SECURITIES AND EXCHANGE COMMISSION

17 CFR Part 230

General Rules and Regulations, Securities Act of 1933

CFR Correction

In Title 17 of the Code of Federal Regulations, Parts 200 to 239, revised as of April 1, 2010, on page 686, in § 230.501, following paragraph (e)(3), reinstate the Note to paragraph (e) to read as follows:

§ 230.501 Definitions and terms used in Regulation D.

* * * * *

(e) * * *

NOTE: The issuer must satisfy all the other provisions of Regulation D for all purchasers whether or not they are included in calculating the number of purchasers. Clients of an investment adviser or customers of a broker or dealer shall be considered the "purchasers" under Regulation D regardless of the amount of discretion given to the investment adviser or broker or dealer to act on behalf of the client or customer.

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[FR Doc. 2011–6830 Filed 3–21–11; 8:45 am]

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DEPARTMENT OF HOMELAND SECURITY

Bureau of Customs and Border Protection

DEPARTMENT OF THE TREASURY

19 CFR Part 141

Entry of Merchandise

CFR Correction

In Title 19 of the Code of Federal Regulations, Parts 141 to 199, revised as of April 1, 2010, on page 6, the second general authority citation for part 141 is removed.

[FR Doc. 2011–6840 Filed 3–21–11; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 179

[Docket No. FDA–1999–F–0056; Formerly Docket No. 1999F–4372]

Irradiation in the Production, Processing, and Handling of Food; Confirmation of Effective Date

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; denial of requests for a stay of effective date and for a hearing; response to objections; confirmation of effective date.

SUMMARY: The Food and Drug Administration (FDA) is denying requests for a hearing on the final rule that amended the food additive regulations to provide for the safe use of ionizing radiation for the control of *Vibrio* species and other foodborne pathogens in fresh or frozen molluscan shellfish. After reviewing objections to the final rule and requests for a hearing, FDA has concluded that the objections do not justify a hearing or otherwise provide a basis for revoking the regulation. FDA also is denying the request for a stay of the effective date of the amendment to the food additive regulations.

DATES: The August 16, 2005, effective date for the final rule published at 70 FR 48057 is confirmed.

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. Introduction

FDA published a notice in the **Federal Register** of October 19, 1999 (64 FR 56351), announcing the filing of a food additive petition (FAP 9M4682) by the National Fisheries Institute and the Louisiana Department of Agriculture and Forestry. In the **Federal Register** of August 16, 2005 (70 FR 48057), FDA issued a final rule permitting the irradiation of fresh or frozen molluscan shellfish for the control of *Vibrio* spp. and other food-borne pathogens. FDA based its decision on data in the petition and in its files. In the preamble to the final rule, FDA outlined the basis for its decision and responded to questions raised in several comments from Public Citizen and the Center for Food Safety (PC/CFS). The preamble to the final rule advised that objections to the final rule and requests for a hearing were due within 30 days of the publication date (*i.e.,* by September 15, 2005).

II. Objections, Requests for a Hearing, and Requests for a Stay

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

Under part 171 (21 CFR part 171) in § 171.110 of the food additive regulations, objections and requests for a hearing are governed by part 12 (21 CFR part 12) of FDA's regulations. Under § 12.22(a), each objection must meet the following conditions: (1) Must be submitted on or before the 30th day after the date of publication of the final rule; (2) must be separately numbered; (3) must specify with particularity the provision of the regulation or proposed order objected to; (4) must specifically state each objection on which a hearing is requested; failure to request a hearing on an objection constitutes a waiver of the right to a hearing on that objection; and (5) must include a detailed description and analysis of the factual information to be presented in support of the objection if a hearing is requested; failure to include a description and analysis for an objection constitutes a waiver of the right to a hearing on that objection.

Following publication of the final rule permitting the irradiation of fresh or frozen molluscan shellfish for the

control of *Vibrio* spp. and other food borne pathogens, FDA received numerous submissions within the 30-day objection period. All but two of these timely submissions express general opposition to the final rule, and are form letters urging the FDA to conduct additional studies on irradiating molluscan shellfish specifically and food in general. Although most of these letters request a hearing, no evidence is identified in support of these objections that could be considered in an evidentiary hearing (§ 12.22(a)(5)). Therefore, they have waived their right to a hearing. The Agency will not discuss these submissions further. FDA received two submissions that met the requirements of § 12.22(a), One of these two submissions is a letter sent jointly by PC/CFS containing 10 numbered objections to the final rule and requesting a hearing on each one. The second is a letter sent by Samuel Epstein (Dr. Epstein), containing six numbered objections, requesting a hearing on each. All but one of the issues raised by Dr. Epstein are identical to certain of those raised in the PC/CFS submission. Both PC/CFS and Dr. Epstein also requested a stay of action on the final rule. FDA addresses the PC/CFS and Dr. Epstein objections and hearing requests in section IV of this document.

FDA also received a large number of submissions after the close of the objection period; their content was identical or similar to the form letters expressing general opposition to the final rule. These tardy submissions failed to satisfy the requirements of 21 U.S.C. 348(f)(1) and need not be considered further by the Agency (*see ICMAD* v. *HEW,* 574 F.2d 553, 558 n.8 (DC Cir), *cert. denied,* 439 U.S. 893 (1978)).

Additionally, most of the issues raised in the PC/CFS and Dr. Epstein objections are similar or identical to issues that have been raised previously and that have been previously addressed in the rule being objected to (70 FR 48057) and in other Agency rulemaking concerning irradiation. The Agency will address these issues briefly; please refer to the cited **Federal Register** documents for a more comprehensive discussion.

III. Standards for Granting a Hearing

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

A party seeking a hearing is required to meet a "threshold burden of tendering evidence suggesting the need for a hearing" (*Costle* v. *Pacific Legal Foundation,* 445 U.S. 198, 214–215 (1980), *reh. denied,* 446 U.S. 947 (1980), citing *Weinberger* v. *Hynson, Westcott & Dunning, Inc.,* 412 U.S. 609, 620–621 (1973)). An allegation that a hearing is necessary to "sharpen the issues" or to "fully develop the facts" does not meet this test (*Georgia Pacific Corp.* v. *U.S. EPA,* 671 F.2d 1235, 1241 (9th Cir. 1982)). If a hearing request fails to identify any factual evidence that would be the subject of a hearing, there is no point in holding one. In judicial proceedings, a court is authorized to issue summary judgment without an evidentiary hearing whenever it finds that there are no genuine issues of material fact in dispute and a party is entitled to judgment as a matter of law (*see* Rule 56, Federal Rules of Civil Procedure). The same principle applies in administrative proceedings (*see* § 12.28).

A hearing request must not only contain evidence, but that evidence should raise a material issue of fact concerning which a meaningful hearing might be held (*Pineapple Growers Association* v. *FDA,* 673 F.2d 1083, 1085 (9th Cir. 1982)). Where the issues raised in the objection are, even if true, legally insufficient to alter the decision, the Agency need not grant a hearing (*see Dyestuffs and Chemicals, Inc.* v. *Flemming,* 271 F.2d 281, 286 (8th Cir. 1959), *cert. denied,* 362 U.S. 911 (1960)). FDA need not grant a hearing in each case where an objector submits additional information or posits a novel interpretation of existing information (*see United States* v. *Consolidated Mines & Smelting Co.,* 455 F.2d 432 (9th Cir. 1971)). In other words, a hearing is justified only if the objections are made in good faith and if they "draw in question in a material way the underpinnings of the regulation at issue" (*Pactra Industries* v. *CPSC,* 555 F.2d 677 (9th Cir. 1977)). Finally, courts have uniformly recognized that a hearing need not be held to resolve questions of law or policy (*see Citizens for Allegan County, Inc.* v. *FPC, 414 F.2d 1125 (DC Cir. 1969); Sun Oil Co.* v. *FPC,* 256 F.2d 233, 240 (5th Cir.), *cert. denied,* 358 U.S. 872 (1958)).

Even if the objections raise material issues of fact, FDA need not grant a hearing if those same issues were adequately raised and considered in an earlier proceeding. Once an issue has been so raised and considered, a party is estopped from raising that same issue in a later proceeding without new evidence. The various judicial doctrines dealing with finality can be validly applied to the administrative process. In explaining why these principles "self evidently" ought to apply to an Agency proceeding, the U.S. Court of Appeals for the District of Columbia Circuit wrote: "The underlying concept is as simple as this: Justice requires that a party have a fair chance to present his position. But overall interests of administration do not require or generally contemplate that he will be given more than a fair opportunity." *Retail Clerks Union, Local 1401* v. *NLRB,* 463 F.2d 316, 322 (DC Cir. 1972). (*See Costle* v. *Pacific Legal Foundation, supra* at 215–220. *See* also *Pacific Seafarers, Inc* . v. *Pacific Far East Line, Inc.,* 404 F.2d 804 (DC Cir. 1968), *cert. denied,* 393 U.S. 1093 (1969)).

IV. Analysis of Objections and Response to Hearing Requests

The letter from PC/CFS contains 10 numbered objections and requests a hearing on each of them. The letter from Dr. Epstein includes six numbered objections and requests a hearing on each. The issues raised in five of the six objections in the letter from Dr. Epstein are identical to issues raised in the letter from PC/CFS; in those cases, the issues will be considered together. FDA addresses each of the objections, as well as the evidence and information filed in support of each, comparing each objection and the information submitted in support of it to the standards for granting a hearing in § 12.24(b) as follows:.

A. Studies on Animals Fed Clams

One objection raised by PC/CFS and Dr. Epstein states that the Agency failed

to consider two animal feeding studies that include toxicological evidence of harmful effects from consumption of irradiated molluscan shellfish. In support of this objection, PC/CFS submitted copies of brief summary reports of the two studies.

The first study is a 1976 reproduction study [1] in which irradiated (4 kiloGray (kGy) and 8 kGy) soft-shell clams were fed to chickens for 2 years. In a note appended to the summary report, the study authors state that the study was replicated (for differing durations) in the F1 and F2 generation birds (*i.e.,* the second and third generation birds bred from the parent generation used in the original study). The objection notes that FDA did not include this study on chickens in the Agency's September 15, 1982, master bibliography of more than 400 studies on the safety of irradiated foods and, that therefore, this study was not assessed by the Task Group for the Review of Toxicology Data on Irradiated Food.[2]

The objection goes on to describe certain of the reported results from the study on chickens, specifically results in the F1 and F2 generations, including the following: Higher hemoglobin values and smaller gonad weights in males of the F1 generation fed irradiated clams; and a decrease in "hatchability" of eggs, enlargement of kidneys in females (an effect that increased with increasing irradiation dose), decreases in egg fertility and embryonic viability, and lower body weights in females, in the F2 generation.

FDA acknowledges that this study was not included in the inventory of studies reviewed by the Bureau of Foods Irradiated Food Task Group in the early 1980s, and agrees that the endpoints cited in the objection were reported by the study authors. However, the Agency does not agree that FDA's failure to assess the study calls into question the safety of irradiated molluscan shellfish, as the objectors contend. The objection fails to note that many of the findings cited in the experimental report were observed both in chickens fed irradiated clams and in chickens fed unirradiated clams, and that the report discusses the need to supplement the diets of the clam-fed chickens with thiamine. Therefore, the observed effects may have been related to the nutritional effects of feeding diets consisting of 50 percent wet-weight of soft-shell clams to chickens. More importantly, if the negative effects cited by the objectors were due to the consumption of irradiated food, one would expect the findings to be reproducible in other studies on irradiated foods; however, such reproducibility is not seen in the large number of feeding studies that have been reviewed by FDA.

The objection also cites a second paper by the same researchers [3] describing a study on feeding clams irradiated at 4 kGy or 8 kGy to beagle dogs. According to the objection, the study showed a significant inverse correlation between the irradiation dose applied to the clams and the blood urea nitrogen (BUN) level of male dogs fed on them. PC/CFS and Dr. Epstein both go on to state that "[t]hough the researchers did not speculate, low blood urea nitrogen levels are usually a symptom of liver damage."

The Agency included this beagle dog study in the review of toxicology studies conducted in the early 1980s. The FDA reviewer noted the reported BUN results and also noted that, although the researchers indicated that organs were weighed and examined histopathologically, no results of the histopathological examination were included in the report. This suggests that the researchers did not find any evidence of liver (or other organ) damage, and in fact the study report includes no information that supports the objectors' contention that liver damage was an underlying condition in the animals tested. Furthermore, the Agency, as part of its rulemaking pertaining to the irradiation of meat and meat products, re-examined the findings reported in this study. As stated in the December 3, 1997, final rule (62 FR 64107 at 64113), FDA concluded that the decrease in BUN levels in this study was not of toxicological significance, and laid out its reasoning in that document and in a memorandum to the record (Ref. 1). Thus, the Agency disagrees with PC/CFS' and Dr. Epstein's contention that this study "* * * found serious toxicity concerns associated with irradiated molluscan shellfish."

A hearing will be denied if the data and information are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)). FDA concludes the data and information are insufficient and, therefore, FDA is denying the request for a hearing on this issue.

B. Microbiologic Safety of Molluscan Shellfish

PC/CFS' second objection asserts that the final rule fails to ensure that the irradiation of molluscan shellfish will result in a product that is microbiologically safe. In support of this objection, PC/CFS cites a 1996 PhD dissertation by Dustin W. Dixon on the effects of irradiation on *Vibrio vulnificus* in shellstock oysters (raw oysters in their shell) harvested in Florida and Texas (Ref. 2). The objection states that there is a potential for microbial outgrowth post-irradiation, and cites Dixon's observation that the *V. vulnificus* count in oysters irradiated at 1.0 kGy and 3.0 kGy rose nearly to the level of that in unirradiated oysters after 2 and 9 days of storage, respectively. The objection states that Dixon concluded that "* * * irradiation processing cannot be considered as a method to sterilize shellstock oysters, and provide a shelf-stable product."

The objection also notes the potential for improper temperature control of irradiated molluscan shellfish prior to consumption by the consumer. The objection states that there is no guarantee that temperature conditions will be properly maintained and asserts that FDA is assuming that Hazard Analysis and Critical Control Point (HACCP) plans [4] will ensure consistent and adequate temperature control.

As noted by PC/CFS, the Dixon dissertation was submitted to the Agency as part of the molluscan shellfish petition. The stated objectives of the research presented in that document were to determine the effects of gamma irradiation on Florida and Texas shellstock oysters in terms of shelf life and microbial consequences. FDA does not dispute the findings of Dr. Dixon, and agrees that irradiation of molluscan shellfish to an absorbed dose of 5.5 kGy will not sterilize molluscan shellfish or create a shelf-stable product. FDA also agrees with Dr. Dixon's conclusion in his dissertation that irradiation may not be sufficient by itself to eliminate *V. vulnificus* in molluscan shellfish and that proper conditions of storage must be maintained after shellfish have been irradiated.

FDA disagrees, however, with PC/CFS' assertion that the final rule must "[en]sure the microbiological safety of fresh oysters." The standards for microbiological safety of molluscan

[1] Fegley, H.C. and Edmonds, R.E., in Food Irradiation Information, International Project in the Field of Food Irradiation, Karlsuhe, Germany, No. 6 (Supplement), 113–115, June 1976.

[2] The Bureau of Foods Irradiated Food Task Group consisted of toxicologists in the Bureau of Foods who reviewed many studies on food irradiation in the early 1980s.

[3] Fegley, H.C. and Edmonds, R.E., in Food Irradiation Information, International Project in the Field of Food Irradiation, Karlsruhe, Germany, No. 6 (Supplement), 111–112, June, 1976.

[4] FDA has established regulations for seafood HACCP in 21 CFR part 123.

shellfish are independent of the final rule permitting the irradiation of molluscan shellfish. Irradiation is but one measure for the control of *Vibrio* spp. and other food-borne pathogens. The rule is not predicated on the approved treatment, by itself, resulting in shellfish that are sterile or shelf-stable. A hearing will not be granted on factual issues that are not determinative with respect to the action requested (§ 12.24(b)(4)). Therefore, FDA is denying the request for a hearing based on this objection.

C. Reasonable Certainty of No Harm

PC/CFS' third objection states that "there is no reasonable certainty in the minds of competent scientists that irradiation is not harmful as applied to molluscan shellfish." In support of this objection, PC/CFS makes several assertions. First, PC/CFS refers to several sets of comments that it submitted to the docket for the molluscan shellfish rulemaking. PC/CFS states that those comments cite 11 "peer-reviewed papers or other publications stating safety concerns associated with irradiated foods" and that these comments refer to "at least 25 other highly 'competent' Ph.D.s or MDs who have stated that they have safety concerns in published literature." The objection states that, although these comments and papers refer to irradiation of food types other than molluscan shellfish, the Agency should have specifically considered the statements of these authors. Second, PC/CFS asserts that FDA misstated what is contained in its literature reference numbered as "Ref 20" in the final rule. Third, PC/CFS, as well as Dr. Epstein, asserts that FDA mischaracterized the findings of the Raltech study. In support of this assertion, PC/CFS submitted a copy of two summary reports from the "Raltech studies" and a 1984 trade press article that quotes Dr. Thayer of USDA. Finally, PC/CFS states that neither FDA's final rule nor the underlying petition actually contains data from, or references to, any toxicity studies on irradiated mollusks.

As evidence that there is not a "reasonable certainty of safety in the minds of competent scientists" PC/CFS notes that they have submitted comments including journal articles and other publications that express concerns with food irradiation. However, the articles do not contain any evidence that could be resolved at a hearing, nor has PC/CFS pointed to any evidence in the cited articles. Nor has PC/CFS pointed to any specific factual information in the cited articles on foods analogous to molluscan shellfish, which the Agency has ignored and which would call into question the Agency's conclusions. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, FDA is denying the request for a hearing based on this objection.

The Agency agrees that reference 20 as cited in the final rule is incorrect. The proper reference is: S.G. Armstrong, S.G. Wylie, and D. N. Leach, "Effects of Preservation by Gamma Irradiation on the Nutritional Quality of Australian Fish," *Food Chemistry* 50 (1994) 351–357. This error does not demonstrate a lack of reasonable certainty of safety. A hearing will be denied if the information submitted is insufficient to justify the factual determination urged (§ 12.24(b)(3)).

The Agency disagrees with PC/CFS' and Dr. Epstein's assertion that the final rule mischaracterizes the findings of the "Raltech study." The Raltech studies were sponsored by the United States Department of Agriculture and conducted by Raltech Scientific Services. In this series of studies, conducted in the late 1970s and early 1980s, irradiation-sterilized chicken (doses ranged from 45–59 kGy) was fed to various types of animals. PC/CFS alleges that there were several negative health effects seen in these studies, including a significant dose-related decrease in the number of offspring of *Drosophila melanogaster* (fruit flies), and a high incidence of testicular tumors and significantly reduced survival in mice.

The Agency evaluated the results of the Raltech studies and has extensively discussed its conclusions regarding these studies in previous rulemaking documents (*see* 51 FR 13376 at 13386, 53 FR 53176 at 53188, and 55 FR 18538 at 18540). The Agency specifically discussed the results of the feeding study in mice and the mutagenicity study in fruit flies (*see, e.g.,* 55 FR 18538 at 18540). The Agency has described its reasoning in finding no evidence in any of the Raltech studies of adverse effects that could be attributed to consumption of irradiation-sterilized chicken. The Agency has found that the quantity and breadth of testing and the number and significance of endpoints assessed would have identified meaningful risks, if any existed. On those few occasions where adverse effects were reported, FDA found that those effects were not attributable to irradiation. PC/CFS does not submit or otherwise identify any factual data that would cause the Agency to alter its conclusions about these studies. Accordingly, FDA is denying the request for a hearing based on this objection (§ 12.24(b)(2)).

Finally, the Agency agrees that there were no toxicological studies conducted using irradiated molluscan shellfish submitted in the petition. As noted in the molluscan shellfish final rule (70 FR 48057 at 48068), the Agency has reviewed a large body of data that are relevant to the assessment of the potential toxicity of irradiated flesh foods. FDA has consistently taken the position that various scientifically validated types of data may properly support a safety determination for a proposed use of a food additive (*see* part 170 (21 CFR part 170) in § 170.20). For example, in the case of food irradiation, the Agency has taken advantage of the extensive research and large body of knowledge concerning the principles of radiation chemistry and the chemical composition of foods. PC/CFS' suggestion that data and information derived from studies of analogous irradiated foods are not sufficient to support a determination that irradiated molluscan shellfish are safe, is unsupported by specific data or other factual information. Further, the question of whether safety has been shown requires the application of the legal standard of safety as defined by FDA's regulations ("reasonable certainty of no harm") to a set of facts (*see* § 170.3(i)). As such, FDA concluded as a matter of law that the proposed use of irradiation to treat fresh and frozen molluscan shellfish with absorbed doses not to exceed 5.5 kGy is safe. A hearing will not be granted on issues of policy or law (§ 12.24(b)(1)). Therefore, FDA is denying the request for a hearing based on this objection.

D. Factors Unique to Molluscan Shellfish

PC/CFS objects to the molluscan shellfish final rule on the grounds that the Agency and the underlying petition failed to consider several factors that could make irradiated molluscan shellfish unsafe. These factors are: (1) Safety of irradiated salt water; (2) chemicals that irradiated molluscan shells may 'off-gas' [5]; (3) effects of irradiation on undigested shellfish stomach contents such as plankton and algae; (4) attenuation of irradiation effects from shell thickness (*i.e.,* that thicker shells may attenuate the effectiveness of irradiation); and (5) lack of data on furan creation from the shells. Dr. Epstein also objects on the basis of the issues relating to chemical byproducts from irradiated molluscan

[5] "Off-gassing" refers to volatile chemicals that may be emitted over time from a source.

shells, and the attenuation of irradiation effects from shell thickness.

First, the Agency notes that there is no basis to suggest that the presence of salts in water will affect the irradiation of molluscan shellfish because ionizing radiation, under the petitioned conditions, does not affect inorganic salts (Ref. 3). Second, the objection provides no information to show that mollusk shells (composed of approximately 95 percent calcium carbonate and 5 percent protein), when irradiated, would produce any chemicals that may off-gas into the meat, nor is there any information to suggest that such chemicals, were they to be formed, would render the food unsafe. Third, the objection provides no evidence that the stomach contents of irradiated molluscan shellfish are materially different from any other irradiated food (*i.e.,* composed predominantly of protein, fat, and carbohydrate). Fourth, the Agency agrees that varying shell thickness may attenuate the effectiveness of irradiation, and that this attenuation would increase with shell thickness. However, the objection provides no evidence that would cause the Agency to find that consumption of irradiated molluscan shellfish is not safe. As explained in section IV.B of this document, it is not necessary that irradiation "[en]sure the microbiological safety of fresh oysters." Parties irradiating molluscan shellstock are responsible for ensuring that treated food receives the minimum irradiation dose reasonably required to accomplish its intended technical effect and not more than the maximum dose specified by the applicable regulation (*see* 21 CFR 179.25(b)) . Finally, the Agency discussed the potential generation of furan in the final rule (70 FR 48057 at 48059) and concluded that irradiated molluscan shellfish do not generate furan at a rate that is higher than the background generation of furan in un-irradiated molluscan shellfish (Ref. 4). Although in the final rule the Agency cited data concerning furan formation from shucked oysters, the objection points to no factual data to suggest that irradiation of mollusks in the shell (which is approximately 95 percent calcium carbonate) would lead to furan formation from irradiation of the shell.

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Neither PC/CFS nor Dr. Epstein has provided a basis for a hearing and FDA is denying the request for a hearing on this objection.

E. Application of 100-Fold Safety Margin for 2-Alkylcyclobutanones

PC/CFS and Dr. Epstein cite 21 CFR 170.22 [6] and object to the molluscan shellfish final rule (70 FR 48057) on the basis that FDA improperly failed to apply a 100-fold safety factor regarding the production of 2-alkylcyclobutanones (2–ACBs) from the irradiation of esterified fatty acids in considering the safety of irradiated molluscan shellfish. In support of their contention that the Agency should have applied a 100-fold safety factor to 2–ACBs, PC/CFS and Dr. Epstein make several assertions. First, the objection asserts that 2–ACBs are found only in irradiated foods and are known to be potentially toxic at certain concentrations and to promote tumor formation in the presence of known carcinogenic substances. The objection also asserts that the flesh of molluscan shellfish is distinct from that of other flesh foods because it contains a "unique combination" of fatty acids and that these fatty acids, when irradiated, produce a unique combination of 2–ACBs. The objection, therefore, maintains that FDA's reliance on the Raltech study to address concerns about 2–ACBs is flawed because that study involved chicken which has a lower stearic acid content than oysters. Finally, the objection asserts that "there are no adequate long-term safety studies that assist in assessing the overall health hazards that consuming 2–ACBs could pose, including likely variations in sensitivities to 2–ACBs among the human consumer population" and refers particularly to children and other vulnerable populations. In relation to this last point, PC/CFS submitted a publication on the susceptibility of children to environmental substances by William Au.[7]

The applicability of § 170.22 is a legal issue, and a hearing will not be granted on issues of law. The Agency notes that § 170.22 refers to safety factors to be used in determining whether a proposed use of a food additive will be safe. In the present instance, 2–ACBs are not the food additive that is the subject of the rulemaking. Therefore, the 100-fold safety factor discussed in § 170.22 does not apply to 2–ACBs. Further, as noted in the molluscan shellfish final rule (70 FR 48057 at 48066), applying a 100-fold safety factor to a processed food or to individual components of a processed food is not feasible or appropriate.

The Agency agrees that 2–ACBs have been reported to be formed in small quantities as a result of irradiation of fats and that these compounds have been identified in irradiated meat and poultry. In the final rule permitting the irradiation of molluscan shellfish, the Agency described in detail its assessment of the significance of the formation of 2–ACBs to a safety assessment of molluscan shellfish, which like poultry and meat, contain appreciable amounts of triglycerides. This assessment included a discussion of the contentions that 2–ACBs may cause DNA damage and may be tumor promoters at certain concentrations (70 FR 48057 at 48065 to 48067). While the objection repeats assertions made in comments to the final rule about the toxicity of 2–ACBs and the failure of the Agency to apply a 100-fold safety factor for 2–ACBs, the objection includes no new information or analysis that would call into question the Agency's rationale for its decision.

The objection states that molluscan shellfish contain a unique combination of fatty acids that differ from those in poultry, and that therefore, the Agency's reliance on the Raltech study to address concerns about 2–ACBs is flawed. In particular, the objection states that chicken meat contains less stearic acid than do oysters. It is true that the Agency considers the Raltech studies useful in assessing the effects of 2–ACBs in animals fed irradiated flesh foods (70 FR 48057 at 48066). In the Raltech studies, animals were fed chicken irradiated at a dose approximately 10 times the dose permitted in the molluscan shellfish final rule, at a level of 35 percent of the diet, for their lifetime. Thus, although the concentration of stearic acid in chickens is lower than in molluscan shellfish, the amount of 2–ACBs in the diets of the animals in the Raltech studies, including those formed from irradiation of stearic acid is likely to be higher than the amount in the human diet from irradiated molluscan shellfish (70 FR 48057 at 48066). As noted previously, there were no adverse toxicological effects seen in the Raltech studies that could be attributed to the consumption of irradiated chicken. In addition, it is important to note that the Agency has not relied solely on the Raltech studies in concluding that irradiation of molluscan shellfish under the conditions permitted in the final rule is safe. As pointed out in the final rule (70 FR 48057 at 48066), the Agency's review included studies in which animals were

[6] That section provides in relevant part 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. * * *" 21 CFR 170.22.

[7] Au, W., Susceptibility of Children to Environmental Toxic Substances, *International Journal of Hygiene Environmental Health;* 205:1–3, 2002.

fed diets containing irradiated beef, pork, poultry, horse meat, and fish, and found no evidence of toxicity attributed to the consumption of these foods, which contain various levels and combinations of fatty acids that may potentially form 2–ACBs. The objection has thus misrepresented the basis for the Agency's decision when it contends that the final rule relies on the Raltech studies to discount concerns about 2–ACBs in irradiated molluscan shellfish.

In the molluscan shellfish final rule, the Agency noted that it had reviewed a multitude of studies on irradiated foods that would have contained radiolytic products including 2–ACBs, and which include long-term safety studies. FDA noted that it had previously concluded that "The results of the available toxicological studies of irradiated flesh foods * * * demonstrate 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). Although the objection alleges that there are no "adequate long-term safety studies that assist in assessing the overall health hazards that consuming 2–ACBs could pose," the objection provides no factual information to call into question the studies on which the Agency has relied, nor does it provide any new information or data to refute the analysis set out in the molluscan shellfish final rule.

The objection also cites the FDA's "rejection" of the 100-fold safety margin as inappropriate, given the need to "protect children and other vulnerable consumers." The paper by Dr. Au, which was submitted in support of this objection, is a commentary discussing the need to consider data and information that indicate that children are more susceptible to toxic contaminants than are adults in setting guidelines for protecting children's health. The objection provides no evidence to show that the Agency's conclusion that molluscan shellfish, irradiated under the conditions permitted by the regulation, are safe, fails to protect children and other vulnerable consumers. The submitted commentary includes no information or data relevant to the safety of irradiated molluscan shellfish.

In sum, the Agency is denying a hearing on the objection that FDA improperly rejected application of the 100-fold safety factor in § 170.22 to 2–ACBs produced in irradiated molluscan shellfish. The interpretation of the applicability of this regulation is a legal issue, and a hearing will not be granted on issues of law. Moreover, PC/CFS and Dr. Epstein have not presented any evidence supporting their contention that the potential levels of 2–ACBs in irradiated molluscan shellfish may render the food unsafe. PC/CFS' request for a hearing merely alleges that there is potential for harm, without providing any evidence that the Agency has not already considered. An objector must make an adequate proffer of evidence to support its allegations and to show that they provide a basis on which to call into question the Agency's conclusions (§ 12.24(b)(2)). Thus, neither PC/CFS nor Dr. Epstein has provided a basis for a hearing and FDA is denying their requests for a hearing based on this objection.

F. Alleged Rejection of Published Evidence

PC/CFS cites their comment submitted on May 14, 2001, and repeats the assertion made in that comment that the Agency ignored or improperly discounted a number of positive *in vivo* and *in vitro* mutagenicity studies, including five peer-reviewed published studies performed by the Indian National Institute of Nutrition (NIN) in which purported mutagenic effects were found in mice, rats, and monkeys, and in malnourished children, consuming freshly-irradiated wheat. In support of the objection, PC/CFS submitted excerpts from 1987 Congressional testimony by S.G. Srikantia, the former Director of NIN, who testified that FDA committed an error of judgment in accepting a report by a committee of Indian scientists discrediting the NIN studies (*see* 53 FR 53176 at 53182). The objection also asserts that FDA neglected to consider a statement made in 1988 by an Australian genotoxicity expert to a Committee of the Australian House of Representatives, stating that the malnourished children study's results seemed reasonable. In addition, the objection refers to two later publications by the NIN researchers rebutting criticisms of the study, and cites a statement by the former Director of NIN stating that the NIN's results were mirrored in a study on hamsters (Ref. 5) that found that polyploidy cells occurred five times more frequently in animals fed irradiated wheat in their diet, and that this increased incidence of polyploidy was related to irradiation dose.

The Agency has previously considered all of the various *in vitro* and *in vivo* mutagenicity studies cited by PC/CFS and discussed its conclusions in detail in previous documents (*see e.g.,* 51 FR 13376 at 13383 and 13385; 53 FR 53176 at 53181–3 and 53191–2; 70 FR 48057 at 48064 and 48067). Several of the studies cited in the comment refer to reports of in vitro mutagenicity of irradiated sugars in solution. The Agency previously has discussed in detail why it has concluded that the irradiation of simple sugars in solution is not a suitable model for predicting and extrapolating toxicity of irradiated foods. In the final rule permitting additional uses of ionizing radiation for the treatment of food, the Agency noted: "In feeding studies where sugars are present in a typically complex food matrix there is no increase in mutagenicity after irradiation. Studies have demonstrated that when a food containing sugars is irradiated, the food does not produce the same toxic effects that occur when these sugars are irradiated in simple solution. Thus, the Agency concluded that irradiated aqueous sugar solutions are unsuitable models for predicting and extrapolating toxicity of irradiated foods and that there is no evidence that radiolytic products from sugars present in irradiated foods cause toxic effects to animals or humans (51 FR 13376 at 13383)."

The objection provides no new evidence or rationale that provides a basis on which to find that FDA's conclusion on the relevance of these studies is incorrect.

The Agency also has previously repeatedly addressed in detail the interpretation of the NIN studies using freshly irradiated wheat and concluded that none of the studies on polyploidy done at NIN were reliable and that the studies do not demonstrate that adverse effects would be caused by ingestion of irradiated foods (51 FR 13376 at 13385; 53 FR 53176 at 53183; 70 FR 48057 at 48068). In the molluscan shellfish final rule, the Agency noted, citing earlier rulemaking: "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 Indian scientists that the studies with irradiated foods do not demonstrate that

adverse effects would be caused by ingesting irradiated foods." (70 FR 48057 at 44067 and 44068)

Dr. Srikantia's testimony states that the FDA was wrong to accept the report of the committee of Indian scientists; he states that NIN has not repudiated the studies on polyploidy and that the Director of NIN submitted a rebuttal to the report of the committee of Indian scientists, and that "[h]ad it seen the Institute's rejoinder to the * * * report, surely, it would have been in a better position to evaluate that report." FDA previously has addressed all issues raised in Dr. Srikantia's testimony (*see e.g.*, 53 FR 53176 at 53182–3). As noted previously (53 FR 53176 at 53183) FDA did not state that NIN had repudiated the studies, nor did it base its own conclusions about the studies on a finding that the data were repudiated by NIN. FDA concluded that the available data from NIN did not provide an appropriate basis on which to conclude that increased polyploidy was caused by ingesting irradiated wheat. Furthermore, FDA in 1986 invited Dr. Srikantia to submit any information to FDA that would be relevant. Dr. Srikantia replied, but did not submit a copy of his rebuttal to the Indian government or any other report (*see* footnote 1, 53 FR 53176 at 53183).

The hamster study by Renner referenced by PC/CFS also has been discussed previously (53 FR 53176 at 53183 and 531834). The study involved the irradiation of hamster diets (composed primarily of carbohydrates) at high doses. The investigator concluded that at doses above 30 kGy there was a "[* * *] transitory effect [* * *] as evidenced by an increased incidence of polyploidy cells" but that "there was no evidence of any mutagenic effect being produced as a result of feeding an irradiated diet." He noted that no effects on incidence of polyploidy were seen at doses below 20 kGy. The objection contains no information that explains why this study is relevant to the molluscan shellfish (composed primarily of protein and fats) irradiated at doses up to 5.5 kGy.

In summary, all of the studies referenced by PC/CFS have been considered previously by FDA and the Agency's rationale for its conclusions on those studies has been discussed at length in previous rulemakings. Neither the objection, nor the testimony of Dr. Srikantia, nor the statement of the Australian expert, includes any new information or data that would refute the Agency's findings about the studies. PC/CFS' request for a hearing merely alleges that there is potential for harm, without providing any evidence that the Agency has not considered previously. An objector must make an adequate proffer of evidence to support its allegations and to show that they provide a basis on which to call into question the Agency's conclusions (§ 12.24(b)(2)). Thus, PC/CFS has not provided a basis for a hearing and FDA is denying PC/CFS' request for a hearing based on this objection.

G. Alleged Warnings on Potential risks

PC/CFS' seventh objection alleges that the "FDA misrepresents important published and unpublished warnings from qualified scientists calling for additional research on 2–ACBs."

The Agency previously has addressed the allegations of the potential harm of the long-term consumption of 2–ACBs that are produced from the irradiation of esterified fatty acids (70 FR 48057 at 48066) and the research performed on 2–ACBs. The Agency concluded: "2–ACBs have been reported as radiolysis products of fats (Refs. 6 and 7). Studies performed by researchers have reported that certain alkylcyclobutanones can cause single strand DNA breaks detectable by the COMET assay (Ref. 8). 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."

The objection provides no additional information on 2–ACBs that the Agency has not addressed previously. The Agency does not consider the statements in the cited papers on 2–ACBs to be warnings; rather, the comments are statements presented by the authors that research should continue on 2–ACBs. These statements do not affect the Agency's determination that 2–ACBs do not cause the food to be unsafe at levels present in irradiated food.

Moreover, PC/CFS' request for a hearing merely alleges that there is potential for harm, without providing any evidence that the Agency has not already considered and determined did not demonstrate a potential for harm. An objector must make an adequate proffer of evidence to support its allegations and to show that they provide a basis on which to call into question the Agency's conclusions (§ 12.24(b)(2)). Thus, PC/CFS has not provided a basis for a hearing and FDA is denying PC/CFS' request for a hearing based on this objection.

H. Alleged Failure To Follow Critical Guidelines for Food Additives

PC/CFS and Dr. Epstein allege that FDA failed to follow "critical guidelines" for food additives. Specifically, the objections assert that although use of an irradiation source is statutorily defined as a food additive, 21 U.S.C. section 321(s), the final rule incorrectly characterizes irradiated molluscan shellfish as "processed foods" (70 FR 48057 at 48069), and as such, applied a lower safety standard. Second, the objections cite § 170.20 and assert that the Agency ignored provisions of that regulation. For example, the objections assert that the rule provides no evidence to support FDA's decision to ignore the current National Academy of Sciences-National Research Council (NAS–NRC) publication "Risk Assessment/Safety Evaluation of Food Chemicals" (*see* § 170.20(a)). Also citing § 170.20, the objections assert that the final rule provides no evidence that FDA gave due weight to anticipated levels and patterns of consumption of irradiated molluscan shellfish (*see* § 170.20 (a)). Third, the objections cite § 170.22 and state that the Agency failed to justify not using a 100-fold safety factor in the final rule. Fourth, the objection maintains that FDA failed to comply with the testing protocols set forth in the Redbook.[8] Finally, the objections state that FDA ignored the recommendations put forth in 1980 by the Bureau of Foods Irradiated Foods Committee (BFIFC) regarding the evaluation of irradiated foods.

A source of radiation used to process food is defined as a food additive in section 201(s) of the FD&C Act (21 U.S.C. 321(s)); the exposure of molluscan shellfish to ionizing radiation is what makes irradiated molluscan shellfish a processed food. The FD&C Act requires that a food additive, including a source of radiation used to process food, must be shown to be safe under the proposed conditions of use before the use can be approved. That is, the Agency must find that there is a reasonable certainty that consumption of an irradiated food is not harmful. FDA applied the same standards and guidelines that the Agency uses to evaluate all food additives to evaluate the safety of a source of ionizing radiation used to treat molluscan shellfish. The Agency's reference to

[8] 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).

irradiated molluscan shellfish as a "processed" food in the final rule did not change the Agency's finding that such shellfish is safe.

The Agency has previously addressed its reasoning in interpreting and applying its own regulations at §§ 170.20 and 170.22 in the molluscan shellfish final rule, in response to comments submitted by PC/CFS (70 FR 48057 at 48066 and 48068). The regulation at § 170.20(a) reads in part: "In reaching a decision on any petition filed under section 409 of the Act, the Commissioner will give full consideration to the specific biological properties of the compound and the adequacy of the methods employed to demonstrate safety for the proposed use, and 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. In reaching a decision, the Commissioner will give due weight to the anticipated levels and patterns of consumption of the additive specified or reasonably inferable."

In the molluscan shellfish final rule, the Agency explained that FDA has consistently taken the position that many scientifically valid types of data may properly support a finding that a proposed use of a food additive is safe. The Agency pointed out that NAS–NRC testing standards and guidelines have been stated in relatively general terms and that in practice, FDA has applied exposure and toxicological criteria that were current for the time, and appropriate for assessing the safety of a particular food additive (70 FR 48057 at 48068). In its objection, PC/CFS repeats its assertion that FDA failed to properly interpret its own regulation, but has provided no new information that would refute the Agency's reasoning. The objection implies that the Agency is obligated to explicitly discuss its consideration of NAS–NRC guidelines in its rules, but there is nothing in § 170.20 that imposes such an obligation on the Agency. The regulation requires the Commissioner of Food and Drugs (the Commissioner) to make a finding that the procedures used by the petitioner give results that are as reliable as, or more reliable than, those reasonably expected from use of the NAS–NRC guidelines. Acceptance of a petition based on alternate procedures implies that the Commissioner has made such a finding.

With respect to the assertion that FDA failed to give due weight to anticipated levels and patterns of consumption of irradiated molluscan shellfish, FDA previously has reviewed a large body of data relevant to the assessment of potential toxicity of irradiated flesh foods. In its evaluations of the safety of a source of radiation to treat food intended for human consumption, the Agency has identified three areas of concern to be addressed: (1) Potential toxicity, (2) nutritional adequacy, and (3) potential microbiological risk from treated foods. Each of these areas was discussed in detail in the molluscan shellfish final rule. FDA asserted that the Agency "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 (70 FR 48057 at 48059)." In its review of studies in which animals were fed diets containing beef irradiated at 56 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 these foods.

FDA has concluded that products formed (typically oxidation products of food constituents) following irradiation of molluscan shellfish are the same as or similar to those found in non-irradiated foods after cooking. Further, radiolysis products in shellfish are essentially the same as those in red meat and poultry, since the composition is roughly the same. Additionally, shellfish make a smaller contribution to the average daily diet; therefore, exposure to radiolysis products from shellfish will be smaller than that from foods for which irradiation currently is regulated. Cooking and other heat processing methods remain the principle means for introducing such substances into the diet (Ref. 9). PC/CFS' assertion provides no basis to challenge FDA's assessment of the safety of irradiated molluscan shellfish.

In like manner, the assertions that FDA failed to follow its regulation in § 170.22, or to comply with recommendations in the Redbook or set forth by the BFIFC committee, have been raised previously by PC/CFS, Dr. Epstein, and others, and have been responded to by the Agency in the molluscan shellfish final rule (70 FR 48057 at 48066 and 48069) and in other previous rulemakings (*see e.g.,* 57 FR 6667 at 6669; 62 FR 64102 at 64105; and Section IV.E., above). The Agency has described its reasoning for concluding that the data and information considered in the evaluation of the petition to permit the irradiation of molluscan shellfish, when considered in its entirety, are sufficient to support the safety of molluscan shellfish irradiated under the conditions specified in the regulation. Once the Agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward with evidence that calls into question FDA's conclusion (*see* § 12.24(b)(2)). PC/CFS and Dr. Epstein provide no new information on how the Agency failed to follow the regulations to establish the safety of irradiating molluscan shellfish to an absorbed dose of 5.5 kGy. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). The objectors must, at a minimum, raise a material issue concerning which a meaningful hearing might be held. Neither PC/CFS nor Dr. Epstein has provided a basis for a hearing and FDA is denying their request for a hearing based on this objection.

I. Wholesomeness

PC/CFS states that "FDA's final rule fails to address recent studies in its possession indicating that irradiation at low dose levels in oysters may cause unpleasant—perhaps unwholesome—byproducts." The objection discusses a report [9] presented at the 2002 annual meeting of the Institute of Food Technologists that suggests that molluscan shellfish irradiated at 2.0 kGy produced an "unpleasant yellow exudate." The objection goes on to discuss other potential organoleptic changes that may occur in irradiated molluscan shellfish (such as "grassy" and "oxidized" odors) as noted in Dixon's 1996 dissertation (Ref. 2). PC/CFS states that FDA's final rule failed to address these issues of "wholesomeness," and requests a hearing on these issues.

FDA previously has acknowledged that irradiation may cause organoleptic changes in foods (62 FR 64107 at 64110). Such organoleptic changes may make the food unappealing and unmarketable; however, undesirable organoleptic changes do not render the food unsafe. Neither the author of the

[9] Andrews, L. S., "Gamma Irradiation Processing to Reduce the Risk of Vibrio Infections from Raw Oysters," (unpublished presentation at the 2002 Annual Meeting), 2002.

report cited by PC/CFS nor PC/CFS itself suggests that there is any evidence that the noted "unpleasant yellow exudate" or other organoleptic changes would render irradiated molluscan shellfish unsafe.

PC/CFS' request for a hearing suggests that there is potential for harm from possible organoleptic changes from irradiation of molluscan shellfish, without providing any evidence to support this suggestion. An objector must make an adequate proffer of evidence to support its allegations and to show that they provide a basis on which to call into question the Agency's conclusions. A hearing will be denied if the Commissioner concludes that the data and information submitted are insufficient to justify the factual determination urged, even if accurate (§ 12.24(b)(3)). FDA concludes that the data and information are insufficient; therefore, FDA is denying the request for a hearing based on this objection.

J. FDA Review Memoranda

PC/CFS alleges that there are errors in some of the FDA review memoranda used to support the final rule. The objection states that these errors call into question the adequacy of the Agency's review processes that led to the Agency's conclusion that irradiated molluscan shellfish are safe. There are four parts to this objection; the Agency will address each part below.

Part one of this objection asserts that "FDA significantly misrepresents published research on the tumor-promoting qualities of 2–ACBs." Specifically, the objection states that an FDA memorandum in the record (Ref. 10) mischaracterizes the findings of a publication submitted by PC/CFS as part of a comment to the petition to irradiate molluscan shellfish (Ref. 11). The objection states that these alleged mischaracterizations "severely bias the Agency's analysis of 2–ACBs."

The disputed memorandum included a discussion of the Raul *et al.* (2002) paper submitted to the Agency by PC/CFS as part of its comment to the molluscan shellfish petition; the memorandum also discussed a commentary on the paper that was submitted with the comment (Ref. 12). The objection cited three selected sentence fragments from the memorandum which PC/CFS maintains are incorrect. The memorandum discussed the authors' observations and the limitations of the Raul, *et al.* study and stated that those limitations and inconsistencies in the data made it difficult to draw conclusions from the study. In the final rule (70 FR 48057 at 48067) the Agency discussed the limitations of the study and its reasoning in concluding that the results of long-term feeding studies were more relevant to a finding of safety than the Raul *et al.* study.

As FDA noted in the final rule (70 FR 48057 at 48067): "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 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."

The Agency maintains that the disputed memorandum taken as a whole, including the sentence fragments highlighted by PC/CFS, accurately and reliably reflects the information in the Raul and Rao publications. Importantly, the factual issues raised by the three disputed statements were not determinative in the Agency's overall conclusions about the relevance of the Raul *et al.* study or to its determination that the irradiated molluscan shellfish under the conditions of the regulation are safe. A hearing will not be granted on factual issues that are not determinative with respect to the action requested (§ 12.24(b)(4)). Thus, PC/CFS has not provided a basis for a hearing and FDA is denying PC/CFS' request for a hearing based on this objection.

Part two of this objection asserts that FDA cites no evidence to dismiss the COMET assay as a valid technique for testing genetic toxicity. The objection asserts that the "technique has broad support within the scientific community" and quotes excerpts from several published reports that state that the COMET assay has utility, and is being increasingly used in the screening of various substances.

The Agency does not dispute the statements quoted by the PC/CFS nor the fact that the COMET assay is being increasingly studied and used to study the cellular response to DNA damage and repair. In the final rule, the Agency has addressed its conclusions pertaining to the COMET assay results (70 FR 48057 at 48065), as they are presented with respect to 2–ACBs and has determined that, when the totality of evidence is examined with other more standard genotoxicity testing methods, "the potential risk of 2–DCB, if any, is very low." The cited quotations do not provide any information related to the safety of consumption of 2–ACBs that may be present in irradiated molluscan shellfish that the Agency has not considered, and the objection contains no information that would cause the Agency to change its safety determination. A hearing will not be granted on factual issues that are not determinative with respect to the action requested (§ 12.24(b)(4)).

Part three of this objection states that certain FDA review memoranda (Chen to Highbarger, 12/21/2001, FAP 9M4697), (Morehouse to Highbarger, 6/l/2002, 9M4697), and (Chen to Highbarger, 4/7/2003, FAP 9M4695) are irrelevant to the analysis of irradiated molluscan shellfish, because they were written as part of the review of other petitions to permit the irradiation of certain other foods. This objection also states that one of the memoranda (Chen to Highbarger, 12/21/2001, FAP 9M4697) is inaccurate, because it states that "the radiolysis products of irradiated lipids and proteins are either the same as, or structurally very similar to, compounds found in foods that have not been irradiated." PC/CFS state that "numerous published articles show—and the FDA now admits—that 2–ACBs are fundamentally unique from any naturally occurring food component." Additionally, the objection states that this memorandum ignores the FDA Redbook's statement that genotoxicity tests can contribute to safety assessments.

The Agency acknowledges that the review memoranda cited were written as part of the review of two petitions to permit the irradiation of certain foods (other than molluscan shellfish) that are pending at the Agency: FAP 9M4695, submitted by the U.S. Department of Agriculture (64 FR 71792) [10] and FAP 9M4697, submitted by the National Food Processors Association on behalf of the Food Irradiation Coalition (65 FR 493 and 66 FR 23943).[11] The objection

[10] FAP 9M4695 requests that 21 CFR part 179 be amended to provide for the safe use of a 4.5 kiloGray (kGy) maximum dose of ionizing radiation to treat unrefrigerated (as well as refrigerated) uncooked meat, meat products, and certain meat food products to reduce levels of foodborne pathogens and extend shelf-life.

[11] FAP 9M4697 requests that 21 CFR part 179 be amended to provide for the safe use of ionizing radiation for control of foodborne pathogens, and extension of shelf-life, in a variety of human foods up to a maximum irradiation dosage of 4.5 kGy for non-frozen and non-dry products, and 10.0 kGy for

Continued

does not explain, however, why the information in those memoranda is irrelevant to the irradiation of molluscan shellfish to an absorbed dose of 5.5 kGy. These review memoranda describe chemistry and toxicology information related to the irradiation of protein, fat, and carbohydrate; these are components of molluscan shellfish. The Agency has repeatedly noted that its conclusions on safety of irradiating molluscan shellfish are based on the evaluation of the totality of evidence before it, and in particular, that information related to the irradiation of flesh foods is relevant to an evaluation of the safety of irradiated molluscan shellfish. The objection provides no information that would suggest the information in the cited memoranda is irrelevant to the molluscan shellfish final rule except to point out that they were written as part of the review of other petitions.

The objection also cites a statement from a memorandum written in 2001 that stated that "* * * radiolysis products of irradiated lipids and proteins are either the same as, or structurally very similar to, compounds found in foods that have not been irradiated" and points out that the Agency has since acknowledged that 2–ACBs have thus far not been found in food that has not been irradiated.[12] As noted in the objection itself, there is no factual issue in dispute, and the objection points to no reason why the statement in the 2001 memorandum calls into question the Agency's subsequent conclusions about the safety of irradiated molluscan shellfish.

Finally, this part of the objection alleges that the 2001 memorandum ignores the FDA Redbook's statement that genotoxicity tests can contribute significantly to safety assessments. The Agency agrees that genotoxicity testing can be useful in the assessment of the safety of food additives. In the molluscan shellfish final rule the Agency discussed the use of genotoxicity tests, and of long-term feeding studies, in the context of the safety assessment of irradiated foods (70 FR 48057 at 48064) concluding: "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."

Thus, the Agency has acknowledged the utility of genotoxicity tests, but also states that when long-term animal feeding studies are available, that these latter studies are more reliable for determining the mutagenic potential of a compound consumed in food. Nothing in the objection would suggest that the Agency's position is in contradiction to the recommendations in the Redbook.

An objector must make an adequate proffer of evidence to support its allegations and to show that they provide a basis on which to call into question the agencies conclusions (§ 12.24(b)(2)). PC/CFS has not provided a basis for a hearing and FDA is denying PC/CFS' request for a hearing based on this objection.

Finally, part four of the objection states that an FDA memorandum (Folmer-Jensen to Highbarger, 8/2/2002, FAP 9M4697) states that other food processing methods (such as freezing, canning and drying) can result in loss of vitamins, but neglects to consider the potential for additional vitamin reduction if irradiated foods were to be subsequently processed by freezing, canning or drying. This part further cites a 1986 trade press article as evidence that irradiation, when combined with other food processing techniques, has a greater effect on reducing levels of vitamins than each process individually. The objection then questions the Agency's conclusion that the contribution of thiamine, niacin and vitamin B6 from fish and shellfish represents an insignificant contribution to the nutritional needs of Americans. The objection cites two studies that showed a substantial reduction in thiamine level in irradiated cod.

The Agency agrees that irradiation may reduce some vitamins in foods. Additionally, further processing may further reduce some vitamins in foods. The extent to which vitamin loss is nutritionally significant depends in part on the relative contribution of the food in question to the overall dietary intake of the vitamin. The Agency has concluded that the reductions of vitamins in molluscan shellfish will cause negligible changes in total dietary intake of the affected vitamins as a result of irradiating molluscan shellfish under the conditions of the regulation. The objection questions the Agency's analysis and conclusion, but offers no data or information to support a contention that permitting the irradiation of molluscan shellfish would have an adverse impact on the nutritional adequacy of the diet. Moreover, the objection contains no information that would cause the Agency to change its conclusion that the consumption of irradiated molluscan shellfish to an absorbed dose of 5.5 kGy is safe.

A hearing will be denied if the Commissioner concludes that the data and information submitted are insufficient to justify the factual determination urged, even if accurate ((§ 12.24(b)(3)). FDA concludes that the data and information are insufficient; therefore, FDA is denying the request for a hearing based on this objection.

K. Chemicals Formed in Irradiated Foods

One objection submitted by Dr. Epstein alleges that FDA has "ignore[d] the fact that irradiation can dramatically increase the concentration of many potentially toxic chemicals." Dr. Epstein specifically mentions benzene and toluene, quoting a statement from D.U. Ahn of Iowa State University: "[B]enzene and toluene * * * could be formed from amino acids upon irradiation * * * Benzene has deleterious effects on human health (Ref. 13)." In support of the quoted statement, the objection references a paper entitled "Effects of Electron Beam Irradiation and Antimicrobials on the Volatiles, Color, and Texture of Ready-to-Eat Turkey Breast Roll."

The Agency acknowledges that benzene, toluene, and other compounds are formed, albeit in very small amounts, when meats are irradiated at sterilizing doses (Ref. 14.). The formation of benzene and other volatile compounds (including toluene) in irradiated foods and their possible risk to human health has been extensively evaluated by FDA and discussed in previous rulemaking (*see* 62 FR 64107 at 64110–64111, 55 FR 18538 at 18542–18543 and 53 FR 53176 at 53197).

frozen or dry products, including: (1) Pre-processed meat and poultry; (2) both raw and preprocessed vegetables, fruits, and other agricultural products of plant origin; (3) certain multi-ingredient food products. The notice stated that the petition does not cover products composed in whole or in part of raw meat, poultry, or fish nor does it cover "ready-to-eat" fish products or ingredients made from fish.

[12] We note that recent studies have demonstrated that 2–ACBs are formed in certain foods that have not been irradiated (*e.g.,* roasted nuts).

Regarding benzene specifically, the Agency has stated: "The select Committee concluded that the small addition of benzene from radiation sterilized beef would contribute only a trivial increment to the normal body burden and is unlikely to increase significantly whatever hazard exists from other sources. FDA is not aware of any evidence that call this conclusion into question" (53 FR 53176 at 53197).

The objection identifies no evidence that the Agency overlooked, and does not provide any new evidence that would indicate benzene, toluene, or other chemicals are formed in irradiated molluscan shellfish in quantities that would pose a risk to human health. Thus, Dr. Epstein's request for a hearing based on this objection is denied because a hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)).

The objection also criticizes the Agency for making "[a] blanket statement which the Agency fails to explain further: "FDA and food 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." Dr. Epstein also takes issue with the Agency's statement that "* * * identification of major radiolysis products will aid in the interpretation of data."

Contrary to Dr. Epstein's remarks, the Agency provided a detailed explanation of its statement about safety testing of irradiated whole foods versus the testing of individual components of those foods in the context of its response to a comment expressing a different view about requirements for testing irradiated food (*see* 70 FR 48057 at 48066). Additionally, the Agency has provided detailed discussions of the role of chemical identification of radiolysis products in the evaluation of data from safety testing (*see* 70 FR 48507 at 48059 and 62 FR 64107 at 64110–64111 and section IV. H of this document).

In conclusion, the submitted objection contains no evidence that the Agency has overlooked and no new evidence that would call into question the Agency's previous conclusion that consumption of irradiated molluscan shellfish is safe. The objection merely alleges that there may possibly be formation of benzene and toluene and alleges a potential of harm. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (§ 12.24(b)(2)); therefore, FDA is denying the request for a hearing based on this objection.

V. Summary and Conclusion

The FD&C Act requires that a food additive be shown to be safe prior to marketing under section 409 of the FD&C Act. Under § 170.3(i), a food additive is "safe" if there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. In the Agency's August 16, 2005, final rule approving the use of irradiation on fresh or frozen molluscan shellfish, FDA concluded that the studies conducted to establish the safety of this additive demonstrate that this use of irradiation is safe for its intended use on fresh or frozen molluscan shellfish.

The petitioner has the burden to demonstrate the safety of the additive to gain FDA approval. Nevertheless, once FDA makes a finding of safety in an approval document, the burden shifts to an objector, who must come forward with evidence that calls into question FDA's conclusion (*American Cyanamid Co.* v. *FDA,* 606 F.2d 1307, 1314–1315 (DC Cir. 1979)).

Despite their many allegations, PC/CFS and Dr. Epstein have not established that FDA overlooked significant information in the record in reaching its conclusion that the use of irradiation on fresh or frozen molluscan shellfish is safe. In such circumstances, FDA has determined that the objections do not raise any genuine and substantial issue of fact that can be resolved by an evidentiary hearing (§ 12.24(b)).

Accordingly, FDA is denying the requests for a hearing. In addition, PC/CFS' and Dr. Epstein's requests for a stay of the effectiveness of the August 16, 2005, regulation until a hearing is held are moot because FDA is denying all hearing requests. Thus, FDA is confirming August 16, 2005, as the effective date of the final rule published at 70 FR 48057.

VI. References

The following references are on display at the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857, under Docket No. FDA–1999–F–0056 (formerly 1999F–4372), and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Memorandum to the file, FAP 4M4428, from P. Hansen, FDA, dated October 31, 1997.
2. Dixon, D.W., "The Influence of Gamma Radiation Upon Shellstock Oysters, and Culturable and Viable but Nonculturable Vibrio vulnificus," a dissertation presented to the Graduate School of the University of Florida, 1996.
3. Diehl, J.F., "Safety of Irradiated Foods," second edition, Marcel Dekker, Inc., New York, 1995.
4. Memorandum for FAP 9M4682 from K. Morehouse, FDA, to L. Highbarger, FDA, July 15, 2005.
5. Renner, H.W., "Chromosome Studies on Bone Marrow Cells of Chinese Hamsters Fed a Radiosterilized Diet," *Toxicology,* 8:213–222, 1977.
6. Miesch, M., Ndiye, B., Hasselmann, C., and E. Marchioni, "2–Alkylcyclobutanones as Markers for Irradiated Food Stuffs—I. Synthesis of Saturated and Unsaturated Standards," *Radiation Physics and Chemistry,* 55:337–344, 1999.
7. Horvatovich, P., M. Miesch, C. Hasselmann, and E. Marchioni, "Supercritical Fluid Extractin of Hydrocarbons and 2–Alkylcyclobutanones for the Detection of Irradiated Foodstuffs," *Journal of Chromatography,* 897:259–268, 2000.
8. 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).
9. Memorandum for FAP 9M4682 and FAP 1M4727, from D. Folmer, FDA, to L. Highbarger, August 2, 2002.
10. Memorandum for FAP 9M4682 from T. Twaroski, FDA, to L. Highbarger, FDA, July 14, 2005.
11. Raul, F., F. Gosse, H. Delincee, 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.
12. 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.
13. Bureau of Food Irradiated Foods Committee, "Recommendations for Evaluation the Safety of Irradiated Food," prepared for the Director, Bureau of Foods, FDA, July 1980.
14. 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.
15. Zhu, M.J., *et al.,* "Effects of Electron Beam Irradiation and Antimicrobials on the Volatiles, Color, and Texture of Ready-to-Eat Turkey Breast Roll," *Journal of Food Science,* 69(5):C382–C387, 2004.
16. Federation of American Societies for Experimental Biology, Life Sciences Research Office, Evaluation of the Health Aspects of Certain Compounds Found in Irradiated Beef, Supplement 1979, 1977.

Dated: March 15, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2011–6625 Filed 3–21–11; 8:45 am]

BILLING CODE 4160–01–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 52

[EPA–R07–OAR–2010–0945; FRL–9281–6]

Approval and Promulgation of Implementation Plans; Nebraska: Prevention of Significant Deterioration; Greenhouse Gas Permitting Authority and Tailoring Rule Revision

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is taking final action to approve revisions to the State Implementation Plan (SIP) for Nebraska, submitted by the Nebraska Department of Environmental Quality (NDEQ) to EPA for final processing on January 14, 2011. These revisions cover two broad categories under Nebraska's prevention of significant deterioration (PSD) preconstruction permitting program. The first applies to revisions relating to permitting of greenhouse gas (GHG) emissions under the PSD program. The second applies to revisions incorporating relevant aspects of EPA's 2002 new source review (NSR) reform rules, submitted by letter dated November 19, 2010.

The GHG SIP revision, which incorporates updates to NDEQ's air quality regulations, includes two significant changes impacting the regulation of GHGs under Nebraska's PSD program. First, the SIP revision provides the State of Nebraska with authority to issue PSD permits governing GHGs. Second, the SIP revision establishes emission thresholds for determining which new stationary sources and modification projects become subject to Nebraska's PSD permitting requirements for their GHG emissions. The first provision is required under the GHG PSD SIP call, which EPA published on December 13, 2010, and which required the State of Nebraska to apply its PSD program to GHG-emitting sources. The second provision is consistent with the thresholds EPA established in the Tailoring Rule, published on June 3, 2010. EPA is approving this SIP revision because this SIP revision meets the requirements of the GHG PSD SIP Call.

In addition, in today's action, EPA is also taking final action to approve Nebraska's adoption of portions of EPA's 2002 NSR Reform rules, published December 31, 2002. EPA has determined that Nebraska's revisions track the Federal NSR Reform Rules. EPA previously determined that the implementation of the Federal NSR Reform Rules will be environmentally beneficial.

DATES: This rule will be effective March 22, 2011.

ADDRESSES: EPA has established a docket for this action under Docket Identification No. EPA–R07–OAR–2010–0945. All documents in the docket are listed on the *http://www.regulations.gov* Web site. Although listed in the index, some information is not publicly available, *i.e.,* Confidential Business Information or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either electronically through *http://www.regulations.gov* or in hard copy at the Air Planning and Development Branch, Air and Waste Management Division, U.S. Environmental Protection Agency, Region 7, 901 North 5th Street, Kansas City, KS 66101. EPA requests that if at all possible, you contact the person listed in the **FOR FURTHER INFORMATION CONTACT** section for further information. The Regional Office's official hours of business are Monday through Friday, 8:30 to 4:30, excluding Federal holidays.

FOR FURTHER INFORMATION CONTACT: For information regarding the Nebraska SIP, contact Mr. Larry Gonzalez, Air Planning and Development Branch, Air and Waste Management Division, U.S. Environmental Protection Agency, Region 7, 901 North 5th Street, Kansas City, Kansas 66101. Mr. Gonzalez's telephone number is (913) 551–7041; e-mail address: *gonzalez.larry@epa.gov.*

SUPPLEMENTARY INFORMATION:

Table of Contents

I. What is the background for today's final action?

EPA has recently undertaken a series of actions pertaining to the regulation of GHGs that, although for the most part distinct from one another, establish the overall framework for today's final action for the Nebraska SIP. The first four of these actions include, as they are commonly called, the "Endangerment Finding" and "Cause or Contribute Finding," which EPA issued in a single final action,[1] the "Johnson Memo Reconsideration," [2] the "Light-Duty Vehicle Rule," [3] and the "Tailoring Rule." [4] Taken together, these actions established regulatory requirements for GHGs emitted from new motor vehicles and new motor vehicle engines; determined that such regulations, when they took effect on January 2, 2011, subject GHGs emitted from stationary sources to PSD requirements; and limited the applicability of PSD requirements to GHG sources on a phased-in basis.

In a separate action, the "GHG PSD SIP Call," [5] EPA called on the State of Nebraska and 12 other States with SIPs that do not provide authority to issue PSD permits governing GHGs to revise their SIPs to provide such authority. In that action, EPA took steps to ensure that in the 13 States that do not have authority to issue PSD permits to GHG-emitting sources at present, either the State or EPA would have the authority to issue such permits by January 2, 2011, or soon thereafter. EPA explained that although for most States, either the State or EPA is already authorized to issue PSD permits for GHG-emitting sources as of that date, Nebraska and the other 12 States have EPA-approved PSD programs that do not include GHG-emitting sources and therefore do not authorize these States to issue PSD permits to such sources. Accordingly, EPA issued the GHG PSD SIP Call to require a SIP revision that applies Nebraska's SIP PSD programs to GHG-emitting sources. EPA also established a SIP submittal deadline. In the proposed SIP call, EPA had stated that the deadline could range from as little as three weeks after the final SIP call was signed to as long as 12 months after the

[1] "Endangerment and Cause or Contribute Findings for Greenhouse Gases Under Section 202(a) of the Clean Air Act." 74 FR 66496 (December 15, 2009).

[2] "Endangerment and Cause or Contribute Findings for Greenhouse Gases Under Section 202(a) of the Clean Air Act." 74 FR 66496 (December 15, 2009).

[3] "Light-Duty Vehicle Greenhouse Gas Emission Standards and Corporate Average Fuel Economy Standards; Final Rule." 75 FR 25324 (May 7, 2010).

[4] "Prevention of Significant Deterioration and Title V Greenhouse Gas Tailoring Rule; Final Rule." 75 FR 31514 (June 3, 2010).

[5] "Action to Ensure Authority to Issue Permits Under the Prevention of Significant Deterioration Program to Sources of Greenhouse Gas Emissions: Finding of Substantial Inadequacy and SIP Call; Final Rule." 75 FR 77698 (December 13, 2010).