

Name of Petitioners: Center for Food Safety and Public Citizen

Address: c/o Peter T. Jenkins, CFS, Suite 302, 660 Pennsylvania Ave. SE, Wash., DC 20003

Date: November 25, 2003

Name of Food Additive and Proposed Use: irradiation of ground beef, including ground beef byproducts; revocation of approval.

Petitions Control Branch
Food and Drug Administration
Department of Health and Human Services
c/o Dockets Management Branch
5630 Fishers Lane, Rm. 1061, HFA 305
Rockville, MD 20852

Dear Sirs/Madams:

The undersigned Center for Food Safety and Public Citizen submit this petition to request the Commissioner of Food and Drugs to modify an existing food additive regulation pursuant to sections 409(b)(1) and 409(c)(1)(A) of the Federal Food, Drug, and Cosmetic Act and to 21 CFR sections 171.1(c)G and 171.130, with respect to the irradiation of ground beef including ground beef byproducts. Specifically, petitioners seek a modification to promptly revoke the approval for irradiation of those foods items. All information concerning this food additive that is pertinent to this petition to modify is attached hereto, in triplicate, and constitutes a part of this petition.

STATEMENT OF GROUNDS

Background

This is a petition by two non-profit, public interest, food safety groups who have long sought to ensure that irradiated foods are safe before any such foods are marketed in the United States. Petitioners seek a regulatory change to modify 21 CFR § 179.26(b)8 in order to revoke the existing approval therein for irradiated ground beef including ground beef byproducts (hereinafter collectively referred to as “IGB”). The current wording of the pertinent regulation allowing irradiation sources to be used is:

[Use] 8. For control of foodborne pathogens in, and extension of the shelf-life of, refrigerated or frozen, uncooked products that are meat within the meaning of 9 CFR 301.2(rr), meat byproducts within the meaning of 9 CFR 301.2(tt), or meat food products within the meaning of 9 CFR 301.2(uu), with or without nonfluid seasoning, that are otherwise composed solely of intact or ground meat, meat byproducts, or both meat and meat byproducts.

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[Limitations] *Not to exceed 4.5 kGy maximum for refrigerated products; not to exceed 7.0 kGy maximum for frozen products.*

The modification petitioners seek is to add the phrase “excluding ground beef and ground beef byproducts” at the end of the “use” paragraph.

This petition presents new facts and data documenting toxicological concerns with IGB. These facts and data include: 1) defects in the 1997 FDA approval for irradiated meat generally; 2) new toxicity information, including on the promotion of cancer, directly relevant to IGB; 3) chemical testing results for IGB retail products being consumed by Americans; 4) expert commentaries on the potential toxicity of IGB as well as other irradiated foods; and 5) increased *trans* fat in IGB. This petition to modify addresses these concerns in turn in relation to FDA’s regulatory standards for food additive petitions.

Applicable Legal Standards

The Federal Food, Drug, and Cosmetic Act defines a source of radiation as a food additive, under § 201(s) (21 USC § 321(s)). Under § 409(c)(3)(A) of the Act (21 USC § 348(c)(3)(A)), a food additive may not be approved for a particular use unless a fair evaluation of the data establishes that the additive is safe for that use.

Under Title 21—Food and Drugs, Part 170--Food Additives, the following key legal standards apply in deciding this petition:

§ 170.20 General principles for evaluating the safety of food additives.

a) 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...

§ 170.22 Safety factors to be considered.

In accordance with section 409(c)(5)(C) of the Act, the following safety factors will be applied in determining whether the proposed use of a food additive will be safe: Except 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; that is, a food additive for use by man will not be granted a tolerance that will exceed 1/100th of the maximum amount demonstrated to be without harm to experimental animals...

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§ 170.3 Definitions.

(i) Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined by scientific procedures or by general recognition of safety. In determining safety, the following factors shall be considered:

- (1) The probable consumption of the substance and of any substance formed in or on food because of its use.*
- (2) The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet.*
- (3) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate.*

Argument

I. Defects in the 1997 FDA Approval for Irradiated Meat

In December of 1997, FDA officials granted a petition by Isomedix, Inc. (FAP 4M4428) to irradiate the flesh and organs from cows, pigs, sheep and horses.¹ In doing so, FDA went beyond the scope of the original petition to also specifically approve “certain meat food products (e.g., ground beef and hamburger)”.² This approval was defective due to weak reasoning on the safety issues and did not comply with the regulatory safety standards quoted above. Nowhere did the decision address acceptable tolerances or margins of safety for the unique, potentially toxic, compounds created in meat as a result of applying the irradiation additive. Nor did it convincingly show that irradiated meat was generally recognized by competent scientists to be safe as required by the applicable legal standards, above.

The discussion in support of FDA’s approval attempted to rationalize or “explain away” at least five earlier feeding studies that did find harmful effects in animals fed irradiated flesh foods.³ FDA

¹ 62 Fed. Reg. 232, pp. 64107-64121; amending 21 CFR § 179.26(b), by adding a new paragraph 8, quoted above.

² 62 FR, p. 64108.

³ 62 FR, p. 64113, References 37, 39, 40, 41, and 43.

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presumed with little scientific analysis that all of those published positive findings were invalid.

Further, the FDA's meat approval relied on 46 safety studies that the agency's own Irradiated Foods Task Group (IFTG) had declared "deficient" 15 years earlier.⁴ Among them were two studies that were also cited in the agency's 1990 approval of irradiation for poultry,⁵ despite specific criticisms by FDA staff scientists who reviewed that petition, i.e.:⁶

- "[T]he in-depth review of this study raised questions about the procedures used; e.g. not all test strains were subjected to positive controls, and the high protein content of the extracts may be a compromising factor for this test." (Phillips, B.J. et al. "An investigation of genetic toxicology of irradiated foodstuffs using short-term test systems. I. Digestion in vitro and the testing of digests in the *Salmonella thyphymurium* reverse mutation test." *Food and Cosmetics Toxicology*, 18:371-375, 1980.)

- "[This study] was of limited value due to procedural flaws." (Thomson, G.M et al. "Mouse teratology study. Final Report." U.S. Army Contract DAMD-17-76-C-6047, 1977.

Also among the 46 "deficient" studies FDA relied on in the meat approval is a study that was rejected by the agency scientists who reviewed the poultry petition:⁷

- "[T]his study was considered to be flawed by experimental design and cannot be used for support of non-mutagenicity." (Phillips, B.J. et al. "An investigation of genetic toxicology of irradiated foodstuffs using short-term test systems. II. Sister chromatid exchange and mutation assays in cultured Chinese hamster ovary cells." *Food and Cosmetics Toxicology*, 18:471-475, 1980.)

Additionally (and ironically) the FDA's meat approval also relied on five studies that the agency's IFTG had not only labeled "deficient," but which the IFTG specifically stated "claimed to show

⁴ The discussion in this section is taken directly from the 2000 Public Citizen et al. report "Broken Record: How the FDA Legalized - and Continues to Legalize - Food Irradiation Without Testing it for Safety," online at <http://www.citizen.org/documents/brokenrecordfinal.PDF> . See pp. 36-37, attached hereto as **Tab 1**.

⁵ 55 FR 18538-18544 (1990).

⁶ FDA Memorandum from Hiltje Irausquin to George Pauli, Dec. 14, 1988.

⁷ FDA Memorandum from Hiltje Irausquin to George Pauli, Dec. 14, 1988.

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adverse effects of irradiated food,” i.e.:⁸

- A 1970 study conducted by the Academy of Medical Science in Moscow, in which rats fed irradiated fish experienced high mortality from pneumonia and other illnesses; “rather unfavorable” metabolism abnormalities, which suggested liver dysfunction; and “an unfavorable effect on gonads, reproductive function and progeny,” including low sperm count, atrophied testes and extended estrous cycles.⁹

- A 1969 study conducted by the United Kingdom Atomic Energy Authority in which the ovaries, uteri and testes of rats fed irradiated cod were significantly more atrophied than rats fed a normal diet.¹⁰

- A 1966 study conducted at the Vanderbilt University School of Medicine for the U.S. Army Surgeon General in which rats fed irradiated beef were significantly more likely to die by the age of 18 months than those fed non-irradiated food.¹¹

- A 1961 study conducted by the Syracuse University Research Institute for the U.S. Army Surgeon General in which rats fed irradiated chicken stew and cabbage experienced significantly lower levels of alkaline phosphatase in their small intestines than those fed a non-irradiated diet, an indication of possible adrenal dysfunction, protein deficiency or malnutrition.¹²

- A 1961 study conducted at the U.S. Army Medical Research and Nutritional Laboratory in Denver in which rats fed a composite irradiated diet containing nine different foods including ground beef, beans and peaches experienced significantly higher levels of the enzyme cytochrome oxidase than those fed a non-irradiated diet,

⁸ FDA Memorandum from Marcia van Gemert to W. Gary Flamm, April 9, 1982.

⁹ Shillinger, I. and Osipova, I.N. “The effect of fresh fish, exposed to gamma radiation, on the organism of albino rats.” *Voprosy Pitaniya*, 29:45-50, 1970.

¹⁰ Hickman, J.R. et al. “Studies on the wholesomeness of irradiated fish.” U.K. Atomic Energy Authority Research Group, Isotope Research Division, Wantage Research Laboratory, Berkshire. AERE-R6015, July 1969.

¹¹ Blood, F.R. et al. “Feeding of irradiated beef to rats.” *Toxicology and Applied Pharmacology*, 8:235-240, 1966.

¹² Phillips, A.W. et al. “Long-term rat feeding studies: Irradiated chicken stew and cabbage.” Office of the Surgeon General, Department of the Army, Contract No. DA-49-007-MD-783, August 15, 1961.

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indicating the possible destruction of essential fatty acids.¹³

The FDA's approval of the Isomedix meat petition, gave no explanation as to how these studies - which again the agency's own IFTG said both were "**deficient**" and that several of them "**show adverse effects** of irradiated food"- could be used to demonstrate the **safety** of irradiated meat. Inadequate safety evidence was before the agency and the agency did not satisfy its own regulatory standards, quoted above. The agency did not and could not point to any "general recognition" or "reasonable certainty" among competent scientists that the evidence published by other scientists on harmful effects of irradiated meat could be rationalized away in the manner that FDA repeatedly did. In sum, the FDA's approval, which included IGB, was wrong at the time.

II. Recent Toxicity Studies Including on the Promotion of Cancer

Since FDA's 1997 meat approval, several key new toxicity studies have been published relevant to IGB. These results directly contradict the following statement in the FDA's meat approval:¹⁴

In general, the types of products generated by irradiation are similar to those produced by other food processing methods.

It had been known since 1972 that irradiation of beef results in the formation of a class of chemicals known as 2-alkylcyclobutanones (2-ACBs).¹⁵ Subsequent research determined that 2-ACBs are formed when certain fats – fats that are ubiquitous in food – are exposed to radiation.

These chemicals are so distinct from natural food components or products generated by other processing methods that they are used as "markers" to determine whether food has been irradiated. By the mid-1990s, the uniqueness of 2-ACBs to irradiated foods had been established.¹⁶ Research

¹³ Read, M.S. et al. "Successive generation rat feeding studies with a composite diet of gamma-irradiated foods." *Toxicology and Applied Pharmacology*, 3:153-173, 1961.

¹⁴ 62 Fed. Reg., at p. 64110.

¹⁵ See LeTellier, P.R. and Nawar, W.W. "2-alkylcyclobutanones from the radiolysis of triglycerides." *Lipids*, 7:75-76, 1972.

¹⁶ See Stevenson, M.H. "Identification of irradiated foods." *Food Technology*, 48: 141-144, 1994; Stevenson, M.H. et al. "The use of 2-dodecylcyclobutanone for the identification of irradiated chicken meat and eggs." *Radiation Physics and Chemistry*, 42: 363-366, 1993; Crone, A.V.J. et al. "Synthesis, characterization and use of 2-tetradecylcyclobutanone together with other cyclobutanones as markers for irradiated liquid whole egg." *Journal of the Science of Food and Agriculture*, 62: 361-367, 1993; Crone, A.V.J. et al. "Detection of 2-dodecylcyclobutanone

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then began into the question of whether these chemicals are toxic, or could cause cancer or genetic damage.

The results, while preliminary, cause great toxicological concern **particularly since FDA's 1997 approval of irradiated meat completely fails to mention or consider 2-ACBs**. In several studies conducted over the past five years, 2-ACBs in concentrated form have been associated with promoting colon cancer development in rats, genetic damage in rats, and genetic and cellular damage in human and rat cells.¹⁷ The most recent and most extensive study was conducted by a team of German and French researchers working under a grant from the European Union (**Tab 2**).¹⁸ Entitled

in radiation-sterilized chicken meat stored for several years." *International Journal of Food Science and Technology*, 27: 691-696, 1992; Stevenson, M.H. and Crone, A.V.J. "Irradiation detection." *Nature*, 344: 202-203, 1990; Stevenson, M.H. "Progress in the identification of irradiated foods." *Trends in Food Science & Technology*, 3: 257-262, 1992; Helle, N. et al. "Identification of irradiated pasteurized egg products: A combined method for use in routine control." *Zeitschrift fur Lebensmittel, Untersuchung und Forschung*, 197: 321-331, 1993; Lembke, P. et al. "Characterization of irradiated food by SFE and GC-MSD." *Journal of Agricultural and Food Chemistry*, 43: 38-45, 1995; Tewfik, I.H. et al. "A rapid supercritical fluid extraction for the qualitative detection of 2-alkylcyclobutanones in gamma-irradiated fresh and sea water fish." *International Journal of Food Science and Nutrition*, 50: 51-56, 1999; Stewart, E.M. et al. "2-alkylcyclobutanones as markers for the detection of irradiated mango, papaya, Camembert cheese and salmon meat." *Journal of the Science of Food and Agriculture*, 80: 121-130, 2000.

¹⁷ See Delincee, H. and Pool-Zobel, B. Genotoxic properties of 2-dodecylcyclobutanone, a compound formed on irradiation of food containing fat. *Radiation Physics and Chemistry*, 52: 39-42, 1998; Delincee, H. et al. Genotoxicity of 2-dodecylcyclobutanone. Food Irradiation: Fifth German Conference, Karlsruhe, November 11-13, 1998; Delincée, H. et al. "Genotoxicity of 2-alkylcyclobutanones, markers for an irradiation treatment in fat-containing food – Part I: cyto- and genotoxic potential of 2-tetradecylcyclobutanone." *Radiation Physics and Chemistry*, 63:431-435, 2002.

¹⁸ The full citation is: D. Burnouf, H. Delincée, A. Hartwig, E. Marchioni, M. Miesch, F. Raul, D. Werner (2001), Etude toxicologique transfrontalière destinée à évaluer le risque encouru lors de la consommation d'aliments gras ionisés - Toxikologische Untersuchung zur Risikobewertung beim Verzehr von bestrahlten fetthaltigen Lebensmitteln – Eine französisch-deutsche Studie im Grenzraum Oberrhein, Rapport final d'étude Interreg II, projet N° 3.171. BFE-R--02-02, Federal Research Centre for Nutrition, Karlsruhe, Germany. An English translation by William Freese Translations is provided.

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“Toxicological Study to Assess the Risks Associated with the Consumption of Irradiated, Fat-containing Foods,” the report by Burnouf et al. contains major new findings. Below is a quote from the English Summary on a new topic, tumor promotion, that has never been assessed in any other irradiated food animal or human feeding studies:

In an experiment with rats treated with a specific colon carcinogen, it was shown that 2-tDCB and 2-tDeCB have a promoter effect on the development of colon tumors. In this experiment, we found a larger number of aberrant crypts and development of more and larger tumors in the animals that received 2-ACBs in combination with the carcinogen azoxymethane (AOM). Although we did not observe initiation of tumor development by 2-ACBs alone, both the in vitro tests and the in vivo experiments with laboratory animals demonstrate that 2-ACBs have potential toxicity. In other feeding studies, it was shown that a very small amount of 2-ACBs can be recovered from fatty tissue, while a similar small amount is excreted in feces. These results indicate that 2-ACBs are largely metabolized or possibly stored in other parts of the body. Therefore, further studies are absolutely necessary in order to elucidate the metabolism of 2-ACBs.

The authors emphasized that further 2-ACB metabolite studies are “absolutely necessary” in order to determine the fate of these substances and in order to elucidate the extent to which they act as tumor promoters in the human body.

Burnouf et al. concluded:

[S]ince our results point to toxic, genotoxic and even tumor-promoting activity of several 2-ACBs, we consider it necessary that further research, including confirmation of our results by other laboratories, be conducted to permit an assessment of the possible risks associated with consumption of irradiated, fat-containing foods.

After a somewhat dismissive and inaccurate review of their report by the European Union’s Scientific Committee on Food in July 2002, the report’s authors, Burnouf et al., made a statement to clarify the significance of their work (**Tab 3**).

[O]ur new data which will be published in peer-reviewed journals, raise some doubts or at least suggest that caution should be exercised before any risk to consumers by exposure to these compounds is denied. At present, knowledge about

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*the potential toxicity of the 2-ACBs (including possible metabolites) and their toxic potency is very limited. Since these compounds are uniquely formed by irradiation and are not inherent in food, in our opinion, complementary studies are needed to make a qualified risk assessment. It needs to be shown that despite the presence of potentially cyto- and genotoxic radiation-induced agents, the consumption of irradiated fat-containing food is safe for consumers.*¹⁹

As the leading researchers to have done any irradiation toxicity assessment in recent decades - and with representation from the well-known food irradiation research program of the Federal Research Center for Nutrition in Karlsruhe, Germany - it is extraordinarily significant that they say that current knowledge is inadequate to show the food is “safe for consumers” and that, pending further research, “risk to consumers” should not be “denied.”

The matrix below, based on the report, illustrates the problems in a nutshell with the particular 2-ACBs detected in IGB.

¹⁹ These results were in fact published in several journal articles, i.e.: Horvatovich P, Raul F, Miesch M, Burnouf D, Delincee H, Hartwig A, Werner D, Marchioni E. Detection of 2-alkylcyclobutanones, markers for irradiated foods, in adipose tissues of animals fed with these substances. *J. Food Prot.*, 65(10): 1610-3, 2002 (**Tab 4**); and Raul F, Gosse F, Delincee H, Hartwig A, Marchioni E, Miesch M, Werner D, Burnouf D. Food-borne radiolytic compounds (2-alkylcyclobutanones) may promote experimental colon carcinogenesis. *Nutrition and Cancer*, 44(2): 189-91, 2002 (**Tab 5**).

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Table 1. Harmful 2-ACBs

Chapter in Burnouf et al. report	Particular 2-ACB				
	2-DCB	2-dDCB	2-tDCB	2-dDeCB	2-tDeCB
2.5 – found in irradiated ground beef	X	X	X*	X	X
2.6.1 – cyto- and genotoxic to human cells		X	X		X
2.6.2 – cytotoxic/oxidative damage to DNA in human cells	X	X	X		X
2.6.3 – cytotoxic to bacteria	X	X	X		
2.6.4 – colon tumor promoter in rats			X		X
2.7 – stored in adipose tissue and present in feces of rats			X		X

* - Note the authors’ comment in chap. 2.5 that 2-tDCB in ground beef was found at “high levels.”

This represents an area of toxicity that FDA never examined in the meat approval or in any other public document. No other scientific researchers have studied these issues. They cannot be dismissed as topics that FDA reviews or other studies have already covered.

In sum, FDA’s statement in the 1997 meat approval that the products of irradiation are similar to those produced by other methods has been shown to be materially false. Thus, FDA must reconsider that statement in light of the new evidence on toxicity 2-ACBs, particularly with respect to IGB that is currently being sold and consumed in the United States as petitioners discuss in the following section.

III. Ground Beef Testing Results

In 2003, Public Citizen and the Center for Food Safety hired a well-established food testing lab, Lebensmittel Consulting of Fostoria, Ohio, to test a variety of commercially-available IGB products for the presence of 2-ACBs:

- fresh, un-irradiated ground beef purchased at a Safeway store in Washington, DC, tested raw and cooked.
- fresh ground beef irradiated with an electron-beam irradiator by SureBeam Corp. of San Diego, purchased at a Safeway store in Washington, DC, and a D’Agostino’s store in New York City, tested raw and cooked.

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- Ground beef irradiated with an electron-beam irradiator by SureBeam Corp. of San Diego, purchased at a Dairy Queen restaurant in Minneapolis, tested cooked.

- Frozen ground beef irradiated with a gamma-ray irradiator by Food Technology Service of Mulberry, Florida, sold under the “New Generation” label, purchased at a Publix store in Florida, tested raw and cooked.

The full report authored by Richard Basel, Ph.D., is attached (**Tab 6**). The two types of 2-ACBs associated with colon tumor promotion in rats, and cellular and genetic damage in human cells, i.e., 2-tDeCB and 2-tDCB (see Table 1 above), were readily detected in all three IGB products, raw and cooked. Again, in the Raul et al. study (**Tab 5**, above), rats that drank solutions of these chemicals in conjunction with exposure to a known colon carcinogen developed more large tumors, more multiple tumors, and more preneoplastic lesions than rats only exposed to the carcinogen. Of the two chemicals, 2-tDeCB had a greater effect.

Additionally, in the Horvatovich et al. study (**Tab 4**, above), 2-tDeCB and 2-tDCB were detected in small quantities in the adipose tissue and feces of the rats. Because most of the chemicals could not be accounted for, the authors strongly recommended that more research be conducted into how the body metabolizes 2-ACBs. It is possible that the chemicals could be stored in other parts of the body, or could give rise to still other chemicals if the body breaks them down. A third type of 2-ACB associated with cellular and genetic damage in human cells – 2-dDCB – also was detected in all three IGB products.

Among the three brands of IGB that had been cooked, a SureBeam sample contained the highest levels of 2-tDeCB and 2-tDCB, while “New Generation” contained the highest level of 2-dDCB. Among the two brands of raw IGB, New Generation contained the highest levels of 2-tDCB and 2-dDCB, while SureBeam contained the highest level of 2-tDeCB. Cooking of IGB generally, but not always, reduced the amount of 2-ACBs. No 2-ACBs were detected in the non-irradiated ground beef, whether raw or cooked.

In view of this evidence of substances shown to be harmful in experimental animals contained in IGB products widely consumed in the United States, FDA must comply with 21 CFR §170.22, which states a:

...safety factor in applying animal experimentation data to man of 100 to 1, will be used; that is, a food additive for use by man will not be granted a tolerance that will exceed 1/100th of the maximum amount demonstrated to be without harm to experimental animals.

Despite the toxicity to rats, no “maximum amount demonstrated to be without harm to experimental animals” for the 2-ACBs has been determined. The toxicological research simply has not been

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undertaken and published. Additionally, no “tolerance” has been granted. FDA must undertake these actions.

Finally, a study out of Kansas State University by Gadgil et al. (**Tab 7**) also found 2-ACBs in raw IGB, although in different measures than found in the Burnouf et al. study and the Lebensmittel report referred to above. FDA must take cognizance of the fact that both the Lebensmittel and the Gadgil et al. studies found the highest 2-ACB levels in their electron beam irradiated samples compared to their gamma irradiated samples. Neither authors could explain this phenomenon. Gadgil et al. stated, at p. 5749, “At this point the reason for the increased level of 2-DCB in the electron beam samples remains unclear.” Richard Basel, Ph.D., the author of the Lebensmittel report, also stated that the reason for the difference is unclear (pers. comm.). The fact that the increases are not explainable demands additional research and special caution regarding the electron beam source. FDA must revoke the IGB approval, which now does not differentiate between irradiation sources, at least until the agency assesses these differences in the two sources as far as their potentially harmful impacts on IGB. Only then will FDA also be able to determine whether different tolerances or margins of safety are merited with respect to absorbed irradiation doses from the gamma and electron beam sources.

IV. Probable Consumption

Again, 21 CFR § 170.3(i) on the definitions of “safe or safety,” above, provides:

In determining safety, the following factors shall be considered:

.....

- (1) The probable consumption of the substance and of any substance formed in or on food because of its use.

Since the FDA’s irradiated meat approval, IGB has dramatically increased in commercial availability and national consumption. While actual sales figures are proprietary company information, IGB is reportedly sold at approximately 8,000 grocery stores throughout the nation.²⁰ In addition, more than 130 Dairy Queen restaurants in Minnesota, New Mexico and South Dakota and 50 Embers America

²⁰ Stores include A&P, Big Y, BI-LO, Bruno’s, Byerly’s, Clemens, Copps, Cub Foods, D’Agostino, Dick’s, Dierbergs, Farm Fresh, Foodtown, Giant, Giant Eagle, Haggen, Hannaford Brothers, Hy-Vee, Jewel-Osco, Kroger, Lowes, Lunds, Marsh, Martin’s, Pathmark, Piggly Wiggly, Price Chopper, Publix, Rainbow, Reasor’s, Redner’s, Safeway, Schnuck, Shaw’s, Shoppers Food and Pharmacy, Shoprite, Stop & Shop, SuperValu, Tops, Victory, Wegman’s, Weis and Winn Dixie. Information in this paragraph is from SureBeam Corp., press releases, at www.surebeam.com/news_events.php and the Minnesota Beef Council’s lists of outlets, at www.mnbeef.org/restaurants_and_retailers.htm.

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restaurants in Minnesota, North Dakota, Iowa and Wisconsin reportedly are serving IGB. And IGB is available through home-delivery services Omaha Steaks and Schwan's. IGB is also being distributed by American Foodservice, Brawley Beef, Huisken, Kenosha, Rochester Meat, Sysco and W.W. Johnson.

Furthermore, as a result of an unfortunate amendment to the 2002 Farm Bill,²¹ the United States is poised to initiate a new program of feeding IGB to schoolchildren *en masse*. While all past consumption of irradiated food in this country has been on a very small scale, representing a minuscule portion of the average American's diet, this is set to change. If school children are fed a steady diet of irradiated staple school items including, but not limited to, hamburgers, chile, beef soups, meatloaf, tacos, taco salad, meat sauce, shepherds pie, meatballs, sloppy joes, beef-stuffed vegetables, beef sausage, goulash, and so on, suddenly a major portion of their diets could be irradiated and the "probable consumption" factor in the safety standard above will be vastly multiplied.²²

For the National School Lunch Program (NSLP) alone, the USDA purchased 142,050,000 pounds of frozen beef products during the 2001-2002 school year.²³ According to 2002 data provided by the Food and Nutrition Service, the removal of the irradiation prohibition could affect up to 27,909,000 American children participating in the NSLP.²⁴ This will convert this program into the largest distribution of irradiated food products ever undertaken in the world. It will also turn millions of children into unwitting experimental subjects to determine whether this technology, whose chemical by-products are still being studied for their potential harmful effects, is safe. What makes this decision even more regrettable is the fact that the poorest, most nutritionally vulnerable, children in our society will not have a choice in the matter, as they are the least able to afford alternatives or to bring lunch from home.

²¹ Farm Security and Rural Investment Act, P.L. 107-171, signed into law on May 13, 2002.

²² A dramatic additional increase in consumption of other irradiated foods would occur if FDA approves the five irradiation petitions pending before it, particularly the "ready-to-eat" foods petition, which alone could affect more one-third of the average American diet; see FAPs 9M4697, 1M4727, 9M4682, 9M4695, and 9M4696. FDA must assess the projected future IGB consumption cumulatively with the potential consumption of these other irradiated foods if FDA approves those petitions. Petitioners here have submitted numerous comments backed by extensive research opposed to those five petitions.

²³ United States Department of Agriculture (USDA), Agricultural Marketing Service, Livestock and Seed Program, www.ams.usda.gov/lsg/cp/beef/BEEF%20Vendor%20state%20Tables%20SY01-02.pdf .

²⁴ USDA, Food and Nutrition Service, www.fns.usda.gov/pd/slfypart.htm .

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Clearly, the European researchers do not believe it is wise to feed irradiated beef to school children. The lead scientist on the 2-ACB colon tumor promotion study, Dr. Francis Raul, Research Director of the French National Institute of Health, is reported by *The New York Times* (**Tab 8**) to have stated:

It is perhaps too early to start irradiating beef to give to children.

FDA and USDA must heed this caution.²⁵ Stubborn adherence to the 1997 meat approval cannot justify exposing millions of American children to unnecessary toxicological risks, particularly in the face of a contrary opinion from the leading tumor promotion researcher.²⁶

V. Other Negative Opinions by Competent Scientists

Section 170.3 on the definitions of “safe or safety,” above, also provides:

In determining safety, the following factors shall be considered: (i) Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.

That standard is simply not met. The consortium of French and German scientists who conducted the European research concluded (Tab 2, above):

[I]t seems not appropriate to draw a final conclusion concerning the risk associated with human consumption of irradiated fat-containing foods. However, since our

²⁵ Petitioners once again remind FDA that in the only controlled study of human children eating a freshly-irradiated diet (irradiated wheat), peer-reviewed and published in a reputable journal, mutagenic effects were found. Bhaskaram, C. and G. Sadasivan. “Effects of feeding irradiated wheat to malnourished children. *American J. of Clinical Nutrition* 28:130-135, 1975. The study specifically examined effects on malnourished children, who are the high-priority recipients of USDA’s nutrition programs such as the NSLP. The results of the study were supported, and criticisms against it rebutted, by the researchers in two later detailed defenses, which the FDA also should consider. Vijayalaxmi and S.G. Srikantia, “A review of the studies on the wholesomeness of irradiated wheat, conducted at the National Institute of Nutrition, India.” *Radiation Phys. Chem.* 34:941-952, 1989; and Vijayalaxmi, “Comparison of studies on the wholesomeness of irradiated wheat: A review.” *Nutrition Research* 19:1113-1120, 1999.

²⁶ Petitioners are not aware of evidence of a single student death resulting during the last 35 years (at least) from eating normal un-irradiated ground beef in the NSLP that was contaminated with pathogens at the source.

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results point towards toxic, genotoxic and even tumor promoting activity of certain 2-ACB, we strongly recommend to carry out further research, including confirmation of our results by other laboratories, to elucidate a possible risk associated with the consumption of irradiated fat-containing foods... To characterize the potential risk, hazards need to be identified, the exposure, the exact dose-response and particularly the kinetics and metabolism of 2-ACB in the living organism should be elucidated. All these studies are deemed necessary to gain insight into the mechanisms of the toxic effects. Numerous questions still remain to be answered, and much research is left to be done, before a qualified risk assessment can be performed.²⁷

Additionally, the scientists stated:

In light of the expected extended application of food irradiation, however, it seems necessary to further clarify the potential toxicity of 2-ACBs and their contribution to a possible risk associated with human consumption of irradiated fat-containing food.²⁸

They further stated:

[W]e feel that our new data ... raise some doubts or at least suggest that caution should be exercised before any risk to consumers by exposure to these compounds is denied... It needs to be shown that despite the presence of potentially cyto- and genotoxic radiation-induced agents, the consumption of irradiated fat-containing food is safe for consumers.²⁹

Other highly-qualified scientists repeat these concerns. Professor William W. Au, Ph.D., of the Department of Preventive Medicine at the University of Texas Medical Branch in Galveston, and an internationally recognized mutagenicity expert, has stated (**Tab 9**):

[In the European Union study on rats,] a portion of the [2-ACBs] crossed the intestinal barrier, entered the blood stream and accumulated in adipose tissue of the animal. Therefore, consumption of irradiated food for a long time can cause significant accumulation of the toxic 2-ACB in the adipose tissues of consumers... [C]onsumption of an improper diet together with food that contains 2-ACB which acts as a tumor promoter can increase the risk for the development of colon cancer. Under this scenario, individuals who would normally outlive the risk for colon cancer

²⁷ Burnouf et al. Consortium report, Tab 2, above.

²⁸ Raul, F. et al. *Nutrition and Cancer* article, Tab 5, above.

²⁹ Burnouf et al. Comment, Tab 3, above.

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might develop the cancer from the promoting effect of 2-ACB. Without a systematic investigation in the population, this serious concern has not been addressed yet... Short-term safety evaluation of components of irradiated food products, rather than on whole food, needs to be systematically conducted. Therefore, regulatory agencies and industries need to ensure that the irradiation process will not produce serious and long-term health effects to consumers.

Dr. Au also expressed concerns about the Raul et al. findings taken together with the fact that cancer promoters are known to be able cause their effects at very low levels (**Tab 10**):

[I]n a different but well-established tumor promotion animal model, the dose that was needed to promote tumors was lower than 0.5 ug per mouse, delivered two times per week for 25 weeks (Saleem et al., 2001).³⁰ Another way to consider the dosage situation is that the concentration of tumor promoters is usually hundreds of times less than the cancer inducing chemicals. Therefore, 2-ACB in irradiated food can potentially be hazardous to humans.

Chinthalapally V. Rao, Ph.D., Associate Chief of the Division of Nutritional Carcinogenesis at the Institute for Cancer Prevention - one of the leading NIH-recognized cancer centers - in Valhalla, New York, stated (**Tab 11**):

[F]urther investigations are warranted to identify and assess the exact levels at which [2-ACBs] may exert tumor promoting effects. Also, a full-length study investigating the cancer promoting effects of 2-alkylcyclobutanones in irradiated foods (per se) and their mechanism(s) of action, is urgently needed to address public health concerns. A thorough investigation of the effect of 2-alkylcyclobutanones at levels consumed by the human population and in models (in vitro and in vivo) of various types of cancers is warranted before proposing that irradiated foods do or do not promote colon cancer.

In the face of these negative, or at least very skeptical, comments by scientists of impeccable credentials - as well as by many other scientists³¹ - it is absolutely clear that the required legal

³⁰ Citation is to: Saleem M, Ahmed SU, Alam A, Sultana S. Tephrosia purpurea alleviates phorbol ester-induced tumor promotion response in murine skin. *Pharmacol. Res.* 43:135-144, 2001.

³¹ Numerous other experts have also called for, at least, more research on irradiation safety. See, e.g., Louria, D.B. "Food irradiation: Perceptions of a qualified opponent." *Infectious Diseases in Clinical Practice*, 2:313-316, 1993; Tritsch, G.L. "Food irradiation." *Nutrition*, 16:698-701, 2000; Steinberg, J., quoted in R. Papazian. "Food irradiation - A hot issue." *Harvard Health Letter*, vol. 17, no. 10, p. 3, 1992. Notably, 26 medical experts and many other prominent

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standard of a “reasonable certainty” of safety for IGB “in the minds of competent scientists” is no longer met, even assuming for the sake of argument that it was met at the time of the 1997 approval. Were FDA to proceed as if the required certainty did exist for IGB it would be wrong as a matter of fact and in violation of the law.

VI. New *Trans* Fat Concerns

In a crucial report on *trans* fatty acids issued last year by the National Academies of Sciences, Institute of Medicine (IOM), the coronary heart disease (CHD) risks presented by these substances are as follows (emphasis added; citations omitted):

*Summary - There is a positive linear trend between trans fatty acid intake and total and LDL cholesterol concentration, and therefore increased risk of CHD, thus suggesting a Tolerable Upper Intake Level (UL) of zero. Because trans fatty acids are unavoidable in ordinary diets, achieving such a UL would require extraordinary changes in patterns of dietary intake. Such extraordinary adjustments may introduce other undesirable effects (e.g., elimination of foods, such as dairy products and meats, that contain trans fatty acids may result in inadequate intakes of protein and certain micronutrients) and unknown and unquantifiable health risks may be introduced by any extreme adjustments in dietary pattern. For these reasons, no UL is proposed. Nevertheless, it is recommended that **trans fatty acid consumption be as low as possible** while consuming a nutritionally adequate diet.³²*

individuals endorsed a detailed warning in a health journal on the dangers of irradiation of foods generally. Epstein, S.S., and W. Hauter. “Preventing pathogenic food poisoning: Sanitation not irradiation.” *Intl. J. of Health Services*, 31:187-192, 2001. Some examples of prominent MD and Ph.D. endorsers of the warning: Neal Barnard, President, Physicians Committee for Responsible Medicine; Donald Dahlsten, Professor and Associate Dean, Univ. of California, Berkeley; Robert Elder, Senior Microbiologist, Neogen Co.; Samuel Epstein, Emeritus Professor of Environmental Medicine, Univ. of Illinois School of Public Health, and Chairman of the Cancer Prevention Coalition; Jay M. Gould, Director, Radiation and Public Health Project; William Lijinsky, past Director of Chemical Carcinogenesis, Frederick Cancer Research Center; Donald Louria, Chairman, Department of Preventive Medicine, New Jersey Medical School; Vincente Navarro, Professor, The Johns Hopkins Univ. and Univ. of Pompeu Fabra, Spain; and Dr. Quentin Young, past President, American Public Health Association.

³² National Academies of Sciences, Institute of Medicine, Panel on Macronutrients. 2002 Letter Report on Dietary Reference Intakes for *Trans* Fatty Acids (July 10).

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As indicated the evidence suggests a Tolerable Upper Intake Level of zero. In any event, *trans* fatty acid consumption should be minimized.

One published study has found that irradiation **doubles** the amount of *trans* fat in irradiated compared to non-irradiated ground beef (**Tab 12**). Doubling the *trans* fat will increase the risk of CHD associated with this harmful fat. Further, an increase in *trans* fat also increases the risks of a variety of other associated human health problems.³³ Especially in light of the IOM recommendation to minimize consumption of *trans* fat, FDA must investigate this issue thoroughly before allowing further sales of IGB, a product on which levels of this fat are not labeled.

VII. Cumulative Effect

Section 170.3(i) on the definitions of “safe or safety,” above, also provides:

In determining safety, the following factors shall be considered: ...

.....

- (2) The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet.

In addition to the potential hazards posed by 2-ACBs in IGB directly, the act of grilling hamburgers typically coats them with polycyclic aromatic hydrocarbons, known carcinogens; further, grilling creates heterocyclic amines, which are mutagens and carcinogens associated with respiratory tract cancers (from the fumes) and are known colon carcinogens.³⁴ The tumor promotion effect of the 2-ACBs, as found by Raul et al., must be investigated in combination with the known colon carcinogens in chargrilled hamburgers. On top of that, the irradiated hamburgers’ potential to contain increased

³³ See Trans Fatty Acid Fact Sheet, on Trans Fat Info Web <http://www.enig.com/0001t1b.html>, maintained by a leading fat researcher, Mary G. Enig, Ph.D., F.A.C.N., Director, Nutritional Sciences Division, Enig Associates, Inc., Silver Spring, MD,

³⁴ See Augustsson, K. et al. “Dietary heterocyclic amines and cancer of the colon, rectum, bladder and kidney: a population-based study.” *The Lancet*, 353:686-687,1999; Ward, M.H. et al. “Risk of adenocarcinoma of the stomach and esophagus with meat cooking method and doneness preference.” *International Journal of Cancer*, 71:14-19, 1997. Nagao, M. and Sugimura, T. “Carcinogenic factors in food with relevance to colon cancer development.” *Mutation Research*, 290:43-51, 1993; also see fact sheets on polycyclic aromatic hydrocarbons prepared by the CDC, Agency for Toxic Substances and Disease Registry, at www.atsdr.cdc.gov/tfacts69.html .

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trans fat must be assessed. It is possible that carcinogenic and other harmful effects will act cumulatively and synergistically.

These safety risks and other concerns in this petition are summarized and restated in the attached new special report by petitioners entitled, “What’s in the Beef? - Scientists Question the Safety of Irradiated Ground Beef” (**Tab 13**). FDA’s alarm bells should be ringing. Charred grilled ground beef - an extremely common American food - potentially poses multiple toxicity hazards if it is first irradiated.

Conclusion

There can be no reasonable claim that IGB meets the safety standard in 21 CFR Part 170 for food additives. Contrary to those standards, established tolerances or safe levels of consumption exist neither for that food item nor for the 2-ACBs and the increased *trans* fat it contains. The “probable consumption” factor for IGB has already increased dramatically in the United States and is on the verge of a huge further increase as a result of the NSLP mass feeding program. This will cause the risks to reverberate across a population of vulnerable children orders of magnitude larger than the population of voluntary purchasers that is currently consuming IGB. Serious potential exists for cumulative harmful effects in the form of increased colon cancer promotion and increased *trans* fat. As shown by the considerable contrary opinions cited herein issued by respected scientists, “reasonable certainty in the minds of competent scientists that the substance is not harmful” plainly does not exist.

In view of the evidence and argument herein, FDA should revoke its approval by, at the end of 21 CFR § 179.26(b)8, adding the phrase “excluding ground beef and ground beef byproducts”.³⁵

Further, FDA should immediately advise the USDA to reverse its decision to allow IGB to be served in the NSLP and other USDA nutritional programs until the issues related to 2-ACBs and other chemicals formed in irradiated beef are addressed adequately. FDA and USDA should recall all IGB already in the NSLP and commercial distribution chains. Using our school children as guinea pigs in an uncontrolled feeding experiment – the largest ever conducted anywhere in the world with any

³⁵ FDA has taken similar action for other food additives such as cyclamate. Approved by the FDA in 1949, cyclamate was banned in 1969 principally based on scientific study indicating it contributed to bladder cancer in rats. 34 Fed. Reg. 202, pp.17063-17064 (Tues., Oct. 21, 1969). Although cyclamate does not cause cancer *per se* it may promote cancer once started. See FDA fact sheet at: www.fda.gov/bbs/topics/ANSWERS/ANS00155.html . Thus, it is similar to, and a precedent for, the present situation regarding 2-ACBs.

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irradiated food – defies common sense and would be immoral until the scientific safety issues are fully resolved.

CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioners which are unfavorable to the petition.

Also attached is petitioners claim for a Categorical Exclusion under the National Environmental Policy Act pursuant to 21 CFR § 25.32 (**Tab 14**). As required by 21 CFR 171.1(i)(2), please publish notice of this petition in the Federal Register within 30 days and advise petitioners of such filing. For additional information regarding this petition, please contact Peter T. Jenkins, CFS, Attorney/Policy Analyst, tel: 202.547.9359; email: peterjenkins@icta.org.

Yours very truly,

Petitioners Center for Food Safety and Public Citizen,

by:

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Attachments (14 tabs)

CC:s: (courtesy copies without attachments)

Mr. Joseph Levitt, CFSAN
Dr. Laura Tarantino, CFSAN
Dr. Alan Rulis, CFSAN
Dr. George Pauli, CFSAN

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**CLAIM OF CATEGORICAL EXCLUSION FROM THE REQUIREMENT TO
PREPARE AN ENVIRONMENTAL ASSESSMENT**

Petitioners Center for Food Safety and Public Citizen assert that this petition should receive a Categorical Exclusion under the National Environmental Policy Act pursuant to 21 CFR § 25.32, as applied to petitions to modify existing food additive approvals. Granting this petition will not have a significant impact on the environment. To our knowledge, there are no extraordinary circumstances that apply to this action that would require submission of an Environmental Assessment.

Dated this 25th day of November, 2003.

On behalf of petitioners:

Peter T. Jenkins, Attorney
Center for Food Safety