

event of a lapse in appropriations, or a day on which the Commission's Washington, DC office is otherwise closed for regular business due to other circumstances. The Commission finds that because the amendment is technical in nature and pertains to the Commission's organization, procedure or practice, publishing the amendment for comment is unnecessary.²¹

The APA also requires publication of a rule at least 30 days before its effective date unless the agency finds otherwise for good cause.²² For the same reasons described above with respect to notice and the opportunity for comment, the Commission finds good cause for this technical amendment to take effect immediately.

IV. Consideration of Burden on Competition, and Promotion of Efficiency, Competition and Capital Formation

Section 3(f) of the Exchange Act,²³ provides that whenever the Commission is engaged in rulemaking and is required to consider or determine whether an action is necessary or appropriate in the public interest, the Commission shall consider, in addition to the protection of investors, whether the action will promote efficiency, competition, and capital formation. Section 23(a)(2) of the Exchange Act requires the Commission, in adopting rules under the Exchange Act, to consider the competitive effects of such rules, if any, and not to adopt a rule that would impose a burden on competition not necessary or appropriate in the furtherance of the purposes of the Exchange Act.²⁴

Because the amendment to Exchange Act Rule 19b-4 is technical in nature, and does not impose any additional requirements beyond those already required, we do not anticipate that the amendment would have a significant effect on efficiency, competition, or capital formation, and we do not anticipate that any competitive advantages or disadvantages would be created.

²¹ For similar reasons, the amendment does not require analysis under the Regulatory Flexibility Act ("RFA") or analysis of major rule status under the Small Business Regulatory Enforcement Fairness Act. See 5 U.S.C. 601(2) (for purposes of RFA analysis, the term "rule" means any rule for which the agency publishes a general notice of proposed rulemaking); and 5 U.S.C. 804(3)(C) (for purposes of Congressional review of agency rulemaking, the term "rule" does not include any rule of agency organization, procedure or practice that does not substantially affect the rights or obligations of non-agency parties).

²² See 5 U.S.C. 553(d)(3).

²³ 15 U.S.C. 78c(f).

²⁴ 15 U.S.C. 78w(a)(2).

List of Subjects in 17 CFR Part 240

Brokers, Confidential business information, Fraud, Reporting and recordkeeping requirements, Securities.

Statutory Basis and Text of Rules

The Commission is amending 17 CFR part 240, pursuant to authority set forth in the Exchange Act, including Sections 19(b) and 23(a).

PART 240—GENERAL RULES AND REGULATIONS, SECURITIES EXCHANGE ACT OF 1934

- 1. The authority citation for part 240 continues to read in part as follows:

Authority: 15 U.S.C. 77c, 77d, 77g, 77j, 77s, 77z-2, 77z-3, 77eee, 77ggg, 77nnn, 77sss, 77ttt, 78c, 78d, 78e, 78f, 78g, 78i, 78j, 78j-1, 78k, 78k-1, 78l, 78m, 78n, 78n-1, 78o, 78p, 78q, 78s, 78u-5, 78w, 78x, 78ll, 78mm, 80a-20, 80a-23, 80a-29, 80a-37, 80b-3, 80b-4 and 80b-11, and 7210 et seq., 18 U.S.C. 1350, and 12 U.S.C. 5221(e)(3), unless otherwise noted.

* * * * *

- 2. Amend § 240.19b-4 by:
 - a. Redesignating paragraph (a) as paragraph (a)(1); and
 - b. Adding new paragraph (a)(2).

The addition reads as follows:

§ 240.19b-4 Filings with respect to proposed rule changes by self-regulatory organizations.

* * * * *

(a) * * *

(2) For purposes of Section 19(b) of the Act and this rule, a "business day" is any day other than a Saturday, Sunday, Federal holiday, a day that the Office of Personnel Management has announced that Federal agencies in the Washington, DC area are closed to the public, a day on which the Commission is subject to a Federal government shutdown or a day on which the Commission's Washington, DC office is otherwise not open for regular business.

* * * * *

Dated: April 7, 2011.

By the Commission.

Elizabeth M. Murphy,
Secretary.

[FR Doc. 2011-8919 Filed 4-12-11; 8:45 am]

BILLING CODE P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 179

[Docket No. FDA-1998-F-0072] (Formerly 98F-0165)

Irradiation in the Production, Processing, and Handling of Food

AGENCY: Food and Drug Administration, HHS.

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

SUMMARY: The Food and Drug Administration (FDA) is responding to objections and is denying requests that it received for a hearing on the final rule that amended the food additive regulations to provide for the safe use of ionizing radiation for the reduction of *Salmonella* in fresh shell eggs. After reviewing objections to the final rule and requests for a hearing, the Agency has concluded that the objections do not raise issues of material fact that justify a hearing or otherwise provide a basis for revoking or modifying the amendment to the regulation.

FOR FURTHER INFORMATION CONTACT: Teresa A. Croce, Center for Food Safety and Applied Nutrition (HFS-265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835, 301-436-1281.

SUPPLEMENTARY INFORMATION:

I. Introduction

In the **Federal Register** of March 20, 1998 (63 FR 13675), FDA published a notice announcing the filing of a food additive petition (FAP), FAP 8M4584, submitted by Edward S. Josephson, University of Rhode Island, Food Science and Nutrition Research Center, to amend the regulations in part 179, *Irradiation in the Production, Processing, and Handling of Food* (21 CFR part 179), to provide for the safe use of ionizing radiation for the reduction of *Salmonella* in fresh shell eggs. In response to the petition, FDA issued a final rule in the **Federal Register** of July 21, 2000 (65 FR 45280), permitting the irradiation of fresh shell eggs for the reduction of *Salmonella* at doses not to exceed 3.0 kiloGray (kGy) (hereafter referred to as the "egg irradiation rule"). 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 stated that objections to the final rule and requests for a hearing were due within 30 days of the

publication date (*i.e.*, by August 21, 2000).

II. Objections and Requests for a Hearing

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

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

Following publication of the final rule permitting the irradiation of fresh shell eggs for the reduction of *Salmonella*, FDA received 26 submissions with objections to the rule within the 30-day objection period. All but one of these submissions either expressed general opposition to the final rule, or objected to the rule based on issues that are outside the rule's scope such as the living conditions and practices in commercial egg production. Although most of these letters requested a hearing, no evidence was identified in support of any of these objections that could be considered in an evidentiary hearing (§ 12.22(a)(5)). Therefore, these objections do not justify a hearing.¹ The Agency will not discuss these

submissions further. The one submission raising specific objections was a letter from Public Citizen (letter to Docket No. 98F-0165, August 17, 2000). The letter from Public Citizen sought revocation of the final rule based on five objections and requested a hearing on issues raised by each objection. A more detailed response to Public Citizen's objections is found in section IV of this document. In addition, FDA also received one letter in support of the egg irradiation rule.

III. Standards for Granting a Hearing

Specific criteria for deciding whether to grant or deny a request for a hearing are set out in § 12.24(b). Under that regulation, a hearing will be granted if the material submitted by the requester shows, among other things, the following: (1) There is a genuine and substantial factual issue for resolution at a hearing; a hearing will not be granted on issues of policy or law; (2) the factual issue can be resolved by available and specifically identified reliable evidence; a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions; (3) the data and information submitted, if established at a hearing, would be adequate to justify resolution of the factual issue in the way sought by the 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. Pac. Legal Found.*, 445 U.S. 198, 214 (1980), *reh. denied*, 446 U.S. 947 (1980), citing *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 620-21 (1973)). An allegation that a hearing is necessary to "sharpen the issues" or to "fully develop the facts" does not meet this test (*Georgia-Pacific Corp. v. U.S. EPA*, 671 F.2d 1235, 1241 (9th Cir. 1982)). 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 Fed. R. Civ. P. 56*). The same principle applies in administrative proceedings (*see* § 12.24).

A hearing request must not only contain evidence, but that evidence should raise a material issue of fact "concerning which a meaningful hearing might be held" (*Pineapple Growers Ass'n v. FDA*, 673 F.2d 1083, 1085 (9th Cir. 1982)). Where the issues raised in the objection are, even if true, legally insufficient to alter the decision, 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)). A hearing is justified only if the objections are made in good faith and if they "draw in question in a material way the underpinnings of the regulation at issue" (*Pactra Industries v. CPSC*, 555 F.2d 677, 684 (9th Cir. 1977)). A hearing need not be held to resolve questions of law or policy (*see Citizens for Allegan County, Inc. v. FPC*, 414 F.2d 1125, 1128 (D.C. Cir. 1969); *Sun Oil Co. v. FPC*, 256 F.2d 233, 240 (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, such as collateral estoppel, can be validly applied to the administrative process (*see Pac. Seafarers, Inc. v. Pac. Far East Line, Inc.*, 404 F.2d 804, 809 (D.C. Cir. 1968), *cert. denied*, 393 U.S. 1093 (1969)). In explaining why these principles ought to apply to an agency proceeding, the U.S. Court of Appeals for the District of Columbia Circuit wrote: "The underlying concept is as simple as this: Justice requires that a party have a fair chance to present his position. But overall interests of administration do not require or generally contemplate that he will be given more than a fair opportunity." *Retail Clerks Union, Local 1401 v. NLRB*, 463 F.2d 316, 322 (D.C. Cir. 1972); *see also Costle v. Pac. Legal Found.*, 445 U.S. at 215-17).

IV. Analysis of Objections and Response to Hearing Requests

The letter from Public Citizen contains five numbered objections and requests a hearing on each of them. FDA addresses each of the objections in this document, as well as the evidence and information filed in support of each, comparing each objection and the information submitted in support of it to

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

the standards for granting a hearing in § 12.24(b).

A. Findings of Study Co-Authored by Donald Thayer

The first objection raised by Public Citizen in response to this rule contends that the Agency misrepresented the findings of the 1990 study co-authored by Donald Thayer (Ref. 1). Specifically, the rule (65 FR 45280 at 45281) states, “* * * *S. enteritidis* was found to have similar sensitivities to ionizing radiation as five other strains of *Salmonella*” (*S.* is referring to *Salmonella*) when, in the original study, Thayer *et al.* state, “*S. enteritidis* was significantly more resistant to ionizing radiation than the other five strains of *Salmonella* tested * * *.” Public Citizen asserts that by stating the findings in this manner FDA gives “* * * the false impression that the same level of radiation can be used to eliminate *S. enteritidis* as other strains of *Salmonella*.”

The full sentence in the final rule states that “*Salmonella* strains, in addition to *S. enteritidis*, in fresh shell eggs should also be reduced by irradiation since *S. enteritidis* was found to have similar sensitivities to ionizing radiation as five other strains of *Salmonella* * * *.” (65 FR 45280 at 45281). The reasoning supporting the statement’s conclusion is that because irradiation reduces *S. enteritidis* it would be expected to reduce other strains of *Salmonella*. To the extent that *S. enteritidis* is more resistant to ionizing radiation than the other strains, the conclusion is strengthened. Further, FDA made clear in the final rule that irradiation of fresh shell eggs at the doses requested in the petition will reduce, but not entirely eliminate, microorganisms in eggs (65 FR 45280 at 45281).

FDA evaluated data provided by the petitioner on the absorbed radiation required to achieve inactivation of *S. enteritidis* in shell eggs. The data showed that irradiation at a dose as low as 1 kGy reduces the viability of *S. enteritidis* by 3- \log_{10} (99.9 percent reduction) (Ref. 2). These data are comparable to the results seen by Thayer, *et al.*, in a similar medium inoculated with *S. enteritidis*, which showed a 3- to 4- \log_{10} reduction of this pathogen at a dose of 1 kGy (Ref. 1). Furthermore, the standards for microbiological safety of fresh shell eggs are independent of the final rule permitting the irradiation of fresh shell eggs. Irradiation is a potential control point in the mitigation of *S. enteritidis* and other food-borne pathogens. The rule is not predicated on the approved treatment, by itself, resulting in fresh

shell eggs that are pathogen-free. FDA is denying the request for a hearing on this point because the action would be the same even if the factual issue were resolved in the manner sought (§ 12.24(b)(4)).

B. Vitamin A Loss

In the egg irradiation final rule, FDA states that the vitamin A retention resulting from the irradiation of shell eggs at a maximum absorbed dose of 1.0 kGy (65 FR 45280 at 45281) yields a relative retention rate of 76 percent following a 24-day storage period. Public Citizen asserts that the final rule misrepresents the vitamin A loss from fresh shell eggs following irradiation at 3.0 kGy because FDA based these conclusions on vitamin A loss from the results of a study that used a maximum dose of 1.0 kGy compared to the maximum petitioned dose of 3.0 kGy, whereas another study in the petition showed that vitamin A retention by the eggs irradiated at 3.1 kGy and stored for 2, 15, and 33 days was 41.8 percent, 35.5 percent, and 20.1 percent, respectively (Refs. 3 and 4).

The studies that Public Citizen refers to were included in the petition and were analyzed and considered when making the safety assessment. FDA acknowledges that stating a vitamin A retention in the range of 20.1 to 35.5 percent is more appropriate in light of the maximum petitioned dose. Importantly, in its review of the petition, FDA considered the health implications from vitamin A loss in eggs at the maximum petitioned dose and concluded that the effect on health from this vitamin loss is not significant because a variety of foods provide vitamin A and the intake of other foods can compensate for any loss (Refs. 5 and 6).

The issue raised by Public Citizen must be a material issue concerning which a meaningful hearing might be held (*Pineapple Growers Ass’n v. FDA*, 673 F.2d at 1085). The Agency recognizes that irradiation can produce nutrient losses under some conditions and has concluded that such effects are not a safety concern under the conditions of this regulation. To justify a hearing on the vitamin A issue, Public Citizen must provide evidence that the nutritional loss in a food irradiated under the conditions of this regulation raises a safety concern because of its cumulative effect on the human diet (*see* 21 U.S.C. 348(c)(5)(B)). While FDA has the ultimate burden of proof when it approves the use of a food additive, once the Agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward

with evidence that raises a material issue of fact with regard to FDA’s conclusion (*American Cyanamid Co. v. FDA*, 606 F.2d 1307, 1314 (DC Cir. 1979)). Public Citizen has submitted no information to support that vitamin A loss in fresh shell eggs irradiated under the conditions of the regulation is a safety concern. Therefore, this objection does not raise a genuine and substantial issue of fact for resolution at a hearing. FDA is denying the request for a hearing on this point because a hearing will not be granted if there is no genuine and substantial factual issue to be resolved (§ 12.24(b)(1)).

C. Analysis of Effects of Irradiation on Egg Yolk Carotenoids

Public Citizen asserts that FDA’s analysis regarding the effects of irradiation on egg yolk carotenoids is flawed because the information used to analyze the nutritional information of egg yolk carotenoids is based on doses of 0.5 kGy and 1.0 kGy, not the petitioned maximum of 3.0 kGy.

FDA acknowledges that Agency’s analysis of the effects of irradiation on egg yolk carotenoids was based on studies performed at lower doses than the petitioned maximum dose of 3.0 kGy; however, because there are a number of commonly consumed foods that are substantial sources of carotenoids in the diet, including yellow corn, carrots, and squash (Ref. 7), FDA has no health concerns about the loss of carotenoids in the diet from the irradiation of eggs. Public Citizen’s request for hearing suggests that there is potential for harm from the loss of carotenoids resulting from the irradiation of shell eggs, 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 of Food and Drugs (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.

D. Request for Updated Analysis for Irradiation of Fresh Shell Eggs Not To Exceed 3.0 kGy

Public Citizen objects to the egg irradiation final rule on the grounds that the Agency did not adequately update “[n]umerous issues raised in the two initial analysis [sic]” after the petition

was amended to allow for doses up to 3.0 kGy from 1.7 kGy.

When the petition (FAP 8M4584) was originally submitted, the maximum petitioned dose was 1.7 kGy. The petition was subsequently amended to increase the maximum dose to 3.0 kGy and additional chemistry and toxicology reviews were performed by FDA following this amendment. Based on these reviews, FDA concluded that the 3.0 kGy dose for shell eggs did not change the general conclusions from the original reviews (Refs. 3 and 6). Public Citizen neither specifies the “[n]umerous issues” nor does it provide any information that would cause the Agency to change its conclusion that the consumption of irradiated shell eggs 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.

E. Bureau of Foods Irradiated Food Committee Report of 1980

Public Citizen alleges that FDA failed to follow all of the recommendations put forth in 1980 by the Bureau of Foods Irradiated Food Committee (BFIFC) regarding the evaluation of irradiated foods. Specifically, Public Citizen quotes the following from a BFIFC report: “Foods irradiated at doses above 100 Krad [1 kGy] and comprising more than 0.01% of the diet are estimated to contain URPs [Unique Radiolytic Products] in sufficient quantity to warrant toxicological evaluation. * * * [T]ests must be performed on extracts in which the concentration of *radiolytic products is maximized*” (Ref. 8).

Public Citizen then states that there is no indication in the egg irradiation rule or its references that such tests were conducted or reviewed by the FDA before the petition was approved.

The assertion that FDA failed to comply with recommendations set forth by the BFIFC committee has been raised previously by Public Citizen and others and has been responded to by the Agency in the molluscan shellfish final rule (70 FR 48057 at 48069, August 16, 2005) and in other previous rulemakings regarding the irradiation of food (*see, e.g.*, 53 FR 53176 at 53179, December 30, 1988, and 62 FR 64102 at 64105, December 3, 1997).

As discussed previously, the BFIFC report was an internal document prepared by FDA scientists that provided recommendations for

evaluating the safety of irradiated foods based on the known effects of food irradiation and on the capabilities of toxicological testing. The report was made available to the public for comment in the **Federal Register** of March 27, 1981 (46 FR 18992). While the report and the comments received on it have aided FDA’s thinking regarding the safety testing of irradiated foods, the report established no requirements. Furthermore, FDA has not adopted regulations that require toxicological testing of a food additive if that additive constitutes a certain portion of the diet, and Public Citizen has not cited any regulation that imposes such a requirement.

In addition, the understanding of radiolytic products produced by the irradiation of foods has evolved since 1980. As noted in the egg irradiation final rule, “[m]ost of the radiolysis products [of shell egg irradiation up to 3kGy] are either the same as, or structurally similar to, compounds found in foods that have not been irradiated, and are formed in very small amounts.” (65 FR 45280). Similarly, in the **Federal Register** of December 3, 1997, for the Agency rulemaking on irradiation of refrigerated or frozen uncooked meat, meat byproducts, and certain meat food products to control food-borne pathogens and extend product shelf-life, FDA concluded that, “[i]n irradiated flesh foods, most of the radiolytic products derived from proteins have the same chemical composition 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.” (62 FR 64107 at 64110, December 3, 1997).

Consistent with section 409 of the FD&C Act, the Agency’s decision on the safety of the irradiation of fresh shell eggs was based on the entire record. FDA reviewed and evaluated studies submitted in the petition as well as additional toxicology studies of irradiated foods, including red meat, chicken, fish and eggs, which are available in Agency files. Included in the data considered by the FDA in review of the petition were at least three studies conducted specifically on irradiated eggs.

Once the Agency makes a finding of safety in an approval document, the burden shifts to an objector to come forward with evidence that calls into question FDA’s conclusion (*see* § 12.24(b)(2)). Although Public Citizen alleged that the rule did not comply with the recommendations in the BFIFC

report, Public Citizen did not present any evidence that these alleged inconsistencies, even if true, would have led to a different conclusion concerning the safety of irradiation of fresh shell eggs. Therefore, FDA is denying this objection and request for a hearing because it raises no factual issue that, even if resolved in the way sought by the objection, would justify the action requested (§ 12.24(b)(4)).

V. Summary and Conclusion

Section 409 of the FD&C Act requires that a food additive be shown to be safe prior to marketing. Under 21 CFR 170.3(i), a food additive is “safe” if “there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.” In the Agency’s July 21, 2000, final rule approving the use of irradiation of fresh shell eggs, FDA concluded, based on its evaluation of the data submitted in the petition and other relevant material, that this use of irradiation is safe for its intended use for the reduction of *Salmonella* in fresh shell eggs.

The petitioner has the burden to demonstrate the safety of the additive to gain FDA approval. However, 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 (*see* section 409(f)(1) of the FD&C Act).

Despite its allegations, Public Citizen has not established that FDA overlooked significant information in the record while reaching its conclusion that the use of irradiation for reduction of *Salmonella* in fresh shell eggs is safe. Therefore, the Agency has determined that the objections requesting a hearing do not raise any genuine and substantial issue of fact that would justify an evidentiary hearing (§ 12.24(b)). Accordingly, FDA is not making any changes in response to the objections and is denying the requests for a hearing.

VI. References

The following references are on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857, under Docket No. FDA-1998-F-0072 (formerly 98F-0165) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. Thayer, D. W., G. Boyd, W.S. Muller, et al. "Radiation resistance of *Salmonella*," *Journal of Industrial Microbiology*, 5: 383–390, 1990.
2. Memorandum for FAP 8M4584 from V. K. Bunning, FDA, to W. Trotter, FDA, April 4, 2000.
3. Memorandum for FAP 8M4584 from K. Morehouse, FDA, to W. Trotter, FDA, April 11, 2000.
4. Memorandum for FAP 8M4584 from K. Morehouse, FDA, to W. Trotter, FDA, May 14, 1999.
5. Memorandum for FAP 8M4584 from I. Chen, FDA, to W. Trotter, FDA, December 11, 1998.
6. Memorandum for FAP 8M4584 from I. Chen, FDA, to W. Trotter, FDA, March 31, 2000.
7. U.S. Department of Agriculture, Agricultural Research Service, USDA National Nutrient Database for Standard Reference, Release 23, Nutrient Data Laboratory Home Page (<http://www.ars.usda.gov/ba/bhnrc/ndl>), 2010.
8. Bureau of Foods Irradiated Foods Committee, *Recommendations for Evaluating the Safety of Irradiated Food*, Prepared for the Director, Bureau of Foods, FDA, July 1980.

Dated: April 8, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2011–8815 Filed 4–12–11; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 610

[Docket No. FDA–2010–N–0099]

Revision of the Requirements for Constituent Materials

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the biologics regulations to permit the Director of the Center for Biologics Evaluation and Research (CBER) or the Director of the Center for Drug Evaluation and Research (CDER), as appropriate, to approve exceptions or alternatives to the regulation for constituent materials. A request for an exception or alternative will be considered for approval when the data submitted in support of such a request establish the safety, purity, and potency of the biological product for the conditions of use, including indication and patient population, for which the applicant is seeking approval. FDA is taking this action due to advances in

developing and manufacturing safe, pure, and potent biological products licensed under the Public Health Service Act (the PHS Act) that, in some instances, render the existing constituent materials regulation too prescriptive and unnecessarily restrictive. This rule provides manufacturers of biological products with flexibility, as appropriate, to employ advances in science and technology as they become available, without diminishing public health protections.

DATES: This rule is effective May 13, 2011.

FOR FURTHER INFORMATION CONTACT: Paul E. Levine, Jr., Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION:

I. Background

In the *Federal Register* of March 30, 2010 (75 FR 15639), FDA published a proposed rule to amend the regulations for constituent materials under § 610.15 (21 CFR 610.15). Constituent materials include ingredients, preservatives, diluents, adjuvants, extraneous protein and antibiotics that are contained in a biological product. FDA is amending the regulation for constituent materials to allow the Director of CBER or the Director of CDER, as appropriate, to approve an exception or alternative to the requirements under § 610.15. An exception or alternative will be considered for approval when the data submitted in support of such a request establish the safety, purity, and potency of the biological product for the conditions for which the applicant is seeking approval. Under the final rule, the Director of CBER or CDER would not approve an exception or alternative when the data or the conditions of use, including indication and patient population, for which the applicant is seeking approval, do not provide a sufficient scientific and regulatory basis for such an approval.

The final rule provides manufacturers of biological products with flexibility, as appropriate, to employ advances in science and technology, as they become available. However, the final rule does not diminish public health protections that are provided by existing laws and regulations. The final rule gives manufacturers the potential to employ advances in science and technology if the data provide a sufficient regulatory basis for approval of the product. This means that each manufacturer's request

for an exception or alternative will be considered on a case-by-case basis to determine whether the product at issue meets the statutory and regulatory criteria for safety, purity, and potency for use in the intended population. The Director of CBER or CDER will only approve a request for an exception or alternative after determining that the particular request meets this prescribed criteria for the intended population. Examples of how the final rule provides flexibility (such as alternatives to the use of preservatives and modifications to the amount of aluminum permitted in certain biological products), without diminishing public health protections, are provided in the paragraphs that follow.¹

Standards for certain constituent materials present in biological products are provided under § 610.15. Section 610.15(a) requires that all ingredients used in a licensed product, and any diluent provided as an aid in the administration of the product, meet generally accepted standards of purity and quality. Any preservative used must be sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient, and in the combination used, it must not denature the specific substances in the product to result in a decrease below the minimum acceptable potency within the dating period when stored at the recommended temperature. Products in multiple-dose containers must contain a preservative, except that a preservative need not be added to Yellow Fever Vaccine; Poliovirus Vaccine Live Oral; viral vaccines labeled for use with the jet injector; dried vaccines when the accompanying diluent contains a preservative; or to an allergenic product in 50 percent or more volume in volume (v/v) glycerin. Furthermore, under § 610.15, an adjuvant must not be introduced into a product unless there is satisfactory evidence that it does not affect adversely the safety or potency of the product.

Section 610.15(a) also requires that the amount of aluminum in the recommended individual dose of a biological product not exceed:

1. 0.85 milligrams if determined by assay;

¹ Although specific examples for use of extraneous protein and antibiotics are not provided, the final rule also allows for flexibility in applying the existing standards for extraneous proteins and antibiotics (§ 610.15(b) and (c)); provided that each request for an alternative or exception to these requirements is supported by data that establish the safety, purity, and potency of the biological product.