

July 27, 2005

Commissioner Lester Crawford
U.S. Food and Drug Administration
5600 Fishers Lane - Room 14-71
Rockville, MD 20857

Dear Commissioner Crawford:

A new study has found that the artificial sweetener aspartame caused statistically significant increases in lymphomas/leukemias in female rats.¹ The lowest level (20 mg/kg body weight) of aspartame that caused an increase was in the ballpark of what many people consume from foods and table-top sweeteners. A lower level (4 mg/kg) caused a 62 percent increase, but that was not statistically significant. In males, a dose of 5,000 mg/kg appeared to cause an increase (from 20.7 percent in the controls to 29 percent in the test group) in the incidence of lymphomas/leukemias, but that increase was not statistically significant. The authors suggest that the methanol metabolite of aspartame might be responsible for the tumors, because in an earlier study methanol caused lymphomas and leukemias in female rats.² The incidence of Non-Hodgkin's lymphomas, according to the National Cancer Institute, has almost doubled over the past 30 years, though increases began prior to the approval and use of aspartame.

The new study by the Cancer Research Centre, European Ramazzini Foundation of Oncology and Environmental Sciences, in Bologna, Italy, cannot be considered definitive, because of the low rate of lymphomas/leukemias in the female controls, the shallow dose-response curve, and the lack of confirmation by other independent researchers. On the other hand, the study was unusually sensitive because it involved large numbers of animals (100 or 150 animals per sex per dosage level). Moreover, the study's sensitivity was reduced because aspartame was not administered until the rats were eight weeks old; if the rats had been exposed to aspartame in utero and during their first eight weeks of life, a time of possibly increased sensitivity to

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¹Soffritti M, Belpoggi F, Esposti DD, et al. Aspartame induces lymphomas and leukaemias in rats. *Eur J Oncol.* 2005;10(2).

² Soffritti M, Belpoggi F, Cevolani D, et al. Results of long-term experimental studies on the carcinogenicity of methyl alcohol and ethyl alcohol in rats. *Ann NY Acad Sci.*2002;982:46-69.



carcinogens, higher tumor rates might have occurred. Another strength of this study is that it was designed and conducted independently, without oversight or sponsorship of aspartame manufacturers. Virtually all of the previous research was sponsored by the makers of aspartame.

Aspartame has been controversial since its original approval a quarter-century ago. An FDA advisory committee had originally concluded that aspartame caused brain tumors, but the FDA staff reexamined the histopathology and persuaded the committee that there was no increase in brain tumors. The new study found brain tumors in 12 out of 1,500 (0.8 percent) treated animals and 0 out of 300 controls. While a dose-response relationship was not observed and the incidence of tumors in the laboratory's historical controls was 1.2 percent, the occurrence of brain tumors only in the test groups of the new study, combined with the debatable occurrence of tumors in company-sponsored tests in the 1970s, indicates the need to reevaluate whether aspartame can cause brain tumors and to conduct further animal studies.

The authors of the new aspartame study stated:

Since the results of carcinogenicity bioassays in rodents, mainly rats and mice, have been shown to be a consistent predictor of human cancer risk, the first results of our study *call for urgent re-examination of permissible exposure levels of [aspartame] in both food and beverages, especially to protect children.* (emphasis added)

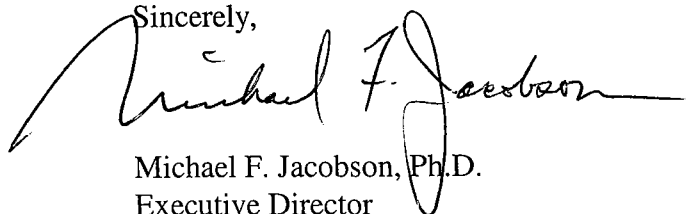
We agree. Considering that aspartame (NutraSweet, Equal) is used in thousands of foods and consumed by 200 million people in the United States and around the world, we urge the FDA make it a top priority to:

- Review the new study immediately and consider employing the precautionary Delaney amendment to remove aspartame from the food supply. We urge that that review be conducted by scientists outside of the Center for Food Safety and Applied Nutrition, which has a long history of defending aspartame's safety.
- Advise consumers—especially those who drink diet sodas made with aspartame—to switch to sucralose, which appears to us to be the safest artificial sweetener (CSPI has concerns about the safety of saccharin and acesulfame-K).
- Urge food manufacturers to replace aspartame with sucralose.
- Ask the government's National Toxicology Program to conduct animal studies of aspartame to extend the new study; such studies should use large numbers of animals, both rats and mice, in utero exposure, and other parameters that would provide confidence in the results. (In the past, according to an article in the Nov. 22, 1996,

Minneapolis Star Tribune, the FDA stopped the NTP on numerous occasions from studying aspartame.) California's Environmental Protection Agency states that all the previous studies have been "inadequate for judging carcinogenicity" and has recommended that new studies of this widely used and controversial food additive be conducted.³

We look forward to swift action by the FDA.

Sincerely,

A handwritten signature in black ink that reads "Michael F. Jacobson". The signature is fluid and cursive, with a long horizontal stroke at the end.

Michael F. Jacobson, Ph.D.
Executive Director

³ http://www.oehha.ca.gov/prop65/docs_state/crnrbatch4final45.html#get (accessed July 27, 2005).