January 11, 2011

Dr. Betty Martini, D. Hum, Founder
Mission Possible International
9270 River Club Parkway
Duluth, Georgia 30097

Re: Aspartame

Dear Dr. Martini,

This letter responds to your faxed letter dated December 4, 2010, regarding your concerns about aspartame, with specific questions about the presence of methanol in Aspartame. Please find responses to your questions below. In addition, you also inquired as to the status of your citizen petition filed with the FDA.

1. How could aspartame possibly have been considered as a suitable food additive in the first place, if the MSDS had been considered?

The MSDS (Material Safety Data Sheet) for methanol alone is not appropriate for the risk assessment of its use in the artificial sweetener aspartame. The dosages, routes of exposure and the uncontrolled nature of the human toxicity data derived from the MSDS are in many instances not relevant. In addition, aspartame as a food additive has been very well studied. With methanol being a component of aspartame, the many studies completed on aspartame inherently also evaluates the safety of methanol as well as the safety of aspartame. The results of these many studies reinforce the FDA's regulatory approval of methanol as a part of the aspartame molecule. Prior to FDA's approval of aspartame, FDA reviewed over 100 toxicological and clinical studies to conclude that aspartame was safe for use as a sweetener. Extensive toxicological and pharmacological studies were done in laboratory animals using far greater doses of aspartame than people could possibly consume. The safety of aspartame has been reviewed repeatedly, not only by the United States, but by other authorities, such as Canadian, United Kingdom, Australian and Japanese regulatory authorities, European Scientific Committee for Foods, European Food Safety Authority, the American Medical Association, and the American Dietetic Association. These agencies all agree that aspartame is safe for the general population with the exception of those individuals with phenylketonuria at the expected levels of exposure. To protect phenylketonurics, any food containing aspartame must bear a conspicuous statement on the label that indicates that the product contains phenylalanine. Thus, the FDA believes that there is a reasonable certainty of no harm to the general population from the use of aspartame as a sweetener.

2. Show us how you established a NOEL for free methanol - 10% of aspartame.

It is the practice of food additive safety assessments to establish the safety profile of the total molecule. The disposition of aspartame within the body assures that each of its components is tested and confirms that the other component molecules are present in safe amounts. Thus, the NOEL (NOAEL as we describe it) is for the whole aspartame molecule. It is clear that if a toxic dose of methanol was being consumed by test animals or during clinical studies with aspartame, the usual symptoms of methanol poisoning would have been observed (and they were not). Although aspartame ingestion results in the production of methanol, the levels formed from actual consumption of aspartame are not of toxicological concern. The acutely toxic doses of methanol (200 to 500 mg/kg body weight) are approximately one hundred times greater than the amount ingested when aspartame is consumed at the 99th percentile level of projected chronic ingestion (10 percent of 34 mg/kg body weight aspartame, or 3.4 mg/kg body weight methanol). Methanol occurs naturally in common foods such as citrus juices, fresh fruits, and vegetables and in larger amounts than those resulting from aspartame consumption and breakdown. For example, a glass of tomato juice provides about 6 times more methanol than an equivalent volume of beverage sweetened 100% with aspartame. The consumption of aspartame would not result in toxicologically significant methanol levels.

3. What science do you have to support the belief that the body handles the free methanol from aspartame in the same way as for methanol in nature?

Metabolic studies performed during research on the safety of aspartame conclude that there is no significant difference in the pharmacokinetics between "free" methanol and "dietary" methanol. The overall disposition of methanol in nature is very similar to the biotransformation of the methyl group of methanol from aspartame. Data indicate that absorption and conversion occur to the same extent with both compounds. Thus, the methyl moiety appears to be rapidly and completely cleaved from aspartame in the gastrointestinal tract, and that this methyl group is oxidized in essentially the same manner as "free" methanol. The only detectable difference in the pharmacokinetic properties between free methanol and dietary methanol derived from the hydrolysis of aspartame is a faster rate of absorption of the free than dietary methanol within the first hour. This difference may be explained by the finding that "free" methanol is readily absorbed from the stomach whereas aspartame must pass into the small intestine before hydrolysis and absorption of the methanol may occur. Based on these pharmacokinetic findings, there is no need or scientific basis to differentiate the free from dietary methanol with respect to the manner in which the body handles the free and aspartame-bound forms.

4. What science did you rely on to be certain that the chronic (daily) ingestion of free methanol was safe at the ADI set - 50 mg/kg?

Aspartame is safe for low-to-moderate intake and very high intake levels would be unlikely because of the organoleptic properties of the substance. The amounts of aspartame used in a specific product are modest and self-limiting due to its high potency as a sweetener. Adding aspartame beyond the levels normally used is counterproductive, as the product taste then becomes unpleasant to the consumer. In the final regulation that approved the use of aspartame in carbonated beverages (48 FR 31376; July 8, 1983) the agency established an

acceptable daily intake (ADI) of 50 milligrams/kilogram of body weight per day (mg/kg/day) for aspartame.

Since the aspartame molecule is ten percent methanol by weight and since the dosages used in the chronic studies were quite high (rat: 1-8 gm/kg b.w., mouse: 1-4 gm/kg b.w. and dog: 1-4 gm/kg b.w.), the exposure of these species to methanol in these four chronic studies was as high as 400 to 800 mg/kg b.w. per day, a very significant dose. Based on an ADI for human exposure of 50 mg of aspartame per kg b.w. per day (or 5 mg/kg b.w. of methanol), these doses represent an 80-to 160-fold exaggeration of methanol exposure in the chronic animal studies when compared with the usual levels of human exposure to methanol through aspartame ingestion. High levels of aspartame intake are unlikely to exceed the ADI if used in food with no limitations other than current good manufacturing practice. The agency concluded that consumption of aspartame would be well below the acceptable intake and that it would be safe for its intended uses.

The agency has fully evaluated the safety issues related to dietary levels of methanol derived from aspartame and previously concluded that these levels do not represent uncommon or toxic levels of exposure. No new credible evidence has been presented or discovered to alter FDA's original evaluation of the risk of methanol toxicity from the decomposition of aspartame.

Please be assured that the FDA continues to closely monitor scientific literature for information that might indicate potential public health concerns with artificial sweeteners like any regulated food ingredient. Should the need arise; the Agency will take the appropriate action to protect public health.

Lastly, in reference to your previously submitted citizen petition, again, we would like to advise you, in accordance with 21 CFR 10.30(e)(2)(iii), that we have not yet reached a decision on your petition, due to a number of competing priorities. However, be advised that your petition and the comments that have been submitted to the docket are currently under active evaluation by our staff.

Thank you for your inquiry to the Food and Drug Administration. I hope the information I have provided is helpful. If you have any additional questions regarding the safety or legality of a particular food additive, please feel free to contact the FDA again.

Sincerely,

Felicia M. Ellison

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