Comment to: Docket No. 99F-5322

THE CENTER FOR FOOD SAFETY

April 7, 2003

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Re: Food Additive Petition 9M4697, Use of ionizing radiation for pre-processed meat and poultry; both raw and pre-processed vegetables, fruits and other agricultural products of plant origin; and certain multi-ingredient food products; Food Additive Petition 1M4727, Use of ionizing radiation for control of foodborne pathogens in crustaceans and processed crustaceans; Food Additive Petition 9M4682, Ionizing radiation for the control of Vibrio and other foodborne pathogens in fresh or frozen molluscan shellfish; Food Additive Petition 9M4695, Use of ionizing radiation to treat unrefrigerated (as well as refrigerated) uncooked meat, meat products, and certain meat food products; and Food Additive Petition 9M4696, Increase the maximum dose of ionizing radiation permitted in the treatment of poultry products

Greetings,

The FDA is considering the five above-referenced food additive petitions to irradiate a much greater portion of the food supply. The Center for Food Safety (CFS), together with Public Citizen, has filed five earlier sets of comments opposing these petitions on grounds of serious safety issues stemming from scientific studies indicating that certain irradiated foods may cause mutagenic, genotoxic, cytotoxic and tumor promoting effects in lab animals as well as in humans.

CFS submits this further comment in **opposition** to the five petitions, including the attached tabbed information, which is incorporated herein by reference. This comment focuses first on the increased risk

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of coronary heart disease and other health problems due to the doubling of *trans* fat resulting from irradiation of ground beef (a product potentially included in the pending food additive petitions 9M4697 and 9M4695). The next section of the comment is on further toxicity risks, relying primarily on older studies whose finding raised alarms that FDA apparently did not heed, but whose impact is amplified by more recent findings. The last section addresses pre-*trans* fat nutritional issues surrounding irradiated foods, based on thoughtful reviews of the nutrient destruction caused by the technology. None of the eight studies cited below were ever addressed in FDA's "omnibus" 1986 irradiation rule (51 FR 13376) nor in any other of its irradiation approvals.

Study 1. Effects of irradiation on *trans* fatty acids formation in ground beef.[1] This recent research tested the levels of various fats and fatty acids in irradiated ground beef. The key finding, summarized in Table 4 therein, is that irradiation at room temperature approximately doubled the prevalence of *trans* fatty acids, from 4.6 % in unirradiated samples to 8.5 % in samples irradiated at 4.5 kGy, the maximum allowable dose for fresh ground beef under FDA regulations.

Study 2. Dietary intake recommendations for *trans* fatty acids.[2] 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, which, again, are doubled in quantity when ground beef is irradiated, are as follows (emphasis added; citations omitted):

> *Similar to saturated fatty acids, there is a positive linear trend between trans fatty acid intake and LDL cholesterol concentrations. Some evidence also suggests that trans fatty acids result in lower HDL cholesterol concentrations (Table 6). Hence, the net result is a higher total cholesterol (or LDL cholesterol):HDL cholesterol ratio. This finding, combined with data from prospective cohort studies (Table 6), has lead to the concern that dietary trans fatty acids are more deleterious with respect to coronary heart disease than saturated fatty acids.*

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[1] Brito, M.S., A.L.C.H. Villavicencio, and J. Mancini-filho. 2002. Effects of irradiation on *trans* fatty acids formation in ground beef. *Radiation Physics and Chemistry* 63: 337-340.

[2] National Academies of Sciences, Institute of Medicine, Panel on Macronutrients. 2002 Letter Report on Dietary Reference Intakes for *Trans* Fatty Acids (July 10), at p. 14: online at: www.iom.edu/iom/iomhome.nsf/Wfiles/TransFattyAcids/$file/TransFattyAcids.pdf . The excerpt attached includes only the pertinent pages on risks, pp. 5-14.

> *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.***

As indicated the evidence suggests a Tolerable Upper Intake Level of **zero**. In any event, *trans* fatty acid consumption should be minimized. This IOM recommendation directly contrasts with the pending petitions which would allow more irradiation of ground beef and other foods, thereby significantly increasing *trans* fatty acid consumption.

It is probable, although not shown in published studies yet, that irradiation of other types of food besides ground beef that contain fatty acids also significantly raises their *trans* fat prevalence. At a minimum information regarding possible *trans* fat increases in all of the foods covered must be obtained by FDA before deciding on the pending petitions, and FDA must consider the cumulative macronutritional effect of American consumers eating such foods in a prospective heavily irradiated diet.

The list of other documented non-cholesterol and non-CHD related health problems associated with *trans* fat is surely well-known to FDA as it proposing a new rule to list the fat on food labels. They include that *trans* fat:[3]

- *lowers the amount of cream (volume) in milk from lactating females in all species studied, including humans, thus lowering the overall quality available to the infant;*
- *correlates to low birth weight in human infants;*
- *increases blood insulin levels in humans in response to glucose load, increasing risk for diabetes;*

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[3] Health problems list from Trans Fatty Acid Fact Sheet, on Trans Fat Info Web http://www.enig.com/0001t1b.html, (last visited March 24, 20003), 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.

- *affects immune response by lowering efficiency of B cell response and increasing proliferation of T cells;*
- *decreases levels of testosterone in male animals, increases level of abnormal sperm, and interferes with gestation in females;*
- *decreases the response of the red blood cell to insulin, thus having a potentially undesirable effect in diabetics;*
- *inhibits the function of membrane-related enzymes such as the delta-6 desaturase, resulting in decreased conversion of, e.g., linoleic acid to arachidonic acid;*
- *causes adverse alterations in the activities of the important enzyme system that metabolizes chemical carcinogens and drugs (medications), i.e., the mixed function oxidase cytochromes P-448/450;*
- *causes alterations in physiological properties of biological membranes including measurements of membrane transport and membrane fluidity;*
- *causes alterations in adipose cell size, cell number, lipid class, and fatty acid composition;*
- *adversely interacts with conversion of plant omega-3 fatty acids to elongated omega-3 tissue fatty acids;*
- *escalates adverse effects of essential fatty acid deficiency; and*
- *increases peroxisomal activity (potentiates free-radical formation).*

To summarize the apparent risks of eating irradiated ground beef that is, for example, grilled are considerable:[4] – **First**, red meat consumption is a well-known risk factor for a myriad of health problems. **Second**, flame grilling coats the beef with polycyclic aromatic hydrocarbons, which are known carcinogens. **Third**, grilling meat creates heterocyclic amines, which are mutagens and carcinogens associated with both respiratory tract cancers (from the smoke) and colon cancer. **Fourth**, as we stated in our last comment of Feb. 26, 2003, irradiated beef contains the unique radiolytic products, 2-alkylcylcobutanones, which are genotoxic in concentration and act as colon tumor promoters if consumed together with known colon carcinogens (as are present in this case). **Fifth**, the doubling of *trans* fat in irradiated compared to non-irradiated ground beef increases the risks of coronary heart disease. **Sixth**, the *trans* fat increase also increases risks of a variety of other health problems, listed above.

These should give FDA pause to reconsider its past approvals for irradiated ground beef as well as other fatty acid-containing foods, in view of the potential cumulative health impacts. Indeed, with such an array of associated risks it appears that irradiated ground beef should be declared unsafe and unwholesome.

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[4] Again, ground beef is potentially covered by the pending food additive petitions 9M4697 and 9M4695.

Additional concerns apply to other irradiated foods as well, such as potatoes, discussed below.

Study 3. Human study finding elevated hemoglobin.[5] As part of the report of her Ph.D. research, Jaarma assessed the impact of eating irradiated potatoes over 14 weeks on seven hematologically healthy volunteers (4 m and 3f). The report states:

> *An increased concentration of hemoglobin, especially in the first period of the investigation, was observed in all the individuals... [H]emoglobin values were significantly higher during the [feeding] period than before [the feeding period]... An additional comparison of the values before with the values after shows that a small effect still remains.*

While unpublished, the study was from a reputable Swedish university and is one of the very few human studies involving irradiated foods. It was one in which several women were subjects, whereas most of the human study subjects have been male. Further, the results showing elevated hemoglobin had high statistical significance.

Study 4. Pig study finding elevated hemoglobin.[6] Study 3's findings were corroborated by this published study by Jaarma and Bengtsson, in which elevated hemoglobin levels again were found, most markedly in breeding female pigs (sows) fed irradiated potatoes over 18 weeks, compared to a control group (p. 117 therein, Fig. 2). The effect was marked during the sows' pregnancies. According to the authors (p. 123):

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[5] Jaarma, M. 1967. Studies of chemical and enzymatic changes in potato tubers and some higher plants caused by ionizing radiation, including studies on the wholesomeness of γ-irradiated potato tubers and effects on some carbohydrates *in vitro. Akademisk Avhandling,* Som med tillstand av kungl. Universitetets i Stockholm (Ph.D. dissertation.). This study was not considered in FDA's 1986 omnibus irradiation ruling, nor was it included in FDA's bibliography of irradiation studies that supported it, although FDA in the past has considered unpublished studies in its safety assessments. The study is cited in an important review paper, P.C. Kesavan and M.S. Swaminathan. 1971. Cytotoxic and mutagenic effects of irradiated substrates and food material. *Radiation Botany* 253:-281. The particular section of the Jaarma paper called "Studies on haemotological effects of γ-irradiated potatoes on human volunteers" begins at p. 13.

[6] Jaarma, M, and G. Bengtsson. On the wholesomeness of γ-irradiated potatoes - II. Feeding experiments with pigs. *Nutr. Dieta* 8:109-129

> *The appreciably faster increasing haemoglobin levels, and the higher final concentrations, which were noted for one or several animals in nearly all of the I [irradiated potato diet] groups, is difficult to explain. The phenomenon is not necessarily a coincidence.*

Study 5. Population study indicating human stillbirths associated with elevated hemoglobin.[7] This is a fundamentally important recent Swedish population-based case control study on the implications of high hemoglobin for pregnant women. Reported in the *Journal of the American Medical Association,* the conclusion of nine years of research on the outcomes of the pregnancies of more than 1,400 women was:

> *High hemoglobin concentration at first measurement during antenatal care appears to be associated with increased risk of stillbirth, especially preterm and small-for-gestational-age (SGA) antepartum stillbirths.*

Earlier studies showed a relationship between high maternal hemoglobin levels and low birth weight, as well as a connection between high hemoglobin levels and hindered circulation in the placenta.[8]

If consumption of irradiated potatoes causes elevated hemoglobin levels in people generally, and in pregnant sows, as Jaarma et al. found in Studies 3 and 4, above, then the findings of Study 5 indicate that consumption of irradiated potatoes by pregnant women would be a risk factor for stillbirths. Particularly in its review of the sweeping FAP 9M4697, which includes use of ionizing radiation for both raw and pre-processed vegetables, fruits, and other agricultural products of plant origin, and multi-ingredient food products, FDA must ensure that it does not permit an easily avoidable national tragedy to occur in the form of an elevated rate of U.S. stillbirths. An array of additional hemoglobin testing for consumption of potatoes and the many other foods that may be irradiated under that petition must be required first. The needed research should emphasize potential effects on pregnant mammals, although it should not be limited to reproductive effects as elevated hemoglobin also can cause an array of other problems, such as blood thickening, bone marrow dysfunction, increasing numbers of clot-forming platelets, and an enlarged liver or spleen.[9]

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[7] Stephansson, O., P.W. Dickman, A. Johansson, and S. Cnattingius. 2000. Maternal hemoglobin concentration during pregnancy and risk of stillbirth. *JAMA* 284:2611-2617.

[8] *Acta Obstetrica Gynecologica Scandinavica*. 1990. 69:127-133.

[9] See the Merck Manual on hemoglobin, online at www.merck.com .

The connection between human stillbirths and elevated hemoglobin was not medically established when FDA conducted its earlier reviews of irradiation, but FDA must not overlook it now. Three mice and rat studies enclosed with our May 16, 2001, comments on these pending irradiation petitions did find elevated rates of stillbirths and other pregnancy failures in lab animals that ate irradiated diets, such as the Bugyaki et al. study.[10] However, hemoglobin levels were not fully assessed in those studies, thus any contribution such levels may have made to the observed stillbirths remains unanalyzed.[11]

Study 6. OECD study on genetic effects produced by irradiated food.[12] This was an early and useful report of available data on genetic effects (mutations and chromosome aberrations) in various organisms after ingesting irradiated foods. The sections of the report on mammals (pp. 7-11), that document positive genetic effect findings never have been adequately addressed by FDA. Effects in mice and rats associated with irradiated diets include cell aberrations, lymphopenia, and dominant lethal mutations. Several of these mutagenicity findings were confirmed in later publications cited in our May 16, 2001, comments on the five pending petitions.[13]

The OECD study concluded (pp. 15-16) that while certainty regarding likely effects of irradiated food on humans was elusive based on the data then available:

> *Hitherto available data indicate, however, that increased rates of mutation and chromosomal aberrations will probably be induced in certain cases. Although*

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[10] Study 2 in the May 16, 2001, comment: Bugyaki, L., A.R. Deschreider, J. Moutschen, M. Moutschen-Dahmen, A. Thijs, and A. Lafontaine. 1968. Do irradiated foodstuffs have a radiomimetic effect? II. Trials with mice fed wheat meal irradiated at 5 Mrad. *Atompraxis* 14:112-118; see also Study 3, therein: Moutschen-Dahmen, M., Moutschen J., and L. Ehrenberg. 1970. Pre-implantation death of mouse eggs caused by irradiated food. *International Journal of Radiation Biology* 18:201-216, and Study 12, Vijayalaxmi and K.V. Rao. 1976. Dominant lethal mutations in rats fed on irradiated wheat. *Int. J. Radiat. Biol.* 29:93-98.

[11] The extent to which mice and rat hemoglobin levels are indicative of correlations in humans is unclear, whereas pigs likely are a better indicator for humans.

[12] Organization for Economic Cooperation and Development (OECD), Steering Committee for Nuclear Energy, Study Group on Food Irradiation. 1965. Genetic effects produced by irradiated food and food components. SEN/IR (65)15. Unpublished report by G.T. Scarascia-Mugnozza, A.T. Najaran, and L. Ehrenberg. Paris, France. This is the best copy available.

[13] See, e.g., the positive studies cited in footnote 10, above.

> *experiments indicate that the genetical effect, in cases where it is induced, is relatively small compared to the effect of direct exposure of animals to radiation, the same experiments indicate that the possible effect will not be negligible.*

Rather than being refuted by subsequent evidence, the OECD's statement regarding likely induction of mutations and chromosomal aberrations has been confirmed in many studies, cited in this and our earlier comments.

We now turn back to (pre-*trans* fat) nutritional issues surrounding irradiated foods, based on thoughtful reviews of the nutrient destruction caused by the technology. The reviews were carried out several years ago, reported in two book chapters attached hereto, but FDA has never addressed them.

Study 7. Nutrition chapter of Food Irradiation - Who Wants It?[14] This 1986 review focuses on reported vitamin losses and concludes they are significant. Key quotes that are particularly relevant as FDA considers the sweeping "ready to eat" petition (FAP 9M4697) and its implications for many types of food that together amount to approximately one-third of the typical American diet are:

> *Losses of 20 to 80% are not uncommon and there are still many gaps in the available scientific data....No studies anywhere have assessed whether there will be a significant impact either on the population as a whole or on vulnerable groups within the population.* (p. 51)

> *The food can thus undergo initial losses on irradiation, accelerated losses during storage, and additional losses because of longer storage times, and then lose further vitamins in cooking.* (p. 52)

The authors noted that the common irradiation industry argument that impacts on population-wide dietary sufficiency would be unlikely because people were not expected to eat much of the food "is dangerously close to saying that irradiated food is all right as long as you don't eat it!" In considering FAP 9M4697, FDA no longer has the luxury of making that assumption.

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[14] Webb, T., T. Lang, and K. Tucker. 1987. *Food Irradiation - Who Wants It?* Thorsons Publishing, Wellingborough, England. Chap. 4. Wholesomeness of irradiated food.

Study 8. Nutrition chapter of Biology of Food Irradiation.[15] The attachment is the bulk of a chapter from the important 1990 synthesis of the irradiation studies by food chemist D.R. Murray. He states his case succinctly:

> *Disproportionate and selective losses of essential nutrients occur in foods as a consequence of irradiation.* (p. 78)

The rest of the chapter supports this in a *tour de force* analysis of negative impacts on fatty acids, vitamins, amino acids, carbohydrates and other essential components, including in combination with cooking, that FDA must address. In considering the evidence as FDA assesses the foreseeable nutritional impacts posed by, in particular, the sweeping "ready to eat" food additive petition, we request the agency to respond to the following questions:

- 1. What would be the impacts of irradiation as proposed in the petition on each important vitamin and other nutritional component in each different food type that is included?

- 2. What would be the projected national rates of consumption of each different food type included in the petition after foreseeable market penetration of the product, e.g., after 5-10 years of marketing?

- 3. How would this projected future consumption vary across age, ethnic, gender, economic status, education status, and other variables in the American population?

- 4. To what extent would the various population groups likely be affected by the nutritional/vitamin impacts identified under question 1., above?

In conclusion, neither you nor American consumers can be reassured that irradiated food is safe and wholesome in view of the combined evidence indicating health and nutrition impacts, as detailed in this and in our previous five sets of comments on the pending petitions. FDA simply cannot ignore scientific papers showing doubled *trans* fat, elevated hemoglobin, mutagenicity, nutrient destruction, and other harms. Public hearings are needed to address the health and nutrition issues we have raised, which could affect tens of millions of consumers, many unknowingly, in particular the potential impacts on pregnant women,

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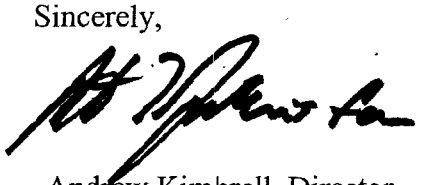
[15] Murray, D.R. 1990. *Biology of Food Irradiation*. Research Studies Press Ltd. Staunton, UK. Chap. 4. Radiolytic products and selective destruction of nutrients. Note: pp. 72-78 are omitted. Unfortunately, the appended copy includes some underlining, but the book is out of print and this is the best version available.

children, and other vulnerable populations.

Thank you for your consideration of this comment in opposition to the above-referenced food additive petitions. We also request to meet with you personally on this matter. To arrange a meeting please contact Peter T. Jenkins, Policy Analyst; tel: 202.547.9359 x13; email: peterjenkins@icta.org.

Sincerely,



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Attachments (8 tabbed studies)

cc: FDA Food Additive Petition Docket No.s: 99F-5522; 01F-0047; 99F-4372; 99F-5321; 99F-5322 (with attachments)