

## **United States Food and Drug Administration Response to "Nancy Markle" Allegations**

I have been requested by the FDA Center for Drug Evaluation and Research to respond to your request for an evaluation of the article written by Nancy Markle received via an e-mail message on the alleged toxicities of the artificial sweetener, aspartame.

My name is David Hattan and I am currently Acting Director of the Division of Health Effects Evaluation in the United States Food & Drug Administration (USFDA) Center for Food Safety and Applied Nutrition. I have worked on questions relating to the safety of aspartame repeatedly since 1978 and am familiar with the safety studies that have been conducted to support the safety of this food additive. There were well over 100 separate toxicological and clinical studies conducted to establish the safety of aspartame before it was approved for regulatory acceptance. Since its approval in 1981 by the USFDA, there have been many additional studies performed to follow up on some of the more creditable reports of aspartame-mediated adverse effects. Below I have tried to succinctly respond to certain of the allegations of toxicity proposed by Nancy Markle.

First, reports of the ingestion of aspartame in patients who later have suffered multiple sclerosis or systemic lupus is obviously not scientifically sustainable evidence that aspartame is responsible for the occurrence of either disease. Both of these disorders are subject to spontaneous remissions and exacerbations so it is entirely possible that when patients stopped using aspartame they might have also coincidentally had remission of their symptoms. There is no credible evidence that I am aware of that suggests that aspartame elicits multiple sclerosis or systemic lupus.

Second, the claim that aspartame ingestion results in the production of methanol, formaldehyde and formate: These claims are factual. In the gastrointestinal tract aspartame is hydrolyzed to one of its component materials, methanol, as well as the two amino acids, phenylalanine and aspartic acid. This methanol is taken up by the cells of the body and metabolized first to formaldehyde and then to formate. The key information that is missing in the description by Ms. Markle is that the levels of ingestion are very modest. In fact, there are other foodstuffs that we ingest that supply as much and sometimes even more methanol; e.g., citrus fruits and juices, and tomatoes or tomato juice. There are even higher quantities of methanol ingested when ethanol is consumed. Thus, in the final analysis this methanol is the same as from other sources and in the quantities consumed from aspartame, it is readily and naturally metabolized via the one-carbon biochemical cycle to entirely innocuous and natural body components.

Third, the claim that the two amino acids, phenylalanine and aspartic acid have neurotoxic effects. This is true in certain individuals and in high enough doses. The only subpopulation of individuals potentially susceptible to adverse effects from phenylalanine is homozygous phenylketonurics and in this case, food itself with much higher levels of phenylalanine from the protein in the diets contributes much higher toxicity for these unfortunate individuals. For those individual phenylketonurics that want to carefully control their intake levels of phenylalanine, they can do that by simply taking into consideration the amount of phenylalanine supplied by the aspartame product or, even more likely, simply refraining from use of these products. The USFDA requires that the aspartame product be labeled specially for phenylketonurics patients so that they will be aware of its presence in these products. As for the other amino acid in aspartame, the levels of aspartic acid ingested with aspartame use are many fold less than those levels responsible for causing adverse effects on the brain of animals and/or man. In fact, it is not clear that the experimentally derived data from animals is relevant to man. In any case, the levels of aspartic acid intake from aspartame are many fold below those needed to mediate neurologic effects.

Fourth, there have been numerous animal and human studies done to evaluate the possibility that aspartame causes seizures or enhances the susceptibility to seizures. In clinical studies

done in adults and children with pre-existing seizures, there was no evidence of contributing to the frequency of occurrence or severity of seizures in seizure-prone individuals. There were additional studies done on seizure-prone experimental animal models to assess the possible influence of aspartame on their seizing activity. Again, the result was the same and no influence was demonstrated on the frequency or severity of seizures.

Fifth, aspartame was comprehensively evaluated for its potential to mediate reproductive effects and birth defects. In all cases of animal testing, there was no evidence of aspartame-mediated effects on the experimental animals at doses many times higher than those to which the human population is exposed.

Sixth, more recent allegations about aspartame mediating an increase in the incidence of brain tumors in the human population has been thoroughly refuted by both government and academic scientists.

The internet provides a convenient means of communicating information of all kinds in a potentially widespread manner. Unfortunately, the recipient of that information has no way of assessing the strength and reality of that information. There are a number of internet web sites that regularly distribute information adverse reactions supposedly mediated by aspartame that is based on anecdotal reports that cannot be confirmed. The legitimate attempts that have been made to confirm and replicate these allegations of adverse reactions from aspartame ingestion have not been successful and the USFDA continues to consider this to be among the most thoroughly tested of food additives and that this information continues to confirm the safety of aspartame.

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