



July 8, 2003

1
1
4
03
JUL -9
PM 12

~~Mr. Joseph Levitt
U.S. Food and Drug Administration
CFSAN HFS-001
Harvey W. Wiley Federal Building
5100 Paint Branch Parkway
College Park, MD 20740-3835~~

~~Dr. Laura Tarantino
U.S. Food and Drug Administration
CFSAN OFAS, HFS-200
Harvey W. Wiley Federal Building
5100 Paint Branch Parkway
College Park, MD 20740-3835~~

~~Dr. Alan Rulis
U.S. Food and Drug Administration
CFSAN OFAS, HFS-200
Harvey W. Wiley Federal Building
5100 Paint Branch Parkway
College Park, MD 20740-3835~~

~~Dr. George Pauli
Associate Director for Science and Policy
U.S. Food and Drug Administration
CFSAN OFAS, HFS-205
1110 Vermont Ave., N.W. Rm. 1250
Washington DC 20201~~

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

Dear Mr. Levitt and Drs. Rulis, Tarantino and Pauli:

This is both a joint comment letter and a request for a high level face-to-face meeting between you and Public Citizen's Executive Director Joan Claybrook and others. Your agency is considering the five above-

MR. JOSEPH LEVITT ET AL.

referenced food additive petitions to irradiate a much greater portion of the food supply, including the huge category of “ready-to-eat foods” (FAP 9M4697) comprising an estimated 37 percent of the average American diet. As you know, our two organizations have filed numerous detailed comments opposing these petitions on grounds of serious safety and nutrition questions.

We request a meeting to discuss the attached paper by Raul et al. newly published in *Nutrition and Cancer*, entitled “Food-borne radiolytic compounds (2-alkylcyclobutanones) may promote experimental colon carcinogenesis.”¹ These findings in their unpublished form were addressed at length in our earlier joint comment to you on the above-referenced petitions dated February 26, 2003.² We won’t repeat them here, except to quote the first and last sentences of the last paragraph, the implications of which we would like to discuss directly with you:

The present report is the first demonstration that pure compounds, known to be exclusively produced on irradiation in dietary fats, may promote colon carcinogenesis in rats.... 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.

We also want to meet in order to discuss the attached new expert opinion by a leading colon cancer/nutrition expert, C.V. Rao, Ph.D., Associate Chief of the Division of Nutritional Carcinogenesis, Institute For Cancer Prevention, American Health Foundation-Cancer Center in Valhalla, New York.³

¹ Raul, F., F. Gossé, H. Delincé, A. Hartwig, E. Marchioni, M. Miesch, D. Werner, and D. Burnouf. 2002. Food-borne radiolytic compounds (2-alkylcyclobutanones) may promote experimental colon carcinogenesis. *Nutrition and Cancer* 44(2): 188-191.

² Pages 3-5 of that comment letter addressed the major unpublished French and German food irradiation report that we had provided to you in English translation: D. Burnouf, H. Delincé, 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.

³ See www.ifcp.us/ResearchFacilities-Profile-CVRao.cfm for more information on Dr. Rao. The Institute’s webpage states: “Institute For Cancer Prevention (IFCP) is the premier institute for cancer prevention research and the only National Cancer Institute designated cancer center dedicated

MR. JOSEPH LEVITT ET AL.

He prepared this as our consultant; we asked him to review the Raul et al. published paper and related materials, as well as to conduct independent literature research. The excerpts below from Dr. Rao's opinion are vital to the safety debate (emphasis added):

*However, it is to be noted that prolonged exposure and thus, the presence of trace amounts of alkylcyclobutanones in the adipose tissue over long periods of time can have deleterious effects, and this requires further investigation. **Ingestion of 2-alkylcyclobutanones present in irradiated foods (specifically from the fatty acid chains) may thus contribute to the risk for the neoplastic growth in colonic (including normal, preneoplastic and neoplastic) epithelia.....***

*It is important to understand whether these compounds are co-carcinogenic and whether they might affect people not at risk from colon cancer differently from those predisposed to it. Irrespective of the pitfalls of the study, it is indeed alarming that 0.005% w/v of solution 2-alkylcyclobutanones given in drinking water to AOM-injected Wistar rats significantly promotes colonic tumors, and total number ACF when compared to rats treated with vehicle alone. **Hence, the results reported in the study by Raul et al. (2003) are very important and the possible public health impacts of their observation needs further investigations with established experimental designs for colon cancer.....***

The exact mechanism(s) by which 2-tDeCB specifically promotes colon cancer warrants further research. Moreover, the prolonged accumulation of these compounds in various tissues (not investigated so far) may lead to genotoxic levels and may possibly promote late but chronic effects.....

*There are several recent reports about the toxicity of 2-alkylcyclobutanones. Ample preliminary evidence exists supporting the possible genotoxic effect of 2-alkylcyclobutanones. However, further investigations are warranted to identify and assess the exact levels at which radiolytic agents 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***

entirely to cancer prevention and control. IFCP is one of only two centers that have two National Institutes of Health-funded core grants, the IFCP Cancer Center Grant and the CNRU, Clinical Nutrition Research Unit Grant.”

MR. JOSEPH LEVITT ET AL.

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.

This is the most definitive public statement yet by an expert that the colon cancer promotion risk requires further careful investigation before anyone asserts that food containing 2-ACBs is safe. We can report to you that our other retained toxicity consultant, Dr. William Au of the University of Texas Medical Branch, concurs completely with Dr. Rao's opinion and has offered supplemental observations beyond Dr. Rao's to the effect that it is likely that certain human subpopulations are more susceptible than others to toxic effects of irradiated foods and, most alarmingly, **that undernourished children may be the most susceptible to the potential colon cancer promotion effect observed in the Raul et al. paper.** This is certainly relevant to the recent USDA decision to allow irradiated ground beef into the National School Lunch Program, which provides a substantial portion of the typical diets of America's undernourished children. Dr. Au may be available to attend the requested meeting and expand on his opinion.

FDA has never examined the colon tumor promotion question on the record; indeed, the question has never been addressed in any other safety study. If FDA were to ignore these findings and expert opinions it would imperil its credibility in the irradiation safety debate.

Further, it is not just our groups along with Drs. Rao and Au that are urging further research. Consumers Union recently recommended in its widely-read *Consumer Reports* that further toxicity research be done on the chemical byproducts of meat irradiation, noting that some scientific researchers and the European Parliament had called for it.⁴ This call resonates with the attached paper by Donald B. Louria, MD, of the New Jersey Medical School entitled "Food irradiation: Unresolved issues."⁵ Dr. Louria points to mutagenic and nutritional risks of high concern, issues he has raised in several articles in the past. He recommends detailed human population studies prior to FDA consideration of any further irradiation approvals.

Also, as stated in the earlier comment letter dated April 7, 2003, submitted by CFS, information on doubling of *trans* fat in irradiated ground beef and other *trans* fat-containing products must be addressed through further published studies. Only then can FDA reliably calculate the expected levels of additional *trans* fat that would be taken in by American consumers after broad market penetration by irradiated products.

You kindly met with Joan Claybrook and others from our organizations about two years pursuant to a

⁴ Anon. 2003. The truth about irradiated meat. *Consumer Reports* Aug., pp. 34-37.

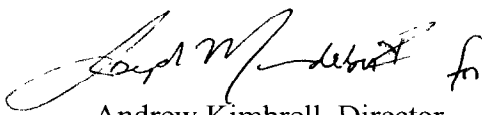
⁵ Louria, D.B. 2001. Food irradiation: Unresolved issues. *Clinical Infectious Diseases* 33:378-380.

MR. JOSEPH LEVITT ET AL.


similar request and the time is now ripe to meet again. We also submit this letter, including the attached information incorporated herein by reference, as a comment to the dockets expressing our **opposition** to FDA approval of the above-referenced petitions until the requested research is completed.

Thank you for your consideration of what we consider to be a very high-priority request to meet with you personally on this matter. To arrange the details of the meeting please contact Tony Corbo, of Public Citizen (tel: 202.454.5131; email: tcorbo@citizen.org).

Sincerely,




Andrew Kimbrell, Director
Center for Food Safety
660 Pennsylvania Ave., S.E.
Suite 302
Washington, DC 20003



Wenonah Hauter, Director
Public Citizen, Critical Mass Energy and Env't Program
215 Pennsylvania Ave., S.E.
Third Floor
Washington, DC 20003

Attachments (3)

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