research institutions direct the use of excised specimens preemptively and exclusively to a particular project or investigator? We think not, because such preemption constrains future, unanticipated uses of these invaluable and long-lived research resources.

We stated our opposition to a regulatory or legal scheme that recognizes exclusive ownership interests in excised tissue specimens. We urge the expansive use of tissue resources, consistent with the reasoning articulated by the courts, based on our conviction that the scientific value of these specimens is unique and irreplaceable, and that their potential contribution to the public library of knowledge should benefit all humankind.

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RESEARCH LETTER

Acrylamide Intake and Breast Cancer Risk in Swedish Women

To the Editor: In 2002, the Swedish National Food Administration (NFA) announced the discovery of acrylamide in commonly consumed baked and fried foods.[1] The World Health Organization has classified acrylamide as a "probable human carcinogen," and under California's Proposition 65, officials are considering imposing warning labels on food items containing acrylamide, including breads, cereals, potato products, and coffee because "these products contain chemicals known by the State of California to cause cancer."[2]

Three case-control studies in humans[3-5] did not find an association between dietary acrylamide and cancer risk. Rats exposed to acrylamide had a higher incidence of several tumors, including those of the mammary gland; the exposure was 3 to 5 orders of magnitude greater than that in humans.[6] We prospectively studied whether acrylamide exposure through diet was associated with higher risk of breast cancer.

Methods. The study cohort consisted of 43 404 Swedish women in the Women's Lifestyle and Health Cohort.[7] The mean age at baseline in 1991 was 39 years, and 9% of women were postmenopausal. Complete follow-up was achieved through linkages with nationwide health registers through December 31, 2002, yielding 490 000 person-years and 667 incident breast cancers.

Participants completed a semiquantitative food frequency questionnaire at baseline that asked about usual intake of foods with elevated acrylamide: coffee, fried potatoes (pan-fried, fries, chips), crisp and soft breads, cereals, biscuits, crackers, pancakes, and meatballs. The Swedish NFA acrylamide database[1] was used to determine median levels in these foods. Daily intake of each food item was multiplied by the median acrylamide level in that item; this was summed across the food items.

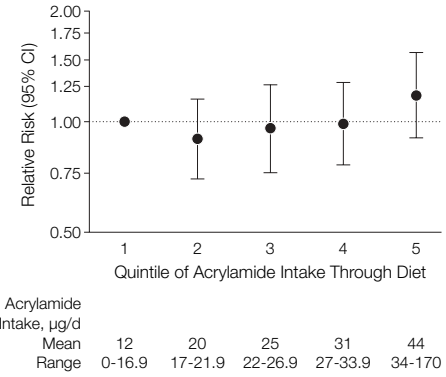
We categorized women into quintiles based on the distribution of acrylamide intake in the entire cohort. Cox proportional hazard models were used to adjust for the following baseline covariates: age, educational attainment, body

Table. Comparison of Quintiles of Estimated Dietary Acrylamide Intake, Swedish Women's Lifestyle and Health Cohort

	Quintiles of Estimated Acrylamide Intake					
Covariates at Enrollment	1 (n = 8510)	2 (n = 8710)	3 (n = 8706)	4 (n = 8799)	5 (n = 8679)	*P* Value*
Acrylamide intake, mean (range), µg/d	12 (0-16.9)	20 (17-21.9)	25 (22-26.9)	31 (27-33.9)	44 (34-170)	N/A
Age, mean (SD), y	39 (5)	39 (5)	39 (5)	39 (5)	39 (5)	.91
Education >12 y, No. (%)	3137 (37.0)	3667 (41.7)	3769 (42.9)	4074 (45.7)	4521 (51.7)	<.001
Body mass index, mean (SD)†	23 (2)	23 (2)	23 (2)	23 (2)	24 (2)	.45
Current smokers, No. (%)	1366 (16.1)	1280 (14.7)	1045 (12.0)	1040 (11.8)	954 (11.0)	<.001
Oral contraceptive use, No. (%)	6966 (82.1)	7279 (83.6)	7289 (83.7)	7351 (83.4)	7164 (82.6)	.36
Nulliparous, No. (%)	1579 (19.0)	1255 (14.5)	1109 (13.2)	1039 (12.0)	969 (11.4)	<.001
Age at 1st birth, mean (SD), y	25 (4)	25 (3)	24 (3)	24 (3)	24 (3)	<.001
Postmenopausal, No. (%)	723 (8.5)	770 (8.8)	802 (9.1)	833 (9.4)	834 (9.4)	<.001
Family history of breast cancer, No. (%)‡	380 (4.6)	405 (4.7)	403 (4.7)	407 (4.7)	375 (4.3)	.80
Dietary intake, mean (SD)						
Alcohol intake, g/d	3 (1)	3 (2)	4 (1)	4 (1)	4 (1)	<.001
Total energy, kcal/d	1332 (1071)	1424 (1030)	1512 (992)	1620 (1080)	1803 (1278)	<.001
Saturated fat, g/d	20 (10)	22 (10)	24 (10)	26 (11)	29 (12)	<.001
Fiber intake, g/d	12 (3)	13 (3)	14 (3)	15 (3)	17 (3)	<.001

Abbreviation: N/A, not applicable.
*Distribution of covariate across quintiles of acrylamide; *P* value for Kruskal-Wallis test.
†Body mass index is calculated as weight in kilograms divided by the square of height in meters.
‡Sister or mother.

Figure. Intake of Dietary Acrylamide and Risk of Breast Cancer Among 43 404 Women, Swedish Women's Lifestyle and Health Cohort, 1991-2002.



Relative risk of breast cancer and 95% confidence intervals, represented by error bars, are plotted on the log scale. Mean acrylamide levels for each quintile of acrylamide is presented along the x-axis below with quintile 1 as the reference group. Data were adjusted for the following covariates: age, education, alcohol intake, smoking status, oral contraceptive use, parity, age at first birth, menopausal status, family history of breast cancer, fiber intake, saturated fat intake, total energy intake.

mass index, alcohol intake, smoking status, oral contraceptive use, parity, age at first birth, menopausal status, family history of breast cancer, total energy intake, and intake of saturated fat and fiber. Wald χ^2 tests were used to assess whether relative risks were significantly different from 1. To assess linear trends, we modeled quintiles of intake as an ordinal variable. The study had 80% power to detect a linear trend for a relative risk of 1.36 or higher between the extreme quintiles. SAS version 8.2 (SAS Institute Inc, Cary, NC) was used for all analyses. An α of .05 was considered statistically significant.

Results. Quintiles differed significantly with respect to baseline measures of educational achievement, smoking status, parity, and intake of total energy, saturated fat, and fiber (TABLE). Mean dietary acrylamide intake was 25.9 µg/d; fewer than 1.5% of participants consumed more than 1 µg/kg per day, a threshold of intake cited in risk assessment models.[6,8] The greatest contribution was from coffee (54% of intake), fried potatoes (12% of intake), and crisp bread (9% of intake).

Compared with the lowest quintile of acrylamide intake, there was no significantly increased risk of breast cancer in the higher quintiles (FIGURE) and no evidence of a linear dose response. For quintile 5 compared with quintile 1, the relative risk was 1.19 (95% confidence interval, 0.91-1.55). Furthermore, there was no association between breast cancer risk and higher intake of any specific foods including coffee, fried potatoes, and crisp bread.

Comment. We found no evidence of an association between the amount of acrylamide consumed by these Swedish women and risk of breast cancer. Strengths of this study include the use of a validated food frequency questionnaire, the prospective study design, and complete cohort follow-up. Using the food frequency questionnaire appears to appropriately rank individuals into high or low acrylamide intake categories[3] even if the actual amount is not precise.

Evidence from animal and risk assessment models suggests that the relative risk for all cancer for those exposed to more than 1 µg/kg per day may only be 1.006 to 1.05,[6,8] less than what our study was powered to ascertain. Nevertheless, we believe that these results exclude a significant public health risk of breast cancer associated with dietary intake of acrylamide. We recommend that the study findings be confirmed in other populations.

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1. Swedish National Food Administration. Acrylamide in food. Available at: http://www.slv.se/engdefault.asp. Accessed April 2002. Accessibility verified January 17, 2004.
2. Office of Environmental Health Hazard Assessment. Acrylamide Workplan. Available at: http://www.oehha.ca.gov/prop65/docs_state/arcyl2.html. Accessibility verified January 17, 2004.
3. Mucci LA, Dickman PW, Steineck G, Adami HO, Augustsson K. Dietary acrylamide and cancer of the large bowel, kidney, and bladder: absence of an association in a population-based study in Sweden. *Br J Cancer*. 2003;88:84-89.
4. Mucci LA, Lindblad P, Steineck G, Adami HO. Dietary acrylamide and risk of renal cell cancer. *Int J Cancer*. 2004;109:774-776.
5. Pelucchi C, Franceschi S, Levi F, et al. Fried potatoes and human cancer. *Int J Cancer*. 2003;105:558-560.
6. Friedman M. Chemistry, biochemistry and safety of acrylamide: a review. *J Agric Food Chem*. 2003;51:4504-4526.
7. Kumle M, Weiderpass E, Braaten T, Persson I, Adami HO, Lund E. Use of oral contraceptives and breast cancer risk: the Norwegian-Swedish Women's Lifestyle and Health Cohort Study. *Cancer Epidemiol Biomarkers Prev*. 2002;11:1375-1381.
8. Ruden C. Acrylamide and cancer risk—expert risk assessments and the public debate. *Food Chem Toxicol*. 2004;42:335-349.