June 2, 2003

Comments on the Draft Revised Codex General Standard for Irradiated Foods; ALINORM 03/12A, Para 78, Appendix V

Greetings:

The Center for Food Safety (CFS) and Public Citizen are pleased to submit this public comment on the above-referenced Draft Revised Codex General Standard for Irradiated Foods, which is due to be considered by the Codex Alimentatrius Commission at its 26th meeting, 30 June – 7 July in Rome.

CFS is a national, non-profit, membership organization established in 1997 to use science and the law to address increasing concerns over the impacts of the global food production system on human health, animal welfare, and the environment. Public Citizen is a national, non-profit, membership organization established in 1971 that advocates for consumer protection and for government and corporate accountability.

CFS and Public Citizen **oppose** the proposed revision of the Codex standards that would remove the existing 10 kiloGray (kGy) irradiation maximum average absorbed dose limit. Important new information indicates that critical concerns remain unresolved as to the safety of irradiated foods.

The European Union in 1999 commissioned a detailed assessment of the toxicity of several "unique radiolytic products" that have been found to be toxic in various contexts. Our earlier comments disclosed some of these toxicity concerns for 2-alkylcyclobutanones (2-ACBs). The recent EU report, entitled "Toxicological Study to Assess the Risks Associated with the Consumption of Irradiated, Fat-containing Foods," was prepared over the last four years by a consortium of German and French scientists from recognized institutions. This report, by Burnouf et al, contains major new findings.[1]

For example, tumor promotion, which has never been assessed in any other irradiated food animal or human feeding studies, represents a new area of toxicity that cannot be dismissed as already covered:

> 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.

These findings have since been published in a peer-reviewed journal:

> All animals received a single intraperitoneal injection of the chemical carcinogen azoxymethane (AOM) at Weeks 3 and 4. At 3 mo after AOM injection, no significant changes were observed in the total number of preneoplastic lesions in the colon of AOM controls and 2-ACB-treated animals. After 6 mo, the total number of tumors in the colon was threefold higher in the 2-ACB-treated animals than in the AOM controls. The colon of four of six AOM control rats exhibited only one small tumor (&6 mm3). Multiple tumors were observed in four and three of six animals treated with 2-tDCB or 2-tDeCB, respectively. Medium (6 < S < 25 mm3) and larger (>25 mm3) tumors were detected only in 2-ACB-treated animals. This is the first demonstration that a compound found exclusively in irradiated dietary fats may promote colon carcinogenesis in animals treated with a chemical carcinogen.[2]

In addition, the authors emphasized that further 2-ACB metabolite studies are "absolutely necessary" in order to determine the fate of these substances, in order to at least elucidate the extent to which they act as tumor promoters in the human body:

> 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.

These findings have since been published in a peer-reviewed journal:

> Laboratory rats received a freshly prepared drinking fluid containing 0.005% 2-tetradecyl- or 2-tetradecenyl-cyclobutanones daily for 4 months… Less than 1% of the 2-alkylcyclobutanones ingested daily were excreted in the feces. In addition, our data indicate that 2-alkylcyclobutanones are able to cross the intestinal barrier, to enter into the bloodstream, and to be stored in the adipose tissue of an animal. However, the amounts of these substances detected in the adipose tissues and in the feces were much smaller than the amounts ingested… [O]ur results indicate that 2-alkylcyclobutanones were not totally stored nor excreted, but either were stored in other parts of the body or underwest metabolic transformation. Further studies are therefore needed to determine the metabolic breakdown products of 2-alkylcyclobutanones and the establish the pathophysiological consequences of the stored 2-alkylcyclobutanones. [3]

In their full report, the authors conclude:

> [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. Unfortunately, these potential risks cannot be assessed at present due to the lack of studies in various areas. In order to characterize the potential risks, the hazards must be identified, and further research is required to precisely determine exposure to these substances, the precise dose-response relationship, and in particular the kinetics and metabolism of 2-ACBs in the living organism. All of this research is necessary to gain insight into the mechanisms of the toxic effects. Numerous questions still remain to be answered, and much research must still be done, before an informed risk assessment can be conducted. However, a start has been made, and we hope to be able to provide answers in the near future.

In response to a review of their report by the EU Scientific Committee on Food in July 2002, the report's authors, Burnouf et al, made a statement to clarify the significance of their work:

> [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 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.[4]

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."

Because these new results raise many more questions than they answered, a path of caution must be taken. These statements give no assurance of safety at all, rather they are a clear call for more studies before safety from now clearly-proven potential risks can be assured.

Here is a summary of 2-ACBs studied and the properties detected:

Chapter of Burnouf et al	**Particular 2-ACB**				
	2-DCB	2-dDCB	2-tDCB	2-dDeCB	2-tDeCB
2.5 – found in 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."

In April of this year, the European Commission's Scientific Committee on Food conducted a review of various issues related to irradiated foods. The Committee stated that there is insufficient evidence to pronounce that foods irradiated above 10 kGy are safe from human consumption:

> As the toxicological and nutritional database relating to foods irradiated below 10 kGy has not been enlarged to any significant degree since the appearance of the 1980 FAO/IAEA/WHO and the 1986 SCF Reports, the Committee considered it not possible, at present, to deviate from its earlier position, that only those specific irradiation doses and food classes should be endorsed, for which adequate toxicological, nutritional, microbiological and technical data are available. The human clinical studies with irradiated foods, although they did not show any adverse effects following the consumption of irradiated foods, do not provide a sufficiently wide database to support a general extension of irradiation with doses up to a maximum overall average dose of 10 kGy to any foodstuff as being safe and wholesome. These studies were so far confined to foodstuffs consumed as part of either an European or Western diet and did not include any exotic or unusual dietary items consumed elsewhere nor did they include novel convenience foods, in which unusual or novel ingredients might be used as components. Since neither adequate compositional data covering any unusual dietary components used in the production processes nor any toxicological data specifically related to these components, when irradiated, were available to the Committee, it was unable to accept the suggested general extension of the safety assessment of irradiated foods to any foodstuffs irradiated at any dose as proposed by the WHO Expert Group of 1994 and the WHO Study Group on high-dose irradiation of 1997.
>
> [O]nly very limited toxicological studies have been carried out with foods irradiated with doses >10 kGy and none have been provided on any of the convenience foods which have been deep frozen and subsequently irradiated with doses above 10 kGy. As the existing toxicological database has been hardly extended it is not possible for the Committee to accept at present the suggested removal of the upper limit of 10 kGy for the production of safe and wholesome irradiated foods. The Committee would be prepared to reconsider its position, when a more adequate database for the evaluation of the safety and wholesomeness of foodstuffs irradiated at doses above 10 kGy has been provided. In addition, the Committee would wish to consider the need for achieving an advantageous technological purpose by the irradiation of foods with doses above 10 kGy. At present, the only technological need recognised by the Committee would be the decontamination by irradiation of spices, dried herbs and vegetable

> seasonings, where doses up to 30 kGy may be needed to ensure a product in a satisfactory hygienic condition.
>
> On the basis of the information presently supplied to it, the Committee is still of the opinion, that it is appropriate to specify a maximum dose for the treatment of certain food products by ionising radiation and that irradiated foodstuffs should continue to be evaluated individually taking into account the technological need and their safety.[5]

Thus, it is not merely scientists and consumer groups who have raised concerns, but also the EU itself.

Public Citizen and CFS made an earlier joint comment to the Codex CCFAC dated May 14, 2001 (at www.centerforfoodsafety.org/li/commcodx.htm) that raised mutagenicity concerns that go far beyond this recent cyclobutanone debate, based on careful review of decades of scientific articles. That comment demonstrated mistakes in the 1999 FAO/WHO/IAEA Technical Report #890, *High-Dose Irradiation: Wholesomeness of Foods Irradiated Above 10 kGy.* At least 10 positive in vivo published studies that found mutagenic effects in mammals – including one in humans – were misclassified or ignored in that 1999 report, upon which the Codex CCFAC explicitly relied in its preliminary approval of removing the 10 kGy limit. These 10 positive studies compare to only 17 published in vivo studies that were reportedly negative for mutagenicity. Similarly, for published in vitro studies, 5 mutagenicity studies were positive and 8 were negative. Overall, more than one-third of published studies indicate mutagenicity of irradiated food substances. This is hardly a record upon which Codex can assert safety.

Further, evidence suggesting that irradiated foods may not be safe for human consumption has been dismissed and misrepresented by the World Health Organization, the International Atomic Energy Agency and the United Nations' Food and Agriculture Organization.

In 1994, 1995 and 1999, the WHO published the three most important documents since international deliberations over food irradiation policy began in earnest in 1961. These documents culminated in an endorsement that any food could be irradiated at any dose. The agencies arrived at this decision after taking research that revealed health problems in animals that ate irradiated foods, and stating that the research actually revealed no health problems that could be attributed to irradiation. In addition to reclassifying studies that found "adverse effects" as "negative," many studies that found negative effects were omitted from key reports published later. These discrepancies occurred 52 times.

In 1994, the WHO published a report entitled *Safety and Nutritional Adequacy of Irradiated Food*.[6] The report stemmed from an FAO/IAEA/WHO meeting held in Geneva two years earlier. The document lists about 150 studies conducted on the safety of irradiated foods, including those involving monkeys, dogs, rabbits, pigs, hamsters, mice, rats and fruit flies. Among these studies, the report lists a wide range of adverse health effects.

In the 1994 report, 11 studies classified as yielding adverse effects were re-classified as negative in an FAO/IAEA/WHO report published in 1999, *High-Dose Irradiation of Food*.[7] Among these studies, the 1994 report lists a wide range of adverse health effects in animals that ate irradiated

foods, including birth defects and genetic damage; fatal internal bleeding and other blood disorders; fewer offspring; stunted growth and weight gain; and liver malfunction.

Additionally, 19 studies that the 1994 report classifies as yielding adverse effects were not listed at all in an FAO/IAEA/WHO report published in 1995, *Review of High-Dose Irradiation of Food*.[8] Among these studies, the 1994 report lists a wide range of adverse health effects in animals that ate irradiated foods, including tumors, mutations and chromosome damage, stunted growth, liver and thyroid malfunction, a blood disorder, prolonged estrous cycles, and atrophied testicles.

And, one study that the 1994 report classifies as yielding an adverse effect – stunted growth in rats fed irradiated oranges for five months – was re-classified in the 1995 report as having no adverse effects.

None of the discrepancies between the 1994 report and 1995 report are specifically explained in the latter. The only reference in the 1995 report to the issue of interpretation of studies states that adverse effects attributable to irradiated foods "were sometimes not shared by other observers or were not confirmed by later work." There is no explanation in the 1995 report of the omission of 19 studies and the re-classification of another.

The discrepancies also appear between the 1995 report and the 1999 report. In the 1995 report, 21 studies that yielded adverse effects were re-classified as negative in the 1999 report. Again, these studies revealed a wide range of health problems in animals that ate irradiated foods, including increased mortality; fatal internal bleeding and other blood problems; decreased fertility and other reproductive problems; lower white blood cell counts; mutations and other genetic damage; liver malfunction; and stunted growth.

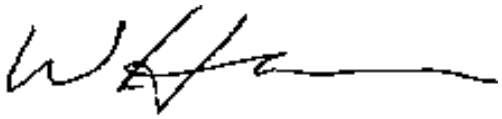
The discrepancies between the 1995 report and 1999 report become more troubling considering that in 27 of the 102 studies listed in 1995, researchers "concluded [that] adverse effects" were observed in animals that ate irradiated foods. One could hardly justify an endorsement of food irradiation when fully one-fourth of experiments revealed health problems in lab animals that ate irradiated foods.

In sum, both new and old evidence indicates a lack of proof of safety for food irradiation. The demonstrated health risks would magnify at higher irradiation levels. Raising the allowable absorbed dose above the existing 10 kGy limit would be imprudent and potentially unsafe at this time. The Center for Food Safety and Public Citizen strongly urge Codex to reject it.

Codex must be mindful of the international scandal that will result if it approves removing the 10 kGy limit, and then the demonstrated potential risks to humans from eating foods irradiated at these newly-approved higher doses become manifest in the subsequent studies recommended by numerous scientists, and supported by the WHO and EU representatives. Indeed, the opinion of many is that the risks already established are beyond what is prudently acceptable.

Thank you for your attention to this comment. For further discussion about the issues herein please contact Peter Jenkins of CFS at peterjenkins@icta.org or Mark Worth of Public Citizen at mworth@citizen.org.

Sincerely,



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[1] Translation was done by William Freese Translations of Mt. Rainier, MD. Mr. Freese has a degree in chemistry and more than 13 years experience translating medical and scientific texts. The untranslated report is online at: www.bfa-ernaehrung.de/Bfe-Deutsch/Information/bfeber91.htm (2nd 2002 paper). 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.

[2] Raul, F. et al. "Food-borne radiolytic compounds (2-alkylcyclobutanones) may promote experimental colon carcinogenesis." *Nutrition and Cancer*, 44(2):189-91, 2002.

[3] Horvatovich P. et al. "Detection of 2-alkylcyclobutanones, markers for irradiated foods, in adipose tissues of animals fed with these substances." *Journal of Food Protection*, 65(10):1610-3, 2002.

[4] D. Burnouf, H. Delincée, A. Hartwig, E. Marchioni, M. Miesch, F. Raul, D. Werner. Comment on a statement of the SCF on a report on 2-alkylcyclobutanones.

[5] "Revision of the opinion of the Scientific Committee on Food on the irradiation of food." Scientific Committee on Food, Health and Consumer Protection Directorate-General, European Commission, SCF/CS/NF/IRR/24 Final, 24 April 2003.
< http://europa.eu.int/comm/food/fs/sc/scf/out193_en.pdf>

[6] *Review of Data on High Dose (10-70 kGy) Irradiation of Food*. Report of a Consulation, Karlsruhe, Germany, 29 August - 2 September 1994. Geneva: World Health Organization, 1995.

[7] *High-Dose Irradiation: Wholesomeness of Food Irradiated with Doses Above 10 kGy*. Report of a Joint FAO/IAEA/WHO Study Group, Geneva, 15-20 September 1997. Geneva: World Health Organization, 1999.

[8] *Review of Data on High Dose (10-70 kGy) Irradiation of Food*. Report of a Consulation, Karlsruhe, Germany, 29 August - 2 September 1994. Geneva: World Health Organization, 1995.