

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Petition to Establish Interim Acceptable)
Levels for Acrylamide In Major Food Sources)

Docket No. 03P-0276

Submitted by the

CENTER FOR SCIENCE IN THE PUBLIC INTEREST

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Dockets Management Branch
United States Food and Drug Administration
Department of Health and Human Services
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CITIZEN PETITION

I. PRELIMINARY STATEMENT

In 1991 the United States Environmental Protection Agency (“EPA”) concluded that human consumption of acrylamide can cause damage to the nervous system, paralysis, and cancer. So the EPA requires that a water supplier ensure—when polyacrylamide is used to remove contaminants from drinking water—that the amount of uncoagulated acrylamide monomer in the water is less than 0.5 parts per billion.

In June 2002 the United States Food and Drug Administration (“FDA”) determined the safe daily intake of acrylamide with respect to neurotoxicity is 12 micrograms per person.

In December 2002 the FDA confirmed that acrylamide is present in 18 classes of food (including infant formula and baby foods) at levels well above that permitted by the EPA for drinking water.¹ Some of those foods—when eaten together at the amounts the average American consumes—provide more acrylamide than the FDA had determined was safe seven months earlier.

Accordingly, the FDA immediately should set interim acceptable limits on the amount of acrylamide for categories of food that provide the most acrylamide to Americans. The FDA should set particularly protective limit for infant formulas and baby foods. The FDA should then deem any food exceeding those levels to be adulterated because it “bears or contains any poisonous or deleterious substance which may render it injurious to health.”² The FDA is

¹ The classes are: some baby foods, all French fries, all potato chips, some infant formulas, some protein foods, some breads and bakery products, all cereals, some snack foods other than potato chips, some gravies and seasonings, some nuts and nut butters, all crackers, some chocolate products, some canned fruits and vegetables, all cookies, all coffee, all frozen vegetables, some dried foods, and some dairy products.

² Section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 342(a)(1).

authorized to seize adulterated food³ and to seek criminal penalties against someone selling it,⁴ as are the many states that have adopted a law based on the Federal Food, Drug, and Cosmetic Act.⁵

II. ACTION REQUESTED

The Center for Science in the Public Interest⁶ (“CSPI”) requests⁷ that the FDA immediately use the best available industry practices as the basis for setting interim acceptable limits⁸ for acrylamide for different classes of food. The FDA should deem any food containing acrylamide in excess of such limits to be adulterated within the meaning of section 402(a) of the Federal Food, Drug, and Cosmetic Act (“FFDCA”).⁹

Acrylamide is of special concern when it appears—as it does—in some infant formulas and baby foods because: (1) babies may rely on those few foods for a substantial proportion of their overall diets, (2) babies tend to consume more food in proportion to their body weights than adults, (3) babies may be more sensitive to the carcinogenic action of acrylamide, and (4) babies may be more sensitive to the neurotoxic impact of acrylamide because of their immature nervous

³ Section 304(a)(1) of the FFDCA, 21 U.S.C. 334(a)(1) .

⁴ Section 303(a)(1) of the FFDCA, 21 U.S.C. 333(a)(1) .

⁵ For example, sections 21a-94 *et seq.* of the Connecticut Food, Drug and Cosmetic Act authorize the Connecticut Commissioner of Consumer Protection to ask a court to seize adulterated food (including a food that “bears or contains any poisonous or deleterious substance which may render it injurious to health”). Section 202-b of the New York Agriculture and Markets Law authorizes the New York Commissioner of Health (subject to review of the courts) to seize adulterated food (including a food that “bears or contains any poisonous or deleterious substance which may render it injurious to health”).

⁶ Petitioner Center for Science in the Public Interest, a nonprofit organization based in Washington, D.C., is supported by 800,000 members and subscribers to its *Nutrition Action Healthletter*. CSPI has been working to improve the nation’s health through better nutrition and safer food since 1971.

⁷ This petition is submitted pursuant to section 4(e) of the Administrative Procedure Act, 5 U.S.C. 553(e), and 21 C.F.R. 10.25 and 10.30 (2002).

⁸ These interim acceptable limits would be action levels, pursuant to section 401(a) of the Federal Food, Drug, and Cosmetic Act (“FFDCA”) and 21 C.F.R. 109.4(c)(1) (2002).

⁹ For enforcement purposes the FDA would indicate the sampling procedures and the permitted variance around the acceptable limit. For example, in enforcing its nutrition labeling requirements, the FDA allows a variation of 20 percent of the stated value in a sample consisting of 12 subsamples. 21 C.F.R. 101.9(g) (2002).

systems. For those foods the FDA should set particularly protective limits for acrylamide.

For other major classes of food the FDA could set as the interim acceptable level for acrylamide the median of all the observed values (using the mean value for a brand when there is more than one sample for the brand).¹⁰ Consider, for example, home-baked French fries—which are a major source of acrylamide because of their high level of acrylamide and their importance in the average American’s diet. In its sample of 12 brands the FDA found the level of acrylamide *before* being baked at home to range from 20 parts per billion (“ppb”) to 218 ppb, with a median value of 77 ppb; therefore, the interim acceptable value would be 77 ppb.¹¹

The FDA could proceed in the following way. First, for some major classes of food the FDA already has a large sample. For example, it has now tested 23 unbrewed coffees, 23 baby foods, 16 brands of potato chip, 12 infant formulas, 12 brands of French fries cooked at home, and 9 brands of restaurant French fries.¹² However, for other important classes of food the current sample is smaller. For example, for cookies the sample is only 7. For those foods the FDA should immediately test more samples and also encourage companies, many of which have been testing their products for acrylamide, to provide data on a confidential basis (levels, but not brands, would be made public).

The FDA should then identify—based on the levels of acrylamide found in the sample and the importance of the food in both the average person’s diet and the diet of major consumers

¹⁰ The FDA could take some value other than the median, such as the lowest observed level or the arithmetic mean of the observed values. Under the former approach, the acceptable level for unbaked French fries would be 20 ppb because that is the lowest level the FDA found in its surveys. Under the latter approach, the acceptable level would be 110 ppb because that is the average of the 12 brands the FDA sampled. The median value has the advantage that it is less sensitive to extreme values and to small changes in the observed values than either the mean value or the lowest value. Rather than using the median (the 50th percentile), the FDA could also take a different percentile as the temporary ceiling, such as the 25th percentile.

¹¹ Six of the 12 brands sampled have values below 77 ppb and six have values above 77 ppb. As there were 12 brands of French fries in the sample, we took as the median value the mean of the sixth brand (74 ppb) and the seventh brand (79 ppb).

¹² All data in this paragraph are based on the combined results of the FDA’s announcements in December 2002 and February 2003.

of the product¹³—the major¹⁴ classes of food (including foods sold in fast-food chains of more than, say, 10 stores¹⁵) for which there is a public health concern for adults. For adults, as explained below in III.H, some of the major classes would include French fries, potato chips, bread, and coffee. For infants and babies, every food should be considered of major concern.

The FDA should then publish in the Federal Register a proposal to establish an initial interim acceptable limit—using the current median observed level—for each of the major classes of food. The FDA should ask for public comment on (1) whether any acrylamide at all should be acceptable in foods intended solely for babies and (2) the proposed initial interim acceptable levels of acrylamide in other categories of food.

The FDA should make it clear that the initial interim acceptable level will be revised downward periodically as the firms with the highest levels of acrylamide either stop selling their product or modify their manufacturing practices so as to get the level of acrylamide below the initial interim acceptable level. Thus, with each iteration the interim acceptable level will fall.

The feasibility of the approach outlined above is supported by activities in Germany. The German government announced last year that:

Our minimization concept to lower acrylamide levels in foods got off to a successful start. Many companies have made intensive efforts to lower acrylamide levels with positive results to show for at the end....The test findings appear to show that it is perfectly possible to cut acrylamide levels substantially at enterprise level, e.g., through the selection of raw materials and temperature control. Major potato chip producers have already made considerable efforts to this effect....In addition, the tests performed by a major crispbread producer seem to confirm that key changes to processes and recipes can be successfully implemented.¹⁶

¹³ For example, the maximum level of acrylamide found by the FDA in unbrewed coffee is 374 ppb. While the average per capita daily consumption of coffee in the United States was 1.9 cups in 1999, the average consumption among coffee drinkers was 3.1 cups per day. See data from Coffee Research Institute (www.coffeeresearch.org/market/usa.htm).

¹⁴ “Major” could be defined as classes of food (e.g., ready-to-eat cereals, bread and rolls, peanut and tree nuts, biscuits and crackers) that contribute 1 microgram or more per day to the average American.

¹⁵ While the FDA does not have direct regulatory authority over the retail sale of food in such stores, it does have jurisdiction over the interstate shipment of such food to each retail store. Moreover, states could enforce the FDA’s standards for retail stores.

¹⁶ Press release of Alexander Müller, State Secretary in the Federal Consumer Protection Ministry (December 4, 2002).

The German government concluded “that in some sectors there is a ‘good manufacturing practice’ that can bring about lower levels of acrylamide. This must be used as a yardstick for the other producers of the same product group.”¹⁷

One should not expect private food companies to call attention to the presence of acrylamide by advising consumers on how to reduce exposure to it. Thus, the FDA should continue making public the results of its tests on the amount of acrylamide, including brands, in various foods so that consumers can make informed choices about both the class of food and the brand within each class. The FDA should also begin to advise consumers, as the German government has done, on how they can modify their cooking practices for potatoes and bread to reduce the amounts of acrylamide to which they are exposed.¹⁸

III. BACKGROUND

A. In 1991 the United States Environmental Protection Agency Set an Upper Limit for Acrylamide in Drinking Water Because Acrylamide May Cause Cancer in People.

The 1974 Safe Drinking Water Act required the EPA to determine safe levels of chemicals in drinking water that may cause health problems. The EPA’s current regulations set a maximum contaminant level goal (“MCLG”) for acrylamide of zero.¹⁹ In order to meet that goal, the EPA requires a water supplier to show that “when acrylamide is added to water, the amount of uncoagulated acrylamide is less than 0.5 ppb.”²⁰ The EPA’s regulations explain that “[a]crylamide has been shown to cause cancer in laboratory animals such as rats and mice when the animals are exposed at high levels over their lifetimes. Chemicals that cause cancer in laboratory animals also may increase the risk of cancer in humans who are exposed over long periods of time. Sufficiently large doses of acrylamide are known to cause neurological injury.”²¹

¹⁷ *Acrylamide in foods, current state of play on the occasion of the press conference held by State Secretary Müller in Berlin on 4 December 2002* at 1.

¹⁸ The German government says, for example, that potatoes should be peeled and soaked in water for one hour before deep-frying or roasting and should also be boiled before roasting. French fries should be baked at a temperature below 200 degrees C (392 degrees F) if top and bottom heat is used. Consumers should avoid excessive browning when baking or toasting bread. Press Release of Alexander Müller, State Secretary in the Federal Consumer Protection Ministry (December 4, 2002).

¹⁹ 40 C.F.R.141.50(a) (2002).

²⁰ EPA *Consumer Factsheet on ACRYLAMIDE*.

²¹ 40 C.F.R. 141.32(e)(23) (2002).

The EPA reached that conclusion after a contested rulemaking in the 1980s. In November 1985 the EPA, after reviewing various studies, said:

The data strongly suggest that acrylamide monomer is carcinogenic in animal species. Because of these potential adverse health effects and the fact that acrylamide is likely to be occurring in water supplies, due to its use as an additive in the drinking water treatment process, EPA is proposing to regulate this contaminant. The RMCL [recommended maximum contaminant level] will be based upon carcinogenic effects and an RMCL of zero is proposed.²²

Several comments on the EPA's proposal argued that a zero MCLG was inappropriate, in part because the carcinogenicity data were weak. The EPA reviewed the scientific studies submitted by those commentators, and in 1989 EPA reaffirmed its earlier carcinogenic conclusion because "the chemical tested positive in more than one species, in more than one strain in one of the species, and by more than one exposure route."²³ In 1991 the EPA issued its final regulation, saying that its conclusion was valid even though it found two human epidemiology studies then available "to be inadequate for determining the potential carcinogenicity of acrylamide in humans."²⁴

A decade later, an epidemiological study provided the first evidence that acrylamide might cause (pancreatic) cancer in humans.²⁵

B. In 1994 the World Health Organization and the United States Government Both Concluded That Acrylamide Probably Causes Cancer in People.

The World Health Organization's International Agency for Research on Cancer

²² 50 Fed. Reg. 46936 (November 13, 1985).

²³ 54 Fed. Reg. 22062 (May 22, 1989).

²⁴ 56 Fed. Reg. 3526 (January 30, 1991).

²⁵ Schulz MR, Hertz-Picciotto I, Wijngaarden EV, Hernandez JC, *Occupational Environmental Medicine* 2001;58:609 (letter commenting on Marsh GM, Lucas LJ, Youk AO, Schall LC, *Occupational Environmental Medicine* 1999;56:181-90). Marsh *et al.* did not find an association between acrylamide and cancer. However, in a reanalysis of the data (using different exposure categories) Schulz *et al.* found a statistically significant link between acrylamide and pancreatic cancer. The study's sensitivity was hampered by inadequate controls of variables and limited population size. The FDA is apparently unaware of the Schulz *et al.* study, as the FDA said in February 2003 that epidemiological "studies did not show increased cancer risk with acrylamide exposure." *FDA Draft Action Plan for Acrylamide in Food – February 24, 2003 Update* (CFSAN) at 2.

concluded in 1994 that “acrylamide is *probably carcinogenic to humans*.” (emphasis in original).²⁶ That same year the United States government’s National Toxicology Program (“NTP”)²⁷ said:

Acrylamide is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. When administered in the drinking water, acrylamide increased the incidences of adrenal pheochromocytomas and mesotheliomas of the tunica of the testes in male rats; pituitary adenomas, mammary adenomas and adenocarcinomas, oral cavity papillomas, uterine adenocarcinomas, and clitoral gland adenomas in female rats; and follicular adenomas of the thyroid in rats of both sexes. When administered by gavage or by intraperitoneal injection, acrylamide increased both the incidence and multiplicity of lung adenomas in mice of both sexes. When administered topically ... acrylamide induced skin squamous cell papillomas and squamous cell carcinomas in female mice. (emphasis in original)²⁸

C. In April 2002 Swedish Scientists Reported Their Discovery of Acrylamide in a Variety Of Fried and Oven-Baked Foods.

On April 24, 2002, scientists at the Swedish National Food Administration and Stockholm University reported the discovery of acrylamide in a variety of fried and oven-baked foods.²⁹ The initial Swedish research suggested that acrylamide formation is particularly associated with traditional high-temperature cooking processes for certain carbohydrate-rich foods.

D. In June 2002 The Same Swedish Scientists Confirmed the Presence of Acrylamide in United States Food That the Center for Science in the Public Interest had provided to Them.

Upon learning of the Swedish discovery, CSPI purchased certain foods—snack chips, taco shells, French fries, and breakfast cereals—and sent them to Sweden to be tested by the same Swedish scientists who had first discovered acrylamide in Swedish food. The Swedish

²⁶ “Acrylamide,” *International Agency for Research on Cancer Monographs*, Cas No. 79-06-1, vol 60 (1994) at 389.

²⁷ The NTP is an interagency program—comprised of the National Institutes of Health (“NIH”), the FDA, and the Centers for Disease Control—that is headquartered at the NIH.

²⁸ “Acrylamide,” *Report on Carcinogens*, 10th ed. (National Toxicology Program 2002).

²⁹ Tareke E, Rydberg P, Karlsson P, Eriksson S, and Tornqvist M, “Analysis of Acrylamide, A Carcinogen Formed in Heated Foodstuffs,” *Journal of Agricultural and Food Chemistry* 2002 Aug 14;50 (17):4998-5006.

tests revealed the presence of acrylamide in those American foods.

E. In June 2002 a Group of Experts Convened by the World Health Organization and the Food And Agriculture Organization Urged That Ways Be Found To Reduce the Amount of Acrylamide in Foods.

Subsequent studies in Norway, Switzerland, the United Kingdom, and the United States confirmed the Swedish discovery of acrylamide in certain foods, and in June 2002 the World Health Organization (“WHO”) and the United Nations Food and Agriculture Organization (“FAO”) convened a meeting of 23 scientific experts. The experts “recognized the presence of acrylamide in food as a major concern in humans based on the ability to induce cancer and heritable mutations in laboratory animals,”³⁰ and they urged investigation of “[t]he possibilities for reducing the levels of acrylamide in food by changes in formulation, processing and other practices.”³¹

The experts also noted that “it is anticipated that children will generally have intakes that are two to three times those of adults when expressed on a body-weight basis. Dietary intakes of acrylamide by some consumers may be several times higher than the average.”³²

F. In June 2002 the United States Food and Drug Administration Set a Safe Level for Acrylamide As a Neurotoxin.

Also in June 2002, the FDA issued a final food additive regulation providing for the safe use of dimethylamine-epichlorohydrin (“DEC”) and acrylamide-acrylic acid resins (“AAR”). The FDA determined that AAR may contain acrylamide, which the FDA said “is a recognized neurotoxin.”³³ However, the FDA approved AAR as a food additive³⁴ because it estimated that the daily exposure to acrylamide from AAR would be less than 2 nanograms per person, which is much less than the 12 micrograms per person that the FDA determined was the safe daily level.³⁵

³⁰ *Health Implications of Acrylamide in Food, Report of a Joint FAO/WHO Consultation* (June 25-27, 2002) (“*FAO/WHO Report*”) at 1.

³¹ *Id.* at 21.

³² *Id.* at 1.

³³ 67 Fed. Reg. 42715 (June 25, 2002).

³⁴ *Id.*

³⁵ Perhaps unaware of the neurotoxicity literature and of the FDA’s work, the FAO/WHO experts concluded “no neurotoxic effects are to be expected from the levels of acrylamide encountered in food.” *FAO/WHO Report* at 1.

G. The Food and Drug Administration Subsequently Measured Acrylamide Levels in a Variety of Foods.

In December 2002, the FDA announced the results of its exploratory survey of 280 products in 18 classes of food, and in March 2003 the FDA announced additional test results in 9 classes of foods. The results revealed significant levels of acrylamide: 130 ppb in a brand of baby food, 1,325 parts ppb in a brand of baked French fries,³⁶ 2,510 ppb in a brand of potato chips, less than 10 ppb in an infant formula, 116 ppb in a brand of baked vegetable burger, 130 ppb in a brand of untoasted bread, 1,057 ppb in a cereal, 1,243 ppb in a brand of snack food other than potato chips, 151 ppb in a seasoning, 457 ppb in a brand of flavored nuts, 620 ppb in a brand of cracker, 909 parts ppb in a brand of cocoa, 83 ppb in brand of canned baked beans, 432 ppb in a brand of cookie, 374 ppb in a brand of (unbrewed) coffee, and 1,184 ppb in a brand of onion soup and dip mix.³⁷

H. The Amount of Acrylamide Found by the Food and Drug Administration Could Lead to Both Thousands of Human Cancers Each Year and Somewhat Less-Quantifiable Risk of Neurologic Illnesses.

At present, one cannot determine with great accuracy the magnitude of harm—cases of cancer and neurotoxicity—caused by acrylamide, because the exact average (and range in) exposure to acrylamide from diet is not known and extrapolating from risks based on animal tests to risks to humans is inexact. Nevertheless, using preliminary data of several types, one can estimate certain risks.³⁸

1. Cancer risk

The FDA has estimated exposure based on CSFII (1989-92 3-day food intakes, 1994-96, 1998 2-day food intakes) and MRCA data (Marketing Research Corporation of America's 1982-

³⁶ This is the value after the French fries were cooked by the FDA. The maximum level for a brand of unbaked French fries was 218 ppb.

³⁷ FDA/CFSAN, *Exploratory Data on Acrylamide in Foods* (December 4, 2002) and FDA/CFSAN, *Exploratory Data on Acrylamide in Foods - February 2003 Update* (March 12, 2003).

³⁸ Thus, there is no need for the FDA to avoid taking action on our petition on the ground it must wait for several years for the results of its proposed studies on the public's exposure to acrylamide. See FDA/CFSAN, *FDA Draft Action Plan for Acrylamide in Food - February 24, 2003 Update* at 4.

87 14-day data).³⁹ Those estimates were 0.32, 0.37 and 0.48 µg/kg/day, or 22, 26, and 34 micrograms per day for an average 70-kg adult. Those figures, together with EPA's cancer-risk estimate,⁴⁰ translate into lifetime cancers of 400,000 (5,300 per year), 470,000 (6,200 per year), and 610,000 (8,200 per year).⁴¹ Of course, differences in acrylamide's metabolism and potency between animals and people might result in larger or smaller numbers of cancers.

CSPI has made its own estimates of dietary acrylamide consumption based on FDA test data and consumption data from the U.S. Department of Agriculture and certain industry groups. (See Table on page 11.) Based on CSFII (1994-96) consumption data for nine categories of foods, plus 10 percent to account for other categories of foods, we estimate a minimum intake of 29 micrograms per person per day (see Table on next page). Because participants in dietary surveys like CSFII typically underestimate food intake, especially of low-nutrition foods like french fries and potato chips, we also adjusted CSFII consumption data in proportion to adjusted energy requirements using data (based on doubly-labeled-water studies) provided in the Institute of Medicine's 2002 report on macronutrients (Chapter 5). Total consumption comes to 37

³⁹ Robie D, DiNovi M. The exposure estimate for acrylamide. Food Advisory Committee meeting on acrylamide, Feb. 24, 2003.
<http://www.cfsan.fda.gov/~dms/acryrob2/sld006.htm> [accessed, May 3, 2003]

⁴⁰ *Integrated Risk Information System (IRIS) on Acrylamide* (U.S. Environmental Protection Agency, National Center for Environmental Assessment, Office of Research and Development, Washington, D.C. 1999).

⁴¹ Calculations using more recent, but unpublished, EPA methods for projecting cancer-risk findings from animals to people may result in estimates several-fold less than the ones calculated here.

Table. Intake of Acrylamide in the Typical American Diet

FOOD	Food Consumption - g/day/person			Acryl.# ug/kg	Acrylamide ug/day/person	
	-----Based On-----				based on CSFII	based on CSPI's Best Estimate
	Diet Survey CSFII 94-9	Disappearance or Retail Sales	CSPI Best Estimate			
French fries	20	42	27	351	7	10
Potato chips	4	10	6	534	2	3
Popcorn, pretzels, corn chips	8	14	10	372	3	4
RTE cereals	16	16	16	85	1	1
Yeast Bread/rolls	63	81	72	84	5	6
Coffee	255	294	275	8	2	2
Peanuts/tree nuts	4	11	6	137	1	1
Cake, cookies, pie, pastries	30	-	36	124	4	4
Biscuits/Crackers	7	18	8	194	1	1
Miscellaneous [~]					3	3
TOTAL Acrylamide Consumption/day:					29	36
CSFII estimate adjusted for underreporting in CSFII⁺⁺			>>>>>		37	

Based on FDA tests (Dec. 2002, Feb. 2003).

~ Estimate (10% of categories listed to account for baby food, cocoa/chocolate, protein foods (veggie burgers, etc.), canned fruits and vegetables, gravies, etc.

++ Based on daily caloric intake (reported in CSFII vs. estimated in IOM 2002 report on Macronutrients).

micrograms per day.⁴² Using that estimate of acrylamide consumption per day and assuming a 70-kilogram person and EPA's figure for lifetime cancer risk, we estimate that dietary acrylamide causes an estimated 8,900 cancers per year, or 670,000 over the population's lifetime.⁴³

In one regard, those estimates may underestimate the cancer risk, because they do not account for the possible increased sensitivity of fetuses and babies to the effects of acrylamide. Fetuses are exposed to acrylamide, because that chemical crosses the placenta.⁴⁴ Also, acrylamide consumed by a nursing mother is present in breast milk, resulting in consumption of up to about 3 micrograms per day, a large amount considering that a baby might weigh one-twentieth as much as an adult.⁴⁵ Furthermore, the FDA found acrylamide at levels of 20 ppb or higher in 14 of the 24 samples of baby food and greater than 0 but less than 10 ppb in two of the 12 infant formulas sampled. While those levels are lower than those in many adult foods, they may be of special concern because: (1) babies may rely on those foods for a substantial proportion of their overall diets, (2) babies tend to consume more food in proportion to their body weights than adults, and (3) babies may be more sensitive to the carcinogenic action of acrylamide. Recently proposed EPA guidance suggests that exposures to mutagenic carcinogens in the first two years of life should be assumed to pose ten times the risk per unit dose as those for adults, and exposures between ages 3 and 15 should be accorded an extra 3-fold weighting factor for equivalent dose per unit body weight.⁴⁶

In sum, using FDA's or CSPI's exposure data and EPA's cancer-risk figure indicates a significant risk, a risk that is far greater than the conventional benchmark of one cancer in a million people over their lifetimes (about 280 cancers for the U.S. population).

⁴² Using another approach, we used our judgment to interpolate between CSFII food-consumption data for the same nine categories of food and either disappearance or retail supplies (details upon request). We added 10 percent for the acrylamide in miscellaneous foods. The final estimate using that method is 36 micrograms per person per day, similar to our first approach.

⁴³ Again, using more recent EPA methods for projecting cancer-risk findings may result in estimates several-fold less and differences in acrylamide's metabolism and potency between animals and people might result in larger or smaller numbers of cancers.

⁴⁴ Sörgel F, Weissenbacher R, Kinzig-Schippers M, *et al.*, "Acrylamide: increased concentrations in homemade food and first evidence of its variable absorption from food, variable metabolism and placental and breast milk transfer in humans," *Chemotherapy*. 2002;48:267-74.

⁴⁵ *Id.*

⁴⁶ Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens, February, 2003. External Review Draft EPA/630/R-03/003.

2. Neurotoxicity

Acrylamide is recognized as a neurotoxin in humans and animals.⁴⁷ Many Americans are now consuming acrylamide at levels higher than the safe level set by the FDA in June.⁴⁸ At that time, the FDA, applying a conventional safety factor to the results from an animal study, concluded that people should not consume more than 12 micrograms per day. Using our exposure estimate of 34 micrograms per day, it appears that the average American is consuming three times as much acrylamide as that safe level. Considering that our estimate might be low and that some people are consuming far more than the average amounts of french fries, potato chips, coffee, bread, and other contaminated foods, some people—probably including some young children—are probably consuming five or even ten times the safe level of acrylamide. Young children are of special concern for exposure to neurotoxic agents because important neurodevelopmental processes continue in the first years of life.

3. Protecting heavy consumers

The exposure levels indicated above are for the average person. The government also has a responsibility to protect consumers whose diets are higher in acrylamide. For example, someone who drank five cups of coffee and ate four ounces of french fries per day would consume about 75 micrograms of acrylamide—six times the safe level for neurotoxicity. FDA's research indicates that a 90th-percentile consumer would consume roughly twice as much as the average person and be at higher risk for the carcinogenic, neurotoxic, and other harmful effects of acrylamide.⁴⁹

I. The Food and Drug Administration Found Large Differences in the Amounts of Acrylamide in Various Products Within Each Class of Food.

The FDA found large differences in the amounts of acrylamide in different products within a class of food. For example, in its two surveys it tested 15 kinds of crackers, and the

⁴⁷ Institute for Health and Consumer Protection, Europeans Chemicals Bureau, Joint Research Centre, European Commission. *Acrylamide. Summary Risk Assessment Report*. 2001. Special Publication 1.01.70.

⁴⁸ 67 Federal Register 42714-7 (June 25, 2002) (Secondary Direct Food Additives Permitted for Direct Addition to Food for Human Consumption). We note that the FDA's determination of an Acceptable Daily Intake of 12 micrograms per person was based on a 22-year-old 92-/93-day rat-feeding study. It is possible, if not likely, that a longer study would have found adverse effects at lower exposure levels. Second, the study did not examine what may be a more sensitive indicator of neurotoxicity: nerve terminal degeneration. (Pers. Comm. R.M. Lopachin) If it had, adverse effects might have been seen at lower exposure levels. Thus, it is possible that the ADI should be lower than 12 micrograms.

⁴⁹ Robie D, DiNovi M., *supra*, note 39.

highest amount of acrylamide—620 ppb—was 24 times the lowest amount (26 ppb). One of the highest levels of acrylamide—909 ppb—was found in one brand of cocoa even though another brand of cocoa had none. Among the 12 brands of unbaked French fries (excluding fast-food restaurants) tested, the highest level—218 ppb—was 11 times greater than the lowest (20 ppb). Among the 16 brands of potato chips tested,⁵⁰ the highest level of acrylamide—2,510 ppb—was 21 times greater than the lowest (117 ppb). Among the nine brands of restaurant French fries tested, the highest level of acrylamide—1,030 ppb—was nine times the lowest (117 ppb).⁵¹ Among the 23 unbrewed coffees tested, the highest level of acrylamide—359 ppb—was seven times the lowest (51 ppb).

Those findings indicate that, with some effort, makers of the most-contaminated products should be able to greatly reduce acrylamide levels in their products. The German government reported in December 2002 that “Many companies have made intensive efforts to lower acrylamide levels with positive results to show for at the end....Yet, the [German] test results [of 1,000 samples] prove that many companies that are concerned apparently still hesitate to take concrete steps to lower acrylamide levels in their produce.”⁵²

IV. THE FOOD AND DRUG ADMINISTRATION SHOULD SET INTERIM ACCEPTABLE LEVELS FOR ACRYLAMIDE IN MAJOR FOOD CATEGORIES.

The FDA now has ample evidence from its own surveys that within a particular class of food some brands contain much less acrylamide than others. The FDA should use that information to quickly establish an interim acceptable level—an action level—for each of the major classes of acrylamide-contaminated food, by using the median of the observed levels.

Current FDA action levels for a particular contaminant sometimes differ for different classes of food. For example, for aflatoxin the FDA has an action level of 0.5 ppb for fluid milk,⁵³ 25 ppb for peanuts and peanut products,⁵⁴ and 20 ppb for other foods.⁵⁵ As another example, the action level for insects in frozen broccoli is 60 or more aphids, thrips, or mites per

⁵⁰ We exclude the two brands of sweet potato chips tested by the FDA, and we have taken the average of the 25 Lay’s Classic Potato Chips tested and treated it as a single brand. The highest level found by the FDA for a bag of Lay’s was only about twice the lowest level found.

⁵¹ We have taken the average level of the restaurant chain when the FDA tested French fries from more than one location.

⁵² Müller, *supra*, note 16.

⁵³ Section 527.400 of *Compliance Policy Guides* (2000).

⁵⁴ *Id.* at Section 570.375.

⁵⁵ *Id.* at Section 555.400.

100 grams,⁵⁶ while for frozen brussels sprouts it is 30 or more aphids and/or thrips per 100 grams.⁵⁷

V. THE FOOD AND DRUG ADMINISTRATION HAS AMPLE LEGAL AUTHORITY TO RESTRICT THE AMOUNT OF ACRYLAMIDE IN FOODS.

A. Acrylamide Is an “Added Substance” Within the Meaning of Section 402(a) of the Federal Food, Drug, and Cosmetic Act.

Section 402(a) of the FFDCFA has two standards for when a food is adulterated, depending on whether or not the “poisonous or deleterious substance” is “added” to the food. The acrylamide that has been found in foods is “added” to foods under both the FDA’s regulations and the standards established by the courts in construing this statutory provision.

The FDA’s regulations say that “A *naturally occurring poisonous or deleterious substance* is a poisonous or deleterious substance that is an inherent natural constituent of a food and is not the result of environmental, agricultural, industrial, or other contamination. An *added poisonous or deleterious substance* is a poisonous or deleterious substance that is not a naturally occurring poisonous or deleterious substance.” (emphasis in original)⁵⁸ Acrylamide is clearly not an “inherent natural substance” of a food such as potatoes. It appears in, say, French fries only through the actions of a manufacturer, as demonstrated by the fact that raw or boiled potatoes contain no detectable (less than 5 ppb) acrylamide, whereas fried potatoes contain hundreds of ppb of acrylamide.⁵⁹

Several federal courts have held that a substance is added if its presence is attributable to the acts of people—as it is in the case of acrylamide. In a recent case, *United States v. Blue Ribbon Smoked Fish, Inc.*, 179 F. Supp. 2d 30, 46 (E.D. N.Y. 2001), a federal district court rejected the defendants’ argument that *Listeria monocytogenes* is not “added” to smoked fish because it may occur naturally in seafood. The court observed that fish are not born with *Listeria monocytogenes* and so upheld the FDA’s claim that the defendants’ smoked fish was adulterated because it contained *Listeria monocytogenes*. The court explained that its decision was consistent with three earlier cases deciding whether a substance was “added” to the food: *United States v. 1232 Cases American Beauty Brand Oysters*, 43 F. Supp. 749 (W.D. Mo. 1942) (oyster shell fragments are not “added” because the oysters are born with shells); *United States v. An Article of Food Consisting of Cartons of Swordfish*, 395 F. Supp. 1184 (S.D. N.Y. 1975) (mercury is “added” because it does not occur naturally in swordfish); *United States v. Union*

⁵⁶ *Id.* at Section 585.260.

⁵⁷ *Id.* at Section 585.275.

⁵⁸ 21 C.F.R. 109.3(c) and(d) (2002).

⁵⁹ Tareke, *supra* note 29, at 5002.

Cheese Co., 902 F. Supp. 778 (N.D. Ohio 1995) (*Listeria monocytogenes* is “added” because it is not an inherent natural constituent of cheese). Other court cases—not cited in *Blue Ribbon Smoked Fish*—also have held that a substance is added. *United States v. Anderson Seafoods, Inc.*, 622 F.2d 157, 160 (5th Cir. 1980) (all mercury in swordfish is “added” because some of it is the result of industrial pollution); *Continental Seafoods, Inc. v. Schweiker*, 674 F.2d 38, 42 (D.C. Cir. 1982) (*Salmonella* is “added” to imported shrimp even if the FDA did not show that its presence in particular shipments was due to human intervention); *United States v. 1,200 Cans*, 339 F. Supp. 131, 136 (N.D. GA 1972) (“presence of *Salmonella* in frozen eggs is a deleterious and poisonous additive...”). See also *Young v. Community Nutrition Institute*, 476 U.S. 974, 976 (1986) (“the parties...agree that, although aflatoxin is naturally and unavoidably present in some foods, it is to be treated as ‘added’ to food”).

Thus, the FDA’s regulations and the legal precedents demonstrate that acrylamide is “added” to foods.

B. Some Foods Are Adulterated Because the Amount of Acrylamide Found by the Food and Drug Administration in the Food “May Render It Injurious To Health” Within the Meaning of Section 402(a) of the Federal Food, Drug, and Cosmetic Act.

While we do not assert that acrylamide is a food additive within the meaning of section 201(s) of the FFDCFA, we do contend that the safety standard the FDA has adopted for food additives should inform its decision about the safety of an added substance. The FDA’s food additive regulations define “safe” or “safety” as meaning “that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.”⁶⁰

In particular, in the context of compounds intended for use in food-producing animals, the FDA has said that a food additive or drug cannot be given to such an animal if it poses a lifetime risk of cancer to humans greater than one in a million,⁶¹ which implies that the FDA will ban such a substance if more than about 280 Americans may get cancer. While we do not concede that the FDA can lawfully apply this *de minimis* standard to substances intentionally added to foods,⁶² the level of acrylamide that the FDA has found in various classes of food indicates—as discussed above in section III.H.—a lifetime incidence of cancer well in excess of 280 Americans.

⁶⁰ 21 C.F.R. 170.3(i) (2002).

⁶¹ 52 Fed. Reg. 49572 (December 31, 1987) (rules for applying section 512(d)(1)(I) of the FFDCFA, 21 U.S.C. 360(b)(d)(1)(I)); codified at 21 C.F.R. Subchapter E, part 500, subpart E.

⁶² See *Public Citizen v. Young*, 831 F.2d 1108, 1120 (D.C. Cir 1987) *cert. denied sub nom. Cosmetic Toiletry and Fragrance Association v. Public Citizen*, 485 U.S. 1006 (1988) (while section 706(b)(5)(B) of the FFDCFA bars approval by the FDA of a color additive that has a human lifetime cancer risk of one in 19 billion, the rejection of FDA’s *de minimis* standard for color additives may or may not apply to section 409(c)(3)(A)’s regulation of food additives).

Indeed, the harm to the public's health resulting from the presence of acrylamide meets the less-protective standard of section 402(a)(1) of the FFDC⁶³ as interpreted by the courts. The courts have found that an added substance "may render [the food] injurious to health" even when there is no quantitative estimate of the extent of such injury (though, of course, in the case of acrylamide quantitative estimates of harm can be made). For example, using only a study done in Iraq on the health effects of different amounts of methylmercury in the human blood and having no evidence of the actual number of illnesses that might occur to Americans from eating swordfish containing mercury, a federal court held that only swordfish containing less than 1.0 part per million of mercury cannot be deemed adulterated. *United States v. Anderson Seafoods, Inc.*, 447 F. Supp. 1151, 1159 (N.D. Fl. 1978), *aff'd*, 622 F.2d (5th Cir. 1980).

In sum, the possible hundreds or thousands of cancers each year and the possible neurologic illnesses that acrylamide may cause indicate that the acrylamide added to food may render the food "injurious to health" within the meaning of section 402(a) of the FFDC.

C. Congress Gave the Food and Drug Administration Ample Authority—in Sections 401(a) and 406 of the Federal Food, Drug, and Cosmetic Act—to Set Interim Acceptable Limits for Acrylamide.

The Supreme Court has held that the FDA has two choices on what to do about what it called "an unavoidable, harmful, added substance."⁶⁴ The Court said that the FDA could either establish a tolerance level pursuant to section 406 or an action level pursuant to section 401(a).⁶⁵

Section 406 of the FFDC directs the Secretary of Health and Human Services to issue regulations setting an acceptable limit for any poisonous or deleterious substance that is added to a food and that cannot be avoided by good manufacturing practices. The Secretary is directed to "take into account the extent to which the use of such substance is required or cannot be avoided in the production of each such [food] article, and the other ways in which the consumer may be

⁶³ A food is adulterated if the added ingredient "may render it injurious to health." 21 U.S.C. 342(a)(1).

⁶⁴ *Young v. Community Nutrition Institute*, 476 U.S. 974, 982 (1986) (having set an action level for aflatoxin of 20 ppb for corn, the FDA can set an action level for aflatoxin of 100 ppb for corn harvested in 1980 in three states and used as animal feed rather than setting a tolerance level).

⁶⁵ *Id.* The Supreme Court reversed the Court of Appeals, 757 F.2d. 354 (D.C. Cir. 1985), which had reversed the District Court and had held that the FDA must issue a tolerance for aflatoxin pursuant to section 406 and could not proceed via informal action levels. In the Court of Appeals the FDA had argued—unsuccessfully—that section 309 of the FFDC, 21 U.S.C. 336, authorized its relying on action levels for "minor violations" of the FFDC.

affected by the same or other poisonous or deleterious substances.”⁶⁶

However, section 701(e) of the FFDCA establishes stricter procedural steps before such a regulation may be issued than are required for the FDA to promulgate an action level.⁶⁷ Thus, the FDA has—with one current exception⁶⁸—in practice relied instead on action levels to inform food manufacturers of the amounts of a particular harmful added substance that will lead the FDA to “regard the food as adulterated.”⁶⁹

The FDA’s criteria for establishing an action level include whether the substance can be avoided by good manufacturing practices and whether the level established “is sufficient for the protection of the public health, taking into account the extent to which the presence of the substance cannot be avoided and the other ways in which the consumer may be affected by same or related poisonous or deleterious substances.”⁷⁰ The FDA’s regulations further provide that “An action level will be withdrawn when a tolerance or regulatory limit for the same substance and use has been established.”⁷¹

Using action levels to set interim acceptable levels for acrylamide seems especially appropriate considering that the food industry may be exploring ways to reduce such levels. One of the FDA’s criteria for when it will set an action level is “that technological or other changes

⁶⁶ Section 406 of the FFDCA, 21 U.S.C. 346.

⁶⁷ 21 U.S.C. 371(e). This statutory provision requires that interested persons must be given an opportunity to present their views orally to the FDA. Pursuant to *Community Nutrition Institute v. Young*, 818 F.2d 943 (D.C. Cir. 1987), *per curiam*, the public can comment on proposed action levels pursuant to section 553 of the Administrative Procedure Act. 21 C.F.R. 109.4(c)(2) (2002).

⁶⁸ Tolerances for polychlorinated biphenyls (PCBs) in eight classes of food and paper packaging material. 21 C.F.R. 109.30 (2002). This final rule was issued in August 1983, more than 11 years after it was initially proposed. 48 Fed Reg. 37020 (August 16, 1983).

⁶⁹ 21 C.F.R. 109.6(d) (2002). In *United States v. Boston Farm Center, Inc.*, 590 F.2d 149 (5th Cir. 1979), the Court of Appeals reversed the District Court and upheld the FDA’s action to enjoin the shipment of corn that contained more aflatoxin than the FDA’s action level of 20 ppb. See also *United States v. An Article of Food Consisting of Cartons of Swordfish*, 395 F. Supp. 1184 (S.D. N.Y. 1975) (swordfish containing mercury above action level of 0.5 ppm is adulterated).

⁷⁰ 21 C.F.R. 109.6(d) and (b)(2) (2002).

⁷¹ 21 C.F.R. 109.6(d) (2002).

that might affect the appropriateness of the tolerance are foreseeable in the near future.”⁷²

D. Congress Directed the Food and Drug Administration To Be Especially Protective of the Health of Infants and Children.

1. Section 412 of the Federal Food, Drug, and Cosmetic Act Authorizes the Food and Drug Administration To Establish Good Manufacturing Practices for Infant Formulas To Ensure That They Do Not Contain Acrylamide.

The FDA tested 12 infant formulas. While it did not detect acrylamide in 10 products, it did find acrylamide in two at levels greater than 0 but below 10 ppb.⁷³ Those levels presumably exceed the safe level of 0.5 ppb set by the EPA for drinking water.

While the amounts the FDA found are small compared to what it found in adult foods, Congress has enacted special food-safety standards to protect infants. Section 412(b)(1) of the FFDCA⁷⁴ directs that the Secretary of Health and Human Services “shall by regulation establish requirements for quality factors for infant formulas to the extent possible consistent with current scientific knowledge...” Section 412(a)(2)⁷⁵ declares that an infant formula is adulterated if “it does not meet the quality factor requirements prescribed by the Secretary under subsection (b)(1).” We urge the FDA—relying on section 412(b)(1)—to set a particularly protective limit on acrylamide in infant formulas and to consider a prohibition of any detectable amounts.

2. Section 408 of the Federal Food, Drug, and Cosmetic Act Directs the Food and Drug Administration to Use an Additional Tenfold Safety Factor to Protect Infants and Children From Pesticide Chemical Residues.

Section 408(a)(1) of the FFDCA declares that any pesticide chemical residue is unsafe unless either the FDA has established a tolerance for such pesticide chemical residue and the amount is below that tolerance or there is in effect an exemption from the requirement for a tolerance.⁷⁶ In establishing such tolerances or exemptions, the FDA is directed to “publish a specific determination regarding the safety of the pesticide chemical residue for infants and children...an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to

⁷² *Id.*

⁷³ The two products were powdered Enfamil and Similac, milk-based formulas with iron.

⁷⁴ 21 U.S.C. 350a(b)(1).

⁷⁵ 21 U.S.C. 350a(a)(2).

⁷⁶ 21 U.S.C. 346a(a)(1).

infants and children.”⁷⁷

While acrylamide is not a pesticide chemical, the legal standard that applies to pesticides should spur the FDA to set a particularly protective limit for acrylamide in foods consumed by infants and children.

VI. CONCLUSION

More than a year has passed since Swedish scientists found significant amounts of acrylamide in foods. For the reasons stated above, the FDA should take prompt action to protect the public from the harmful effects of the avoidable amounts of acrylamide now found in many foods that are important parts of the American diet. The FDA should set interim acceptable limits on the levels of acrylamide in frequently consumed foods and should set particularly protective limits for acrylamide in infant formulas and other foods intended for babies.

VII. ENVIRONMENTAL IMPACT

The action requested is subject to a categorical exclusion under 21 C.F.R. 25.32(m) and (n) and therefore does not require the preparation of an environmental assessment.

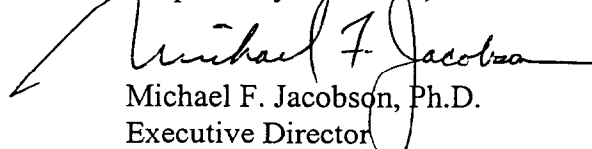
VIII. ECONOMIC IMPACT

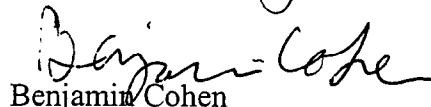
No statement of the economic impact of the requested action is presented because none has been requested by the Commissioner.⁷⁸

IX. CERTIFICATION

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

Respectfully submitted,


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⁷⁷ Section 408(b)(2)(C), 21 U.S.C. 346a(b)(2)(C).

⁷⁸ 21 C.F.R. 10.30(b) (2002).