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; denial of request for a stay of effective date and for a hearing; response to objections; confirmation of effective date.

SUMMARY: The Food and Drug Administration (FDA or we) is responding to objections and is denying requests that it received for a hearing on the final rule that appeared in the **Federal Register** of August 22, 2008 (73 FR 49593), and that amended 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. After reviewing objections to the final rule and requests for a hearing, we have concluded that the objections do not raise issues of material fact that justify a hearing or otherwise provide a basis for revoking or modifying the amendment to the regulation. We are denying the request for a stay of the effective date of the amendment to the food additive regulations. We are also confirming the effective date of August 22, 2008, for the final rule.

DATES: Effective date of final rule published in the **Federal Register** of August 22, 2008 (73 FR 49593) confirmed: August 22, 2008.

FOR FURTHER INFORMATION CONTACT: Teresa A. Croce, Center for Food Safety and Applied Nutrition (HFS–265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740–3835, 240–402–1281.

SUPPLEMENTARY INFORMATION:

I. Introduction

In a notice published in the **Federal Register** of January 5, 2000 (65 FR 493), which was subsequently amended May 10, 2001 (66 FR 23943), we announced that a food additive petition (FAP 9M4697), had been filed by the National Food Processors Association (now merged into the Grocery Manufacturers Association) on behalf of The Food Irradiation Coalition, 1350 I St. NW., Suite 300, Washington, DC 20005 (petitioner). The petition proposed to amend the food additive regulations in part 179, *Irradiation in the Production, Processing and Handling of Food* (21 CFR part 179), 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 dose of 4.5 kiloGray (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) and 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 fresh iceberg lettuce and fresh spinach up to a maximum dose of 4.0 kGy. In response to this request, we issued a final rule in the **Federal Register** of August 22, 2008 (73 FR 49593), permitting the irradiation of fresh iceberg lettuce and fresh spinach (hereafter referred to as ''fresh lettuce and fresh spinach'') for control of food-borne pathogens and extension of shelf life up to a maximum dose of 4.0 kGy. We based our decision on data in the petition and in our files. In the preamble to the final rule, we outlined the basis for our decision and stated that objections to the final rule and requests for a hearing were due within 30 days of the publication date (i.e., by September 22, 2008).

II. Objections, Requests for a Hearing, and Request for a Stay of Effective Date

Section 409(f)(1) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 348(f)(1)) provides that, within 30 days after publication of an order relating to a food additive regulation, any person adversely affected by such order may file objections, ''specifying with particularity the provisions of the order deemed objectionable, stating reasonable grounds therefor, and requesting a public hearing upon such objections.''

Under 21 CFR 171.110 of the food additive regulations, objections and requests for a hearing are governed by part 12 (21 CFR part 12) of FDA's regulations. Under § 12.22(a), each objection must meet the following conditions: (1) Must be submitted on or before the 30th day after the date of publication of the final rule; (2) must be separately numbered; (3) must specify with particularity the provision of the regulation or proposed order objected to; (4) must specifically state each objection on which a hearing is requested; failure to request a hearing on an objection constitutes a waiver of the right to a hearing on that objection; and (5) must include a detailed description and analysis of the factual information to be presented in support of the objection if a hearing is requested; failure to include a description and analysis for an objection constitutes a waiver of the right to a hearing on that objection.

Following publication of the final rule permitting the irradiation of fresh lettuce and fresh spinach for control of food-borne pathogens and extension of shelf life, we received numerous submissions with objections to the rule within the 30-day objection period. The majority of these submissions were form letters expressing concern regarding one or more of the following issues: (1) Labeling of produce being irradiated and (2) potential vitamin depletion resulting from irradiation. Many of the form letters also expressed general opposition to the final rule, or objected to the rule based on issues that are outside the rule's scope such as the regulation and management of the meat industry, the number of inspectors currently available to perform inspections, and the proximity of cattle farms to produce farms. Although most of these letters requested a hearing, no evidence was identified in support of any of these objections that could be considered in an evidentiary hearing (§ 12.22(a)(5)). Therefore, these objections do not justify a hearing.[1] We will not discuss these submissions further.

There were two submissions raising specific objections. One was a letter from the Center for Food Safety (CFS) (letter to Docket No. FDA–1999–F–2405; September 17, 2008) and the second was a letter from Food & Water Watch (FWW) (letter to Docket No. FDA–1999–F–2405; September 22, 2008). The letter from CFS sought revocation of the final rule pertaining to two areas, which were enumerated as five specific objections. CFS requested a hearing on the issues

[1] FDA also received letters after the close of the objection period that expressed general opposition to the fresh lettuce and fresh spinach irradiation rule. Tardy objections fail to satisfy the requirements of 21 U.S.C. 348(f)(1) and need not be considered by the Agency (see *ICMAD* v. *HEW,* 574 F.2d 553, 558 n.8 (D.C. Cir.), cert. denied, 439 U.S. 893 (1978)).

raised by each objection. The letter from FWW agreed with all objections raised in the letter from CFS, and requested a hearing and stay of effective date for one additional topic not described in the CFS letter. A more detailed response to both CFS' and FWW's objections is found in section IV. We also received two letters in support of the fresh lettuce and fresh spinach rule.

III. Standards for Granting a Hearing

Specific criteria for deciding whether to grant or deny a request for a hearing are set out in § 12.24(b). Under that regulation, a hearing will be granted if the material submitted by the requester shows, among other things, the following: (1) There is a genuine and substantial factual issue for resolution at a hearing; a hearing will not be granted on issues of policy or law; (2) the factual issue can be resolved by available and specifically identified reliable evidence; a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions; (3) the data and information submitted, if established at a hearing, would be adequate to justify resolution of the factual issue in the way sought by the requester; a hearing will be denied if the data and information submitted are insufficient to justify the factual determination urged, even if accurate; and (4) resolution of the factual issue in the way sought by the person is adequate to justify the action requested; a hearing will not be granted on factual issues that are not determinative with respect to the action requested (e.g., if the action would be the same even if the factual issue were resolved in the way sought).

A party seeking a hearing is required to meet a ''threshold burden of tendering evidence suggesting the need for a hearing'' (*Costle* v. *Pac. Legal Found.,* 445 U.S. 198, 214 (1980), reh. denied, 446 U.S. 947 (1980), citing *Weinberger* v. *Hynson, Westcott & Dunning, Inc.,* 412 U.S. 609, 620–21 (1973)). An allegation that a hearing is necessary to ''sharpen the issues'' or to ''fully develop the facts'' does not meet this test (*Georgia-Pacific Corp.* v. *U.S. EPA,* 671 F.2d 1235, 1241 (9th Cir. 1982)). In judicial proceedings, a court is authorized to issue summary judgment without an evidentiary hearing whenever it finds that there are no genuine issues of material fact in dispute and a party is entitled to judgment as a matter of law (see Fed. R. Civ. P. 56). The same principle applies in administrative proceedings (see § 12.24).

A hearing request must not only contain evidence, but that evidence should raise a material issue of fact ''concerning which a meaningful hearing might be held'' (*Pineapple Growers Ass'n* v. *FDA,* 673 F.2d 1083, 1085 (9th Cir. 1982)). Where the issues raised in the objection are, even if true, legally insufficient to alter the decision, we need not grant a hearing (see *Dyestuffs and Chemicals, Inc.* v. *Flemming,* 271 F.2d 281, 286 (8th Cir. 1959), cert. denied, 362 U.S. 911 (1960)). A hearing is justified only if the objections are made in good faith and if they ''draw in question in a material way the underpinnings of the regulation at issue'' (*Pactra Industries* v. *CPSC,* 555 F.2d 677, 684 (9th Cir. 1977)). A hearing need not be held to resolve questions of law or policy (see *Citizens for Allegan County, Inc.* v. *FPC,* 414 F.2d 1125, 1128 (D.C. Cir. 1969); *Sun Oil Co.* v. *FPC,* 256 F.2d 233, 240–41 (5th Cir. 1958), cert. denied, 358 U.S. 872 (1958)).

Even if the objections raise material issues of fact, we need not grant a hearing if those same issues were adequately raised and considered in an earlier proceeding. Once an issue has been so raised and considered, a party is estopped from raising that same issue in a later proceeding without new evidence. The various judicial doctrines dealing with finality, such as collateral estoppel, can be validly applied to the administrative process (see *Pac. Seafarers, Inc.* v. *Pac. Far East Line, Inc.,* 404 F.2d 804, 809 (D.C. Cir. 1968), cert. denied, 393 U.S. 1093 (1969)). In explaining why these principles ought to apply to an Agency proceeding, the U.S. Court of Appeals for the District of Columbia Circuit wrote: ''The underlying concept is as simple as this: Justice requires that a party have a fair chance to present his position. But overall interests of administration do not require or generally contemplate that he will be given more than one fair opportunity.'' (*Retail Clerks Union, Local 1401* v. *NLRB,* 463 F.2d 316, 322 (D.C. Cir. 1972).) (See *Costle* v. *Pac. Legal Found.,* 445 U.S. at 215–20. See also *Pac. Seafarers, Inc.* v. *Pac. Far East Line, Inc.,* 404 F.2d 804 (D.C. Cir. 1968), cert. denied, 393 U.S. 1093 (1969).)

In summary, a hearing request must present sufficient credible evidence to raise a material issue of fact, and the evidence must be adequate to resolve the issue as requested and to justify the action requested.

IV. Analysis of Objections and Response to Hearing Requests

The letter from CFS contains five numbered objections with requests for a hearing on each of them, and also appears to have two broad objections. FWW's letter agrees with all objections presented by CFS and presents one additional objection; they request a hearing and stay of effective date on each objection. We address CFS' two broad objections first, followed by the specific objections, as well as the evidence and information filed in support of each, comparing each objection and the information submitted in support of it to the standards for granting a hearing in § 12.24(b).

A. CFS' Broad Objections

Although CFS' letter was formatted as five numbered objections with requests for a hearing on each, CFS appears to have two broad objections to the final rule providing for the safe use of ionizing radiation for control of food-borne pathogens and extension of shelf life in fresh lettuce and fresh spinach. In brief, CFS claims that: (1) We have improperly relied on studies in other fruits and vegetables and (2) we have improperly relied on studies at doses below 4.0 kGy. CFS appears to raise these objections to attempt to call into question our assessment of the nutritional impact of the final rule and ultimately our determination that the irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe.

We disagree that we have improperly relied on studies in other fruits and vegetables. We have consistently taken the position that various scientifically validated types of data may properly support a safety determination for a proposed use of a food additive (see 21 CFR 170.20(a)). Further, we have consistently taken the position that data obtained from specific foods irradiated under specific conditions may be extrapolated and generalized to draw conclusions regarding the safety of foods of a similar type irradiated under related conditions (see 62 FR 64107 at 64110; December 3, 1997, and 70 FR 48057 at 48059; August 16, 2005). Other scientific bodies have used this approach as well. As explained in our final rule permitting the irradiation of molluscan shellfish (70 FR 48057 at 48058), the World Health Organization, in its review of the safety data on irradiated food, found that safety data on one food type can be extrapolated to other foods of similar composition and that individual studies of irradiated foods can be integrated into one database (Ref. 1). In the fresh lettuce and fresh spinach final rule, we concluded that the body of data and information we considered in our review demonstrated the safety of fresh lettuce and fresh spinach irradiated up to a maximum dose of 4.0 kGy. CFS' suggestion that such information is not

sufficient to support a safety determination is unsupported by specific data or other factual information.

We also disagree that we improperly relied on studies at doses below 4.0 kGy. In analyzing the nutritional adequacy of irradiated fresh lettuce and fresh spinach, we evaluated the totality of evidence, which included studies of plant-based foods irradiated at a wide range of doses (i.e., doses above and below 4.0 kGy), information about the susceptibility of vitamins in lettuce and spinach to irradiation, information about the susceptibility of vitamins in plant matrices in general to irradiation, and estimates of the significance of fresh lettuce and fresh spinach as sources of these vitamins. For the assessment of the significance of fresh lettuce and fresh spinach as sources of vitamins, we considered the levels of the vitamins present in food, published information about the relative contribution of fresh lettuce and fresh spinach to the total dietary intake of these vitamins, and published studies and reviews summarizing the limited bioavailability of certain vitamins from green leafy vegetables. Importantly, we noted that folate, provitamin A carotenoids, and vitamin K all have limited bioavailability from green leafy vegetables; hence the contribution of these foods to overall intake of these vitamins is diminished, despite the presence of the vitamins in high amounts in foods such as spinach (Ref. 2).[2] For example, in 2001 the Institute of Medicine (IOM) concluded that provitamin A bioavailability from dietary sources (i.e., not supplemental forms) is half that previously thought (Ref. 3), and that very low bioavailability (<10 percent) is associated with raw green leafy vegetables (Ref. 4). Similar findings of limited bioavailability have been reported for folate and vitamin K from green leafy vegetables, particularly relative to supplements and other food sources, as discussed in our nutrition memorandum (Ref. 2).

We considered studies performed at doses ranging from 0.5 kGy to 56 kGy to ascertain the relative amount of vitamin loss at those doses. Specifically, we assessed studies performed at doses above 4.0 kGy for folate, provitamin A carotenoids, vitamin K, and vitamin C. As such, we did not rely solely on studies conducted below 4.0 kGy to perform the nutritional assessment; rather we considered all available data pertaining to potential nutrient loss for those vitamins. The available data included information on the levels of vitamins following treatment with doses below 4.0 kGy, information on the levels of vitamins following treatment with doses above 4.0 kGy, information on the limited bioavailability of certain vitamins and provitamins from green leafy vegetables, and information pertaining to the relative contribution of these sources to the total dietary intake of individual vitamins. Our assessment of the available data does not provide reason for a safety concern regarding potential vitamin loss from irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy. CFS provided no information to support its assertions that our reliance on studies in other fruits and vegetables and studies performed at doses below 4.0 kGy would call into question our assessment of the nutritional impact of the final rule and ultimately our determination that irradiated fresh lettuce and fresh spinach at 4.0 kGy is safe. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, we are denying CFS' objection and request for a hearing based on this objection.

B. First Numbered Objection: CFS' Contention That FDA Failed To Determine the Magnitude of Nutrient Losses at or Near the Maximum Permitted Dose of 4.0 kGy

The first objection raised by CFS contends that FDA ''fails to determine the magnitude of nutrient losses to be expected from irradiation of fresh spinach or iceberg lettuce at or near the upper limit approved in the rule: 4 kGy.'' They expound upon this objection by asserting that the majority of the studies cited in our nutrition memorandum (Ref. 2) were performed at doses below 2 kGy and on fruits and vegetables other than fresh spinach and fresh lettuce. The objection includes CFS' assertions regarding the following ''nutrients'': Carotenoids/vitamin A,[3] folate, vitamin K, and vitamin C. CFS' discussion for each nutrient contains additional objections.

CFS further contends that we failed to determine the magnitude of nutrient losses to be expected from irradiating fresh spinach and fresh lettuce at or near the petitioned maximum dose because we did not address the synergistic effects of irradiation and heating. According to CFS, we should have considered that ''irradiation-induced nutrient losses will be superadded to those from other industrial or home food processing methods.'' CFS' assertion that we failed to determine the magnitude of nutrient losses at or near the petitioned maximum dose ultimately attempts to call into question our determination that the irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe.

Contrary to CFS' contention and, as demonstrated in our nutrition memorandum (Ref. 2), we evaluated both the extent of nutrient loss and the nutritional importance of any such losses resulting from irradiation of fresh lettuce and fresh spinach at doses up to 4.0 kGy. Our review of a large body of data relevant to the nutritional adequacy and wholesomeness of irradiated foods has demonstrated that irradiation does not significantly alter the macronutrients (i.e., proteins, fats, and carbohydrates) of the food at the petitioned doses. However, it has been shown that some vitamins are susceptible to irradiation. The susceptibility of a vitamin to irradiation depends on factors such as the chemical structure of the vitamin, the conditions of processing, the conditions and duration of storage, and the composition of food. To determine whether or not partial vitamin loss is significant, it is essential to consider the relative contribution of the vitamin from the irradiated food to the total dietary intake of the vitamin and the sensitivity of that vitamin to irradiation.

Therefore, our analysis focused primarily on vitamins that are present in relatively high amounts in fresh lettuce and/or fresh spinach, which were identified using the criteria for nutrient content claims (§ 101.54 (21 CFR 101.54)),[4] and that contribute more than a trivial amount to the total dietary intake of that vitamin (i.e., more than 1 to 2 percent). The nutrients which meet both criteria are: Vitamin A, vitamin K, and folate. Therefore, our discussion of the nutritional impact of the proposed conditions of irradiation on fresh lettuce and fresh spinach focused on these three nutrients.[5] For each of these

[2] Only vitamin K is present in high amounts in iceberg lettuce.

[3] We note that while CFS refers to these components as nutrients, not all carotenoids are vitamin A precursors and not all carotenoids have been shown to be essential to the human diet.

[4] In accordance with § 101.54(b), foods containing ≥ 20 percent of the Reference Daily Intake or Daily Reference Value per reference amount customarily consumed, 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.

[5] Spinach contains high levels of vitamin C, but 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 in the United

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nutrients, we evaluated the dietary requirements, dietary sources, and susceptibility of vitamins to irradiation, and we found that there would be no significant impact on the dietary intake of those nutrients.

1. Provitamin A Carotenoids/Vitamin A

In the analysis specific to irradiation-induced loss of provitamin A, CFS objects to the use of six studies, five of which did not involve the irradiation of fresh lettuce or fresh spinach. We have reviewed a large body of data relevant to the safety of irradiated foods.[6] When evaluating the safety of a source of radiation to treat food intended for human consumption, we address three general areas: (1) Potential toxicity, (2) nutritional adequacy, and (3) effects on the microbiological profile of the treated food. We have consistently taken the position that various scientifically validated types of data may properly support a safety determination for a proposed use of a food additive. For example, in the case of food irradiation, we have taken advantage of the extensive research and large body of knowledge concerning the principles of radiation chemistry and the chemical composition of foods. CFS' suggestion that data and information derived from studies of analogous irradiated foods are not sufficient to support a determination that irradiated fresh lettuce and fresh spinach is safe is unsupported by specific data or other factual information.

Furthermore, vitamin A exists in food sources in two different forms: (1) Preformed vitamin A (retinol) and (2) provitamin A (carotenoids).[7] Preformed vitamin A is found in some animal-derived foods (e.g., organ meats, dairy products, eggs) and in fortified foods such as ready-to-eat cereals, whereas provitamin A carotenoids are found in foods such as dark-green vegetables, orange vegetables, orange fruits, and red palm oil (Ref. 3). There is a diverse set of foods that contributes to the total dietary intake of vitamin A in a balanced diet, including vitamin A-rich foods and provitamin A carotenoid-rich foods. Among the wide range of plant-based foods containing provitamin A carotenoids, fresh lettuce and fresh spinach are among the poorer dietary sources, due to limited bioavailability of carotenoids from these foods, as discussed earlier and reviewed by the IOM (Ref. 4). Hence, even for fresh spinach, which has a relatively high concentration of provitamin A, the actual contribution of this food to total vitamin A intake is minor due to limited bioavailability (Ref. 2). Therefore, considering the insensitivity of vitamin A and provitamin A carotenoids found in spinach to irradiation and the limited contribution of these particular foods to the total dietary intake of vitamin A, the small losses of vitamin A that might result from the irradiation of fresh lettuce or fresh spinach are not nutritionally significant (Ref. 2).

Additionally, CFS asserts that there is ''no discussion of the apparent discrepancy between no carotenoid loss in carrots at 2 kGy and 'low to moderate losses in beta and alpha-carotene' * * * in carrots irradiated at less than half that dose, 0.8 kGy.''[8] We were aware of the discrepancies between the two studies during our review. However, we concluded that differences in observed losses between the studies did not call into question our assessment of the nutritional impact of the final rule and determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe. The two studies differed in treatment dose but also other factors, including storage time, temperature during irradiation and storage, and analysis of total carotenoids (Ref. 8) versus individual carotenoids (Ref. 9), which could impact the reported levels of carotenoids. Despite differences in study design, losses of total carotenoids (alpha-carotene plus beta-carotene) were less than 20 percent in both studies. Losses of alpha-carotene (28 percent) were reported to be slightly higher than losses of beta-carotene (8 percent) in the Baraldi et al. paper (Ref. 9); however, it is important to note that alpha-carotene is present in lower amounts than beta-carotene in carrots and has half the retinol activity equivalence of beta-carotene (discussed further in this document). Further, alpha-carotene is not present in meaningful amounts in either spinach or iceberg lettuce; hence; this provitamin was not highlighted in the nutrition memorandum.

The nutritional significance of provitamin A carotenoids is that provitamin A carotenoids, including alpha and beta-carotenes, are precursors of vitamin A. Even at the highest observed losses in the cited studies (28 percent for alpha-carotene), one would not expect substantive losses of vitamin A in the total diet, in part due to inefficient conversion of alpha-carotene to retinol and the limited bioavailability of alpha-carotene from plant sources. In recognition of these limitations, the IOM has established a retinol activity equivalence of 24 micrograms of alpha-carotene (from food) to 1 microgram of retinol (meaning 24 micrograms of alpha-carotene in carrots yield only 1 microgram of retinol in the body). In contrast, the IOM estimates that 12 micrograms of food-borne beta-carotene yield one microgram of retinol in the body. Despite the relatively high concentration of beta-carotene in spinach, the bioavailability of beta-carotene from green leafy vegetables is generally considered to be low relative to other food sources of beta-carotene (even lower than raw carrot) due to inhibitory effects of the food matrix (i.e., the components of the food) on carotenoid release from food. Release of the carotenoids from the food matrix is a step that precedes the incorporation of carotenoids into mixed lipid micelles and their subsequent absorption (Refs. 4 and 10). This topic has been addressed in section IV.A and in an extensive review by the IOM (Ref. 3). Considering the limited bioavailability of provitamin A carotenoids from fresh lettuce and fresh spinach, the limited contribution

States (Ref. 5); hence, vitamin C was not an area of focus in the final rule, although it was addressed in the our nutrition memorandum.

[6] 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. 6). In the 1990s, WHO reanalyzed the safety data on irradiated foods, including additional studies (see 51 FR 13376 at 13378, April 18, 1986) and 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. 1). Furthermore, our Bureau of Foods Irradiated Foods Committee assessed hundreds of toxicology studies in our files and determined that studies involving irradiated foods did not demonstrate adverse effects (Ref. 7). These studies, taken as a whole, serve as an independent method to assess toxicological safety. The studies considered in that evaluation include those that have been relied on by FDA in previous evaluations of the safety of irradiated foods, including lettuce, spinach, molluscan shellfish, shell eggs, meat, and poultry (see 73 FR 49593, August 22, 2008; 70 FR 48057, August 16, 2005; 65 FR 45280, July 21, 2000; 62 FR 64107, December 3, 1997; 55 FR 18538, May 2, 1990; and 51 FR 13376), along with additional data and information from our files and from other information available to us, including published reports regarding studies in which animals were fed a wide variety of foods irradiated at different doses.

[7] There are also two types of carotenoids: Provitamin A carotenoids that are vitamin A precursors, meaning that they contribute to vitamin A activity, and nonprovitamin A carotenoids that are not vitamin A precursors and, therefore, do not contribute to vitamin A activity.

[8] The studies to which CFS refers are the Hajare et al. study (Ref. 8) that looked at the loss in total carotenoids in carrots irradiated at 2.0 kGy and the Baraldi et al. study that was reviewed by Diehl (Ref. 9) and was conducted at 0.8 kGy showing low to moderate losses in beta- and alpha-carotene. Our nutrition memorandum (Ref. 2) notes that the study conducted at 0.8 kGy showing low to moderate losses in beta- and alpha-carotene was reviewed within the Diehl reference.

of these foods to the total dietary intake of vitamin A, and the relative radiation resistance of plant-based carotenoids, we determined that the loss of carotenoids would not be a safety concern. We also note that although provitamin A carotenoids are susceptible to partial losses due to irradiation, these losses are somewhat variable and can be minimized by control of various irradiation conditions (e.g., temperature, packaging, headspace gas). Therefore, while there were variable (but not extensive) losses observed in the two carrot studies, this apparent discrepancy does not call into question the outcome of this final rule. CFS' objection attempts to call into question our assessment of the nutritional impact of the final rule and implies that there is a safety issue due to a discrepancy in losses between the two cited studies; however, they do not provide any information or data to support their objection. We are therefore denying CFS' objection and request for a hearing because a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)).

Further, CFS asserts that we failed to determine the magnitude of nutrient losses from irradiating fresh lettuce and fresh spinach because the discussion of carotenoids was limited to total carotenoid levels as opposed to analyzing specific carotenoids with ''particular nutritional relevance,'' such as lutein and zeaxanthin. To support this objection, CFS cites a study performed by Semba and Dagnelie (Ref. 11), that, according to CFS, demonstrates the nutritional relevance of lutein and zeaxanthin because ''[l]ow dietary intake and plasma levels of lutein and zeaxanthin have been associated with low macular pigment density and increased risk of age-related macular degeneration, and on this basis these carotenoids have been considered good candidates for designation as a [sic] 'conditionally essential' nutrients.'' CFS fails to note that the same journal article states that these carotenoids ''*may* play a role in the pathogenesis of age-related macular degeneration,'' that ''studies are *beginning to suggest* that they fit the criteria for conditionally essential nutrients'' and that ''[s]hould controlled clinical trials show lutein and/or zeaxanthin supplementation protects against the developments or progression of ARMD [age-related macular degeneration] and other eye diseases, then lutein and zeaxanthin *could be considered* as conditionally essential nutrients for humans'' (emphasis added) (Ref. 11). Thus, none of these statements supports CFS' claim that there currently is a scientific basis which would provide a substantial rationale for us to perform analysis on individual carotenoids. Furthermore, it should be noted that both lutein and zeaxanthin are nonprovitamin A carotenoids, meaning that neither contributes to vitamin A activity.

Additionally, in the most recently published report from the IOM on Dietary Reference Intakes (DRIs), which updated recommendations for the intake of vitamin C, vitamin E, selenium, and discussed carotenoids, the IOM stated: ''[a] large body of observational epidemiological evidence suggests that higher blood concentrations of β-carotene and other carotenoids obtained from foods are associated with lower risk of several chronic diseases. This evidence, although consistent, cannot be used to establish a requirement for β-carotene or carotenoid intake because the observed effects may be due to other substances found in carotenoid-rich food, or to other behavioral correlates of increased fruit and vegetable consumption * * * [a]lthough no DRIs are proposed for β-carotene or other carotenoids at the present time, existing recommendations for increased consumption of carotenoid-rich fruits and vegetables are supported . . .'' (Ref. 4).

After reviewing the relevant scientific studies, the IOM did not establish a requirement for carotenoid intake; therefore, unless the carotenoids contributed to vitamin A levels in the diet, we did not analyze specific carotenoids. For these reasons, there was no evidence that individual carotenoids needed to be analyzed when we made our safety decision on irradiation of fresh lettuce and fresh spinach at the petitioned doses. Accordingly, we are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

2. Folate

CFS offers three arguments to support their view that we erroneously concluded that irradiation-induced folate loss in fresh lettuce and fresh spinach is not nutritionally significant. First, CFS asserts that we did not consider any studies of irradiation-induced folate losses in iceberg lettuce. Second, CFS asserts that only one of the cited studies pertained specifically to fresh spinach. Third, CFS contends that we failed to discuss certain results from the study performed by Müller and Diehl (Ref. 12).

First, CFS asserts that ''though iceberg lettuce contains considerably less folate than spinach * * *, lettuces as a group supply a larger percentage of folate than the spinach/greens groups to the average American diet,'' and therefore we should have considered studies of irradiation-induced folate losses in iceberg lettuce. However, we note that iceberg lettuce is just one leafy vegetable within the category of ''lettuces'' (which includes Romaine, butterhead, green leaf, etc.); among the lettuces, iceberg lettuce contains the lowest concentration of folate. In our nutrition memorandum (Ref. 2), we explain that iceberg lettuce is not considered to be a ''good source'' of folate in accordance with § 101.54(c) and that enriched and fortified foods (e.g., cereal grains and grain-based products) make the greatest contribution to folate in the diet. Furthermore, the form of folate used for fortification is more bioavailable than naturally occurring food folates. While we did not provide an analysis for iceberg lettuce, we did analyze the potential folate loss in spinach, which is considered to contain relatively large amounts of folate. We concluded that irradiation of spinach at doses up to 4.0 kGy would not have a significant impact on the dietary intake of folate in the U.S. diet. It follows that iceberg lettuce, which does not meet the criteria for a ''good source'' of this nutrient, would not have a significant impact on the dietary intake of folate either. Therefore, the information provided by CFS that lettuces ''as a group'' supply a larger percentage of folate than the spinach/greens group is not sufficient to demonstrate that we should have considered irradiation-induced losses in iceberg lettuce. Accordingly, we are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

Second, CFS asserts that only one study was presented that considered irradiation-induced folate loss in fresh spinach. While we cited two studies considering folate loss, CFS asserts that only one study is relevant because it was performed in fresh spinach. In the final rule, we explained our position that many scientifically valid types of data may properly support a finding that a proposed use of a food additive is safe. CFS has not provided any evidence that our consideration of studies considering folate loss is inadequate to determine the magnitude of nutrient losses from irradiating fresh lettuce and fresh

spinach at the petitioned doses. CFS has also not provided any additional studies that we should have considered in assessing folate loss. We are therefore denying CFS' objection and request for a hearing because a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)).

Third, CFS contends that our discussion of the study performed by Müller and Diehl (Ref. 12) did not include certain results. CFS asserts that the study reported a 12 percent loss of folate in fresh spinach when irradiated at 2.5 kGy, but we did not discuss the 21 percent loss of folate in fresh spinach when irradiated at 5.0 kGy or the 13 percent loss of folate when dehydrated spinach was irradiated at 10 kGy. The Müller and Diehl study was included in the petition and was analyzed by FDA when we made our safety assessment. We acknowledge that a greater loss of folate was shown when fresh spinach was irradiated at a higher dose (i.e., 5.0 kGy) when compared to the lower dose of 2.5 kGy. The nutrition memorandum cited the 2.5 kGy result, since it was within the range of doses under consideration in the petition and highlighted the general stability of food folate. The 5.0 kGy dose, although greater than the dose under consideration in the petition, still shows that nearly 80 percent of folate is maintained, thus supporting the general stability of this vitamin to moderate doses of irradiation. In our review of the petition, we considered the health implications from folate loss in spinach at the maximum petitioned dose (4.0 kGy), and concluded that such folate loss is not nutritionally significant because: (1) Fresh lettuce and fresh spinach contribute minimally to the dietary intake of folate; and (2) folate is found to be consistently stable to irradiation under various conditions that have been detailed in published studies.

Therefore, the information provided by CFS that a greater loss of folate was shown when fresh spinach was irradiated at a higher dose does not call into question our assessment of the nutritional impact of the final rule and determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe. Accordingly, we are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

3. Vitamin K

CFS objects to the final rule based on our nutrition memorandum for vitamin K because CFS asserts that: (1) The Knapp and Tappel study (Ref. 13) cited in the nutrition memorandum involved the irradiation of pure vitamin K in an isooctane solution and not in a food matrix; (2) the Richardson et al. study (Ref. 14) cited in the nutrition memorandum involved indirect measurement of vitamin K activity in spinach and other vegetables after freezing, irradiation at 28 or 56 kGy, or heat-processing; (3) we ''failed to consider'' conflicting results in two studies (Richardson et al. (Ref. 15) and Metta et al. (Ref. 16)) from the same period as the Richardson et al. study (Ref. 14) cited in the nutrition memorandum; and (4) we failed to consider the 2007 study by Hirayama et al. (Ref. 17) that raises ''similar questions'' regarding the nutritional impact of irradiating fresh lettuce and fresh spinach.

First, CFS contends that the Knapp and Tappel study that involved the irradiation of pure vitamin K in an isooctane solution rather than a food matrix is of ''limited value for assessing irradiation-induced loss of Vitamin K in irradiated spinach or iceberg lettuce.'' We disagree with CFS' assessment. To the contrary, we maintain that this study establishes vitamin K as one of the least sensitive fat-soluble vitamins to irradiation, and therefore is relevant for assessing irradiation-induced losses. Even though the study was performed in an isooctane solution, the relative sensitivities of the vitamins to irradiation do not change; rather, the food matrix can offer protection to the vitamin, lessening the effects of irradiation because the radiation effects will be distributed to all components of the food, i.e., the principle of mutual protection (Ref. 18). We reviewed this study and found it to be adequate to determine comparative radiosensitivities under uniform conditions for vitamins A, D, E, K, as well as carotene. Therefore, the information provided by CFS that the Knapp and Tappel study involved the irradiation of vitamin K in an isooctane solution rather than a food matrix does not call into question the value of the Knapp and Tappel study in helping us assess the nutritional impact of the final rule. We are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

Second, CFS contends that the Richardson et al. study (Ref. 14) is of limited value because the study ''estimated'' the vitamin K content through indirect measurement of the prothrombin times of chick plasma, and the study reported ''anomalous results.'' According to CFS, the authors of the study reported an increase in vitamin K activity in irradiated spinach over time in addition to variability in the values obtained from different assays. CFS cites these findings to support its contention that we erroneously determined the magnitude of vitamin K loss from irradiation of fresh lettuce and fresh spinach under the petitioned conditions.

We disagree that the indirect measurement of vitamin K activity in spinach precludes this study from being useful in the assessment of potential nutrient losses. In our review of this study, we considered the prothrombin time measurement in the chick bioassay, even though indirect, to be relevant for assessing vitamin K activity in foods since the chick is sensitive to dietary vitamin K deprivation. Moreover, the prothrombin time measurement is a common parameter for measuring vitamin K status for clinical purposes (Refs. 3 and 19). Furthermore, we acknowledge the variability in the data cited by CFS; however, CFS' objection fails to note that the authors of the study in question concluded that ''regardless of the variability in results * * * there was no appreciable loss of vitamin K activity in the foods preserved by any process or when stored for 15 months'' (Ref. 14). Variability in results is not grounds for a study to be ignored; important information about general trends may still be gleaned from this study, which consistently found vitamin K activity was not reduced by irradiation relative to frozen or heat-processed controls. As part of their objection, CFS specifically notes that vitamin K activity after 15 months of storage was higher than directly after irradiation at both irradiation doses; however, it should be noted that irradiation may either accelerate or decelerate metabolic changes within the food, a factor which may account for differences observed following storage (Ref. 9). For example, it is known that vitamin K resides in the chloroplasts and has tight association with the thylakoid membranes. This tight association may account for the limited bioavailability of vitamin K from green leafy vegetables (Ref. 20). Processing techniques such as irradiation (particularly at high doses) may result in disruption of thylakoid membranes, an

effect which may become more evident after long term storage and may account at least in part for variability in observed vitamin K activity after storage. As such, the information provided by CFS that the Richardson et al. study involved indirect measurement of vitamin K activity does not call into question the value of the Richardson et al. study in helping us assess the nutritional impact of the final rule. We are therefore denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

Third, CFS contends that we failed to consider conflicting results from two studies cited by CFS: A study performed by Richardson et al. (Ref. 15); and a study performed by Metta et al. (Ref. 16). Although neither of these studies was cited in our nutrition memorandum, we were aware of both studies when evaluating the nutritional impact of irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy. We disagree with CFS' conclusions that the Richardson et al. study demonstrated that the ''Vitamin K activity of diets containing small quantities of Vitamin K was markedly decreased by irradiation with sterilizing doses of gamma rays.'' CFS' objection fails to note that, in the experimental report, the authors concluded that ''practically none of the vitamin K activity was lost by the irradiation process when vitamin K_1 was the source of the vitamin in the diet.'' The article also concluded that ''[s]ince the incidence of hemorrhage was higher in the chicks receiving the untreated spinach than it was in those receiving the irradiated spinach, it was concluded that no destruction of vitamin K occurred by the irradiation process.''

In addition, the Metta et al. study (Ref. 16) reported vitamin K deficiency in rats induced by the feeding of irradiated beef. However, we deemed the study irrelevant to the assessment of vitamin K loss in fresh lettuce and fresh spinach because the Metta et al. study assessed the vitamin K destruction of the more labile form of vitamin K found in meat (menaquinone). There are a number of different forms of vitamin K, including, but not limited to: Phylloquinone (vitamin K_1)—the only important molecular form found in plants, menaquinones (vitamin K_2)—which refers to a series of compounds produced by gut bacteria but also to a form of vitamin K_2, termed ''menaquinone-4'' that is produced in animal tissues from conversion of dietary vitamin K (K_1, K_3), and menadione (vitamin K_3), a synthetic form (Refs. 3, 21, and 22).

Phylloquinone is the form of vitamin K that is found in spinach and other leafy greens, whereas menaquinone, although present in minor amounts, is the dominant form found in beef along with lesser amounts of dietary phylloquinone. The radiosensitivities differ among various forms of vitamin K. For example, Richardson et al. reported menadione (vitamin K_3) is more readily destroyed by ionizing radiation than either phylloquinone (vitamin K_1) or vitamin K_5 (a vitamin K analog) (Ref. 15). The Metta et al. study assessed the destruction of vitamin K found in meat and the effect on rats fed a limited diet; the lability of vitamin K in beef[9] has been noted in numerous published reviews, including those of WHO (Ref. 23), Thayer et al. (Ref. 24); and Diehl et al. (Ref. 9). We determined that the Metta et al. study was not relevant to the assessment of potential irradiated-induced phylloquinone losses in fresh lettuce and fresh spinach, and did not highlight this reference in our nutrition memorandum.

We do not agree with CFS' contention that our nutritional assessment of irradiated fresh lettuce and fresh spinach is called into question by these studies. Neither of these studies includes any information or data that would call into question our findings regarding the nutritional impact of irradiation under the petitioned conditions. We are therefore denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

Lastly, CFS asserts that a study conducted by Hirayama et al. (Ref. 17) was not reviewed by FDA in the approval process to permit ionizing radiation to treat fresh lettuce and fresh spinach, and therefore calls into question our nutritional assessment and ultimately our safety conclusion. In the Hirayama et al. study, germ-free mice were fed pelleted, sterilized animal feed. According to CFS, vitamin K_3, a synthetic form of vitamin K, was eliminated when the pure compound was added to the feed and irradiated at 50 kGy. CFS notes that the study also showed that vitamin K_1, the form found in spinach, was reduced by approximately 68 percent after the pelleted feed was exposed to irradiation doses of 50 kGy. CFS objects to the final rule, asserting that this study demonstrates the need for more research to determine the ''differential sensitivities'' of the two forms of vitamin K. We do not agree that our nutritional assessment and the safety of irradiated fresh lettuce or fresh spinach up to a maximum dose of 4.0 kGy are called into question by this study.

As previously mentioned in this document, research has demonstrated that different forms of vitamin K have variable sensitivities to irradiation. For example, the Richardson et al. study (Ref. 15) cited by CFS investigated the effects of ionizing radiation on vitamin K when different sources were used (i.e., probing the ''differential sensitivities''). The sources of this vitamin were K_1, K_3, K_5, dehydrated alfalfa leaf meal, and fresh spinach. The authors concluded that menadione (K_3) was more readily destroyed by irradiation than either vitamin K_1 or K_5, and practically no destruction of vitamin K (phylloquinone) occurred when the dietary source was natural (i.e., from alfalfa leaf meal and spinach). Clearly, it is understood that different forms of vitamin K can have variable sensitivity to irradiation, and we were aware of this fact when evaluating the nutritional adequacy of irradiated lettuce and spinach (Ref. 25). In addition, the petition proposes to irradiate spinach in its natural form, and the Richardson et al. study, which provides the most pertinent results (Ref. 15), demonstrated that there was practically no destruction of vitamin K from this natural source. Furthermore, the WHO report we evaluated during review of the petition contained information regarding the varied properties of these different forms of vitamin K (Ref. 20). Therefore, the Hirayama et al. study raised by CFS does not call into question our assessment of the nutritional impact of the final rule; we continue to conclude from all of the available evidence that the irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy will have no significant impact on the total dietary intake of vitamin K and is safe. We are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

4. Vitamin C

CFS asserts that the final rule does not provide an assessment of vitamin C loss from irradiation and further alleges that our assessment of irradiation-induced vitamin C loss in our nutrition memorandum is erroneous. CFS argues

[9] We note that although Metta et al. does not identify the form of vitamin K in beef tissue, other studies have reported menaquinone-4 as the predominant form of vitamin K in beef tissue.

that the studies we reviewed regarding irradiation-induced loss of vitamin C showed varied results and that one source of variation in that loss is whether ascorbic acid (AA) was measured or whether AA plus dehydroascorbic acid (DHAA) was measured. Measuring AA plus DHAA yields the total ascorbic acid (TAA). Specifically, CFS states that, in light of the divergent data, experiments for irradiation of fresh lettuce and fresh spinach should be conducted measuring TAA. CFS also contends that a source of variation in vitamin C can arise from ''differential Vitamin C loss in different fruits and vegetables.''

We evaluated the vitamin C loss in irradiated fresh lettuce and fresh spinach and the evaluation was provided in our nutrition memorandum (Ref. 2). However, because fresh lettuce and fresh spinach are not major contributors to vitamin C in the U.S. diet, the question of vitamin C loss from these foods was not discussed in the final rule. While spinach has a relatively high concentration of vitamin C, the combined food group of ''spinach/greens'' contributes less than 2 percent to the total intake of vitamin C in the diet. Other major food sources (e.g., citrus fruit, fortified juice drinks, tomatoes, peppers, potatoes, broccoli) provide the majority of vitamin C in the U.S. diet. We therefore determined that little if any reduction in intake of vitamin C in the U.S. diet is expected to result from irradiation of fresh lettuce and fresh spinach under the petitioned conditions of use.

We agree that the studies cited in our nutrition memorandum appear to report divergent results; however, for all these studies, we provided an explanation for each set of differences. For example, our nutrition memorandum states that, ''[m]any of the early studies of the effects of irradiation on vitamin C levels measured AA levels only and consequently reported artificially high decreases in vitamin C,'' and ''AA losses of irradiated foods relative to controls may be quite different depending on whether AA levels are recorded immediately after irradiation or after typical storage conditions.'' The memorandum also states that, ''[i]n the most recent studies conducted on spinach and iceberg lettuce, when irradiation has been conducted at doses reflective of those that would be practical for maintaining acceptable sensory properties, reported losses were minimal.'' Thus, the information provided by CFS, that the studies we reviewed regarding irradiation-induced loss of vitamin C showed varied results, does not call into question our assessment of the nutritional impact of the final rule or our conclusion that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe. We evaluated the totality of evidence and determined that the irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy was safe. We are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

5. Synergistic Effects of Irradiation and Heating

CFS contends that we do not address the synergistic effects of irradiation and heating, stating that nutrient losses would be even greater for dual processing compared to irradiation alone. In support of this objection, CFS cites a table in ''Safety of Irradiated Foods'' by Diehl (Ref. 9) specifically showing synergistic losses of vitamin E. We are aware that synergistic losses have been noted for vitamin E and thiamin, two vitamins that are particularly sensitive to irradiation; however, synergistic effects have not been observed for all vitamins or in all food types (Ref. 24). To determine the potential impact of irradiation at levels up to 4.0 kGy on the nutritional value of fresh lettuce and fresh spinach, we considered all vitamins known to be present in these foods, and primarily focused on vitamins that are present in relatively high amounts in one or both of these foods and vitamins for which lettuce and spinach contribute more than a trivial amount to the total dietary intake of those vitamins (i.e., more than 1 to 2 percent). There are a number of commonly consumed foods that are substantial sources of vitamin E (e.g., certain nuts and oils, margarines) (Ref. 5); these foods are discussed in the reference cited by CFS. Substantial sources of thiamin include yeast breads, ready-to-eat cereals, pastas and grains, certain meats, and milk (Ref. 5). Neither of the two vitamins particularly sensitive to irradiation, vitamin E and thiamin, has been identified as being present in relatively high amounts in fresh lettuce and/or fresh spinach and as contributing more than a trivial amount to the total dietary intake of these vitamins. Therefore, the information provided by CFS, that synergistic losses have been found for vitamin E, does not call into question our assessment of the nutritional impact of the final rule and determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe. Accordingly, we are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

C. Second Numbered Objection: CFS' Assertion That FDA Underestimated the Nutritional Contribution of Fresh Spinach and Fresh Lettuce to the Diet

CFS also objects that we underestimated the nutritional contribution of fresh lettuce and fresh spinach to the diet. Specifically, CFS states that we failed to consider spinach's ''dramatically rising nutritional contribution'' to the average American diet over time and failed to consider subpopulations which rely more heavily on spinach for nutrition than the statistically average American. Thus, CFS attempts to call into question our assessment of the nutritional impact of the final rule and ultimately our determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe.

According to CFS, we employed two criteria to consider which nutrients were assessed: (1) Nutrients for which spinach/iceberg lettuce are an ''excellent source;'' and (2) nutrients for which spinach/iceberg lettuce contribute greater than 1 to 2 percent of the statistically average American's diet. CFS asserts that we should have provided a rationale for considering only nutrients for which spinach is an ''excellent source'' and should have considered vitamins for which spinach is also a ''good source.'' CFS has mischaracterized the criteria we used for our nutritional assessment, which was explained in our nutrition memorandum (Ref. 2). We explained in the nutrition memorandum that we considered all vitamins known to be present in lettuce and spinach in relatively high amounts (greater than or equal to 10 percent of the daily value for vitamins), including vitamins for which lettuce and/or spinach were ''good'' or ''excellent'' sources, and that contribute greater than 1 to 2 percent to the total dietary intake of those vitamins. Vitamins that did not meet these two criteria were not explicitly discussed in the nutrition memorandum. While fresh spinach is a ''good source'' of vitamin E, vitamin B_6, and riboflavin, fresh spinach did not contribute more than 1 to 2 percent to the total dietary intake of these vitamins. Therefore, we did not explicitly discuss these nutrients in the nutrition memorandum. CFS has not presented any evidence to call into question the criteria we used for our nutritional assessment. Therefore, we are denying CFS' objection and request

for a hearing because a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)).

In addition, CFS objects to our second criteria, asserting that we rely on a ''13-year old 'snapshot' that misses the growing importance of [spinach] to the nutritional adequacy of American diets.'' In support of this objection, CFS submitted a study performed by the Economic Research Service (ERS) of the United States Department of Agriculture (USDA) (Ref. 26). This study provides basic economic information about the market distribution of spinach in the United States. CFS points out that this study indicated an increase in the consumption of spinach from the 1970s through 2002. Table 1 of the ERS study presents ''per capita use'' [10] of spinach in the United States. The per capita use values for fresh market (i.e., fresh spinach) for 1994, 1995, and 1996 are 0.75, 0.67, and 0.63 pounds, respectively, and the corresponding per capita use values for total spinach are 1.71, 1.66, and 1.77 pounds, respectively. While CFS focused on the value for per capita use of total spinach, the fresh market value is more pertinent to this discussion, as fresh spinach is the subject of this regulation. The ERS study indicates that the total fresh market per capita value for spinach increased from 0.75 pounds in 1994 to 1.49 pounds in 2002. CFS asserts that we did not consider this increase in fresh spinach consumption in the nutritional assessment.

CFS further asserts that this rise in consumption of spinach could be used to provide a rough approximation of the dietary and nutritional contribution of spinach during these years (i.e., 1997 to 2002). CFS provides estimations for percent contribution of spinach to vitamin A and vitamin C intake and suggests that contributions of spinach to vitamin E, riboflavin, and vitamin B_6 intake may have increased to provide more than 1 to 2 percent of the percent daily value as well.

However, we note that our nutritional assessment included a key conservative assumption that compensates for the increase in fresh spinach consumption cited by the ERS study. Specifically, we assumed that all spinach and iceberg lettuce in the food supply would be irradiated (i.e., 100 percent commercial application). For the years of 1994, 1995, and 1996, we conservatively estimated 100 percent commercial application; values for total per capita use of spinach were 1.71, 1.66, and 1.77 pounds, respectively, during those years, and we assumed all spinach could be irradiated when evaluating the nutritional impact of irradiating fresh lettuce and fresh spinach. These values for total per capita use of spinach each exceed the value for fresh market consumption in 2002 and therefore, our assessment encompassed the increased per capita use of fresh spinach through use of this conservative approach. Since our approach did not underestimate fresh spinach consumption in our nutritional assessment, the data and information provided by CFS do not call into question our assessment of the nutritional impact of the final rule and determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe. Moreover, CFS' assertion that the rise in spinach consumption indicates increased contributions of spinach to the dietary intake of vitamins is not based on actual data. The estimates provided by CFS are purely speculative; the estimates do not account for recent changes in calculation of vitamin A equivalency and presume no other changes in the U.S. diet (during the same time period) related to intakes of other foods containing vitamin A and provitamin A and certain water-soluble vitamins listed by CFS. Because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)), and a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)), we are denying CFS' objection and request for a hearing.

CFS also objects to the final rule by alleging that we did not consider atypical consumers of spinach such as Asian women, women 60 years of age or older, and vegetarians. We are aware that there is variation in the amount of fresh spinach consumed by different U.S. subpopulations; however, CFS provided no evidence that spinach is a more significant source of certain vitamins for any particular subpopulation. Indeed, to establish the contribution and significance of spinach as a source of specific vitamins in the diet, the complete diet must be considered. For example, when assessing the relative contribution of spinach and other leafy greens to the vitamin A content of the diet, the dietary intake of other major contributors of vitamin A (including vitamin A rich foods such as organ meats and dairy products) and provitamin A rich foods (such as carrots, tomatoes, and fortified ready-to-eat cereals) should be included. In addition, according to the IOM, bioavailability of provitamin A carotenoids should be taken into account. In the absence of data on the complete diet, it is not possible to determine the percent contribution of spinach and lettuce to the dietary intake of vitamins for these population subgroups and whether the relative contribution of spinach and lettuce to the dietary intake of these vitamins varies for the subpopulations cited by CFS. While the ERS study indicates that Asian women and women 60 years of age or older consume a relatively greater amount of fresh spinach compared to statistically average Americans, CFS did not establish that the small losses of some vitamins that could result from the petitioned use of irradiation of fresh spinach would be nutritionally significant (i.e., exceed a trivial amount for the total diet) for any of these population subgroups. Thus, the information provided by CFS regarding certain subpopulations that consume more spinach is not sufficient to support CFS' assertion that we failed to protect ''atypical'' consumers and therefore underestimated the nutritional contribution of fresh lettuce and fresh spinach to the diet. We are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

D. Third Numbered Objection: CFS' Contention That FDA Failed To Conduct a Cumulative Assessment of Irradiation-Induced Nutrient Loss

CFS also objects that we ''failed to conduct a cumulative assessment of irradiation-induced nutrient losses in fresh spinach and iceberg lettuce in combination with irradiation-induced nutrient losses in other foods already approved for irradiation * * *.'' CFS contends that by ''breaking out'' fresh lettuce and fresh spinach from the original petition, the nutritional impact will appear lessened, even if the impact of irradiating all the foods covered in the original petition is significant. Accordingly, CFS believes that we should conservatively assume that the entire supply of any given food will be irradiated at the maximum permitted dose when approving a petition. CFS'

[10] ''Per capita use'' was calculated using two major datasets on food consumption in the United States: (1) Food disappearance data, which measures the flow of raw and semi-processed food commodities through the U.S. marketing system, and (2) the Continuing Survey of Food Intakes by Individuals, which records food intake over a specific period and collects demographic information, information on where a food item was purchased, how it was prepared, and where it was eaten (Ref. 26).

contention therefore attempts to call into question our assessment of the nutritional impact of the final rule and our determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe.

We explained in the final rule our criteria for evaluating whether irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy would have an adverse effect on the nutritional quality of the diet. Our analysis focused on the effects of irradiation on those nutrients for which at least one of these foods may be identified as an ''excellent source'' or a ''good source'' and for which they contribute more than a trivial amount to the total dietary intake (i.e., the nutrients that had the potential to impact the diet). We based our decision on both the data and information submitted in the petition, as well as other data and information in our files. We determined that, based on the available data and information, the effects of irradiation on nutrient levels in fresh lettuce and fresh spinach treated under the proposed conditions will be insignificant and will not adversely affect the nutritional quality of the overall U.S. diet.

CFS alleges that ''breaking out'' fresh lettuce and fresh spinach from the foods covered in the original petition lessens the apparent overall nutritional impact of irradiated foods. However, the vitamin loss resulting from this regulation is negligible and therefore will not affect any cumulative assessment. CFS also asserts that we should conservatively assume that the entire supply of any given food will be irradiated at the maximum permitted dose during the approval of a petition. We agree with CFS and have chosen to employ this approach when assessing nutritional losses induced by irradiation. The nutrition memorandum notes that we, in our reviews and analysis of nutritional data, operate under the assumption that the entire supply of a given food may be irradiated at the maximum permitted dose. Contrary to what CFS appears to assert, the discussion of data at lower doses in the nutrition memorandum does not negate this assumption; rather, it reflects a review of published data on irradiation of various plant foods at both lower and higher doses. CFS has not submitted sufficient information to support the conclusion that nutrient loss in fresh lettuce or fresh spinach irradiated under the petitioned conditions, in combination with nutrient losses in other foods already approved for irradiation, would call into question our assessment of the nutritional impact of the final rule and would be a safety concern. Accordingly, we are denying CFS' objection and request for a hearing because a hearing will not be held on the basis of mere allegations or denials or general descriptions of positions or contentions (§ 12.24(b)(2)).

E. Fourth Numbered Objection: CFS' Assertion That FDA Failed To Determine Risk of Food-Borne Disease From Radiation Resistant Pathogens

In another overall objection to the final rule, CFS objects to our safety evaluation of irradiated fresh lettuce and fresh spinach, stating that ''FDA has failed to determine whether irradiation of fresh spinach and iceberg lettuce . . . will increase the risk of food-borne disease from radiation-insensitive pathogens such as *Clostridium botulinum*. . . .'' Specifically, CFS asserts that our analysis did not adequately address the possibility that the suppression of radiation-sensitive bacteria by irradiation might offer enhanced growth conditions for pathogens that are more resistant to irradiation, such as *C. botulinum* (the bacterium that produces the toxin which causes the disease botulism). CFS presents three arguments to support this objection: (1) We did not provide a discussion of radiation-insensitive pathogens other than *C. botulinum;* (2) the study by Petran et al. (Ref. 27), which we cited to support our conclusion that irradiation will not increase the risk of botulism, did not involve irradiation of fresh lettuce or fresh spinach; and (3) the microbiology memorandum (Ref. 28) contained contradictory statements. We will address each argument in this document.

First, CFS asserts that we erred by not evaluating irradiation's potential effect on radiation-insensitive pathogens other than *C. botulinum.* Historically, it has been our practice to evaluate microbiological pathogens that have been identified as a potential hazard for a specific type of food and which are also of public health significance (see, for example, 70 FR 48057, August 16, 2005 (amending the food additive regulations to provide for the safe use of ionizing radiation for control of *Vibrio* species and other food-borne pathogens in fresh or frozen molluscan shellfish); 65 FR 64605, October 30, 2000 (amending the food additive regulations to provide for the safe use of ionizing radiation to control microbial pathogens in seeds for sprouting); 65 FR 45280, July 21, 2000 (amending the food additive regulations to provide for the safe use of ionizing radiation for the reduction of *Salmonella* in fresh shell eggs); 62 FR 64107, December 3, 1997 (amending the food additive regulations to provide for the safe use of a source of radiation to treat refrigerated or frozen uncooked meat, meat byproducts, and certain meat food products to control food-borne pathogens and extend product shelf life); 55 FR 18538, May 2, 1990 (amending the food additive regulations to provide for the safe use of sources of ionizing radiation for the control of food-borne pathogens in poultry); and 50 FR 29658, July 22, 1985 (amending the food additive regulations to permit gamma radiation treatment of pork to control *Trichinella spiralis*)). In the microbiology memorandum, we provide a discussion of the food-borne disease outbreaks and pertinent pathogens most commonly associated with the consumption of fresh lettuce and fresh spinach. The microbiology memorandum identifies *Escherichia coli* O157:H7, *Listeria monocytogenes,* and *Salmonella enterica* serovars as pathogens of public health significance, and discussed these pathogens in detail. We also discuss *C. botulinum* in the microbiology memorandum and in the final rule, not because *C. botulinum* has been identified as a reasonable hazard for either fresh lettuce or fresh spinach, but because this pathogen has been identified as being both radiation-insensitive and of public health significance, and to demonstrate the impact that elimination of native microflora may have on the ability of this type of pathogen to proliferate and elaborate toxin. However, it is not our burden to discuss possibly irrelevant pathogens. CFS does not provide information related to additional radiation-insensitive pathogens of public health significance that may be present in fresh lettuce or fresh spinach that we have not considered, and the objection contains no information that would cause us to change our safety determination. We are therefore denying CFS' objection and request for a hearing because a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)).

Second, CFS asserts that the Petran et al. study (Ref. 27), which we cited in support of our conclusion that irradiation will not increase the risk of botulism, did not involve irradiation of fresh lettuce or fresh spinach, and therefore, did not address the safety concern that irradiation may provide enhanced growing conditions for radiation-insensitive pathogens due to the ''elimination'' of spoilage and other

bacteria. CFS also objects to the final rule based on this study because *C. botulinum* multiplies more rapidly on shredded cabbage than romaine lettuce, asserting that this observation demonstrates that pathogens can have markedly different growth patterns on different vegetables, underscoring the illegitimacy of extrapolating from data on one vegetable to another.

The Petran et al. study (Ref. 27) assesses the potential for growth and toxin production of heat-shocked *C. botulinum* spores in fresh-cut romaine lettuce and shredded cabbage. While the produce was not irradiated, the study was chosen because it offers a non-competitive environment for *C. botulinum* elaboration, reflecting conditions that would be generated if produce were irradiated in the presence of *C. botulinum* spores. *C. botulinum* is a Gram-positive anaerobic sporeformer, and this study examined the potential for outgrowth and toxin production under conditions of temperature abuse in both aerobic and anaerobic conditions. As stated in our microbiology memorandum, there was no toxin production detected in either the vented or non-vented packaging at 12.7 °C (~55 °F) or lower after 28 days. Toxin was produced only under conditions of extreme temperature abuse after all samples became unmistakably inedible, i.e., after 14 days at 21 °C (~70 °F). The study demonstrated that even under ideal growth conditions for *C. botulinum* where the levels of native microflora were greatly reduced, toxin production was not elaborated until after the produce was clearly inedible. Moreover, CFS has not presented evidence or a rationale that changes our conclusion that the ''growth and toxin expression by Gram-positive anaerobic sporeformers would not present a likely additional hazard in this application of irradiation.''

CFS also objects to the use of the Petran et al. study because it did not involve fresh lettuce or fresh spinach; rather, the study explored the potential for growth and toxin production by *C. botulinum* in samples of romaine lettuce and cabbage packaged in aerobic and anaerobic conditions exposed to temperature abuse, which represent ideal conditions for growth and toxin production by *C. botulinum*. CFS uses the example of *C. botulinum* multiplying more rapidly on shredded cabbage than on romaine lettuce as evidence that one cannot extrapolate from data on one type of leafy green vegetable to draw conclusions about other leafy green vegetables (i.e., fresh lettuce and fresh spinach). We recognize that in the study, toxin was produced in the non-vented cabbage sample after 7 days of storage at 21 °C (nearly 70 °F), a timeframe that was shorter than the timeframe for toxin production in romaine lettuce. However, we do not agree that these results indicate the illegitimacy of extrapolating data from one type of leafy green vegetable to another leafy green vegetable. CFS fails to note that all of the samples for which toxin production was observed were clearly inedible prior to toxin production, and that toxin was not produced for at least 28 days in any of the samples that were vented. Indeed, the study demonstrated that it is extremely unlikely for an anaerobic sporeformer to grow and produce toxin in lettuce products that are handled properly (i.e., not stored at 70 °F for 7 days) and are of acceptable quality for consumption. Furthermore, all leafy green vegetables (e.g., iceberg lettuce, spinach, romaine lettuce, and cabbage) are grown and harvested under similar conditions and therefore the probability of contamination with *C. botulinum* is similar. As stated in the microbiology memorandum, this type of contamination is unlikely. CFS did not provide any data to demonstrate that *C. botulinum* has been identified as a hazard in green leafy vegetables or that the likelihood of toxin production would be greater for either fresh lettuce or fresh spinach than it is in romaine lettuce or cabbage. CFS' objection did not include any new information or data that would call into question our findings about this study. Accordingly, the information provided by CFS, that the Petran et al. study did not involve the irradiation of fresh lettuce or fresh spinach, is not sufficient to call into question our determination that irradiating fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is safe. We are therefore denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

Further, it is important to note that the standards of microbiological safety of fresh lettuce and fresh spinach are independent of the final rule permitting the irradiation of fresh lettuce and fresh spinach. Irradiation is just one potential control contributing to the mitigation of food-borne pathogens, and its intended technical effect is to reduce, not eliminate, spoilage and pathogenic bacteria. Therefore, the final rule is not predicated on irradiation, by itself, resulting in fresh lettuce and fresh spinach that are pathogen-free.

The final portion of the CFS objection contends that the our microbiology memorandum contains contradictory statements, and therefore, the question of whether the growth of *C. botulinum* or other radiation-insensitive pathogens present on irradiated fresh lettuce or fresh spinach would be enhanced by the suppression of competing bacteria remains unanswered. CFS asserts that when discussing the Petran et al. study, the microbiology memorandum states that the spoilage microorganisms ''attain previous levels within days of treatment,'' but when discussing the Zhang et al. study (2006) (Ref. 29), the memorandum states that ''relative reductions [in numbers of viable bacteria during 9 days of storage] persisted . . .'' CFS contends that these statements are contradictory and that our conclusion that spoilage microorganisms ''attain previous levels within days of treatment'' is erroneous.

CFS' objection implies that both statements cannot be true and that we misinterpreted the Zhang et al. study. However, we disagree that either statement is false. The Zhang et al. study (Ref. 29) reported substantially lower total bacterial counts for the irradiated samples as compared to the unirradiated control on the same day. Our microbiology memorandum's statement that ''relative reductions [in numbers of viable bacteria during 9 days of storage] persisted . . .'' is, therefore, correct. However, while these lower levels of bacteria persisted, the native microflora was also recovering as evidenced through the increase in total bacterial counts over the storage period. In the case of the 0.5 kGy and 1.0 kGy irradiation trials, bacterial counts attained initial levels (i.e., the control level on day zero) within days of treatment. For the 1.5 kGy sample, the total bacterial counts did not reach the control level by the end of the 9-day storage period, but the total bacterial counts increased as storage time increased. The results of the 1.5 kGy sample therefore demonstrate the veracity of both of the memorandum's statements: The native microflora was able to recover and the substantially lower bacterial counts persisted throughout the 9-day storage period. At the end of the 9-day storage period, the unirradiated control was reported to have 7.60 Log CFU/g [11] or approximately 4 million colony forming units per gram, which resulted in the spoilage of tissue. On the same day, the

[11] The data were obtained by calculating the log of the colony forming units per gram (LogCFU/g). Therefore, any whole number reported is indicative of magnitude.

sample irradiated at 1.5 kGy contained approximately 50 thousand colony forming units per gram, which was lower than the unirradiated control, but significantly larger than the nearly 200 colony forming units that were present immediately following irradiation. Thus, the statements in the microbiology memorandum are both correct, and we maintain that the memorandum accurately and reliably reflects the information in the cited publication. Accordingly, we are denying CFS' objection and request for a hearing because the data and information submitted by CFS are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)).

F. Fifth Numbered Objection: CFS' Contention That FDA Failed To Consider Alternatives to Irradiation of Fresh Lettuce and Fresh Spinach

CFS' final objection contends that we have failed to consider alternatives to irradiation of fresh lettuce and fresh spinach. However, we evaluate a particular food additive only for its safety. Section 409(c)(1) of the FD&C Act requires FDA to establish a regulation prescribing, with respect to one or more proposed uses of the food additive involved, the conditions under which such additive may be safely used. The FD&C Act does not require us to consider alternatives as a factor in deciding whether to grant a food additive petition. We evaluated the safety of irradiating fresh lettuce and fresh spinach at a maximum dose not to exceed 4.0 kGy based on three appropriate areas relevant to safety: (1) Potential toxicity; (2) nutritional adequacy; and (3) effects on the microbiological profile of the treated food. Based on the data and studies submitted in the petition and other information in our files, we properly concluded that the proposed use of irradiation to treat fresh lettuce and fresh spinach with absorbed doses that will not exceed 4.0 kGy is safe. Therefore, we are denying CFS' objection and request for a hearing because CFS raises a factual issue that is not determinative with respect to the action requested (e.g., the action would be the same even if the factual issue were resolved in the way sought) (§ 12.24(b)(4)).

G. FWW's Assertion That FDA Failed To Address Potential Organoleptic Degradation

FWW submitted objections to the final rule in a letter dated September 22, 2008, which concurred with objections put forth by CFS, and included an additional objection. FWW asserts that there is a basis to stay the approval of the final rule and to convene a public evidentiary hearing on the issue of the quality of the irradiated produce at the dose levels approved and whether there is technology currently available to achieve the pathogen reduction desired while still preserving the organoleptic properties of the produce. FWW asserts that approval of this petition raises issues of safety and deception to the consumer under section 409 of the FD&C Act because irradiating fresh lettuce and fresh spinach at the petitioned doses may result in organoleptic degradation and may not achieve pathogen reduction.

In support of its objection, FWW cites a 2008 study by Gomes et al. (Ref. 30), which according to FWW, demonstrated that doses higher than 1 kGy were necessary to ensure elimination of food-borne pathogens from bagged spinach leaves. Additionally, FWW quotes Dr. Mike Doyle, Director of the Center for Produce Safety at the University of Georgia, who stated that, ''in a commercial processing plant, products are stacked in cartons for treatment, so the dose must be strong enough to irradiate every part of the package and that could lead to some products being 'overly treated,' which could render the product unappetizing.'' Thus, FWW asserts that pathogen reduction may require strong irradiation doses that will result in organoleptic degradation.

It appears from the objection that FWW has misinterpreted the intended technical effect from irradiation of fresh lettuce and fresh spinach to be the elimination of microbial contamination instead of the control of microbial contamination, as stated in the final rule. FWW provides no information to call into question our conclusions that the irradiation of fresh lettuce and fresh spinach is safe and will achieve the intended technical effect of controlling microbial contamination at doses not to exceed 4.0 kGy. In addition, we acknowledge that radiation-induced chemical changes, if sufficiently large, may cause changes in the organoleptic properties of the food. However, such organoleptic changes do not necessarily render the food unsafe, and FWW has not provided any evidence that would establish a link between organoleptic changes and the safety of irradiated foods. Moreover, food processors have an incentive to minimize the extent of the chemical changes in the food to avoid undesirable effects on taste, odor, color, or texture. Therefore, we are denying FWW's objection and request for a hearing because a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)).

FWW also asserted that irradiation is not effective against all food-borne pathogens (e.g., viruses) and could lead consumers to an incorrect conclusion that a product is safe even though it may still be contaminated. While we recognize that irradiation is not effective against viruses, the final rule permitting the irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy is not predicated on the irradiation treatment eliminating all potential pathogens. In the final rule, we concluded that the use of irradiation up to a maximum dose of 4.0 kGy on fresh lettuce and fresh spinach was safe. During the review, we considered chemical, toxicological, nutritional, and microbiological effects resulting from the application of ionizing radiation to fresh lettuce and fresh spinach. It was demonstrated that the petitioned use of irradiation would not raise safety concerns and that the treatment achieved its intended technical effects (i.e., reduction of microorganisms and extension of shelf life). Therefore, we are denying FWW's objection and request for a hearing. FWW has not provided any evidence to demonstrate that the final rule would lead consumers to an incorrect conclusion that a product is safe even though it may still be contaminated; a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)). In addition, FWW's assertion that irradiation is not effective against all food-borne pathogens is not determinative with respect to the action requested; a hearing will not be granted unless resolution of the factual issue in the way sought is adequate to justify the action requested (§ 12.24(b)(4)).

V. Summary and Conclusion

Section 409 of the FD&C Act requires that a food additive be shown to be safe before marketing. Under 21 CFR 170.3(i), a food additive is ''safe'' if ''there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.'' In our August 22, 2008, final rule approving the use of irradiation of fresh lettuce and fresh spinach up to a maximum dose of 4.0 kGy, we concluded, based on our evaluation of the data submitted in the petition and other relevant material, that the petitioned use of irradiation is safe for its intended use for the control of food-borne pathogens and extension of shelf life in fresh lettuce and fresh spinach.

The petitioner has the burden to demonstrate the safety of the additive to gain FDA approval. However, once we make a finding of safety in an approval document, the burden shifts to an objector, who must come forward with evidence that calls into question our conclusion (see section 409(f)(1) of the FD&C Act).

CFS and FWW have not established that we overlooked or misinterpreted significant information in the record to reach our conclusion that the use of irradiation up to a maximum dose of 4.0 kGy for control of food-borne pathogens and extension of shelf life in fresh lettuce and fresh spinach is safe. Therefore, we have determined that the final rule should not be modified or revoked based on the objections. We are also denying the requests for a hearing because the objections do not meet the standard for granting a hearing as discussed in this document. In addition, FWW's request for a stay of the effectiveness of the August 22, 2008, regulation until a hearing is held is moot because we are denying all hearing requests. Thus, we are confirming August 22, 2008, as the effective date of the regulation.

VI. 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 (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, under Docket No. FDA–1999–F–2405 (formerly 1999F–5522) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at *http://www.regulations.gov*. References without asterisks are not on display; they are available as published articles and books.

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Dated: February 19, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2014–03976 Filed 2–24–14; 8:45 am]

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DEPARTMENT OF THE TREASURY

Financial Crimes Enforcement Network

31 CFR Parts 1010 and 1030

RIN 1506–AB14

Anti-Money Laundering Program and Suspicious Activity Report Filing Requirements for Housing Government Sponsored Enterprises

AGENCY: Financial Crimes Enforcement Network (''FinCEN''), Treasury.

ACTION: Final rule.

SUMMARY: FinCEN, a bureau of the Department of the Treasury (''Treasury''), is issuing this Final Rule