Rules and Regulations

Federal Register
Vol. 70, No. 157
Tuesday, August 16, 2005

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 71

[Docket No. FAA–2005–21703; Airspace Docket No. 05–ACE–19]

Modification of Legal Description of the Class D Airspace; and Class E Airspace; Topeka, Forbes Field, KS

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Direct final rule; confirmation of effective date.

SUMMARY: This document confirms the effective date of the direct final rule which revises Class D and Class E airspace at Topeka, Forbes Field, KS.

DATES: *Effective:* 0901 UTC, October 27, 2005.

FOR FURTHER INFORMATION CONTACT: Brenda Mumper, Air Traffic Division, Airspace Branch, ACE–520A, DOT Regional Headquarters Building, Federal Aviation Administration, 901 Locust, Kansas City, MO 64196; telephone: (816) 329–2524.

SUPPLEMENTARY INFORMATION: The FAA published this direct final rule with a request for comments in the **Federal Register** on July 12, 2005 (70 FR 39914). The FAA uses the direct final rulemaking procedure for a non-controversial rule where the FAA believes that there will be no adverse public comment. This direct final rule advised the public that no adverse comments were anticipated, and that unless a written adverse comment, or a written notice of intent to submit such an adverse comment, were received within the comment period, the regulation would become effective on October 27, 2005. No adverse comments were received, and thus this notice confirms that this direct final rule will become effective on that date.

Issued in Kansas City, MO on August 3, 2005.

Elizabeth S. Wallis,

Acting Area Director, Western Flight Services Operations.

[FR Doc. 05–16158 Filed 8–15–05; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 71

[Docket FAA 2005–21522; Airspace Docket No. 05–AWP–6]

Establishment of Class E Surface Area, South Lake Tahoe, CA

AGENCY: Federal Aviation Administration (FAA) DOT.

ACTION: Final Rule; correction.

SUMMARY: The Federal Aviation Administration (FAA) published in the **Federal Register** of July 7, 2005, a document establishing Class E Surface Area at South Lake Tahoe, CA. The location of the airport was incorrectly published, this action amends the legal description and corrects the longitude coordinate. The amended description replaces all references to South Lake Tahoe, CA airport.

EFFECTIVE DATE: September 15, 2005.

FOR FURTHER INFORMATION CONTACT: Larry Tonish, Airspace Specialist, Airspace Branch, AWP–520.1, Air Traffic Organization, Western Terminal Operations, Federal Aviation Administration, 15000 Aviation Boulevard, Lawndale, California 90261, telephone (310) 725–6539.

SUPPLEMENTARY INFORMATION: The FAA published a document in the **Federal Register** of July 7, 2005, Docket FAA 2005–21522; Airspace Docket No. 05–AWP–06 (70 FR 39175), establishing Class # Surface Area at South Lake Tahoe, CA. In that rule the longitude coordinate was incorrectly published. The correct coordinate should be 119°59′44″. This document corrects the longitude coordinate.

Correction to the Final Rule

■ In consideration of the foregoing, the Federal Aviation Administration amends 14 CFR part 71 as follows:

PART 71—DESIGNATION OF CLASS A, CLASS B, CLASS C, CLASS D AND CLASS E AIRSPACE AREAS; AIRWAYS; ROUTES; AND REPORTING POINTS

■ 1. The authority citation for 14 CFR, part 71 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40103, 40113, 40120; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389.

§ 71.1 [Corrected]

■ 2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9M, Airspace Designations and Reporting Points, dated August 30, 2004, and effective September 16, 2004, is amended as follows:

Paragraph 6002 *Class E Airspace Designated as Surface Areas.*

* * * * *

AWP CA E2 South Lake Tahoe, CA [Established]

South Lake Tahoe Airport, CA
(Lat. 38°53′38″ N., long. 119°59′44″ W.)

Within a 4.3-mile radius of the South Lake Tahoe Airport.

* * * * *

Issued in Los Angeles, California, on August 1, 2005.

John Clancy,

Area Director, Western Terminal Operations.

[FR Doc. 05–16154 Filed 8–15–05; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 179

[Docket No. 1999F–4372]

Irradiation in the Production, Processing, and Handling of Food

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of ionizing radiation for control of *Vibrio* species and other foodborne pathogens in fresh or frozen molluscan shellfish (e.g., oysters, mussels, clams, etc.). This action is in

response to a petition filed by the National Fisheries Institute and the Louisiana Department of Agriculture and Forestry.

DATES: This rule is effective August 16, 2005. Submit written or electronic objections and requests for a hearing by September 15, 2005. See section VI of this document for information on the filing of objections.

ADDRESSES: You may submit written or electronic objections and requests for a hearing identified by Docket No. 1999F–4372, by any of the following methods:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.
- E-mail: *fdadockets@oc.fda.gov*. Include Docket No. 1999F–4372 in the subject line of your e-mail message.
- FAX: 301–827–6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

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

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

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

SUPPLEMENTARY INFORMATION:

Table of Contents

I. Background

In a notice published in the **Federal Register** of October 19, 1999 (64 FR 56351), FDA announced that a food additive petition (FAP 9M4682) had been filed by the National Fisheries Institute, 1901 North Fort Myer Dr., Arlington, VA 22209, and the Louisiana Department of Agriculture and Forestry, P.O. Box 3334, Baton Rouge, LA 70821. The petition proposed that the food additive regulations in part 179, *Irradiation in the Production, Processing, and Handling of Food* (21 CFR part 179), be amended to provide for the safe use of approved sources of ionizing radiation for control of *Vibrio* and other foodborne pathogens in fresh or frozen molluscan shellfish.

II. Safety Evaluation

Under section 201(s) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(s)), a source of radiation used to treat food is defined as a food additive. The additive is not added to food literally, but is rather a source of radiation used to process or treat food such that, analogous to other food processing technologies, its use can affect the characteristics of the food. In the subject petition, the intended technical effect is for control of foodborne pathogens, including but not limited to *Vibrio* bacteria, that might be present in fresh or frozen molluscan shellfish.

In evaluating the safety of a source of radiation to treat food intended for human consumption, the agency must identify the various effects that may result from irradiating the food and assess whether any of these effects pose a public health concern. In this regard, the following three areas of concern need to be addressed: (1) Potential toxicity, (2) nutritional adequacy, and (3) potential microbiological risk from the treated food. Each of these areas is discussed in detail in this document. FDA has fully considered the data and studies submitted in the subject petition as well as other data and information relevant to safety.

A. Analyses of Data by the World Health Organization

Based on a joint FAO/IAEA/WHO[1] Committee's conclusion on the toxicological, microbiological safety and nutritional adequacy of irradiated foods, the Codex Alimentarius Commission (Codex) published its standard for irradiated foods in 1983 (revised in 2003) for adoption by Codex member countries (Refs. 1 and 2). This standard was based on the conclusion that the irradiation of any food commodity at an overall average dose of up to 10 kiloGray (kGy) presents no concerns. The newly revised standard (2003) states that the

> [m]inimum absorbed dose should be sufficient to achieve the technological purpose and the maximum absorbed dose should be less than that which would compromise consumer safety, wholesomeness [of the food] or would adversely affect structural integrity, functional properties, or sensory attributes. The maximum absorbed dose delivered to a food should not exceed 10 kGy, except when necessary to achieve a legitimate technological purpose.

(Ref. 2) The original version of the standard explains in a footnote that ''wholesomeness [in the context of the standard] refers to safety for consumption of irradiated foods from the toxicological point of view * * * and that irradiation up to an overall average dose of 10 kGy introduces no special nutritional or microbiological problems.''

FDA did not adopt the 1983 Codex recommendations because, at that time, it had not sufficiently analyzed the issues of nutritional adequacy and microbiological safety for all foods at all doses, nor had the agency pursued the analysis of toxicity beyond the examination of individual studies (62 FR 64107 at 64112, December 3, 1997).

At the request of one of its member states, WHO conducted a subsequent review and analysis of the safety data on irradiated food (Ref. 3). WHO

[1] FAO is the Food and Agriculture Organization of the United Nations; IAEA is the International Atomic Energy Agency; and WHO is the World Health Organization.

considered the extent to which data on one type of food can be extrapolated to other foods and the extent to which individual studies of irradiated foods can be integrated into a single database to be evaluated as a whole, as opposed to separate evaluations of a series of individual studies (62 FR 64107 at 64112). This review included all of the studies in FDA's files considered to be reasonably complete by the agency, as well as those studies that appeared to be acceptable but had some deficiencies interfering with interpretation of the data (51 FR 13376 at 13378, April 18, 1986). WHO's review also included data from the U.S. Department of Agriculture (USDA) and from the Federal Research Centre for Nutrition at Karlsruhe, Germany (62 FR 64107 at 64112). WHO concluded that while levels of some vitamins are decreased when food is irradiated at doses relevant for food irradiation, few vitamins are severely affected, with the exception of thiamine and vitamin E. However, these losses are small (on the order of 10 to 20 percent or less) at or below an overall average absorbed dose of 10 kGy and are comparable to losses seen with other forms of food processing, such as thermal processing and drying (Ref. 3).

B. Radiation Chemistry

Scientists have compiled a large body of data regarding the effects of ionizing radiation on different foods under various conditions of irradiation. These data indicate that the effects of ionizing radiation on the characteristics of treated foods are a direct result of the chemical reactions induced by the absorbed radiation. The types and amounts of products generated by radiation-induced chemical reactions (''radiolysis products'') depend on both the chemical constituents of the food and on the specific conditions of irradiation. The principles of radiation chemistry also govern the extent of change, if any, in both the nutrient levels and the microbial load of irradiated foods. For a detailed discussion and evaluation of radiation chemistry, nutrition, toxicology, and microbiology related to irradiation of flesh-based foods under various conditions of use, see the agency's final rule permitting the irradiation of meat (62 FR 64107). In the current rulemaking, FDA has reviewed relevant data and information regarding radiation chemistry as it applies specifically to fresh or frozen molluscan shellfish irradiated at absorbed doses not to exceed 5.5 kGy.

The major components of fresh or frozen molluscan shellfish are water, protein, and lipid. Irradiation of water produces reactive hydroxyl and hydrogen radicals. These radicals can either recombine to form water, hydrogen gas, or hydrogen peroxide, or react with other components of molluscan shellfish. While the most significant effect of radiation-processing on the protein and lipid components of fresh or frozen molluscan shellfish results from the chemical reactions induced by hydroxyl radicals generated from the radiolysis of the water, radiolysis products of protein and lipid may also result from directly absorbed radiation. These radiolysis products, however, form in very small amounts and are usually the same as compounds found in foods that have not been irradiated (Ref. 4).

The amounts of radiolysis products generated in a particular food are directly proportional to the radiation dose. Therefore, FDA can draw conclusions about the amounts of radiolysis products expected to be generated at radiation doses relevant to the subject petition by extrapolating from data obtained at higher doses for foods of similar composition irradiated under similar conditions. In general, the types of products generated by irradiation are similar to those products produced by other methods of food processing, such as canning, cooking, etc., because all chemical reactions caused by the addition of energy must follow the laws of chemistry. The radiation chemistry of food is also strongly influenced by the physical state of the food (solid, liquid, dry, or frozen) during irradiation. For example, the extent of chemical change that occurs in a particular food in the dry or frozen state will be less than the change that occurs in the same food when liquid water is present, all other conditions (including dose and ambient atmosphere) being equal, because indirect reaction products from water will be minimized (Ref. 5).

During the course of reviewing chemical effects of irradiation as part of the evaluation of this and other petitions, FDA became aware of a reference that suggested that irradiating apple juice may produce furan (Ref. 6). Because furan has been shown to cause cancer in laboratory animals, FDA initiated research on whether the referenced report was accurate and whether furan was a common radiolysis product in food. FDA has confirmed that certain foods form furan in low quantities when irradiated and also that some foods form furan when heated. Studies on the irradiation of molluscan shellfish show that if furan is formed when molluscan shellfish are irradiated, it is formed at levels that are undetectable, or below the background levels of natural furan formation (Ref. 7). Therefore, the consumption of irradiated molluscan shellfish will not increase the amount of furan in the diet and is not an issue with this petition.

In the **Federal Registers** of May 2, 1990 (55 FR 18538), and December 3, 1997 (62 FR 64107), FDA issued final rules permitting the use of ionizing radiation for the control of foodborne pathogens in poultry and meat, respectively (referred to henceforth as the poultry and meat final rules). In the poultry final rule, the agency concluded that poultry irradiated at a dose not to exceed 3 kGy was safe. In the meat final rule, the agency concluded that refrigerated uncooked meat, meat byproducts, and meat food products, as defined in Title 9 of the Code of Federal Regulations (CFR), irradiated at doses up to 4.5 kGy are safe, and that frozen meat, meat by-products, and meat food products irradiated at doses up to 7.0 kGy are safe. Because meat is high in protein, lipid, and water, the radiation chemistry of proteins, lipids, and water (in both the liquid and frozen state) was extensively discussed in the meat final rule. The radiation chemistry of proteins and lipids discussed in the meat final rule is also relevant to other flesh foods, including foods such as poultry and fish, that may be referred to as ''meat'' in common usage, but that do not conform to the definition of meat in Title 9 of the CFR. Molluscan shellfish, depending on the species, differ from other flesh foods in that they contain between 2 and 6 percent carbohydrate, up to 20 percent protein, and up to 10 percent fat; the remainder is primarily water. While the carbohydrate level is higher than in other flesh foods, the level is still low.

1. Protein

With respect to proteins, several types of reactions can occur as a result of irradiation. One type of reaction is the breaking of a small number of peptide bonds to form polypeptides of shorter length than the original protein. Radiation-induced aggregation or cross-linking of individual polypeptide chains can also occur; these processes result in protein denaturation. In irradiated flesh foods, most of the radiolytic products derived from proteins have the same chemical composition regardless of the protein sources, but are altered in their secondary and tertiary structures. These changes are similar to those that occur as a result of heating, but in the case of irradiation, such changes are far less pronounced and the amounts of reaction products generated are far lower (Refs. 4 and 8). Studies have established that

there is little change in the amino acid composition of fish irradiated at doses below 50 kGy (Ref. 9), which is well above the petitioned maximum absorbed dose for molluscan shellfish. Therefore, no significant change in the amino acid composition of fresh or frozen molluscan shellfish is expected to occur under the conditions set forth in this regulation.

2. Carbohydrate

The main effects of ionizing radiation on carbohydrates in foods have been reviewed previously in the literature and by WHO (Refs. 5, 10, and 11). One of the main effects of ionizing radiation is the abstraction of hydrogen from the carbon-hydrogen bonds of the carbohydrate, resulting in directly ionizing and exciting the carbohydrate molecule. Carbohydrate radicals may result from ionization of monosaccharides such as glucose or polysaccharides such as starch. Radiolysis products formed from starches of different origin are reported to be qualitatively similar (Refs. 5 and 11). In polysaccharides, the glycosidic linkages between constituent monosaccharide units may be broken, resulting in the shortening of polysaccharide chains and reduction in the viscosity of polysaccharides in solution. Starch may be degraded into dextrins, maltose, and glucose. Sugar acids, ketones, and other sugar monosaccharides may also be formed as a result of ionizing radiation. Irradiation of carbohydrates at doses up to 10 kGy has minimal effect on the carbohydrate functionality. The overall effects of ionizing radiation are the same as those caused by cooking and other food processing treatments. Carbohydrates that are present as a component of food are less sensitive to the effects of irradiation than pure carbohydrates (Ref. 5). No significant change in the carbohydrate composition of fresh or frozen molluscan shellfish is expected to occur under the conditions set forth in this regulation, i.e., a maximum absorbed dose of 5.5 kGy.

3. Lipid

The meat final rule also discussed the radiation chemistry of lipids (predominantly triglycerides in meat). A variety of radiolysis products derived from lipids have been identified, including fatty acids, esters, aldehydes, ketones, alkanes, alkenes, and other hydrocarbons (Refs. 12 and 13). Identical or analogous compounds, however, are also found in foods that have not been irradiated. In particular, heating food produces the same types of compounds, but in amounts far greater than the trace amounts produced from irradiating food (Refs. 4 and 14). In addition, alkylcyclobutanones (ACBs), which are formed in small quantities when fats are exposed to ionizing radiation, have been identified in meat and poultry. The specific ACBs formed will depend on the fatty acid composition of the food. For example, 2-dodecylcyclobutanone (2–DCB) has been reported to be formed from palmitic acid in amounts from 0.3 to 0.6 microgram per gram lipid per kGy (µg/g lipid/kGy) from irradiated chicken (Ref. 15). Other researchers have found that (2—DCB) is formed at significantly lower rates, 0.04 µg/g lipid/kGy from ground beef (Ref. 16). For comparison, ground beef tallow contains approximately 25 percent palmitic acid and chicken fat contains approximately 22 percent palmitic acid.

One major difference between fish (including shellfish and finfish) and other flesh foods is the predominance of polyunsaturated fatty acids (PUFAs) in the lipid phase of fish. PUFAs are a subclass of lipids that have a higher degree of unsaturation in the hydrocarbon chain than the saturated (e.g., stearic acid) or monounsaturated (e.g., oleic acid) fatty acids. Due to the higher level of unsaturation, PUFAs are generally more readily oxidized than saturated fatty acids. Therefore, PUFAs could be more radiation-sensitive than other lipid components, as observed in some studies of irradiated oil. However, evidence from meat studies suggests that the protein component of meat may protect lipids from oxidative damage (Ref. 5). Because the lipid fraction of meat consists primarily of saturated and monounsaturated fatty acids with negligible quantities of PUFAs, FDA did not explicitly address the radiation chemistry of PUFAs in its previous reviews.

The effects of irradiation on PUFAs in fish have been described in several studies reviewed by FDA. Adams *et al.* studied the effects of radiation on the concentration of PUFAs in herring and showed that irradiation of herring fillets at sterilizing doses (50 kGy), well above the petitioned maximum dose for molluscan shellfish, had no effect on the concentration of PUFAs (Ref. 17). Similarly, Armstrong *et al.* conducted research on the effects of radiation on fatty acid composition in fish and concluded that no significant changes occurred in the fatty acid profiles upon irradiation at 1, 2, or 6 kGy (Ref. 18). The authors also concluded that variations in fatty acid composition between individual samples were greater than any radiation-induced changes.

Sant'ana and Mancini-Filho studied the effects of radiation on the distribution of fatty acids in fish (Ref. 19). They studied two monounsaturated fatty acids and seven PUFAs (including three different omega-3 fatty acids) before and after irradiation at doses up to 3 kGy. The authors observed insignificant changes in the concentration of total monounsaturated fatty acids and an approximately 13 percent decrease in total PUFAs at the highest dose, largely attributable to a loss of the long chain PUFAs, including docosahexaenoic acid. The overall change for essential fatty acids (e.g., linoleic and linolenic acids) was minimal (less than 3 percent). The authors also observed an increase in lipid oxidation based on levels of thiobarbituric acid reactive substances, but noted that antioxidants such as tocopherol protect against lipid oxidation (Ref. 4).

In addition, a study summarized in an International Consultative Group on Food Irradiation monograph compared the fatty acid composition of unirradiated and irradiated herring oil (Ref. 20). The profile for 12 fatty acids was compared to controls 1 day and 28 days after irradiation. Only two fatty acids appeared to have decreased by day 28 following irradiation at 50 kGy (Ref. 4).

Research conducted by FDA on various species of seafood also demonstrated that the concentrations of PUFAs are not significantly affected by irradiation (Refs. 21 and 22). Therefore, based on the totality of evidence, the agency concludes that no significant loss of PUFAs is expected to occur in the diet under the conditions of irradiation set forth in this regulation. In summary, FDA's review of the radiation chemistry of proteins and lipids in the subject petition raises no issues that have not been considered previously in the meat and poultry final rules (Ref. 4).

C. Assessment of Potential Toxicity

In the safety evaluation of irradiated meat and poultry, the agency examined all of the available data from toxicological studies relevant to the safety of irradiated flesh-based foods, including studies on fish high in PUFAs. These included 24 long-term feeding studies, 10 reproduction/teratology studies, and 15 genotoxicity studies with flesh-based foods irradiated at doses from 6 to 74 kGy. No toxicologically significant adverse effects attributable to irradiated flesh foods were observed in any of the studies (62 FR 64107 at 64112 and 64114).

The proposed maximum absorbed dose of 5.5 kGy for fresh and frozen molluscan shellfish in the subject petition is somewhat higher than the currently permitted maximum dose for the irradiation of non-frozen meat. However, FDA previously evaluated the long-term toxicological studies of flesh foods fed at a range that includes absorbed doses that are either similar to or considerably higher than the absorbed dose requested in this petition. In addition, the absorbed dose exceeded 50 kGy in many studies with no adverse effects reported. Therefore, these data demonstrate that molluscan shellfish irradiated at levels up to the dose proposed in this petition will not present a toxicological hazard (Ref. 8).

In summary, FDA has reviewed a large body of data relevant to the assessment of potential toxicity of irradiated foods. While all of the studies are not of equal quality or rigor, the agency concludes that the quantity and breadth of testing and the number and significance of endpoints assessed would have identified any real or meaningful risk. The overwhelming majority of studies showed no evidence of toxicity. On those few occasions when adverse effects have been reported, FDA finds that those effects have not been consistently produced in related studies conducted at a higher dose or longer duration, as would be expected if the effects were attributable to irradiation (62 FR 64107 at 64112 and 64114). Therefore, based on the totality of evidence, FDA concludes that irradiation of fresh and frozen molluscan shellfish under the conditions proposed in this petition does not present a toxicological hazard.

D. Microbiological Profile of Molluscan Shellfish

Vibrio bacteria predominate in estuarine environments, and consequently, are naturally present in most finfish and shellfish (Ref. 23). Most cases of reported diseases attributed to *Vibrio* species are associated with consumption of raw molluscan shellfish, particularly raw oysters. Although *Vibrio* species from shellfish infect relatively few individuals, they can cause severe illness, including mortality. Of the 12 *Vibrio* species known to cause human infections, 8 have been associated with consumption of food. *V. parahaemolyticus* and *V. vulnificus* are most commonly isolated from oysters. *V. vulnificus* is associated with 95 percent of all seafood-related deaths in the United States (Ref. 24).

In general, the subject petition relies on published or other publicly available information or material from previous food additive petitions to address microbiological issues. The petitioner has documented that *Vibrio* species in uncooked molluscan shellfish provide a significant public health risk. *Vibrio* bacteria are highly sensitive to ionizing radiation and are usually eliminated by doses as low as 0.5 kGy. Published D_{10} values[2] for *V. parahaemolyticus* and other *Vibrio* species range from 0.02 to 0.4 kGy (Ref. 25).

Control of contaminating *Salmonella* or *Listeria* generally requires higher doses than for *Vibrio* species, because the D_{10} values are higher, about 0.5 to 1.0 kGy and 0.4 to 0.6 kGy, respectively (Ref. 26). Several publications referenced in the subject petition state that these three genera can be eliminated by doses well under 10 kGy. Numerous studies demonstrate that a dose of 5 kGy will reduce a population of *Salmonella* serotypes, *Staphylococcus aureus*, *Shigella*, and *Vibrio* by at least six log cycles. Other studies report 5-log reductions for *Listeria* and *Salmonella* at 2.3 kGy and 2.8 kGy. In addition, D_{10} values for irradiation cited in published literature for several *Salmonella* serotypes in various fresh foods ranged from 0.2 to 0.9 kGy. Therefore, irradiation at doses up to the dose limit in the regulation could significantly reduce the populations of these organisms (Ref. 25).

Clostridium botulinum (*C. botulinum*) type E can sometimes be found in seafood. Because this organism is relatively resistant to radiation, as compared to non-spore forming bacteria, the petitioner provided data regarding the likelihood that *C. botulinum* would grow and produce toxin in irradiated molluscan shellfish. Included in the petition's references is an in-depth discussion of the likelihood for outgrowth and toxin production by *C. botulinum* type E in fish (Ref. 27). The author cites studies conducted in his laboratory on the effect of storage temperature and irradiation on toxin production by *C. botulinum* type E in fish. In these studies, no toxin was detected after incubation with fish of up to 10^5 organisms at 0 degrees Celsius for 8 weeks, well beyond the shelf life of these products. At 5 degrees Celsius, no toxin was produced for up to 6 weeks of storage in inoculated fish that had not been irradiated or for up to 7 weeks when irradiated at 2 kGy. Thus, it took longer for toxin to be produced in the irradiated fish than in fish that were not irradiated. Additionally, the time required for toxin production, 7 weeks, is far beyond the shelf life of fresh seafood. Therefore, irradiation would not increase the risk from botulinum toxin.

Current Hazard Assessment and Critical Control Point plans in effect for molluscan shellfish require storage under proper conditions, including maintenance at controlled temperatures. Therefore, irradiation can serve as an effective method for the primary intended use of eliminating populations of *Vibrio* species and other pathogens in molluscan shellfish without adding a significant risk from the growth of and toxin production by *C. botulinum* type E (Ref. 25).

The subject petition includes data and information that support the effectiveness of the proposed irradiation of fresh and frozen molluscan shellfish at a maximum absorbed dose of 5.5 kGy to control *Vibrio* species and other foodborne pathogens. While the data show that irradiation is effective in reducing the levels of *Vibrio* species and other bacteria in fresh and frozen molluscan shellfish, the data also show that irradiation will not increase the risk of toxin production from germinated spores of *C. botulinum* type E.

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

E. Nutritional Considerations

Lipids are a component of molluscan shellfish contributing approximately 20 to 30 percent to the caloric value of molluscan shellfish. PUFAs are a significant source of omega-3 and omega-6 fatty acids and are therefore nutritionally important components of the fat of molluscan shellfish. As noted in section II.A of this document, PUFA levels were not reduced significantly by ionizing radiation. Additionally, the amount of omega-3 and omega-6 PUFAs can vary widely within a single species and between species of molluscan shellfish. The omega-3 fatty acid content among most species varies within a factor of 2, and the total PUFA content can vary by more than a factor of 10 (omega-3 and omega-6 PUFAs) within an individual species. Furthermore, molluscan shellfish are only one of several fish sources of long chain PUFAs. Because of the variety of seafood sources of long chain PUFAs, the variation of fatty acid content in molluscan shellfish, and the observed insensitivity of PUFAs to irradiation, FDA concludes that irradiation of fresh

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

and frozen molluscan shellfish under the conditions proposed will not adversely affect the nutritional adequacy of the diet with respect to PUFAs (Ref. 8).

Molluscan shellfish contain several B-vitamins including thiamine, niacin, vitamin B6, and vitamin B12.[3] Individual food intake data is available from nationwide surveys conducted by the USDA. These surveys were designed to monitor the types and amounts of foods eaten by Americans and food consumption patterns in the U.S. population. FDA routinely uses these data to estimate exposure to various foods, food ingredients, and food contaminants. The relative contribution of the food category ''shellfish and fish (excluding canned tuna)'' is less than 3 percent of the dietary intake for thiamine, niacin, and vitamin B6 (Ref. 28). Fish and shellfish are, however, significant contributors to vitamin B12 intake among U.S. adults, contributing to approximately 20 percent of the total vitamin B12 intake.

Irradiation of any food, regardless of the dose, has no effect on the levels of minerals that are present in trace amounts (Ref. 5). Levels of certain vitamins, on the other hand, may be reduced as a result of irradiation. The extent to which this reduction occurs depends on the specific vitamin, the type of food, and the conditions of irradiation. Not all vitamin loss is nutritionally significant, however, and the extent to which a reduction in a specific vitamin level is significant depends on the relative contribution of the food in question to the total dietary intake of the vitamin. While thiamine is among the most radiation sensitive, the more nutritionally significant vitamin in fish and shellfish, vitamin B12, is extremely resistant to radiation.

Based on the available data and information, FDA concludes that irradiation of fresh or frozen molluscan shellfish under the conditions set forth in the regulation in this document will have no adverse impact on the nutritional adequacy of the diet.

III. Comments

FDA has received numerous letters, primarily form letters, from individuals that state their opinions regarding the potential dangers and unacceptability of irradiating food. None of these letters contain any substantive information that can be used in a safety evaluation of irradiated molluscan shellfish.

Additionally, FDA received several comments from Public Citizen (PC) and the Center for Food Safety (CFS) requesting the denial of this and other food irradiation petitions. The comments were largely of a general nature and not necessarily specific to the petitioned requests. Some of the comments specifically questioned a report of a Joint FAO/IAEA/WHO Study Group on the wholesomeness of foods irradiated with doses above 10 kGy. Because the comments were addressed to the Docket for this rulemaking, the comments and FDA's response are discussed as follows:

A. Studies Reviewed in the 1999 FAO/IAEA/WHO Report on High-Dose Irradiation

(1) One comment states that the petition should be denied because there are four positive studies mentioned but mischaracterized in the 1999 FAO/IAEA/WHO report on high-dose irradiation. The comment states:

> The 1999 FAO/IAEA/WHO report is the most detailed recent review of food irradiation safety. CFS [Center for Food Safety] anticipates that FDA will seek to rely on it. It is critical that FDA understand the defects in that report before making a determination on the above-referenced additive petition...the four studies were incorrectly classified as ''negative for high-dose irradiation effect, possible effect of nutrition or diet.''* * *
>
> The 1999 FAO/IAEA/WHO report acknowledged the Anderson *et al.* study (on laboratory animal diets) showed ''*evidence of weakly mutagenic effect*'' with one diet that was irradiated, yet it classified the study as ''*negative for high-dose irradiation effect, possible effect of nutrition or diet*'' (p. 117). However, no indication exists that the irradiated standard PRD laboratory diet that produced the mutagenic effect was otherwise deficient. Further, the unirradiated control PRD diet did not produce the mutagenic effect. Anderson *et al.* found irradiation of the diet produced the effect. The 1999 FAO/IAEA/WHO report's classification of the study as ''negative'' was unfounded. (Emphasis in original.)

In the study performed by Anderson *et al.* (1981) mice were fed four laboratory diets irradiated at 10 kGy, 25 kGy, and 50 kGy (Ref. 29). Mice were also fed unirradiated diets as a negative control. Additionally, mice were injected intraperitoneally with a known mutagen, cyclophosphamide, at 200 mg per kg of body weight (mg/kg body weight) as a positive control. The study report stated that mice consuming one diet (PRD diet)[4] irradiated at 50 kGy resulted in a slight increase in post-implantation deaths over the unirradiated diet when compared to the positive control. The other three irradiated diets showed no significant increases in early post-implantation death. The comment provides no information to explain why the Anderson *et al.* study on radiation-sterilized laboratory diets should be considered relevant to the conditions proposed in this petition for the irradiation of molluscan shellfish to a maximum absorbed dose that will not exceed 5.5 kGy. Moreover, the comment provides no analysis of the study and no information to demonstrate that the ''weakly mutagenic effect'' associated with the laboratory diet irradiated at 50 kGy is attributable to irradiation of the diet.

(2) The comment states that ''[a] thorough discussion of the Bugyaki *et al.* study in a 1970 FAO/IAEA/WHO Expert Committee report highlighted it as a significant positive finding.'' The comment goes on to state:

> The 1999 FAO/IAEA/WHO report admitted that Bugyaki *et al.* showed ''*chromosomal abnormalities in germ cells due to formation of peroxides and radicals,*'' but - without explanation - classified the study as ''*negative for high-dose irradiation effect, possible effect of nutrition or diet*'' (p. 118). That is plain inconsistency; the 'peroxides and radicals' resulted from the irradiation (see Bugyaki *et al.*, at p. 118: ''*... some of the changes produced by radiation — the free radicals for example — will disappear with time.*'' [translated from French]). Further, the same Expert Committee agreed 29 years earlier that Bugyaki *et al.* demonstrated ''*certain disturbing effects*'' of high dose irradiation. That Committee did not discount the effects as artifacts of nutrition or diet, as the 1999 Committee did. The 1999 FAO/IAEA/WHO report's classification of this study as 'negative' again lacks a rational foundation. (Emphasis in original.)

In Bugyaki *et al.*, a 1968 report on irradiated wheat, mice were fed a diet containing 50 percent freshly irradiated wheat meal (50 kGy); the balance was basic food powder (the basic food powder was described by the author to contain 55 percent vegetable matter, 35 percent animal matter, and 10 percent complementary nutrients) (Ref. 30). Control animals were fed a diet containing 50 percent wheat that had not been irradiated with the balance being the basic food powder. Because the authors were concerned that compression into pellets may affect the irradiated foods, the animals were fed the food in powder form. The authors note that there were readily observable

[3] Dietary sources of nutrients have been evaluated using the 1994/1996 Continuing Survey of Food Intakes by Individuals database.

[4] The PRD diet is a formulation of 5.125 g/100 g Barley, 10.0 g/100 g maize meal, 18.125 g/100 g oats (Sussex Ground), 20.0 g/100 g wheat, 20.0 g/100 g wheat feed, 5.0 g/100 g white fish meal (crude protein 66 percent), 2.5 g/100 g yeast, 10.0 g/100 g soya extract, 7.5 g/100 g dry skimmed milk (crude protein 33), 0.75 g/100 g salt (NaCl), and a 1.0 percent vitamin mineral supplement.

physical and chemical changes in the wheat meal irradiated at 50 kGy.

The authors state that both the treated and untreated animals developed tumors. However, the tumors found in the treated animals were different than the tumors found in the untreated animals. The authors note that the treated animals had a slight increase in anatomic-pathological lesions; however, they go on to state that there was no well defined damage. Additionally, they state that there were alterations in the meiotic chromosomes of the treated animals. The authors conclude that animals consuming a large part of their diet irradiated at doses as high as 50 kGy may deserve special attention.

The comment provides no information to demonstrate why the Bugyaki *et al* study on freshly irradiated wheat at 50 kGy is relevant to the conditions proposed in this petition for the irradiation of molluscan shellfish to a maximum absorbed dose that will not exceed 5.5 kGy. Foods irradiated at such a high dose often require careful control of temperature and atmosphere to prevent compositional changes that would make them unsuitable for food use. The agency notes that several long term feeding studies using foods irradiated under appropriate conditions at doses greater than 50 kGy demonstrated no toxicological effects that could be attributed to the irradiated foods.

(3) The comment states:

> The 1999 FAO/IAEA/WHO report states the study performed by Moutschen-Dahmen *et al.* showed ''*increased pre-implantation embryonic deaths; not confirmed by cytological analysis*'' and classified the study as ''*negative for high-dose irradiation effect, possible effect of nutrition or diet*'' (p. 115). The suggestion of an effect of nutrition or diet is unsupported. (Emphasis in original.)

The agency has previously addressed the study by Moutschen-Dahmen *et al.* (51 FR 13376 at 13387) and noted:

> There was no increase in post-implantation losses. Post-implantation losses, determined by counting dead embryos, are believed to be the most reliable and sensitive indicator of dominant lethality. The authors found only pre-implantation losses, which are much less sensitive than post-implantation losses and merely a measure of total implants dead or alive subtracted from the total number. In addition to the possibility that results of the study could be spurious, any number of factors other than dominant lethality may cause pre-implantation losses, such as a decrease in the number of eggs ovulated.
>
> If these effects were real, one would expect to see some effect on post implantation losses at a lower dose because post-implantation losses are a much more sensitive indicator than pre-implantation losses, as mentioned previously.

The agency concluded:

> Although the findings reported may be statistically significant, the authors were uncertain as to what to attribute these results. They concluded that the most probable mechanism by which these effects could be produced would be via chromosomal aberration. The studies necessary to establish an association between these effects and chromosomal aberrations were not conducted. Additional treatment levels below that conducted as mentioned previously to detect post-implantation losses or examinations of the 24 to 48 hour fertilized eggs could have proved better evidence of causality, but these studies were not conducted. Thus, although pre-implantation losses were observed, FDA concludes that there is no biological significance to this observation because it was not reproducible.

The comment provides no information to demonstrate why the Moutschen-Dahmen *et al.* (Ref. 31) study (1970) in which mice were fed a laboratory chow diet, of which 50 percent was irradiated at 50 kGy is relevant to the conditions proposed in this petition for the irradiation of molluscan shellfish to a maximum absorbed dose that will not exceed 5.5 kGy. The study was designed to look for mutations that would be lethal to the animals. Further, the comment provides no information to demonstrate that the pre-implantation deaths were caused by dominant lethal mutations that were induced by the consumption of irradiated food. Finally, the comment provides no evidence to refute the agency's previous conclusion.

(4) With regard to another study (Ref. 32), the comment states that:

> The 1999 FAO/IAEA/WHO report admits the study showed ''*significant increase in the mutation frequency induced by the high dose irradiated foods*,'' but nevertheless classified the study as ''*negative for high-dose irradiation effect, possible effect of nutrition or diet*'' (p. 115). This is patently contradictory; the 'negative' classification again lacks explanation. (Emphasis in original.)

In the study performed by Johnston-Arthur *et al.* (1975), Swiss albino mice were starved for 36 hours and then fed normal and irradiated (7.5 kGy, 15 kGy, and 30 kGy) laboratory chow for 7 hours (Ref. 32). The mice were then injected intraperitoneally with *Salmonella typhimurium* TA 1530 and the bacteria were incubated in the mice for 3 hours. The mice were then sacrificed and the bacteria were harvested and tested using the host-mediated assay test for mutagenicity. The results indicated a significant increase in the mutation frequency in the bacteria that were exposed to the 30 kGy-sterilized food. No significant differences were observed in the bacteria that were harvested from the mice fed the 7.5 kGy and 15 kGy diet when compared with the control.

The comment provides no information to demonstrate why the Johnston-Arthur *et al.* study on the irradiation sterilization of lab chow at 30 kGy is relevant to the irradiation of molluscan shellfish to a maximum absorbed dose that will not exceed 5.5 kGy. Moreover, mutation studies with *S. typhimurium* are intended to screen for possible mutations affecting animals that can be tested in long term animal studies. However, several properly conducted long term feeding studies performed on animals fed with foods irradiated at higher doses (up to 56 kGy) have shown no mutagenic effects to the subject animals.

Finally, the agency notes that the subject of this regulation is the petition (FAP 9M4682) regarding shellfish and not the 1999 FAO/IAEA/WHO report on high-dose irradiation. In its review of the published literature on the safety of irradiated foods, the agency finds that properly conducted animal feeding studies showed no evidence of toxicity attributable to irradiated food. On the few occasions when studies reported adverse effects, the effects were not consistently reproduced in related studies conducted with similar foods irradiated to doses equal to or higher than those for which the adverse effects were reported, as would be expected if the reported effect were a toxic effect caused by a radiolysis product (62 FR 64107 at 64112 and 64114).

B. Review Article

One comment submitted a paper (Kevesan and Swaminathan, 1971) that reviewed studies performed in the 1950s and 1960s on irradiated substrates and irradiated foods (Ref. 33). The comment states that numerous studies from the 1950s and 1960s found a variety of toxic effects in animal feeding and in vitro studies, which on the whole cast doubt on the safety of the technology. The comment asks FDA to ''take a closer look at the host of past positive studies cited therein.''

The comment further states:

> [A]ttempts to discount all of the past positive findings as aberrations, products of chance, or artifacts of diet will no longer suffice. These studies need further FDA review particularly in view of the 2003 Codex Alimentarius standard revision that allowed for higher absorbed doses of radiation than previously permitted.

The agency notes that the subject of FAP 9M4682 is the irradiation of molluscan shellfish to a maximum absorbed does of 5.5 kGy, not the recently revised Codex standard. Furthermore, the authors of the paper referenced by the comment do not come to the conclusion that the comment implies. Rather, the study's authors

(Kevesan and Swaminathan) conclude that ''major deficiencies in the way some of the experiments have been designed and conducted coupled with inadequacy of genetic data urgently necessitates further investigations before concluding that the irradiated food materials 'can be consumed with impunity'.''

FDA agrees with the conclusions of the review article in the context of studies performed prior to 1970. However, many properly conducted studies have been performed after this review was written. As previously noted in this document, the agency finds that properly conducted animal feeding studies showed no evidence of toxicity attributable to irradiated food. On the few occasions when studies reported adverse effects, the effects were not consistently reproduced in related studies conducted with similar foods irradiated to doses equal to or higher than those for which the adverse effects were reported, as would be expected if the reported effect were a toxic effect caused by a radiolysis product (62 FR 64107 at 64112 and 64114). The comment provides no additional information that would cause the agency to change its conclusion on the safety of irradiated food.

C. Irradiated Strawberry

One comment submitted a paper (Verschuuren, Esch, and Kooy, 1971) describing the effects of feeding rats irradiated strawberry-powder and irradiated strawberry-juice (Ref 34). The comment states that rats fed ''irradiated strawberry powder supplement showed a statistically significant growth deficit compared to the control animals fed the same diet, including the powder supplement, but which was unirradiated.'' The comment goes on to state:

FDA's internal reviewers in 1981 and 1982 (reviews are attached to study) twice classified the Verschurren (*sic*) *et al.* study as one the agency should ''accept'' without reservations, only to be later overridden by a third reviewer who was able to reclassify the study as ''reject.'' This change was based on the third reviewer's suggestion that the study was hampered by ''inadequate diet and restricted food intake,'' a surprising suggestion as nothing in the study supported that conclusion

The comment misrepresents the conclusion of one of the reviewers who did the initial review of the study. Initially, the study was accepted by two reviewers. However, upon further review by one of the initial reviewers and a third reviewer, this paper was rejected in the secondary review because of inadequate diet and restricted food intake. The comment provides no information that would alter the agency's conclusion that some of the diets were incomplete and restricted. Moreover, the comment provides no information that explains why the consumption of irradiated strawberry-powder is relevant to the consumption of irradiated molluscan shellfish with a maximum absorbed dose of 5.5 kGy.

D. Reproduction Performance

One comment states that a study conducted at Columbia University in 1954 ''supports other studies that yielded adverse health effects, which our organizations have previously submitted to this docket.''

The comment submitted part of a report, ''Termination Report—Part 1, Food Irradiation and Associated Studies, September 15, 1954,'' which was conducted at Columbia University for the U.S. Atomic Energy Commission. The report compares the fertility of ''Professor Sherman's high generation rats'' that were fed either ''Sherman diet 16'' or a ''modified Sherman diet''[5] (milk powder was replaced by skim milk powder and irradiated butterfat). The report concluded that there was a significant decrease in the fertility of the rats fed the irradiated diet. The report also mentions that there is significant vitamin E destruction; however, the comment did not include the entire results and discussion section with the authors' discussion.

FDA reviewers have previously reviewed a subsequent publication of a report of this study (Ref. 35). At the time of the study, it was not well recognized that irradiation of fat in the presence of air can stimulate oxidation leading to rancidity and high levels of peroxides. Such rancidity can lead to nutritional deficiencies due to the animals reducing their food consumption and destruction of vitamins. FDA reviewers concluded that it appears that littermates were mated and that the females were mated almost continually, allowing little time for rest between litters. If there was a nutritional or oil peroxidation and palatability problems with the diet, it would be exacerbated by the continuous breeding of the females. Considering the report's mention of considerable vitamin E destruction, the effects seen appear to be the result of a nutritionally inadequate diet, not toxicity, and would not be relevant to irradiation of molluscan shellfish.

[5] The control diet was ''Sherman diet 16,'' consisting of 1000 g ground whole wheat, 200 g whole milk powder, and 20 g salt. The ''irradiated diet'' consisted of 1000 g ground whole wheat, 147 g skim milk powder, 53 g irradiated butterfat, and 20 g salt.

E. Mutagenicity Studies

One comment states that the petition should be denied because the number of positive mutagenicity studies (including those discussed previously that were identified by the comment as mischaracterized or ignored) compares favorably with the number of negative studies. The comment states that ''[m]ore than one-third of both *in vivo* and *in vitro* studies are positive'' for mutagenicity, suggesting there is ''bias in the official posture in support of the safety of irradiation.''

The suggestion of the comment that FDA showed a ''bias in the official posture'' on the safety of the consumption of irradiated food is not supported by any substantive information.

The Bureau of Foods Irradiated Foods Committee (BFIFC) recommended that foods irradiated at a dose above 1 kGy be evaluated using a battery of mutagenicity tests to assess whether long-term feeding studies in animals were necessary (Ref. 36). Mutagenicity studies are primarily used to screen for potential mutagenic effects. Animal feeding studies are more reliable for determining the true mutagenic potential of a compound that is consumed in food (Ref 37). Moreover, one cannot draw valid conclusions from data simply by summing positive and negative results without fully evaluating the individual studies and assessing what conclusions such studies support and considering the totality of evidence. If the occasional report of a mutagenic effect were valid and significant to health, one should have seen consistent adverse toxicological effects in the many long term and reproduction studies with animals. This has not been the case.

F. International Opinions

The comment states that the petition should be denied because ''[a] majority of Parliamentary Members voted for a provision that the EU's list of foods authorised (*sic*) for irradiation should not be expanded,'' and ''[a] working group of the Codex Alimentarius Commission's Contaminants and Food Additives Committee in November, 2002, recommended *against* approval of a Codex proposal to remove the present 10 kiloGray radiation dose cap, which would allow any foods to be irradiated at any dose — regardless of how high. (Emphasis in original.)''

The agency notes that the subject of this regulation is the petition (FAP 9M4682) to permit irradiating shellfish at a dose up to 5.5 kGy, not whether the maximum dose in the Codex General Standard for Irradiated Foods should be

raised above 10 kGy. The act requires FDA to issue a regulation authorizing safe use of an additive when safety has been demonstrated under the proposed conditions of use. FDA notes that the Codex General Standard for Irradiated Foods has recently been revised (Codex 2003) by supplanting reference to a maximum overall average dose of 10 kGy with the statement that ''[t]he maximum absorbed dose delivered to a food should not exceed 10 kGy, except when necessary to achieve a legitimate technological purpose.'' (Ref. 2). The comment fails to demonstrate why the debate within Codex leading up to this change is relevant to the conditions proposed in this petition for the irradiation of molluscan shellfish to a maximum absorbed dose that will not exceed 5.5 kGy.

One comment states that the petition should be denied because of a report published by the Organisation for Economic Co-Operation and Development (OECD) which states:

Hitherto available data indicate, however, that increased rates of mutation and chromosomal aberration will probably be induced in certain cases. Although experiments indicate that the genetical (*sic*) effect, in cases where it is induced, is relatively small compared to the effect of direct exposure of animals to radiation, the same experiments indicate that the possible effect will not be negligible.

The comment goes on to state that ''[r]ather than being refuted by subsequent evidence, the OECD's statement regarding likely induction of mutations and chromosomal aberration has been confirmed in many studies, cited in this and our earlier comments.''

The 1965 OECD report, entitled ''Steering Committee for Nuclear Energy Study Group on Food Irradiation,'' reflects scientific understanding at the time it was written (Ref. 38). The document is a compendium of published and unpublished (at the time) reports on the effect of irradiated substances on a variety of organisms. The report concluded that ''it is impossible to arrive at any definite conclusion as to the presence or absence of genetic effects if irradiated food were used for human consumption or for animal feeding.'' Furthermore, the report states that more rigorous studies should be performed and when contradictory results are found, the reasons should be determined. Since the report was compiled in 1965 numerous studies have been performed on the effects of consuming irradiated foods in multiple animal species and in humans. Starting in the 1980's, FDA has reviewed these and other studies, and while many of these studies cannot individually establish safety, they still provided important information that, when evaluated collectively, supports a conclusion that there is no reason to believe that irradiation of flesh foods presents a toxicological hazard. The comment provides no evidence to refute the agency's conclusion.

G. Alkylcyclobutanones

One comment states that ''certain chemical by-products formed in food that has been irradiated, known as cyclobutanones, could be toxic enough to cause significant DNA damage, potentially leading to carcinogenic and mutagenic effects.'' In addition, the comment states that ''[t]wo major international food safety groups — CCFAC (Codex Committee on Food Additives and Contaminants), and SCF (The Scientific Committee on Food of the European Commission) — deemed the indications of toxicity strong enough to necessitate considerable additional study.''

2–ACBs have been reported as radiolysis products of fats (Refs. 39a and 39b). Studies performed by researchers have reported that certain alkylcyclobutanones can cause single strand DNA breaks detectable by the COMET[6] assay (Ref. 40). Several animal feeding studies have been conducted with fat-containing foods irradiated at doses far higher than would be used on molluscan shellfish. If 2–ACBs, at the level present in irradiated foods, were of sufficient toxicity to cause significant DNA damage, one would expect to have seen adverse effects in those studies where animals were fed meat as a substantial part of their diet. Moreover, the COMET assay has not yet reached the level of reliability and reproducibility that is needed to be considered a standard procedure for testing potential genotoxins. At present, the assay is of value primarily in basic research of cellular response to DNA damage and repair, in both *in vitro* and *in vivo* systems (Ref. 41).

Also, contrary to what is implied by the comment, the Scientific Committee on Foods of the European Commission concluded, in July 2002, ''[a]s the adverse effects noted refer almost entirely to *in vitro* studies, it is not appropriate, on the bases of these results, to make a risk assessment for human health associated with the consumption of 2–ACBs present in irradiated fat-containing foods.'' The genotoxicity of 2–ACBs has not been established by the standard genotoxicity assays nor are there any adequate animal feeding studies in existence to determine no-observed-adverse-effect levels (NOAELs) for various alkylcyclobutanones. Reassurance as to the safety of irradiated fat-containing food can be based on the large number of feeding studies carried out with irradiated foods which formed the basis for the wholesomeness assessments of irradiated foods published by FAO/IAEA/WHO.

Moreover, researchers have recently demonstrated that 2–DCB does not induce mutations in the *Salmonella* mutagenicity test or intrachromosomal recombination in *Saccharomyces cerevisiae* or the *Escherichia coli* tryptophan reverse mutation assay (Refs. 42 and 43). A further study, published in 2004, has demonstrated that the Ames assay showed no difference between 5 concentrations of 2–DCB and the controls, including samples incubated with S9. The results indicate that 2–DCB does not produce point or frameshift mutations in *Salmonella* and is not activated by S9. The study also investigated the toxicity of 2–DCB and concluded ''that the potential risk from 2–DCB, if any, is very low'' (Ref. 44).

One comment states that 2–DCB is a unique radiolysis byproduct of palmitic acid, and ''[b]ecause palmitic acid appears in molluscan shellfish in varying quantities and high percentages, the FDA should refrain from considering the petition until potential cytotoxicity and genotoxicity of 2–DCB in each type of shellfish covered by the petition is thoroughly studied.''

FDA agrees that 2–DCB is a radiation by-product of triglycerides with esterified palmitic acid and that molluscan shellfish contain significant amounts of such triglycerides. FDA previously reviewed studies in which animals were fed diets containing irradiated meat, poultry, and fish which contain triglycerides with palmitic acid (62 FR 64107 at 64113), and concluded that no adverse effects were associated with the consumption of these irradiated flesh foods. The comment provides no evidence to refute the agency's conclusion regarding the irradiation of molluscan shellfish to a maximum absorbed dose that will not exceed 5.5 kGy.

One comment states that two studies by Delincée *et al.* on the potential genotoxicity of 2–DCB were mischaracterized in the 1999 FAO/IAEA/WHO report. The comment states that while ''[t]he 1999 FAO/IAEA/WHO report properly labeled Study 5 as demonstrating a '*possible effect of high-dose irradiation*.'* * * it rationalized this by saying the level of the lipid

[6] Single cell gel electrophoresis or 'Comet assay' is a rapid and very sensitive fluorescent microscopic method to examine DNA damage and repair at individual cell level.

present in the experiment was three orders of magnitude greater than the normal lipid level in chicken meat.'' In addition, the comment states that ''[s]tudy 6 did not, in fact, use an '*extremely high level*' of 2–DCB as claimed in the WHO Secretariat's proof note. The level of 2–DCB, according to the researchers, was carefully calibrated and multiplied by the appropriate toxicological safety factor, to determine the safety of chicken irradiated for shelf sterilization.'' In summary, the comment states that ''Delincée *et al.* conclude that applying the standard toxicological safety factor of 100 below the 'no-effect level' means that 2–DCB failed the standard safety test'' and should be denied under § 170.22 (21 CFR 170.22).

In the first study cited, Delincée *et al.* incubated rat and human colon cells for 30 minutes in solutions containing 0.3-1.25 mg/ml 2–DCB and determined by the COMET assay that there were single strand DNA breaks (Ref. 45). The authors also state that they observed a cytotoxic effect at increased concentration. Cytotoxicity can confound the results of the COMET assay such that standard protocols attempt to use concentrations below that producing cytotoxicity (Ref. 46). Delincée notes that the 2–DCB concentration in the lipid fraction of chicken irradiated at 58 kGy (Raltech study) is 17 µg/g lipid (Refs. 45 and 47). Thus, the concentration of 2–DCB used in the assay was 17 to 73 times higher than that in the lipid fraction of radiation sterilized chicken. As the average dose in the Raltech study was 10 times higher than the maximum dose requested in the shellfish petition, the concentration of 2–DCB and other alkylcyclobutanones would be far lower in the lipid fraction of shellfish than in the experiment by Delincée. Moreover, the concentration reported in the study cited is the concentration in a liquid solvent (solvent not reported) in direct contact with colon cells. As one would not consume pure irradiated lipid from shellfish, the concentration of any 2–DCB from shellfish would be diluted substantially by the major components in shellfish and further by other components being consumed simultaneously. Thus, cells in the colon of humans would be in contact with concentrations more than a thousand times lower than those used in Delincée's study. In the Raltech study in mice, chicken constituted 35 percent of the diet by dry weight, and there were no adverse toxicological effects that could be attributed to the consumption of irradiated chicken.

In the second paper (Ref. 40), the authors administered 2–DCB to rats by pharyngeal tube at doses of 1.12 and 14.9 mg/kg body weight. They reported the higher concentration as equivalent to the amount found in 800 broiler chickens treated at 60 kGy (equivalent to approximately 40,000 wild eastern oysters irradiated at the maximum dose requested by the petition). They harvested colon cells from the rats 16 hours later and performed the COMET assay. Although the authors observed single strand DNA breaks at the higher concentration, no effect was seen at the lower concentration.

In its review of studies in which animals were fed diets containing beef irradiated at 56 kGy, pork at 56 kGy, poultry at 6 kGy, fish at 6 kGy, horse meat at 6.5 kGy, fish at 56 kGy, and others (62 FR 64107 at 64113), the agency found no evidence of toxicity attributable to the consumption of various flesh foods, which contain esterified palmitic acid and other fatty acids, and which should also contain 2–DCB and other alkylcyclobutanones.

Furthermore, the comment misrepresents the paper's conclusions. The comment states that the ''failure to pass the 100-fold safety factor'' means that 2–DCB fails the standard set under § 170.22, and therefore, the petition should be denied. Contrary to what the comment implies, the authors did not conclude that the ''test failed the 100-fold safety factor.'' Rather, the dose applied to the animals was set on the basis of calculations such that the lower dose would be equivalent to 100 times the amount of all 2–ACBs consumed if all fat in the diet were irradiated at a pasteurizing dose (3 kGy); and the larger dose was set to be 100 times the total alkylcyclobutanones from radiation sterilization (60 kGy) of all dietary fat. The authors noted that there was no effect at the lower dose and that the higher dose was equivalent to the amount from 800 radiation-sterilized broiler chickens and questioned this approach to the use of safety factors.

FDA notes that § 170.22 provides that ''[e]xcept where evidence is submitted which justifies use of a different safety factor, a safety factor in applying animal experimentation data to man of 100 to 1 will be used.'' FDA and food safety scientists worldwide have long agreed that the evaluation of the safety of irradiated foods requires consideration of the whole food, not the testing of each component (although identification of major radiolysis products will aid in the interpretation of data) (Ref. 5). Applying a 100-fold safety factor to a processed food is neither feasible nor rational. Similarly, testing each component of a food separately is impossible. There are too many components to test them all, and many food components that occur naturally will cause adverse effects if tested in isolation at an exaggerated dose. For example, naturally occurring food components, such as solanine from potatoes, tomatine from tomatoes or various vitamins and minerals, would cause toxic effects if consumed in amounts 100 times greater than normal. Thus, requiring a 100-fold safety factor for each component of a food (that occurs naturally or is produced through processing) is not appropriate.

An affidavit written by Dr. William Au that was submitted by CFS and PC, states that radiolysis compounds (e.g., 2–DCB) are formed during the irradiation of food and that ''[t]heir potential health hazard has not been adequately evaluated. Without conclusive evidence of the potential health consequences of these products, the safety of irradiated food cannot be assured.''

The affidavit provides no basis to conclude that the multitude of studies on irradiated foods (which contain the radiolysis products referred to) are inappropriate for the evaluation of the safety of those foods. In FDA's review of the consumption of irradiated flesh foods for a previous petition on irradiated meat, FDA concluded that ''the results of the available toxicological studies of irradiated flesh foods also demonstrates that a toxicological hazard is highly unlikely because no toxicologically significant adverse effects attributable to consumption of irradiated flesh foods were observed in any of these studies'' (62 FR 64107 at 64114). As those foods would have contained the radiolysis products, including 2–DCB, produced by the irradiation of fats, Dr. Au is incorrect in stating that its potential hazard to health has not been evaluated.

One comment references a paper published in 2004 that summarizes the European testing of 2–ACBs. The comment quotes language from the paper stating that ''the in vitro and in vivo experiments with laboratory animals demonstrated that 2–ACBs have potential toxicity,'' and the comment states that ''the paper concludes that as far as the possibility of health hazards from consuming irradiated food, 'further research is highly required''' (Ref. 48). The comment concludes by asserting that ''unfortunately, no comprehensive research on the toxicity of 2–ACBs has been undertaken to date, leaving this uncertainty as a huge obstacle to FDA's making a reliable decision on the five pending petitions.''

FDA disagrees that the conclusions of this paper would prevent completing

the safety review of FAP 9M4682. The conclusions submitted by the comment selectively quote from the authors' conclusions. The authors state:

Although our results point towards toxic, genotoxic and even tumor promoting activity of certain highly pure 2–ACBs, it should be emphasized that these experimental data are **inadequate to characterize a possible risk associated with the consumption of irradiated fat containing food**. Other food components may influence the reactions of 2–ACBs not evident from our experiments on purified 2–ACBs. More knowledge is also needed about the kinetics and metabolism of 2–ACBs in the living organism. It would, therefore, **at present be premature to draw the final conclusion that 2–ACBs are a health hazard on consumption of irradiated food**, but further research is highly required.

(Emphasis added) As previously noted in this document, FDA has reviewed studies in which animals were fed diets containing irradiated meat, poultry, and fish which contain triglycerides (62 FR 64107 at 64113). The agency concluded that no adverse effects were associated with the consumption of these irradiated flesh foods. The comment provides no additional information that would alter the agency's conclusion that the consumption of irradiated fat-containing foods does not present any health hazard.

H. Promotion of Colon Cancer

One comment submitted a paper entitled *Foodborne Radiolytic Compounds (2-Alkylcyclobutanones) May Promote Experimental Colon Carcinogenesis* (Ref. 49) and a commentary by Chinthalapally V. Rao, Ph.D. (Ref. 50) that states that the petition should not be approved until additional research is performed on a purported correlation between the consumption of ACBs and the promotion of colon carcinogenesis.

Raul *et al* designed their study to determine if 2–ACBs, specifically 2-tetradecylcyclobutanone (2–tDCB) and 2-(tetradec-5'-enyl)-cyclobutanone (2–tDeCB), will promote the carcinogenic effects of azoxymethane (AOM), which is known to induce colon preneoplastic lesions, adenomas, and adenocarcinomas in rats (Ref. 49). The paper states that the ''[p]resent report is the first demonstration that pure compounds, known to be exclusively produced on irradiation in dietary fats, may promote colon carcinogenesis in animals.''

Many different chemicals, some of which occur naturally in the human body, are known to promote carcinogenesis (Ref. 51). Additionally, Dr. Rao states that colon cancer is largely influenced by dietary lipids such as animal fat. Moreover, FDA notes that Dr. Rao states that the precursor lipids (which will be consumed in millions of times greater amount than the 2–ACBs, 2–tDCB and 2–tDeCB) are influential in the promotion of colon cancer.

The data showed no significant difference in tumor incidence between treatment groups. Raul *et al* reported no apparent difference in the number of aberrant crypt[7] foci (ACF)[8] per centimeter of colon, except that the 6 month treatment group receiving 2-tDeCB showed an increase in the total number of aberrant crypts (Refs. 52 and 53). However, the study has design flaws that make it difficult to understand the relevance of the data. Both FDA and Dr. Rao note that these flaws include: (1) Use of a limited number of animals (6 male Wistar rats per group); (2) use of a poor animal model (Wistar rats); and (3) alcohol, the vehicle in the study, has been linked to tumor promotion in many studies. Most importantly, as Raul *et al* point out in the discussion in their paper, the exposure of rats to 2–ACBs (milligrams per kilogram body weight) was three orders of magnitude higher than human exposure would be (micrograms per kilogram body weight).

Given the limitations of the animal model and study design, ambiguous data, and the absence of close relationship between the chemical exposure used in the study and the expected human exposure, the agency finds that the comment provides no substantial or reliable scientific information to show that there is reason to believe that the consumption of 2–ACBs will promote colon cancer. Moreover, the agency notes that long term feeding studies performed using irradiated foods that contain 2–ACBs did not show any promotion of colon cancer. The results of these latter long term feeding studies are more relevant than results from the Raul paper because the 2–ACBs were fed in the diet as in human exposure and the levels of exposure would still have been increased over usual dietary levels.

I. Indian National Institute of Nutrition Studies

One comment states that the petition should be denied because six positive studies conducted by the Indian National Institute of Nutrition (NIN) were ignored in the 1999 FAO/IAEA/WHO report. The comment states that FDA should give full consideration to the NIN studies, most notably the children's study using freshly irradiated food. The comment also states that the validity of these studies is supported by expert commentary and two published defenses by the NIN researchers.

A commentary by Dr. William Au submitted with the comment states ''[s]ome reports in the peer-reviewed literature on mutagenic activities of irradiated foods were not considered in the 1999 FAO/IAEA/WHO report (Bhaskaram and Sadasivan, 1975; Vijayalaxmi, 1975, 1976, 1978; Vijayalaxmi and Sadasivan, 1975; Vijayalaxmi and Rao, 1976).'' ''Although the observations from these studies are not confirmed by some publications in the literature, the positive findings have support from other publications (Bugyaki *et al.*, 1968; Moutschen-Dahmen, *et al.*, 1970; Anderson *et al.*, 1980; Maier *et al.*, 1993). Furthermore, repeated observations of activities that have significant public health implications such as polyploidy in somatic cells, genetic alterations in germ cells and reproductive toxicity should not be ignored, but should be considered seriously and explicitly by FDA with respect to the pending food irradiation petitions.''

The agency notes that the subject of this regulation is the petition (FAP 9M4682) submitted by NFI regarding shellfish, not the 1999 FAO/IAEA/WHO report on high-dose irradiation. The studies cited by the comment are not related to irradiated shellfish or other irradiated flesh foods.

The comment implies that FDA has not considered the cited studies despite the fact that FDA previously discussed the reason why some of the study reports could not be used to support a decision on irradiated foods (51 FR 13376 at 13385 and 13387). In 1986 FDA addressed the studies performed at the NIN (Ref. 54) and stated:

A committee of Indian scientists critically examined the techniques, the appropriateness of experimental design, the data collected, and the interpretations of NIN scientists who claimed that ingestion of irradiated wheat caused polyploidy in rats, mice, and malnourished children. After careful deliberation, this committee concluded that the bulk of these data are not only mutually contradictory, but are also at variance with well-established facts of biology. The committee was satisfied that once these data were corrected for biases that had given rise to these contradictions, no evidence of increased polyploidy was associated with ingestion of irradiated wheat.

The agency agreed with the conclusions of the committee of scientists that the studies

[7] A crypt is a cell that is used as a pathological marker. A crypt focus is a grouping of crypts. An aberrant crypt is a crypt that has altered luminal openings, thickened epithelia and are larger than adjacent normal crypts.

[8] Aberrant crypt foci of the colon are possible precursors of adenoma and cancer, and ACF have been observed in animals exposed to colon specific carcinogens, e.g. AOM.

with irradiated foods do not demonstrate that adverse effects would be caused by ingesting irradiated foods.
(51 FR 13376 at 13385)

Moreover, the agency notes that adverse effects which should have been seen if the conclusions drawn by the NIN researchers were valid were not observed in studies performed using similar foods irradiated at higher doses and consumed for longer periods of time. Finally, we note that the paper by Maier cited in the comment by Dr. Au concluded that ''* * * the consumption of irradiated wheat does not, therefore, pose any health risk to humans.''

J. Toxicity Data

One comment states that the petition should be denied because it does not contain specific data about the potential toxicity of irradiated molluscan shellfish. The comment concludes that ''FDA cannot credibly assess the safety and wholesomeness of foods covered by the petition if no toxicology data were included in the petition.''

The petitioner (FAP 9M4682) did not submit copies of toxicological data specific to irradiated shellfish. However, as noted earlier, FDA has reviewed a large body of data relevant to the assessment of the potential toxicity of irradiated flesh foods. The agency disagrees with the statement that ''FDA cannot credibly assess the safety and wholesomeness of foods covered by the petition if no toxicological data were included in the petition.'' There was no reason to submit additional copies of studies that have previously been reviewed by FDA. The comment provides no basis to challenge FDA's reliance on these studies to assess the safety of irradiated molluscan shellfish.

One comment states that the petition should be denied because ''* * * in the course of legalizing the irradiation of numerous classes of food over a 14-year span, the FDA relied on dozens of studies declared 'deficient' by agency toxicologists.''

FDA notes that the animal feeding studies reviewed in support of this petition (FAP 9M4682) were not considered deficient by agency scientists. Rather, they were considered acceptable or accepted with reservation by the agency scientists because even though all studies may not have met modern standards in all respects, they provided important information. Those studies categorized by FDA scientists as deficient were not relied on in the review of this petition. Although some of the studies accepted with reservation might not have been reported in full, used fewer animals, or examined fewer tissues than is common today, they still provide important information that, when evaluated collectively, supports the conclusion that consumption of molluscan shellfish irradiated under the conditions proposed in this petition is safe (Ref. 55).

K. Failure to Meet Statutory Requirements

One comment submitted by CFS and PC states that the petition should be denied because Delincée *et al* (Ref. 40). stated that ''* * * the results urge caution and should provide impetus for further studies.'' The comment further states that if established irradiation researchers and numerous medical experts urge caution and further research on the safety of irradiated food, then ''reasonable certainty,'' as required by 21 CFR 170.3(i), is missing.

The comment quotes selectively from the conclusions of Delincée regarding ACBs and omits other portions more relevant to this petition. For example, the sentence immediately prior to the sentence quoted states: ''The requisite concentrations are very much higher than those that can be reached through the consumption of irradiated foods that contain fat.'' Additionally, the authors note in the referenced article that ''[i]t should be mentioned once again that in many animal feeding experiments with irradiated foods in which it is known that cyclobutanones was also in the feed, no evidence has been found to indicate an injury from irradiated foods that have been consumed.'' In a comment to the docket in response to the statement made by CFS and PC, Dr. Delincée states that ''[u]nfortunately, the authors Worth and Jenkins did not take my precautions into account but made a story about the 'dangerous' cyclobutanones. In my opinion they greatly exaggerate the risks of 2-alkylcyclobutanones (2–ACB), which we still do not know very much about'' (Ref. 56).

One comment requests that the agency remove the food additive petition from the expedited review process.

FDA has established a process to give priority to petitions for technologies intended to reduce pathogen levels in foods (64 FR 517, January 5, 1999). FDA notes that petitions under expedited review are subject to all controls and requirements regarding safety data applicable to comparable petitions in the standard review process. Accordingly, valid scientific evidence, as defined by § 171.1 (21 CFR 171.1), is required to support the approval of an expedited petition. Likewise, the standards for safety and for data presentation are identical to the standard review process. The comment provides no information to support removing the petition from the expedited review process.

One comment requests that FDA review all of part 179 to determine if the regulations adequately protect the public health based on the best available scientific information.

This comment is outside the scope of this petition.

One comment states that the petition should be denied because ''FDA did not review studies that met the protocols established by the National Academy of Sciences/National Research Council (NAS/NRC) as required by 21 CFR 170.20.''

The comment provides no information to demonstrate that the studies reviewed by the agency in support of this petition (FAP 9M4682) fail to meet the standards set forth under § 170.20 (21 CFR 170.20). Section 170.20 states:

> The Commissioner will be guided by the principles and procedures for establishing the safety of food additives stated in current publications of the National Academy of Sciences-National Research Council. A petition will not be denied, however, by reason of the petitioner's having followed procedures other than those outlined in the publications of the National Academy of Sciences-National Research Council if, from available evidence, the Commissioner finds that the procedures used give results as reliable as, or more reliable than, those reasonably to be expected from the use of the outlined procedures.

FDA has consistently taken the position that many scientifically valid types of data may properly support a finding that the proposed use of a food additive will cause ''no harm'' to consumers. For example, § 170.20 which sets forth the general scientific criteria that FDA uses in evaluating a food additive petition, cites the ''principles and procedures * * * stated in 'current' publications of the National Academy of Sciences, National Research Council'' as a guide that the agency uses in its safety evaluation of food additives. NAS has written testing standards for both public and agency use, but these testing requirements have been stated in relatively general terms. In practice, FDA has applied toxicological criteria and exposure information that were current for the time in assessing the safety each food additive. The agency has continuously adjusted food additive testing recommendation as necessary to reflect both the steady progress of science and the most current information about population exposure to additives (Ref. 57).

FDA concludes that the data considered for this regulation, when

evaluated in its entirety, are sufficient to support the safety of consumption of irradiated molluscan shellfish at a maximum absorbed dose that will not exceed 5.5 kGy.

One comment states that the petition should be denied because the battery of experiments prescribed by the BFIFC to assess the potential toxicity and mutagenicity of irradiated food was based on the assumption that only 10 percent of the food supply would likely be irradiated and fell ''[f]ar short of those battery prescribed by the FDA's Red Book, but the FDA [did] not comply with the *abbreviated* battery of experiments before legalizing the irradiation of pork, fruit and vegetables, poultry, red meat, eggs, sprouting seeds and juice.''

The agency notes that the subject of this regulation is the petition (FAP 9M4682) on shellfish, not the BFIFC report (Ref. 36) nor the FDA Red Book (Ref. 37).

The BFIFC report is an internal document prepared by FDA scientists that provides recommendations for evaluating the safety of irradiated foods based on the known effects of radiation on food and on the capabilities of toxicological testing. While the report and the commentary on it have aided FDA's thinking regarding the testing of irradiated foods, the report established no definitive requirements. BFIFC recognized that it may not be necessary to perform reproduction and chronic toxicity studies in cases where there was evidence that irradiated foods provided no mutagenic or other toxic effects that could be seen in shorter studies. Therefore, BFIFC recommended that in the absence of chronic and reproductive feeding studies, foods irradiated at a dose above 1 kGy be evaluated using a battery of mutagenicity tests, as well as 90-day feeding studies in two species (one rodent and one non-rodent). BFIFC also recommended that chronic studies would only be indicated when two of the four mutagenicity tests showed mutagenic effects, and that the reproductive toxicity tests would only be indicated when the 90-day studies showed a potential for effects on the reproductive system. Furthermore, BFIFC also recommended that foods should be considered generically as a class, based on their composition i.e., proteins, lipids, and carbohydrates. Consistent with these recommendations, FDA has considered several relevant chronic feeding studies, as well as the macronutrient composition of molluscan shellfish in the safety determination for this regulation. Therefore, there is no need to conduct additional mutagenicity studies to determine whether chronic studies are needed.

Finally, FDA's Red Book represents the agency's current thinking on the information needed for the safety assessment of *food ingredients*, not processed foods, such as irradiated molluscan shellfish, and it does not bind the petitioner to follow specific procedures that are recommended in the Red Book. Furthermore, even if the Red Book applied to processed foods, alternative approaches would be permissible if such approaches satisfy the requirement of the applicable statute and regulations. The comment contains no evidence to demonstrate that the studies considered for this regulation, when evaluated in totality, are insufficient to support the safety of consumption of irradiated molluscan shellfish at an absorbed dose no to exceed 5.5 kGy.

L. Trans Fatty Acids

One comment states that the petition should be denied because there is evidence that the consumption of *trans* fatty acids increases the risk of coronary heart disease and recent research shows that irradiation increases the amount of trans fatty acids present in ground beef (Ref. 58).

The paper submitted by the comment purports to show a 3.4 percent increase in the amount of *trans* fatty acids when ground beef is irradiated at 1 kGy at 25 degrees Celsius, and a greater increase in *trans* fatty acids at higher doses. For example, the paper states that unirradiated beef contains 4.60 ± 0.31 percent *trans* fatty acid, 4.40 ± 0.31 percent *trans* fatty acid when stored for 60 days, and 5.00 ± 0.31 percent *trans* fatty acid when stored for 90 days. When beef was irradiated at 3 kGy, they report 8.00 ± 0.00 percent *trans* fatty acid for all three storage times. When beef was irradiated at 8 kGy, they report 11.00 ± 0.50 percent *trans* fatty acid at day zero, 10.50 ± 0.50 percent trans fatty acid when stored for 60 days, and 10.00 ± 0.31 percent trans fatty acid when stored for 90 days.

The fat in beef has a natural background of *trans* fat that ranges from 3 percent to 10 percent and research performed by the agency shows no change in the amount of *trans* fatty acids present when ground beef is irradiated at 25 degrees Celsius (Ref. 59). Additionally, Consumer Reports (August 2003) found no *trans* fats were produced when ground beef was irradiated. The agency has reviewed the paper submitted by the comment and concludes that the researchers did not demonstrate that there was an increase in the amount of *trans* fatty acid present in irradiated ground beef, or that irradiation showed a dose dependent response. In fact, the paper fails to demonstrate that the researchers were measuring the quantity of *trans* fatty acids (Ref. 60). Therefore, the agency concludes that there is no basis to deny the petition based on increased amount of *trans* fatty acids in irradiated ground beef.

M. Elevated Hemoglobin

One comment states that the petition should be denied because the consumption of irradiated food may contribute to an increase in the number of still-born children. The comment provides three studies to substantiate this comment: (1) An unpublished report states that the consumption of irradiated potatoes increased the hemoglobin concentrations in healthy human volunteers; (2) a published study that shows that elevated hemoglobin levels were found in pigs consuming irradiated potatoes; and (3) a published study appearing to show that ''high hemoglobin concentration at first measurement during antenatal care appears to be associated with increased risk of stillbirth, especially preterm and small-for-gestational age antepartum stillbirths.''

The comment suggests that the consumption of a high carbohydrate diet may increase hemoglobin levels and this may lead to an increase in the frequency of still born children among pregnant women who consume irradiated carbohydrates. FDA notes that consumption of shellfish would not contribute significant carbohydrates to the diet because the maximum proximate carbohydrate composition of shellfish is 10 percent or less.

The first study (1967) compares the hemoglobin and hematocrit levels of 7 human volunteers who, for 14 weeks, consumed potatoes that had been irradiated at 14 kGy (Ref. 61). The study does not include a baseline prior to feeding; it provides a single measurement. The hemoglobin values reported show a slight increase during the period of consumption of irradiated potato, but they are still within the normal range of hemoglobin values (Ref. 62). Additionally, there is no concurrent control group to demonstrate that the irradiated potatoes were the cause of the increase in hemoglobin values.

The second study (1966) submitted by the comment compares piglets fed both irradiated and non-irradiated potatoes (Ref. 63). The authors conclude that the pigs fed irradiated potatoes did not differ significantly from the control animals in the parameters measured,

except that the pigs fed irradiated potatoes grew slightly faster, had a more rapid increase in hemoglobin levels, and had a higher hemoglobin concentration at the end of the experiment. The authors state that ''[t]he second generation pigs provided no indication that the irradiated potatoes might give rise to deleterious effects'' (Ref. 64).

The third study entitled ''Maternal Hemoglobin Concentration During Pregnancy and Risk of Stillbirth'' (2000) compares the hemoglobin concentration during antenatal care, the change in hemoglobin concentration during pregnancy and the risk of still birth (Ref. 64). The study compares the hemoglobin concentrations at first measurement of 702 primiparous (bearing first child) women with stillbirths occurring at 28 weeks or later to 702 primiparous women with live births. The authors concluded that high hemoglobin concentrations at first measurement appeared to be associated with an increased risk of stillbirth, especially preterm and small-for-gestational-age antepartum stillbirths. The authors note that the study was limited to primiparous women with singleton (first) pregnancies and that the conclusions can only be interpreted within that small sub-population. FDA also notes that the study did not investigate other potential confounding variables such as nutrition or physical activity.

FDA acknowledges that hemoglobin concentrations were not reported in studies such as the Bugyaki *et al.* study that reported gestational effects. However, FDA notes that none of the long term reproductive studies performed with irradiated foods that were found to be acceptable or acceptable with reservation in 1982 showed effects on reproduction. This is substantiated in the second study identified by the comment. Therefore, given the limitations in design of the additional two studies, the agency finds no basis to conclude that the consumption of irradiated shellfish will increase hemoglobin levels. Similarly, FDA finds no basis to the purported association between increased hemoglobin levels and an increase in stillbirth rates.

N. Dangers of Radiation

In an affidavit written by Dr. William Au that was submitted by CFS and PC, he states that ''[i]onizing radiation is a teratogen, mutagen, and carcinogen whereas some other procedures for food decontamination/sterilization such as heat and steam are not. Whenever other processing methods or combination of methods are equally effective in reducing the risk of foodborne disease are available, the use of radiation procedure should be avoided.''

While methods other than treatment with ionizing radiation are available to eliminate or reduce microbial contamination of food, the existence of such methods is not a reason to prohibit safe alternatives. Additionally, the act does not authorize FDA to arbitrarily limit other safe alternatives. The fact that radiation can be teratogenic, carcinogenic, or mutagenic when applied directly to living organisms is not relevant to the safety of irradiated shellfish. Most food processing techniques (such as grinding, slicing, boiling, roasting) would be harmful to living mammals but that is unrelated to the safety of the food. Irradiating the shellfish will not expose consumers to additional amounts of radiation.

O. Nutritional Deficiency

One comment states that the petition should be denied because the BFIFC ''* * *cautioned that even if 10 percent of the food supply were irradiated: 'When irradiation results in the significant loss of micronutrients, enrichment may be considered appropriate.''' The comment goes on to state that to date, FDA has authorized the irradiation of several classes of food that comprise more than half of the U.S. food supply. ''If the FDA approves the pending 'ready-to-eat' petition [FAP 9M4697], an estimated 80-90 percent of the U.S. food supply would be eligible for irradiation.'' The comment further states that ''no analysis has been done of the nutritional deficiencies that would be created among the populace should 80-90 percent of the food supply be irradiated.''

The comment provides no information to conclude that irradiating 80-90 percent of the diet is probable or feasible. Additionally, molluscan shellfish are a small part of the food supply. The comment provides no basis for the statement that consumers will suffer nutritional deficiencies from being exposed to irradiated food.

FDA agrees that treatment of food with ionizing radiation, as with heat processing, decreases the levels of some nutrients and irradiation must be evaluated by considering the nutritional consequences on the diet as a whole. The agency has specifically addressed the impact of irradiation on vitamins and other nutritional components in the **Nutrition** section in this document. Irradiation has essentially no effect on the quantity of fatty acids, amino acids, and carbohydrates in foods and no effect on the overall dietary intake of these macronutrients. While irradiation may reduce the levels of some vitamins, similar to heat processing, the agency concludes that the irradiation treatment of shellfish would have no significant effect on dietary intake of vitamins. The comment provides no evidence to refute the agency's conclusion that the consumption of irradiated molluscan shellfish would not result in nutritional deficiencies. The effects of ionizing radiation on the nutritional qualities of the foods that are the subject of other petitions, such as FAP 9M4697, will be evaluated as part of the safety evaluation for those petitions.

Another comment states that a statement by D. R. Murray in *Biology of Food Irradiation*[9] suggests that ''disproportionate and selective losses of nutrients occur in foods as consequence of irradiation.''

The comment provided the bulk of a chapter from this book and states that FDA must address the negative impact on fatty acids, vitamins, amino acids, carbohydrates and other essential components on food as a consequence of irradiation and in combination with cooking. The comment requests that the agency respond to the following four questions regarding the nutritional impact of irradiated foods.

- ''What would be the impacts of irradiation as proposed on each important vitamin and other nutritional component in each different food type that is included?''
- ''What would be the projected national rates of consumption of each different food type included in the petition after foreseeable market penetration of the product, e.g., after 5-10 years of marketing?''
- ''How would this projected future consumption vary across age, ethnic, gender, economic status, education status, and other variables in the American population?''
- ''To what extent would the various population groups likely be affected by the nutritional/vitamin impacts identified under question 1, above?''

In the review of this petition (FAP 9M4682), FDA considered whether the nutritional quality of irradiated molluscan shellfish would differ in any meaningful way from that of non-irradiated molluscan shellfish and concludes that consumption of irradiated molluscan shellfish will not result in nutritional deficiencies. FDA notes that foods are commonly processed more than once, such as by heating in the factory followed by

[9] Murray, D. R., *Biology of Food Irradiation*, Research Studies Press Ltd. Staunton, UK, Chapter 4, Radiolytic products and selective destruction of nutrients, 1990.

cooking one or more times in the home, without an adverse effect on the diet. The comment provides no rationale as to why irradiation should be considered differently from heat processing in this regard, nor why the major data research projects envisioned in the final three questions are necessary to evaluate the safety of irradiated shellfish.

IV. Conclusions

Based on the data and studies submitted in the petition and other information in the agency's files, FDA concludes that the proposed use of irradiation to treat fresh and frozen molluscan shellfish with absorbed doses that will not to exceed 5.5 kGy is safe, and therefore, the regulations in § 179.26 should be amended as set forth in this document.

In accordance with § 171.1(h), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the Information contact person (see **FOR FURTHER INFORMATION CONTACT**). As provided in § 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

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

V. Environmental Impact

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

VI. Objections

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

VII. References

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

1. WHO, ''Wholesomeness of Irradiated Food: Report of a Joint FAO/IAEA/WHO Expert Committee,'' World Health Organization Technical Report Series, No. 659, World Health Organization, Geneva, 1981.

2. Codex 2003, ''Codex General Standard for Irradiated Foods (CODEX STAN 106-1983, Rev.-2003)'' and ''Recommended Code of Practice for the Operation of Radiation Facilities Used for the Treatment of Foods (CAC/RCP 19-1979, Rev.-2003).'' *Codex Alimentarius Commission*, Food and Agriculture Organization and World Health Organization, Rome, 2003.

3. *Safety and Nutritional Adequacy of Irradiated Food*, World Health Organism, Geneva, 1994.

*4. Memorandum for FAP 9M4682 from D. Folmer, FDA, to L. Highbarger, FDA, August 2, 2002.

5. Diehl, J.F., *Safety of Irradiated Foods*, Second Edition, Marcel Dekker, Inc., New York, 1995.

6. Seibersdorf Project Report, International Programme on Irradiation of Fruit and Fruit Juices, Chemistry and Isotopes Department, National Centre for Nuclear Energy, Madrid, Spain, vol. 8, 1966.

*7. Memorandum for FAP 9M4682 from K. Morehouse, FDA, to L. Highbarger, FDA, July 15, 2005.

*8. Memorandum for FAP 9M4695 from I. Chen, FDA, to L. Highbarger, FDA, April 7, 2003.

*9. Uderdal, B., J. Nordal, G. Lunde, and B. Eggum, ''The Effect of Ionizing Radiation on the Nutritional Value of Fish (Cod) Protein,'' *Lebensmittel-Wissenschaft Technologie*, 6:90-93, 1973.

10. Von Sonntag, C., ''Free-radical Reactions of Carbohydrates as Studies by Radiation Techniques, *''Advances in Carbohydrate Chemistry Biochemistry*, 37:7-77, 1980.

11. WHO, ''High-dose Irradiation: Wholesomeness of Food Irradiated With Doses Above 10 kGy,'' World Health Organization Technical Report Series, No. 659, World Health Organization, Geneva, 1999.

*12. Delincée, H., ''Recent Advances in Radiation Chemistry of Lipids,'' in *Recent Advances in Food Irradiation*, edited by P.S. Elias and A.J. Cohen, Elsevier, Amsterdam, pp. 89-114, 1983.

*13. Kavalam, J.P., and W.W. Nawar, ''Effects of Ionizing Radiation on Some Vegetable Fats,'' *Journal of the American Oil Chemical Society*, 46:387-390 (1969).

*14. Nawar, W.W., ''Thermal Degradation of Lipids. A Review,'' *Journal of Agricultural Food Chemistry*, 17(1): 18-21, 1969.

*15. Crone A.V.J., Hamilton, J.T.G., and M.H. Stevenson, ''Effect of Storage and Cooking on the Dose Response of 2-Dodecylcylobutanone, a Potential Marker for Irradiated Chicken, *Journal of Science and Food Agriculture*, 58:249-252, 1992.

*16. Gadgil, P., Hachmeister, K.A., Smith, J.S., and D.H. Kropf, ''2-Alkylcyclobutanones as Irradiation Dose Indicators in Irradiated Ground Beef Patties,'' *Journal of Agriculture and Food Chemistry*, 50:5746-5750, 2002.

*17. Adams, S., G. Paul, D. Ehlerman, ''Influence of Ionizing Radiation on the Fatty Acid Composition of Herring Fillets,'' *Radiation Physics Chemistry*, 20:289-295, 1982.

*18. Armstrong, S.G., Wylie, S.G., and D.N. Leach, ''Effects of Preservation by Gamma-Irradiation on the Nutritional Quality of Australian Fish,'' *Food Chemistry*, 50:351-357, 1994.

*19. Sant'Ana, L.S. and J. Mancini-Filho ''Influence of the Addition of Antioxidants in Vivo on the Fatty Acid Composition of Fish Fillets'' *Food Chemistry*, 68:175-178, 2000.

*20. Status Report on Food Irradiation by Member Countries of the International Consultative Group on Food Irradiation, IAEA Headquarters, Vienna, Austria, October 20-22, 1998.

*21. Morehouse, K.M., Y. Ku, ''Gas Chomatographic and Electron Spin Resonance Investigations of Gamma-Irradiated Shrimp,'' *Journal of Agriculture and Food Chemistry*, 40(10), 1963-1971, 1992.

22. Morehouse, K.M., ''Identification of Irradiated Seafood,'' in *Detection Methods for Irradiated Foods: Current Status*, edited by C.H. McMurray, E.M. Stewart, R. Gray, and J. Pearce, The Royal Society of Chemistry, Cambridge, UK, pp. 249-258, 1996.

*23. Buck, J.D., ''Potentially Pathogenic *Vibrio* spp. In Market Seafood and Natural Habitats from Southern New England and Florida,'' *Journal of Aquatic Food Product Technology*, 7(4):53-61, 1998.

24. Oliver, J.D. and Kaper, J.B., ''Vibrio Species,'' In M.P. Doyle, L. Beuchat and T.J. Montville (ed.) Food Microbiology, Fundamentals and Frontiers, 2d Ed., ASM Press, Herndon, VA, 2001.

*25. Memorandum for FAP 9M4682 from R. Merker, FDA, to L. Highbarger, FDA January 2, 2003.

26. Tauxe, R.W., *Emerging Infectious Diseases*, 7:516-21, 2001.

27. Diehl, J.F., *Safety of Irradiated Foods*, Marcel Decker, New York, Basel, 1990.

*28. Cotton, P.A., Subar, A.F., Friday, J.E., Cook, A., ''Dietary Sources of Nutrients Among US Adults, 1994 to 1996,'' *Journal of the American Dietetic Association*, 104:921-930, 2004.

*29. Anderson D, M.J.L. Clapp, M.C.E. Hodge, and T.M. Weight, ''Irradiated Laboratory Animal Diets—Dominant Lethal Studies in the Mouse,'' *Mutation Research*: 80:333-345, 1981.

*30. Bugyaki L., A.R. Deschreiaer, and J. Moutschen, ''Do Irradiated Foodstuffs Have a Radiomimetic Effect: II. Trials With Mice Fed Wheat Meal Irradiated at 5 MRad,'' *Atompraxis*, 14, 112, 1968.

*31. Moutschen-Dahmen M., J. Moutschen, and L. Ehrenberg, ''Pre-implantation Death of Mouse Eggs Caused by Irradiated Food,'' *International Journal of Radiation Biology*, 18:201-216, 1970.

*32. Johnston-Arthur T, M. Brena-Valle, K. Twanitz, R. Hruby, and G. Stehuk, ''Mutagenicity of Irradiated Food in the Host-mediated Assay System,'' *Studia Biophysica Berlin*, 50:137-141, 1975.

*33. Kesavan, P.C. and M.S. Swaminathan, ''Cytotoxic and Mutagenic Effects of Irradiated Substances and Food Material,'' *Radiation Botanay*, vol. 11, pp. 253-281, 1971.

*34. Verschuurn, H.G., G.J. Esch, and J.G. Kooy, *Ninety Day Rat Feeding Study on Irradiated Strawberries; Food Irradiation; 7 (1-2); pp. A17-A21, 1966.*

*35. Memorandum from Food Additives Evaluation Branch, HFF–156 to C. Takaguchi, Petition Control Branch, December 28, 1982.

*36. Bureau of Foods Irradiated Foods Committee, *Recommendations for Evaluating the Safety of Irradiated Food*, Prepared for the Director, Bureau of Foods, FDA, July 1980.

37. Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food, ''Red Book II,'' U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition, 1993, revised 2001.

*38. Organisation for Economic Co-Operation and Development, European Nuclear Energy Agency, Steering Committee for Nuclear Energy Study Group on Food Irradiation, *On Genetic Effects Produced by Irradiated Foods and Food Components, Scarascia-Mugnozza, G.T., A.T. Natarajan, and L. Ehrenberg, 1965.*

*39a. Miesch, M., B. Ndiye, C. Hasselmann, and E. Marchioni, ''2-Alkylcyclobutanones as Markers for Irradiated Food Stuffs - I. Sysnthesis of Saturated and Unsaturated Standards,'' *Radiation Physics and Chemistry*, 55:337-344, 1999.

*39b. Horvatovich, P., Miesch, M, Hasselmann, C., and E. Marchioni, ''Supercritical Fluid Extractin of Hydrocarbons and 2-alkylcyclobutanones for the Detection of Irradiated Foodstuffs,'' *Journal of Chromatography*, 897:259-268, 2000.

*40. Delincée H, B.L. Pool-Zobel, and G. Rechkemmer ''Genotoxicity of 2-dodecyclcyclobutanone,'' *Food Irradiation: Fifth German Conference*, Report BFE-R-99-01, Federal Nutrition Research Institute, Karlsruhe, Germany, unpublished, 1998.

*41. Memorandum for FAP 9M4682 from R. Sotomayer, FDA, to L. Highbarger, FDA, April 28, 2003.

*42. Sommers C.H., and R.H. Schiestl, ''2-Dodecylcyclobutanone Does Not Induce Mutations in the Salmonella Mutagenicity Test or Intrachromosomal Recombination in Saccharomyces Cerevisiae, *Journal of Food Protection*, 67(6):1293-8, 2004.

*43. Sommers, H., ''2-Dodecylcyclobutanone Does Not Induce Mutations in the *Escherichia coli* Tryptophan Reverse Mutation Assay,'' *Journal of Agriculture and Food Chemistry*, 51:6367-6370, 2003.

*44. Gadgil, P. and J.S. Smith, ''Mutagenicity and Acute Toxicity Evaluation of 2-Dodecylcyclobutanone,'' *Journal of Food Science*, 69(9), 713-716, 2004.

*45. Delincée H, and BL Pool-Zobel, ''Genotoxic Properties of 2-Dodecyclcyclobutanone, a Compound Formed on Irradiation of Food Containing Fat,'' *Radiation Physics and Chemistry*, 52:39-42, 1998.

*46. Henderson, L., A. Wolfreys, J. Fedyk, C. Bourner and S. Windebank ''The Ability of the Comet Assay to Discriminate Between Genotoxins and Cytotoxins,'' *Mutagenesis*, 13:89-94, 1998.

*47. Victoria, A., J. Crone, J.T.G. Hamilton, and M. Hilary Stevenson, ''Detection of 2-dodecylcyclobutanone in Radiation Sterilized Chicken Meat Stored for Several Years,'' *International Journal of Food Science and Technology*, 27:691-696, 1992.

*48. Marchioni, E., F. Raul, D. Burnouf, M. Miesch, H. Delincée, A. Hartwig, D. Werner, ''Toxicological Study on 2-alkylcyclobutanones—Results of a Collaborative Study;'' *Radiation Chemistry and Physics*, 71:147-150, 2004.

*49. Raul, F., F. Gosse, H. Delincée, A. Hartwig,, E. Marchioni, M. Miesch, D. Werner, and D. Burnouf, ''Food Borne Radiolytic Compounds (2-Alkylcyclobutanones) May Promote Experimental Colon Carcinogenesis,'' *Nutrition and Cancer*, 44(2):181-191, 2002.

*50. Rao, C., ''Do Irradiated Foods Cause or Promote Colon Cancer?,'' Division of Nutritional Carcinogenesis, Institute for Cancer Prevention, American Health Foundation-Cancer center, Valhalla, NY, Unpublished, 2003. FDA notes that this article has now been published as a commentary in *Nutrition and Cancer*, 46(2):107-109, 2003.

51. Casserett & Doull's Toxicology, the Basic Science of Poisons, 2001.

*52. Memorandum for FAP 9M4682 from T. Twaroski, FDA, to L. Highbarger, FDA, July 14, 2005.

*53. Mori H., Y. Yamada, T. Kuno, and Y. Hirose, ''Aberrant Crypt Foci and B-catenin Accumulated Crypts; Significance and Roles for Colorectal Carcinogenesis,'' *Mutation Research*, 566:191-208, 2004.

*54. Kesavan, P.C. and P.V. Sukhatame. ''Summary of the Technical Report on the Data of NIN,'' Hyderabad and BARC, Bombay on the Biological Effects of Freshly Irradiated Wheat, Report submitted to the Indian Ministry of Health and Family Planning, 1976.

*55. Memorandum for FAP 4M4428, from D. Hattan, to FAP 4M4428; Further Evaluation of Toxicological Studies, November 20, 1997.

*56. Comment submitted by Henry Delincée to the docket.

57. Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food, ''Red Book I,'' U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition, 1982.

*58. Britto M.S., A.L.C.H. Villavicencio, and J. Mancini-filho, ''Effects of Irradiation on *Trans* Fatty Acids in Ground Beef,'' *Radiation Physics and Chemistry*, 63:337-340, 2002.

*59. Memorandum for FAP 9M4682 from K. Morehouse, FDA, to L. Highbarger, FDA, July 15, 2005.

*60. E-mail from Paul Kuznesof to L. Highbarger to be added to FAP 9M4682, April, 28, 2003.

*61. Jaarma, M., ''Studies of Chemical and Enzymatical Changes in Potato Tubers and Some Highber Plants Caused by Ionizing Radiation, Including Studies on the Wholesomeness of γ-Irradiated Potato Tubers and Effects on Some Carbohydrates *in vitro*, Biokemiska Institutionen, Kuugl, Univeritetet I Stockholm, Stockholm, Sweden, 1967.

*62. Memorandum 2 for FAP 9M4682 from T. Twaroski, FDA, to L. Highbarger, FDA, July 14, 2005, 2005.

*63. Jaarma, M., G. ''Bengtsson On the wholesomeness of γ-irradiated Potatoes II. Feeding Experiments with Pigs'' *Nutritio et Dieto—European Review of Nutrition and Dietetics*, 8:109-129, 1966.

*64. Stephansson, O., Dickman, P.W., Johansson, A., and S. Cnattingus, ''Maternal Hemoglobin Concentration During Pregnancy and Risk of Stillbirth,'' *Journal of the American Medical Association*, 248(20):2611-2617, 2000.

List of Subjects in 21 CFR Part 179

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

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

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

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

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

■ 2. Section 179.26 is amended in the table in paragraph (b) by adding a new item ''11.'' under the headings ''Use'' and ''Limitations'' to read as follows:

§179.26 Ionizing radiation for the treatment of food.

* * * * *

(b) * * *

Use	Limitations
* * *	* *
11. For the control of Vibrio bacteria and other foodborne micro-organisms in or on fresh or frozen molluscan shellfish.	Not to exceed 5.5 kGy.
* * *	* *

* * * * *

Dated: August 11, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–16279 Filed 8–12–05; 1:19 pm]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 1240

Turtles Intrastate and Interstate Requirements

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; technical amendment.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulation regarding the intrastate and interstate distribution of turtles to reflect a change in responsibility for administering the provisions of the regulations from FDA's Center for Food Safety and Applied Nutrition (CFSAN) to FDA's Center for Veterinary Medicine (CVM). FDA is taking this action to enable the agency to more effectively administer the provisions of this regulation.

DATES: This rule is effective August 16, 2005.

FOR FURTHER INFORMATION CONTACT: Joseph Paige, Center for Veterinary Medicine (HFV–230), Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–276–9210, e-mail: *jpaige@cvm.fda.gov*.

SUPPLEMENTARY INFORMATION: FDA is amending its regulations regarding the intrastate and interstate distribution of turtles (§ 1240.62 (21 CFR 1240.62)) to reflect the transfer of regulatory responsibility from CFSAN to CVM. Except as otherwise provided, § 1240.62 requires that viable turtle eggs and live turtles with a carapace length of less than 4 inches not be sold, held for sale, or offered for any other type of commercial or public distribution. FDA is amending this regulation because current expertise for addressing issues regarding this regulation is within CVM. Reassigning regulatory responsibility to CVM more effectively utilizes agency resources in administering the provisions of the regulation.

Publication of this document constitutes final action on this change under the Administrative Procedures Act (5 U.S.C. 553). FDA has determined that notice and public comment are unnecessary because this amendment to the regulation is nonsubstantive. It merely reflects an organizational change.

List of Subjects in 21 CFR Part 1240

Communicable diseases, Public health, Travel restrictions, Water supply.

■ Therefore, under the Public Health Service Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 1240 is amended as follows:

PART 1240—CONTROL OF COMMUNICABLE DISEASES

■ 1. The authority citation for 21 CFR part 1240 continues to read as follows:

Authority: 42 U.S.C. 216, 243, 264, 271.

§ 1240.62 [Amended]

■ 2. Section 1240.62 is amended as follows:

a. In paragraphs (c)(1)(i), (c)(1)(ii), (c)(1)(v), and (c)(2) by removing ''Director of the Center for Food Safety and Applied Nutrition'' each time it appears, and adding in its place ''Director of the Center for Veterinary Medicine''.

b. In paragraph (c)(1)(ii) by removing ''5100 Paint Branch Pkwy., College Park, MD 20740'', and adding in its place ''7519 Standish Pl., Rockville, MD 20855''.

Dated: August 9, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–16142 Filed 8–15–05; 8:45 am]

BILLING CODE 4160–01–S

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 52

[R07–OAR–2005–IA–0003; FRL–7953–7]

Approval and Promulgation of Implementation Plans; State of Iowa

AGENCY: Environmental Protection Agency (EPA).

ACTION: Direct final rule.

SUMMARY: EPA is approving the State Implementation Plan (SIP) revision submitted by the state of Iowa for the purpose of approving the 2001 and 2004 updates to the Linn County Air Quality Ordinance. These revisions will help to ensure consistency between the applicable local agency rules and Federally-approved rules, and ensure Federal enforceability of the applicable parts of the local agency air programs.

DATES: This direct final rule will be effective October 17, 2005, without further notice, unless EPA receives adverse comment by September 15, 2005. If adverse comment is received, EPA will publish a timely withdrawal of the direct final rule in the **Federal Register** informing the public that the rule will not take effect.

ADDRESSES: Submit your comments, identified by Regional Material in EDocket (RME) ID Number R07–OAR–2005–IA–0003, by one of the following methods:

1. Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the on-line instructions for submitting comments.

2. Agency Web site: *http://docket.epa.gov/rmepub/*. RME, EPA's electronic public docket and comment system, is EPA's preferred method for receiving comments. Once in the system, select ''quick search''; then key in the appropriate RME Docket identification number. Follow the on-line instructions for submitting comments.

3. E-mail: *Hamilton.heather@epa.gov*.

4. Mail: Heather Hamilton, Environmental Protection Agency, Air Planning and Development Branch, 901 North 5th Street, Kansas City, Kansas 66101.

5. Hand Delivery or Courier: Deliver your comments to Heather Hamilton, Environmental Protection Agency, Air Planning and Development Branch, 901 North 5th Street, Kansas City, Kansas 66101.

Instructions: Direct your comments to RME ID No. R07–OAR–2005–IA–0003. EPA's policy is that all comments received will be included in the public