ambient atmosphere. Irradiation in an atmosphere of high oxygen content generally produces both a greater variety, and greater amounts, of radiolysis products in the food than would be produced in an atmosphere of lower oxygen content. This is because irradiation initiates certain oxidation reactions that occur with greater frequency in foods with high fat content (Refs. 1 and 5).

With few exceptions, the radiolysis products generated in a particular food are the same or very similar to the products formed in other types of food processing or under common storage conditions. These radiolysis products are also typically formed in very small amounts (Ref. 1).

Radiation-induced chemical changes, if sufficiently large, however, may cause changes in the organoleptic properties of the food. Because food processors want to avoid undesirable effects on taste, odor, color, or texture, there is an incentive to minimize the extent of these chemical changes in food. Thus, the doses used to achieve a given technical effect (e.g., inhibition of sprouting, reduction in microorganisms) must be selected carefully to both achieve the intended effect and minimize undesirable chemical changes. Typically, the dose or dose range selected will be the lowest dose practical in achieving the desired effect. Irradiation also is often conducted under reduced oxygen levels or on food held at low temperature or in the frozen state.

2. Radiation Chemistry of the Major Components of Iceberg Lettuce and Spinach

The major components of iceberg lettuce and spinach, as with most fruits and vegetables, are water (approximately 91 to 96 percent) and carbohydrate (up to approximately 4 percent), with protein also present as a minor component. The lipid content of both iceberg lettuce and spinach is quite low (less than 0.5 percent) (Ref. 6).

Because of the high water content of iceberg lettuce and spinach, their radiation chemistry is dominated by the radiation chemistry of water, in which reactive hydroxyl and hydrogen radicals are the primary radiolysis products. These radicals are most likely to recombine to form water, hydrogen gas, or hydrogen peroxide; they may, however, also react with other components of iceberg lettuce and spinach (e.g., carbohydrates). While most of the chemical effects of radiation-processing on iceberg lettuce and spinach are expected to result from the reactions induced by hydroxyl and hydrogen radicals, other food components (e.g., carbohydrates, proteins, and lipids) may also absorb radiation directly and generate small amounts of other radiolysis products.

a. *Carbohydrates*. Carbohydrates are molecules composed of sugar units, which are grouped and categorized according to their size. The simplest and smallest are the monosaccharides (simple sugars such as glucose) and disaccharides (such as sucrose). Larger complex carbohydrates (pectin, fiber, and starch) consist of chains of monosaccharide units and are referred to as polysaccharides. The main effects of ionizing radiation on carbohydrates in foods have been studied extensively and discussed at length in the scientific literature (Refs. 7 and 8), as well as in reviews by such bodies as the World Health Organization (WHO) (Ref. 9). In the presence of water, carbohydrates react primarily with the hydroxyl radicals generated by the radiolysis of water. The result is abstraction of hydrogen from the carbon-hydrogen bonds of the carbohydrate, forming water and a carbohydrate radical. Direct ionization of carbohydrates to form carbohydrate radicals also is possible, but occurs to a far lesser extent (Refs. 10, 11, and 12).

In polysaccharides, the links between constituent monosaccharide units may be broken, resulting in the shortening of polysaccharide chains. Starch may be degraded into dextrins, maltose, and glucose. Sugar acids, ketones, aldehydes, and other sugar monosaccharides may also be formed as a result of ionizing radiation. Various studies have reported that radiolysis products formed from starches of different origin are qualitatively similar. The nature and concentration of the main radiation-induced products showed no marked differences among the various starches. In addition, 40 different products have been analyzed in irradiated starches and have been found to be produced by heat treatment or natural oxidation of starch during storage, as well as by irradiation (Refs. 8 and 10).

The overall effects of ionizing radiation on carbohydrates are basically the same as those caused by cooking and other food processing treatments (Refs. 1 and 10). Irradiation of carbohydrates at doses up to 10 kGy has minimal effect on the carbohydrate functionality and the resulting products are smaller carbohydrates or other compounds also produced from carbohydrates through oxidation and/or heat treatment. FDA concludes that no significant change in carbohydrate nutrient value or functionality is expected to occur in iceberg lettuce and spinach irradiated at doses up to 4 kGy.

b. *Proteins*. FDA has previously provided detailed discussions of the radiation chemistry of proteins in its rulemakings on the use of ionizing radiation to treat meat and molluscan shellfish (''the meat rule,'' 62 FR 64107; December 3, 1997, and ''the molluscan shellfish rule,'' 70 FR 48057; August 16, 2005, respectively). Studies conducted with high-protein foods (e.g., meat, poultry, and seafood), have established that most of the radiolysis products derived from food proteins have the same amino acid composition and are altered only in their secondary and tertiary structures (i.e., denatured). These changes are similar to those that occur as a result of heating, but in the case of irradiation, even at doses up to 50 kGy, such changes are far less pronounced and the amounts of reaction products generated are far lower (62 FR 64107; Refs. 10 and 13). FDA concludes that there will be few reaction products generated from the small amounts of protein in iceberg lettuce and spinach and that no significant change in the amino acid composition of these two foods is expected to result from irradiation at doses up to 4.0 kGy.

c. *Lipids*. FDA also has previously provided a detailed discussion of the radiation chemistry of lipids in the meat and molluscan shellfish rules. In summary, a variety of radiolysis products derived from lipids have been identified, including fatty acids, esters, aldehydes, ketones, alkanes, alkenes, and other hydrocarbons (Refs. 1 and 14). Identical or analogous compounds are also found in foods that have not been irradiated. In particular, heating food produces generally the same types of compounds, but in amounts far greater

than the trace amounts produced from irradiating food (Refs. 10 and 15).

There is, however, a class of radiolysis products derived from lipids, 2-alkylcyclobutanones (2–ACBs), that has been reported to form in small quantities when fats are exposed to ionizing radiation, but not when they are exposed to heat or other forms of processing. The specific 2–ACBs formed will depend on the fatty acid composition of the food. For example, 2-dodecylcyclobutanone (2–DCB) is a radiation by-product of tryiglycerides with esterified palmitic acid. Researchers have reported that 2–DCB is formed in small amounts (less than 1 microgram per gram lipid per kGy (μg/g lipid/kGy) from irradiated chicken (Ref. 16) and in even smaller amounts from ground beef (Ref. 17). Both of these foods are of relatively high total fat and palmitic acid content.[2]

In the molluscan shellfish rule, the agency provided a detailed discussion of its assessment of the significance of the formation of 2–DCB to the safety evaluation of irradiated molluscan shellfish, a food which, like chicken and ground beef, contains significant amounts of triglycerides with esterified palmitic acid. In that assessment, FDA considered all of the available data and information, including the results of genotoxicity studies and previously reviewed studies in which animals were fed diets containing irradiated meat, poultry, and fish. All of these foods contain appreciable amounts of lipids that contain triglycerides with palmitic acid. While 2–DCB and other alkylcyclobutanones would be expected to be present in these irradiated foods, FDA found no evidence of toxicity attributable to their consumption.

As noted previously in this document, iceberg lettuce and spinach contain little fat (less than 0.5 percent); neither food contains appreciable amounts of palmitic acid.[3] Because of the low lipid content and the very low palmitic acid content of iceberg lettuce and spinach, FDA concludes that formation of alkylcyclobutanones generally, and 2–DCB specifically, from irradiation of these foods would be in amounts much smaller than those formed from irradiation of foods of higher fat content and would not pose a toxicological concern.

Overall, FDA concludes that no significant differences are expected to occur between the kinds and amounts of lipids and lipid byproducts in non-irradiated iceberg lettuce and spinach compared to iceberg lettuce and spinach irradiated at doses of 4.0 kGy.

3. Consideration of Furan as a Radiolysis Product

During the course of reviewing the chemical effects of irradiation as part of the evaluation of this and other petitions, FDA became aware of a report that suggested irradiating apple juice may produce furan (Ref. 18). Because furan has been shown to cause tumors in laboratory animals, FDA initiated research on whether the report was accurate and whether furan was a common radiolysis product in food. The petitioner also conducted testing and the United States Department of Agriculture (USDA) initiated additional research. FDA has confirmed that certain foods form furan in low quantities when irradiated. Studies conducted by FDA scientists and other researchers show that some foods form furan when heated and still other foods form furan during storage at refrigeration temperatures (Refs. 19 and 20). Testing of irradiated lettuce and spinach show that if furan is formed when these foods are irradiated, it is formed at levels that are below the limit of detection in the tests, or below the background levels of natural furan formation during storage (Refs. 19, 21, and 22). Therefore, FDA concludes that the consumption of irradiated iceberg lettuce and spinach will not increase the amount of furan in the diet.

B. Toxicological Considerations

The available information from the results of chemical reactions described in section II.A of this document suggests that there is no reason to suspect a toxicological hazard due to consumption of an irradiated food. While chemical analyses have not identified the presence of radiolysis products in amounts that would raise a toxicological concern, the agency notes that the large body of data from studies where irradiated foods were fed to laboratory animals provides an independent way to assess toxicological safety. These studies include those relied on by the agency in previous evaluations of the safety of irradiated foods (see 70 FR 48057, 65 FR 45280, 62 FR 64107, 55 FR 18538, and 51 FR 13376) and additional data and information in FDA files or other published reports regarding studies in which animals were fed a wide variety of foods irradiated at different doses.

The agency's analysis incorporates the principles that toxicological data collected from studies on a given food may be applied to the toxicological evaluation of foods of similar generic class and that data from foods irradiated at high doses can be applied to the toxicological evaluation of foods of similar generic class receiving lower doses (62 FR 64107; Ref. 10). The agency's analysis also draws upon the integrated toxicological database derived from the extensive body of work reviewed by the agency (Ref. 23) and by the WHO[4] in previous evaluations of the safety of irradiated foods. Thus, the agency has re-examined the available data from toxicological studies that are particularly relevant to the safety of irradiated iceberg lettuce and spinach, specifically fruits and vegetables which, as a group, are relatively carbohydrate-rich foods of high water content. The agency's analysis also takes into account the known effects of other conditions of irradiation to compare the results of different studies.

FDA has evaluated a large number of studies in which various irradiated fruits or vegetables,[5] alone or in combination with other irradiated foods, were fed to animals (Refs. 25 and 26). These studies were conducted in a variety of animal species, with foods irradiated at doses ranging from 0.15 to 50 kGy. In the vast majority of these studies, no adverse effects were reported. Three studies reported observations that merit further discussion. FDA has concluded that the effects reported in these three studies were either not attributable to

[2] Beef is generally composed of approximately 15 to 25 percent fat, depending on the cut. Chicken, depending on the cut and whether skin is included, is approximately 5 to 19 percent fat. The palmitic acid content of the fat in beef and chicken is in the range of 22 to 25 percent (Ref. 6)

[3] Iceberg lettuce contains approximately 0.016 percent palmitic acid, and spinach contains approximately 0.046 percent palmitic acid (Ref.6)

[4] During the early 1980s, a joint Food and Agriculture Organization/International Atomic Energy Agency, World Health Organization (FAO/IAEA/WHO) Expert Committee evaluated the toxicological and microbiological safety and nutritional adequacy of irradiated foods. The Expert Committee concluded that irradiation of any food commodity at an average dose of up to 10 kGy presents no toxicological hazard (Ref. 24). In the 1990s, at the request of one of its member states, WHO conducted a new review and analysis of the safety data on irradiated food. This more recent WHO review included all the studies in FDA's files that the agency considered as reasonably complete, as well as those studies that appeared to be acceptable but had deficiencies interfering with the interpretation of the data (see 51 FR 13376 at 13378). The WHO review also included data from USDA and from the Federal Research Centre for Nutrition at Karlsruhe, Germany. WHO concluded that the integrated toxicological database is sufficiently sensitive to evaluate safety and that no adverse toxicological effects due to irradiation were observed in the dose ranges tested (Ref. 9).

[5] The irradiated fruits and vegetables in these studies included: Peaches, strawberries, bananas, cherries, prunes, potatoes, carrots, onions, black beans, corn, green beans, and cabbage.

irradiation or were otherwise not of toxicological significance.

In the first study, dogs fed a diet containing 10 percent onions (dry weight basis, irradiated at 0.25 kGy) for 90 days were reported to develop anemia, as did control dogs fed nonirradiated onions (Ref. 27). Other effects such as increased spleen weights, myeloid metaplasia, and reticuloendothelial hyperplasia were reported but, again, in both control and treated dogs. FDA has concluded that the effects cannot be attributed to irradiation because similar effects were reported in both dogs fed irradiated onions and dogs fed non-irradiated onions (Ref. 25).

The second study was a multi-generation reproduction study in which rats were fed a diet containing 35 percent oranges (dry weight basis) (Ref. 28). Animals in the control group were fed non-irradiated oranges; animals in the treated groups were fed oranges irradiated at 1.40 or 2.79 kGy. The authors reported decreased reproductive performance in the second breeding, as measured by several parameters,[6] for rats fed irradiated oranges as well as those fed the control diet. Because the effects were observed in both animals fed irradiated food and animals fed non-irradiated food, FDA has concluded that they cannot be attributed to irradiation (Refs. 25 and 26). The authors also reported a small, but statistically significant difference in one additional parameter of reproductive performance in treated animals, body weight of pups at weaning. The pups made up for the weight depression after weaning. FDA has concluded that this reported effect is not of toxicological significance for the following two reasons: (1) It was a very small difference in the overall poor reproductive performance of all animals in the second breeding, and (2) the pups from the treated groups made up for the slight weight depression after weaning. In another segment of this study, the authors reported a small, but statistically significant reduction in body weight gain for third generation animals in the treated groups (but not the parent or second generation animals). FDA has concluded that this effect is not of toxicological significance for the following two reasons: (1) There was no apparent dose response,[7] and (2) the differences in body weights were within the normal range of variation for feeding studies (Ref. 26).

In a third study (Ref. 29), weanling rats fed a mixture of cabbage irradiated at 6 kGy and chicken stew irradiated at 56 kGy for 19 days were reported to have reduced levels of alkaline phosphatase in duodenal tissue. In its evaluation of the safety of irradiated meat, FDA reviewed this study in detail and concluded that the effect observed was not of toxicological significance (62 FR 64107 at 64113).

In summary, FDA has reviewed a large body of data relevant to the assessment of potential toxicity of irradiated fruits and vegetables. While all of the studies are not of equal quality or rigor, the agency has concluded that the quantity and breadth of testing and the number and significance of endpoints assessed would have identified any real or meaningful risk. The overwhelming majority of studies showed no evidence of toxicity. On those few occasions when adverse effects were reported, FDA finds that those effects cannot be attributed to irradiation. Based on the totality of the evidence, FDA concludes that irradiation of iceberg lettuce and spinach under the conditions proposed in this petition does not present a toxicological hazard.

C. Nutritional Considerations

It is well known that the nutritive values of the macronutrients in the diet (protein, fats, and carbohydrates) are not significantly altered by irradiation at the petitioned doses (Refs. 30, 31, and 32). Minerals (e.g., calcium and iron) are also unaffected by irradiation. Levels of certain vitamins, on the other hand, may be reduced as a result of irradiation. The extent to which this reduction occurs depends on the specific vitamin, the type of food, and the conditions of irradiation. Not all vitamin loss is nutritionally significant, however, and the extent to which a reduction in a specific vitamin level is significant depends on the relative contribution of the food in question to the total dietary intake of the vitamin.

Nutrition-related information relevant to fruits and vegetables submitted in the petition included analyses of consumption data for these broad categories and of vitamin levels in specific irradiated foods from these categories. The petitioner's overall analysis focused on the the following vitamins the petitioner identified as being present in relatively high levels in fruits and vegetables generally: Thiamine; folate; and vitamins C, E, and A (the latter as provitamin carotenoids). Most of the studies with irradiated fruits or vegetables submitted in the petition focused on the levels of vitamin C or provitamin A carotenoids (sometimes also referred to as carotenes), because fruits and vegetables, as a combined category, are good sources of these micronutrients. Some studies of the effects of irradiation on the levels of vitamin E and on folate were also submitted.

FDA has carefully reviewed the data and information submitted in the petition, as well as other data and information in its files, to determine whether irradiation of iceberg lettuce and spinach would have an adverse effect on the nutritional quality of the diet. FDA's evaluation focused on the effects of irradiation on those nutrients for which at least one of these foods may be identified as an ''excellent source''[8] and for which they contribute more than a trivial amount to the total dietary intake (i.e., greater than 1 to 2 percent)[9]: Vitamin A (from beta-carotene, a provitamin A carotenoid), vitamin K, and folate. FDA's evaluation has also considered the relative radiation sensitivities of these vitamins.

Many fruits and vegetables are good sources of vitamin A (including provitamin A carotenoids). Spinach is considered an excellent source of vitamin A based on its relatively high content of the provitamin A carotenoid beta-carotene. Nevertheless, it contributes no more than 3.5 percent to the total U.S. dietary intake of vitamin A[10] (Refs. 33, 34 and 35).

Although vitamin A has been identified as one of the most radiation-sensitive of the fat-soluble vitamins, carotenoids in plant products demonstrate fairly high resistance to the effects of irradiation. One study of carrots irradiated at 2 kGy reported that carotenoids were stable to irradiation

[6] Incidence of female sterility (percent), established fertility of males (percent), incidence of still births per litter, and pups born alive reaching weaning age (percent).

[7] The effect was more pronounced in rats fed oranges irradiated at the lower of the two test doses, the opposite of what one would expect if the effect were related to irradiation.

[8] In accordance with 21 CFR 101.54(b), foods containing ≥ 20 percent of the Reference Daily Intake (RDI) or Daily Reference Value (DRV) per reference amount customarily consumed (RACC), the amount of food customarily consumed per eating occasion such as in one meal or snack) may be labeled as ''excellent source of'', ''high in'' or ''rich in'' a given nutrient. By this criterion, spinach is an excellent source of vitamins A, C, K, and folate. Iceberg lettuce is an excellent source of vitamin K only.

[9] Although spinach contains relatively high amounts of vitamin C, its contribution to the total dietary intake of this vitamin is negligible. The combined group of spinach and ''greens'' (e.g., kale, chard, chives) contributes less than 2 percent to the total dietary intake of vitamin C; the contribution of iceberg lettuce is essentially zero (Ref. 33).

[10] The primary food sources of vitamin A (including provitamin A carotenoids) in the U.S. diet are carrots, organ meats, dairy products, eggs, and ready-to-eat cereals. Together, these food sources contribute approximately 60 percent of the total dietary intake of vitamin A (expressed in retinol equivalents).

and that total carotenoid content of irradiated carrots did not differ from controls through 16 days of storage (Ref. 36). In another study, carotenoid losses in mangoes and papayas irradiated at doses up to 2 kGy were reported to be negligible (0 to 15 percent) while considerable losses resulted from freezing or canning with various additives (Ref. 37). In other studies, minor carotenoid losses in broccoli irradiated at doses of 2 and 3 kGy were observed relative to controls on the day of treatment only, while no marked effects on total carotenoid content of irradiated samples were observed at days 4, 9, and 14 of storage (Ref. 38), and irradiation at doses up to 1 kGy did not affect the total carotenoid content of spinach stored under refrigeration for 15 days (Ref. 39). In several studies, other processing or storage parameters were reported to affect the proportions of individual carotenoids more strongly than irradiation treatment (Ref. 31). FDA concludes that the small losses of vitamin A that might result from the proposed irradiation of iceberg lettuce or spinach will have little impact on the total dietary intake of this vitamin.

Spinach and iceberg lettuce contribute approximately 12 percent and 8 percent, respectively, to the dietary intake of vitamin K (Ref. 40). Vitamin K is widely distributed in other plant and animal foods, however, and deficiencies of vitamin K in humans are extremely rare[11] (Ref. 33).

Vitamin K has also been identified as one of the least radiation sensitive of the fat-soluble vitamins (Ref. 41). In one study, which examined the effects of irradiation, freezing, and canning on vitamin K activity in spinach, along with other vegetables, there was no appreciable radiation-induced loss in Vitamin K activity at doses as high as 28 or 56 kGy, doses much higher than the maximum dose requested in this petition (Ref. 42). FDA concludes that irradiation of iceberg lettuce and spinach up to a maximum dose of 4.0 kGy will have no impact on the total dietary intake of vitamin K (Ref. 33).

Spinach is an excellent source of folate.[12] Nevertheless, in the context of the total diet, spinach contributes only a little more than 2 percent of the total dietary intake of folate (Refs. 33 and 34).[13] Studies that examined radiation-induced losses of folic acid in dehydrated asparagus irradiated to 5 kGy or dehydrated spinach irradiated at 10 kGy found no loss of folate as measured by compositional analysis or in a bioavailability assay in rats (Ref. 43). Another recent study that examined the effects of irradiation of fresh vegetables at 2.5 kGy, reported folate losses of approximately 10 percent in fresh spinach, green cabbage, and Brussels sprouts (Ref. 44). The folate losses observed in this study are comparable to or less than the folate losses that have been reported for vegetables following various heat treatments (Refs. 45 and 46). FDA concludes that radiation-induced loss of folate in iceberg lettuce or spinach will have no significant impact on the dietary intake.

In summary, based on the available data and information, FDA concludes that amending the regulations, as set forth below, to allow for the use of ionizing radiation to treat iceberg lettuce and spinach up to a maximum dose of 4 kGy will not have an adverse impact on the nutritional adequacy of the overall diet.

D. Microbiological Considerations

Leafy green vegetables such as iceberg lettuce or spinach can serve as an ideal habitat for the growth of various microorganisms. Among the common, naturally-occurring microflora of vegetables, *Pseudomonas*, *Enterobacter*, and *Erwinia* species predominate. Various molds and yeasts may also be found on leafy green vegetables. Pathogens, which may also be present in the agricultural environment, can contaminate fresh produce that is grown, harvested, and in some cases undergoes preliminary processing (e.g., cutting or trimming) in that environment. Iceberg lettuce and spinach are often consumed raw and after only minimal preparation (e.g., rinsing) and, therefore, lack the final microbial elimination step provided for other foods by cooking.

Contamination of fresh produce with several specific pathogens continues to be a public health problem. Infections from *Salmonella enterica* serovars and *Escherichia coli* O157:H7, for example, have not decreased since 1996. Most of the recent serious outbreaks of illness attributed to consuming lettuce or spinach have resulted from contamination by *E. coli* O157:H7. Three notable outbreaks involving this microorganism occurred in 2006; one of these was associated with bagged fresh spinach, the other two with lettuce used in fast food restaurants. Contamination of leafy greens with *Listeria monocytogenes* or *Salmonella* serovars also continues to be a public health problem. Even though other pathogens may be present, the three microorganisms named here are those that have been most commonly associated with recent outbreaks from the consumption of raw spinach or lettuce (Ref. 47).

Data and information relevant to microbiological considerations presented in the petition included published studies of radiation-induced reductions in levels of different microorganisms in a variety of fruits and vegetables under different conditions of irradiation. Some of these studies also investigated the use of irradiation in combination with other antimicrobial treatments. FDA has evaluated the information in the petition, along with other data and information in its files and in the published literature in assessing the microbiological issues presented by the petitioner.

There is a large body of work regarding the radiation sensitivities of non-pathogenic food spoilage microorganisms and pathogenic foodborne microorganisms. Generally, the common spoilage organisms such as *Pseudomonas* and the important pathogens in or on leafy greens are quite sensitive to the effects of ionizing radiation. Information in the petition and other information in FDA files shows that *E. coli* O157:H7 is highly sensitive to ionizing radiation, with published D_{10} values[14] ranging from 0.12 to 0.32 kGy, depending on the specific food matrix, physical state of the food, temperature, and other factors. Control of contaminating *Salmonella* serovars or *Listeria* spp. generally requires higher doses than for *E. coli* O157:H7. This is shown by the higher D_{10} values which are in the range of 0.16 to 0.65 kGy, again, depending on the specific food, physical state, temperature, and other factors (Refs. 48 to 51).

Several recent studies have focused on the effects of ionizing radiation on pathogen levels in lettuce and spinach, specifically. In a series of studies by one group of researchers, the average D_{10} values for *E coli* O157:H7 and *L. monocytogenes* were reported to be 0.1 kGy and 0.2 kGy, respectively and the D_{10} value for Salmonella reported to be ca. 0.25–0.3, depending on the lettuce

[11] Other green vegetables such as broccoli, collards, salad greens, and kale contain substantial amounts of vitamin K. Other foods that also contribute to vitamin K intake include: Vegetable oils, grains, liver, cheese, and eggs.

[12] One RACC of raw spinach (85 grams (g) can contain 41 percent of the RDA for folate. One RACC of iceberg lettuce, however, contains only about 6 percent of the RDA for folate; iceberg lettuce is not considered a good source of this vitamin. (Ref. 6)

[13] Enriched and fortified foods (e.g., cereal grains and grain-based products) make the greatest contribution to folate in the diet.

[14] D_{10} is the absorbed dose of radiation required to reduce a bacterial population by 90 percent.

type (Refs. 52 and 53). In another study, treatment with ionizing radiation at a dose of 1.5 kGy produced a 4-$\log_{10}$ reduction in colony-forming units (CFU) on romaine lettuce and a 3-$\log_{10}$ reduction in CFU on baby spinach leaves (Ref. 54). Another recent study examined the effects of irradiation on bagged, ready-to-eat spinach leaves inoculated with E. coli O157:H7 and found that, for single leaves, doses as low as 0.9 kGy resulted in a 5- to 6-$\log_{10}$ reduction in the levels of this pathogen, while a dose of 1.2 kGy resulted in its reduction below the limits of detection of the test (Ref. 39). Collectively, these studies, together with earlier work, establish that levels of *E. coli* O157:H7, *L. monocytogenes*, and *Salmonella* serovars in or on iceberg lettuce or spinach will be reduced by irradiation at dose levels of 0.1 to 1.5 kGy, with the largest reductions occurring at the higher dose levels.

Still other studies have examined the effects of irradiation on extension of shelf life and sensory attributes of various types of vegetables, including iceberg lettuce and spinach. In one study, the authors reported a reduction in total aerobic bacterial counts of over 2-$\log_{10}$ CFU per gram (CFU/g) in fresh-cut lettuce irradiated at 1.0 kGy and over 3-$\log_{10}$ CFU/g reductions at 1.5 kGy (Ref. 55). In a separate study, the same researchers found similar results on total aerobic bacterial counts and significant reductions in coliform counts on fresh-cut lettuce when irradiated with similar doses. In this particular study, the authors also followed numbers of viable bacteria for 9 days storage, noting that for irradiated samples, relative microbial reductions persisted while total numbers of bacteria increased by about 2-$\log_{10}$. Over the same storage period, coliforms remained below the level of detection in irradiated samples (Ref. 56). Recent studies by other researchers have examined the effects of irradiation on levels of pathogens and sensory attributes of fresh-cut iceberg lettuce, including studies in modified atmosphere packaging. One of these studies demonstrated deterioration in several sensory attributes (e.g., firmness, color) when iceberg lettuce is irradiated at levels of 3 or 4 kGy (Ref. 57). Additional related studies on iceberg lettuce and other vegetables by the same group of researchers indicate irradiation above 1.5 or 2 kGy (depending on the specific vegetable) can negatively affect sensory properties (Refs. 58 and 59). Taken together, the studies described above indicate that irradiation in the expected practical dose range will reduce, but not entirely eliminate, spoilage microorganisms.

In evaluating the subject petition, FDA has carefully considered whether irradiation of iceberg lettuce and spinach under the conditions proposed in the petition could result in significantly altered microbial growth patterns such that these foods would present a greater microbiological hazard than comparable food that had not been irradiated. In considering this question, FDA has focused on whether the proposed irradiation conditions would increase the probability of significantly increased growth of, and subsequent toxin production by, *Clostridium botulinum* because this organism is relatively resistant to radiation as compared to non-spore-forming bacteria. FDA has concluded that the possibility of increased microbiological risk from *C. botulinum* is extremely remote because: (1) The conditions of refrigerated storage necessary to maintain the quality of iceberg lettuce or spinach are not amenable to the outgrowth and production of toxin by *C. botulinum* and, (2) sufficient numbers of spoilage organisms will survive such that spoilage will occur before outgrowth and toxin production by *C. botulinum* (Refs. 48 and 60).

Based on the available data and information, FDA concludes that irradiation of iceberg lettuce and spinach conducted in accordance with good manufacturing practices will reduce or eliminate bacterial populations with no increased microbial risk from pathogens that may survive the irradiation process.

III. Comments

FDA has received numerous comments, primarily form letters, from individuals that state their opinions regarding the potential dangers and unacceptability of irradiating food. FDA has also received several comments from individuals or organizations that state their opinions regarding the potential benefits of irradiating food and urging FDA to approve the petition. None of these letters contain any substantive information that can be used in a safety evaluation of irradiated iceberg lettuce and spinach.

Additionally, FDA received several comments from Public Citizen (PC) and the Center for Food Safety (CFS) requesting the denial of this and other food irradiation petitions. Overall, the comments were of a general nature and not necessarily specific to the requests in the individual petitions. Many of these comments from PC and CFS were also submitted to the docket for the agency rulemaking on irradiation of molluscan shellfish (Docket No. 1999F–4372, FAP 9M4682). The topics raised in these comments included the following: Studies reviewed in the 1999 FAO/IAEA/WHO report on high-dose irradiation; a review article that analyzed studies of irradiated foods performed in the 1950's and 1960's; the findings of a 1971 study in which rats were fed irradiated strawberries; the findings regarding reproductive performance in a 1954 study in which mice were fed a special irradiated diet; issues regarding mutagenicity studies; certain international opinions; issues related to ACBs, including purported promotion of colon cancer; the findings of certain studies conducted by the Indian Institute of Nutrition in the 1970's; general issues regarding toxicity data; FDA's purported failure to meet statutory requirements; data from a 2002 study purportedly showing an irradiation-induced increase in trans fatty acids in ground beef; studies regarding purported elevated hemoglobin levels and their significance; and an affidavit describing the opinions of a scientist regarding the dangers of irradiation and advocating the use of alternative methods for reducing the risk of foodborne disease. For a detailed discussion of the agency's response to the above general comments, the reader is referred to the molluscan shellfish rule (70 FR 48057 at 48062–48071). Because these comments do not raise issues specific to irradiated iceberg lettuce or spinach and because the agency has already responded to these comments in detail, they will not be addressed further here.

FDA also received two letters from PC and CFS that were submitted only to the docket for this rulemaking (Docket No. FDA–1999–F–2405 (formerly Docket No. 1999F–5522), FAP 9M4697). Many of the issues raised in these letters were also raised in comments submitted by PC and CFS to the docket for the agency rulemaking on irradiation of molluscan shellfish. Other issues raised in these letters were specific to the request in FAP 9M4697; these particular comments were not responded to in the molluscan shellfish rule. Below, the agency responds to the specific comments raised in these two letters from PC and CFS that were not addressed in the molluscan shellfish rule.

The agency also received an additional letter from Food and Water Watch (formerly PC) and CFS after the rule for the irradiation of molluscan shellfish published. The comments in this letter are also addressed below.

A. 2-Alkylcyclobutanones

During the evaluation of this petition and several others requesting various applications of irradiation, the agency received several comments on issues related to 2–ACBs. The agency has previously addressed most of these comments in the molluscan shellfish rule (70 FR 48057 at 48062–48071), and that discussion will not be repeated here. However, after the publication of the molluscan shellfish rule, the agency received an additional comment on 2–ACBs. This comment included a report that contained data on 2–ACBs present in irradiated turkey, hotdogs, and papayas.

As noted in section II. A of this document, 2–ACBs are formed in small quantities when fats are exposed to ionizing radiation. Of the three foods examined in the study submitted with the comment, only papayas are from the same generic class as iceberg lettuce and spinach. (Turkey and hotdogs are foods high in protein and fat that have little in common with leafy greens.) The report presents data indicating that 2–ACB concentrations in papaya flesh are indistinguishable from zero. There is no additional information in the paper other than concentrations of various alkylcyclobutanones in the three foods mentioned.

As previously noted in this document and in the molluscan shellfish rule, FDA has reviewed studies in which animals were fed diets containing irradiated foods of high fat content (meat, poultry, and fish). The agency concluded that no adverse effects were associated with the consumption of these high fat foods. Iceberg lettuce and spinach contain far less fat than meat, poultry, fish or molluscan shellfish. As previously noted in section II.B of this document, FDA has reviewed studies in which animals were fed diets containing irradiated fruits and vegetables. No adverse effects were associated with consumption of these food types. The comment provides no additional information that would alter the agency's conclusion that the consumption of irradiated iceberg lettuce and spinach does not present a health hazard.

B. List of Foods Covered by the Petition

One comment stated that ''FDA has no definitive list of foods that are covered by the petition,'' citing a personal communication of March 19, 2001. The comment goes on to state that ''[a] **Federal Register** filing of May 10, 2001, pertaining to the [above-referenced] petition establishes that the FDA [sic] no understanding as to which specific foods are covered by the petition.''

FDA disagrees with this comment. The **Federal Register** document of May 10, 2001, corrected an inadvertent exclusion of certain foods from the scope of the original filing notice. FDA also notes that a listing of each and every food covered by a food additive petition has never been required and is not necessary. The agency frequently evaluates food additive petitions intended to cover broad categories of food types. Further, this partial response authorizing irradiation of iceberg lettuce and spinach up to a maximum dose of 4.0 kGy addresses two specific foods, rendering the issue moot.

C. Toxicity Data

One comment states that the petition should be denied because ''[t]he petitioner submitted no toxicology data on any of the products that are ostensibly covered by the petition.''

FDA acknowledges that the petitioner did not submit new toxicological data specific to the foods in the petition. The petitioner made extensive reference to studies considered in earlier evaluations of the toxicological safety of irradiated foods by FDA, WHO, and others. As noted earlier, FDA has reviewed a large body of data relevant to the assessment of the potential toxicity of irradiated foods, including irradiated fruits and vegetables. There was no reason to submit additional copies of studies that had previously been reviewed by the agency.

One comment states that the petition should be denied ''because the validity of three of the studies referenced by the petitioner was questioned by the FDA's Irradiated Foods Task Group (IFTG) in 1982.'' The comment lists three studies, one of which ''was labeled 'reject' by the IFTG'' and two of which were ''labeled 'accept with reservation' by the IFTG.''

FDA does not disagree that the IFTG had questions regarding these three studies. FDA does not agree, however, that these 1982 findings by the IFTG provide a basis to deny the petition or the partial request that is the subject of this rulemaking. FDA has not relied on studies that were rejected by the IFTG in assessing the safety of irradiated iceberg lettuce and spinach or any other irradiated food. Some studies were accepted with reservation by the agency scientists on the IFTG because they did not meet modern standards in all respects; specifically, they may have used fewer animals, or examined fewer tissues than is common today. Nevertheless, these studies still provide important information that, when evaluated collectively, supports the conclusion that consumption of iceberg lettuce and spinach irradiated under the conditions proposed in this petition is safe. As noted earlier, FDA has reviewed a large body of data relevant to the assessment of the potential toxicity of irradiated fruits and vegetables, and to an assessment of the potential toxicity of irradiated iceberg lettuce and spinach specifically. The comment provides no basis to challenge FDA's conclusion that iceberg lettuce and spinach irradiated under the conditions set forth in the regulations in this document are safe.

Another comment stated that the petitioner claimed that a fourth study, conducted by Renner et al. (Ref. 61) ''provided [no] evidence of toxicity induced by irradiation.'' The comment took issue with the petitioner's characterization of this study, stating ''[t]he study found, however, 'significant' effects on DNA synthesis and 'significant loss of body weight' among rodents that ate irradiated food compared to that that ate non-irradiated food.''

The Renner et al. study consisted of six in vivo genetic toxicity tests that were carried out in several different animal species with irradiated or non-irradiated cooked chicken, dried dates, and cooked fish. FDA has previously evaluated the results of these tests and does not agree with comment's characterization of the study findings, which appear to be presented out of context.

In the Renner et al. study, the authors concluded that ''[n]one of the tests provided any evidence of genetic toxicity induced by irradiation.'' Further, the authors did not attribute a ''significant loss of body weight'' to consumption of irradiated food, but stated, rather, that ''[t]he nutritional effects of exposing Chinese hamsters for 7 days to a diet consisting entirely of dried dates were evidenced by a significant reduction in food intake and, consequently, a significant loss of body weight.'' The effect was observed in both animals fed non-irradiated dates and animals fed irradiated dates. The authors also reported various effects on DNA synthesis resulting from feeding Chinese hamsters diets consisting entirely of dried dates or cooked chicken, irradiated or not. Thus, the authors concluded that these effects were also not attributable to irradiation. Further, the authors state that ''In only one case in the nine tests described in this report and in two previous papers* * *was an effect seen that could be attributed to an irradiated foodstuff. This was with irradiated fish in the DNA metabolism test.'' The authors concluded that the specific

effect observed with irradiated fish in the DNA metabolism test was not an indication of genotoxic activity, but rather, that it ''* * *provided evidence for absence of genotoxic potential in fish so processed.'' The comment provides no basis to conclude that the studies and information reviewed by the agency and discussed previously in this document are not adequate to assess the safety of irradiated iceberg lettuce and spinach.

D. Hardy Pathogens

One comment submitted a copy of a newsletter published by the Food Safety Consortium. The comment stated that ''when irradiation is applied to meat in commercial plants, the pathogens present have evolved to survive the irradiation better, thus the irradiation does not achieve the levels of de-contamination that are predicted, and advertised, by the meat irradiation industry based on the lab studies.'' The article in the newsletter states that pathogens in a food processing plant are generally more resistant to stressful conditions than laboratory grown bacteria.

The comment provides no data that can be used in a safety assessment of irradiated food in general or irradiated iceberg lettuce and spinach, specifically. FDA also believes that the comment incorrectly characterizes the science behind the article in the newsletter. Scientists understand that bacteria grown under stressful conditions (e.g., high acidity, elevated temperatures) can manifest resistance to treatments that would be lethal to the same type of bacteria grown under less stressful conditions. Thus, any bacteria grown in nutrient-rich media under optimal conditions in the laboratory may be somewhat less resistant to any given treatment, including irradiation, than the same bacteria grown in nutrient-poor or other harsh conditions in a non-optimal environment.

FDA also notes that under the regulations set forth in § 179.25, radiation treatment of food must conform to a scheduled process, which is a written procedure to ensure that the radiation dose range selected by the food irradiation processor is adequate under commercial processing conditions (including atmosphere and temperature) for the radiation to achieve its intended effect on a specific product and in a specific facility.[15] The regulations further require that the scheduled process be established by qualified persons having expert knowledge in radiation processing requirements of food and specific for that food and for the facility in which it is to be irradiated.

E. Effects on Organoleptic (Sensory) Properties

One comment argued that the petition should be denied because of ''organoleptic damage'' that raises ''serious concerns about the general wholesomeness of irradiated foods.''

The agency acknowledges that organoleptic changes can occur in irradiated foods. However, this comment provides no information that would establish a link between organoleptic changes in, and the safety of, irradiated foods. Consideration of organoleptic changes, in and of themselves, is beyond the scope of this rulemaking.

IV. Conclusions

Based on the data and studies submitted in the petition and other information in the agency's files, FDA concludes that the proposed use of irradiation to treat iceberg lettuce and spinach with absorbed doses that will not exceed 4.0 kGy is safe, and therefore, the regulations in § 179.26 should be amended as set forth below in this document. In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the use of irradiation on iceberg lettuce and spinach in a partial response to the petition will be made available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the information contact person (see **FOR FURTHER INFORMATION CONTACT**). As provided in § 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

V. Environmental Impact

The agency has carefully considered the potential environmental effects of this action. The agency has determined under 21 CFR 25.32(j) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VI. Objections

Any person who will be adversely affected by this regulation may file with the Division of Dockets Management (see **ADDRESSES**) written or electronic objections. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents are to be submitted and are to be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

VII. References

The following sources are referred to in this document. References marked with an asterisk (*) have been placed on display at the Division of Dockets Management (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. References without asterisks are not on display; they are available as published articles and books.

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[15] Food irradiation processors are also subject to FDA's regulation requiring Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Human Food (CGMP) (21 CFR part 110) and other applicable regulations regarding proper food handling and storage conditions.

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List of Subjects in 21 CFR Part 179

Food additives, Food labeling, Food packaging, Radiation protection, Reporting and record keeping requirements, Signs and symbols.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 179 is amended as follows:

PART 179—IRRADIATION IN THE PRODUCTION, PROCESSING AND HANDLING OF FOOD

■ 1. The authority citation for 21 CFR part 179 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 343, 348, 373, 374.

■ 2. Section 179.26 is amended in the table in paragraph (b) by adding a new item ''12.'' under the headings ''Use'' and ''Limitations'' to read as follows:

§ 179.26 Ionizing radiation for the treatment of food.

* * * * *

(b) * * *

Use	Limitations
* * * * * * *	
12. For control of food-borne pathogens and extension of shelf-life in fresh iceberg lettuce and fresh spinach.	Not to exceed 4.0 kGy.

* * * * *

Dated: August 19, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–19573 Filed 8–21–08; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 314, 601, and 814

[Docket No. FDA–2008–N–0032] (formerly Docket No. 2008N–0021)

RIN 0910–ZA32

Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations regarding changes to an approved new drug application (NDA), biologics license application (BLA), or medical device premarket approval application (PMA). This final rule provides that a supplemental application submitted under certain FDA regulations is appropriate to amend the labeling for an approved product to reflect newly acquired information and to add or strengthen a contraindication, warning, precaution, or adverse reaction if there is sufficient evidence of a causal association with the drug, biologic, or device, as defined in other FDA regulations and guidance documents.

DATES: This rule is effective September 22, 2008.

FOR FURTHER INFORMATION CONTACT:

For information regarding devices: Nicole Wolanski, Center for Devices and Radiological Health (HFZ–402), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 240–276–4010.

For information regarding biologics: Christopher Joneckis, Center for Biologics Evaluation and Research (HFM–1), Food and Drug Administration, 1401 Rockville Pike, Rockville MD 20852, 301–827–0373.

For information regarding drugs: Laurie Burke, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6462, Silver Spring, MD 20933, 301–796–0900.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of January 16, 2008 (73 FR 2848), FDA proposed amending its regulations regarding changes to an NDA, BLA, or PMA to codify the agency's longstanding view concerning when a change to the labeling of an approved drug, biologic, or medical device may be made in advance of the agency's review and approval of such change (the January 2008 proposed rule). With respect to drugs, § 314.70(c)(6)(iii) (21 CFR 314.70(c)(6)(iii)) provides that certain labeling changes related to an approved drug may be implemented upon receipt by the agency of a supplemental new drug application (sNDA) that includes the change. The corresponding regulation for biological products, § 601.12(f)(2) (21 CFR 601.12(f)(2)), provides that products with certain labeling changes may be distributed before FDA approval. Similarly, with respect to devices, § 814.39(d) (21 CFR 814.39(d)) provides that certain labeling changes may be placed into effect upon submission of a PMA supplement, but prior to the sponsor's receipt of a written FDA order approving the supplement. The supplements described by §§ 314.70(c), 601.12(f)(2), and 814.39(d) are commonly referred to as ''changes being effected supplements''