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## Let Them Eat Cake? A Historical Analysis of FDA's Decision to Approve Aspartame

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<b>Citation</b>	Let Them Eat Cake? A Historical Analysis of FDA's Decision to Approve Aspartame (1997 Third Year Paper)
<b>Accessed</b>	February 19, 2015 9:32:43 AM EST
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That sugar occupies a cherished role in the human diet hardly needs mention. After all, nearly 2,500 tastebuds located at the tip of the human tongue are dedicated to the pursuit of sweetness. The first recorded mention of sugar, a description of a crown of glistening sugar crystals, dates back to a sacred Hindu text from 800 B.C.<sup>1</sup> Of course, the sumptuous deserts and candies which fulfill our sugar cravings come at a high caloric cost, a cost which has become less and less affordable to the growing millions who seek to watch their weight. As far back as the mid 1800's, people recognized the tension between the desire to eat delicious foods, and the often contravening desire to eat healthfully. "The pleasures of the appetite are legitimate pleasures," wrote Mrs. Horace Mann, but "God did not implant the sense of Taste in man to ruin the beautiful structure of his body, or to impair the noble faculties of his soul."<sup>2</sup> It is not surprising, therefore, that the intersection of the dietary movement with the human sweet tooth would eventually lead to a demand for low calorie artificial sweeteners.

Unfortunately for dieters and diabetics alike, the two sweeteners which preceded aspartame to the market each were found to present health risks. Faced with evidence of possible carcinogenicity, FDA banned cyclamate in 1969.<sup>3</sup> Saccharin was the next sweetener to come under FDA fire. Implicated by two 1972

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<sup>1</sup>Diane Ackerman, *A Natural History of the Senses*, Vintage Books, 1990, p. 135. The Hindu text is the Atharvaveda.

<sup>2</sup>The Culinary Historians of Boston Newsletter, Volume XVII, Number 3, January, 1997, p.10.

<sup>3</sup>See 34 FR 17063. In 1985, FDA's Cancer Assessment Committee held that cyclamate itself is not carcinogenic; however, the National Academy of Sciences concluded that it may contribute to the production of tumors: See Peter Barton Hutt, Richard A. Merrill, *Food and Drug Law: Cases and Materials*, Foundation Press, 1991, p. 923.

animal studies, saccharin finally faced an FDA ban in 1977, after a third animal study completed in Canada indicated “unequivocally that saccharin causes bladder tumors in the test animals.”<sup>4</sup> Unwilling to wrest the only remaining sugar alternative away from the American consumer, Congress passed the Saccharin Study and Labeling Act, which imposed a moratorium on the saccharin ban, recently extended until May 1997, and required that the risks of cancer be clearly labeled on saccharin products.<sup>5</sup> So, with one sweetener ominously labeled and another banned outright, American consumers were hungry for a new, safer artificial sweetener.

A food additive petition landed on the Food and Drug Administration’s desk on February 9, 1973 that seemed to offer an answer to America’s culinary prayers. Illinois company G.D. Searle sought approval for an odorless, white crystalline powder, composed of two amino acids, L-aspartic acid and L-phenylalanine, which offered all the sweetness of sugar at a fraction of the caloric price<sup>6</sup>. While not quite as sweet as saccharin, aspartame could boast that it lacked its competitor’s bitter after-taste. More importantly, Searle planned to market aspartame as a safer choice than saccharin, which, as mentioned, was not yet subject to the Congressional labeling regulation but was already clouded by accusations of carcinogenicity. The road to aspartame’s approval, however, would be long and arduous, engendering scientific, legal and ethical disputes

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<sup>4</sup>42 FR 19996, April 15, 1977. FDA explains that if everyone in the United States consumed one saccharin-sweetened beverage once a day over a lifetime, there would be between zero and 1,200 additional cases of bladder cancer a year, i.e. the risk for an individual consumer would be between zero and four in 10,000.

<sup>5</sup>The warning label, which is scripted even more finely than this footnote, reads: “Use of this product may be hazardous to your health. This product contains saccharin, which has been determined to cause cancer in laboratory animals.”

<sup>6</sup>38 FR 5921, March 5, 1973

that continue to resonate fifteen years later. In FDA's approval of aspartame, and in its continued support of the product today, there emerges a recurring question: how much scientific evidence is enough to invoke the regulatory powers of the agency against a popular and much desired substance?

Despite the din of controversy surrounding the introduction and proliferation of aspartame in the American marketplace, its discovery occurred without fanfare, and quite by accident. In 1965, while testing a new anti-ulcer drug at the G.D. Searle Company, chemist James Schlatter created an intermediate chemical –aspartylphenylalanine-methyl-ester (aspartame)- and spilled a little of the powder on the outside of the test tube. Licking his finger later in the day to pick up a piece of paper, he noticed an intensely sweet taste and realized it was the aspartame powder.<sup>7</sup> Soon after, Searle began studying aspartame for use as an artificial sweetener. Searle announced its discovery in the publication *Science* in 1970<sup>8</sup>, and entered into discussions with the Food and Drug Administration, culminating in the 1973 petition for approval of aspartame for use in all foods.

In 1981, Searle finally gained approval for the additive for use in dry foods. In 1983, the FDA approved Searle's petition for use in carbonated beverages, which would exponentially increase aspartame consumption in the United States and abroad. A few months later, a third petition was granted for use of aspartame as an inactive ingredient in human drug products.<sup>9</sup> Finally, on June

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<sup>7</sup>Stegink, Lewis D., Filer L., 1984. "Aspartame: Physiology and Biochemistry," Marcel Dekker, Inc., N.Y., p. 4.

<sup>8</sup>"Aspartylphenylalanine methyl ester: a low calorie sweetener," *Science*, Volume 170, p. 81.

<sup>9</sup>See for 48 FR 31376 for approval in carbonated drinks and see 48 FR 54993 for approval

28, 1996, the Food and Drug Administration amended the food additive regulations to allow the use of aspartame as a general sweetener, thereby collapsing most of the twenty-three previously designated uses into a single use category for food.<sup>10</sup> Well over 100 million people consumer aspartame-sweetened products today, a popularity which translates into over a billion dollars a year for the industry. Monsanto, which bought G.D. Searle in 1985 and created the NutraSweet Kelco Company as a subsidiary<sup>11</sup>, is currently testing aspartame in China, the world's largest market.<sup>12</sup>

Despite aspartame's ultimate success in entering the food supply, few products in FDA history have generated such controversy. While the FDA and Monsanto stand firmly by the sweetener, a number of consumer groups, prominent scientists, and political leaders have raised scientific and ethical concerns about FDA's decision to approve the sweetener. First, they argue that the old studies upon which FDA approval rested were flawed and that new studies are needed to address aspartame's relationship to brain tumors and a range of other purported side-effects. Second, aspartame opponents contend that political considerations, particularly the "revolving door" between the public and private food and drug sectors, fueled the FDA approval of what they perceive to be an unsafe additive.

Accusations that aspartame endangers the public health vary in tenor

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as inactive ingredient in drugs.

<sup>10</sup>Amendment of § 172.804 (21 CFR 172.804), as announced in 61 FR 33654, June 28, 1996.

<sup>11</sup>According to Steve Wilson's 1984 interview with Robert Shapiro, head of Searle's NutraSweet Group, sale of aspartame products yielded 70% of Searle's annual profits before it sold out to Monsanto. "Sweet Suspicions," a Steve Wilson report included in the Congressional Record, Senate Proceedings and Debates of the 99th Congress, First Session, August 1, 1985.

<sup>12</sup>Transcript of *CBS 60 Minutes*, "How Sweet Is It?", December 29, 1996, p. 8.

and credibility<sup>13</sup>. Some consumers have organized to form aspartame awareness groups and have even established WebSites on the Internet. One site goes so far as to label aspartame a “chemical weapon” and instructs consumers to “think of aspartame as the drug-equivalent of AIDS!”<sup>14</sup> Another WebSite lists a plethora of aspartame-induced symptoms, ranging from dizziness, memory loss, personality changes, impotency, and hair-loss, to death. The site also cautions that “aspartame disease mimics symptoms” or exacerbates a number of diseases, such as arthritis, Lupus, Alzheimer’s, Lyme disease, and depression.<sup>15</sup> Mary Nash Stoddard, former judge on the State of Texas Board of Adjustments, board member of the National Natural Foods Association, and founder of the Aspartame Consumer Safety Network, agrees that aspartame may both cause individual symptoms and effect sets of symptoms that resemble diseases, such as chronic fatigue syndrome. Contending that the FDA and aspartame manufacturers are deliberately keeping the public in the dark about the health hazards, she remarks: “aspartame approval and persistence on the market has everything to do with money and politics, and almost nothing to do with science and reason.”<sup>16</sup>

FDA has, in fact, received over 7,000 complaints from consumers re-

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<sup>13</sup>In a modern version of the Boston Tea Party, a group of activists, joined by Emory Law School professor David Bederman, dumped an unsavory mixture of Diet Coke, NutraSweet, and rBGH-enhanced milk all over the sidewalk in Atlanta, Georgia on August 17, 1995. The group was protesting both the use of aspartame and BGH in foods and the “food slander” laws, on the books in Georgia and ten other states, which make it a civil crime to criticize or denigrate food without a “scientific basis.” The protesters argue that these laws are the handiwork of the food industry lobby and are calculated to keep consumers “cowed.” (Gar Smith, “Food Slander is Now a Crime,” ELJ Fall 95, downloaded from <http://www.igc.apc.org/ei/journal/slander.html>)

<sup>14</sup>See <http://www.dorway.com/nuindex1.html/menu> on, copyright 1996, David O. Reitz, the Internet. I was informed that I was the 5379th visitor to the site.

<sup>15</sup>See <http://www.tiac.net/users/mgold/aspartame/aspartame.html>.

<sup>16</sup>*Nutrition and Healing*, November, 1995, interview with Mary Nash Stoddard, p.4.

porting adverse reactions to aspartame, including dizziness, headaches, and seizures.<sup>17</sup> Dr. Richard Wurtman, a scientist at the Massachusetts Institute of Technology, is worried about potential adverse effects of aspartame on some consumers. After voicing concerns about the sweetener in the mainstream media in 1984, he became inundated with letters from individuals claiming to have experienced unpleasant symptoms which they attributed to the aspartame in their diets. These complaints, similar to the complaints received by the FDA and by Searle itself, described numbness, insomnia, rashes, menstrual problems, nausea, and headaches.<sup>18</sup> A number of those reporting symptoms insisted that they had confirmed their reactions by cutting aspartame out of their diets for a time to see if the symptoms vanished, then starting up again to see if they would return.

The *Annals of Internal Medicine* reported a severe example of allergic reaction to aspartame in 1985. In “the first confirmed case of aspartame-induced granulomatous panniculitis<sup>19</sup>,” Dr. Nelson Lee Novick described a healthy 22 year-old female who developed “numerous, bilateral, nontender nodular lesions” on both of her legs lasting approximately two months. The patient, who insisted she had neither used any medications in the previous six months nor had suffered any recent trauma or infection, stated that she had consumed between

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<sup>17</sup>“How Sweet Is It?”, p.2. Aspartame complaints account for up to 75% of all FDA consumer complaints annually, according to Stoddard, above, and *Nexus Magazine*, “The Bitter Truth about Artificial Sweeteners,” Volume 2, p.28 (Oct.-Nov., 1995)

<sup>18</sup>*Common Cause Magazine*: “How Safe is Your Diet Soft Drink?”, July/August 1984, included in the Congressional Record, Senate Proceedings and Debates of the 99th Congress, First Session, May 7, 1985, p.50. Copies of complaints to the FDA and Searle obtained by *Common Cause* under the Freedom of Information Act.

<sup>19</sup>*Annals of Internal Medicine*, “Aspartame-Induced Granulomatous Panniculitis,” Vol. 102, No.2, February 1985, included in the Congressional record, May, 1985, p.21.

36 and 44 fluid oz. of soft drink sweetened with saccharin nearly every day for the past six years. Ten weeks before presenting herself for medical evaluation, she had switched from her former diet soda to the same manufacturer's new aspartame-sweetened soda. Her diet had otherwise not changed.

Two weeks after switching sweeteners, the patient noticed deep nodules on her left thigh which proceeded to enlarge and spread on both legs. After her first medical examination, she was advised to stop consuming aspartame for four weeks, and the lesions disappeared. She was then instructed to resume drinking the aspartame-sweetened beverages, and her lesions reappeared within ten days. Again she refrained from aspartame, and again her lesions vanished. To further test the hypothesis that aspartame had caused the phenomenon, she was next administered 50 mg capsules of aspartame, supplied by Searle, four times a day. In ten days, she again suffered from an outbreak of the nontender nodules all over her legs. The lesions cleared up after cessation of the doses. Having studied the patient's blood test results and other constitutional symptoms, Novick ruled out a number of non-aspartame causes. While not concluding with certainty that aspartame was the culprit, he states, "the formation of toxic metabolites of aspartame, either during the drug's shelf-life or as metabolic byproducts, offers one possible explanation for the reaction seen in this patient." He also notes that Searle had previously received numerous unconfirmed reports of "dermal eruptions" by consumers of aspartame.

Aspartame critics also claim that aspartame can induce seizures in non-epileptics and lower seizure thresholds for epileptics. M.I.T.'s Dr. Wurtman,



who has studied 80 individuals who had seizures after consuming aspartame, is concerned about a potential causal link. Wurtman, who testified on behalf of the aspartame industry in the early 1980's and who admits to dusting his strawberries with Equal, argues that uncertainties still hover around the sweetener.<sup>20</sup> He does not argue for a ban, but urges that placebo-controlled studies be initiated to determine aspartame's relationship to seizures, as well as to a range of other adverse reactions.<sup>21</sup> But the Epilepsy Foundation of America defends the sweetener, as do the American Medical Association, the United Kingdom Committee on Toxicology of Chemicals in Foods, the Scientific Committee for Food of the European Economic Communities, and the Canadian Health Protection Branch. Those organizations "have all affirmed the safety of aspartame for the general population."<sup>22</sup>

Those who stand by aspartame's safety record say that the age-old "placebo effect" among consumers, coupled by wide-scale media focus on the product, means that the new kid on the block gets blamed for every ailment that comes along. Former Searle executive attorney Robert Shapiro explains: "I believe if we were to introduce lettuce to the market tomorrow with a big national publicity campaign, and nobody had ever seen lettuce before, and people started eating lettuce, my guess is you would get exactly the same kinds of complaints."<sup>23</sup> Another explanation offered for the complaints is the sheer fact

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<sup>20</sup>*Common Cause*, p. 40. fix

<sup>21</sup>Letter from Dr. Richard Wurtman to Senator Howard Metzenbaum, April 22, 1985, included in the Congressional Record, May, 1985.

<sup>22</sup>Reina Berner, Dr. Richard Reuben, The Epilepsy Institute, in a letter to the *Washington Post*, April 30, 1986, reprinted at the Honorable Tony Coelho's urging in the Congressional record, June 20, 1986. Coelho remarks, "as one who has epilepsy, I would like to dispel the unnecessary concern about aspartame..."

<sup>23</sup>Congressional record, May, 1985, p.51.

that out of over 100 million aspartame users worldwide<sup>24</sup> there are bound to be those who are allergic, just as there are those who are allergic to dairy products or peanuts. Dr. Gerald E. Gaull, former vice president for nutrition and medical affairs for aspartame at Searle conceded that “a few people may be...sensitive to it...For those few people, the issue is not one of safety but rather of food selection.”<sup>25</sup> Critics of aspartame, however, continue to lobby for additional testing and assert that both the FDA and the industry are underestimating the severity and the prevalence of consumer “sensitivities.”

Looming even more largely than accusations that aspartame induces incidentalized adverse reactions are suspicions that aspartame causes brain tumors in laboratory rats, and may cause brain tumors in human beings. The most recent claim hails from long-time aspartame critic, Dr. John Olney, a neuropathologist and psychiatrist at Washington University’s School of Medicine. Olney and a team of Washington University researchers recently examined brain tumor data gathered by the National Cancer Institute and published an analysis which has generated great controversy among physicians and scientists.<sup>26</sup> They report that three to five years after aspartame was approved, the incidence of brain tumors rose by 10%, translating into approximately 1,500 additional cases a year. The team also points out that there has been a distinct change in the specific kinds of tumors reported over this time period. In particular, there has been a decrease in the more benign, preliminary tumors, astrocytomas and a

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<sup>24</sup>*Minneapolis -St. Paul Star -Tribune*, “NutraSweet Is Suspected in Rise in Brain Tumors,” November 5, 1996.

<sup>25</sup>*Science Times*, “Sweetener Worries Some Scientists,” February 5, 1985.

<sup>26</sup>Study published in the *Journal of Neuropathology and Experimental Neurology*, Vol.55, No.11, November 1996.

concurrent marked increase in the more aggressive and deadly glioblastomas. While not claiming certainty that aspartame is responsible for this rise in brain cancer, Olney and his colleagues believe it is the most likely candidate and argue for more aspartame research. Leading epidemiologist Dr. Debra Davis of the Strang-Cornell Cancer Prevention Center agrees that “without any question” brain cancer is on the rise in industrialized countries. She also believes that, while there could be a spectrum of environmental factors at work, “one of them may be, for some people, increased consumption of aspartame.”<sup>27</sup>

The FDA and the aspartame industry insist that the rise in brain cancer has nothing to do with consumption of the artificial sweetener. According to Deputy Commissioner David Friedman, the Olney hypothesis is simply “not a convincing line of evidence.”<sup>28</sup> FDA released the following position statement offering a different interpretation of the brain tumor data, contending that the National Cancer Institute’s statistics “show that overall incidence of brain and central nervous system cancers began increasing in 1973 and continued to increase through 1985 in the United States. Since 1985 the trend line has flattened for these cancers, and in the last two years recorded (1991 to 1993), the incidence has slightly decreased.”<sup>29</sup> Virginia Weldon, head of public policy at Monsanto, also dismisses the Olney paper, remarking that “even the most respected and distinguished investigators occasionally make mistakes, and in this instance, I think Dr. Olney has made a mistake.”<sup>30</sup>

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<sup>27</sup>“*How Sweet Is It?*”, p. 2.

<sup>28</sup>*FDA Week*, January 3, 1997, p. 5.

<sup>29</sup>*Id.*, at 6.

<sup>30</sup>“*How Sweet Is It?*”, p.7.

Other critics of Olney's research suggest that advances in diagnostic technology mean that doctors are simply detecting more tumors today than they used to, which may account for much of the 10% increase. But Olney responds that computerized tomography was used in the early to middle 1970's and magnetic resonance imaging technology became widely used in the early eighties, the impact of which on tumor detection had already been felt by the time aspartame entered the equation. Moreover, he argues, if diffusion of advanced diagnostic systems were the explanation, one would expect to see a rise in the smaller, preliminary astrocytomas which the newer technology now better detects.<sup>31</sup> Yet it is the incidence of the larger, more readily detectable glioblastomas that has risen so sharply in the years after the introduction of aspartame into the American marketplace. Finally, Dr. Olney contends that these are the same types of tumors that were found in laboratory rats in one of the controversial toxicity studies done on aspartame in the 1970's.

Does Olney want the FDA to impose an immediate ban on the suspicious sweet powder? "No," he explains, "and I'm not saying that aspartame has been proven to cause brain tumors. I'm saying that there is enough basis to suspect aspartame, that it needs to be reassessed. The FDA needs to reassess it, and this time around, FDA should do it right."<sup>32</sup>

Dr. Olney and other aspartame critics believe that the FDA did not properly assess the safety of aspartame "the first time around," when Searle first applied

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<sup>31</sup> "Increasing Brain Tumor Rates: Is There a Link to Aspartame?", by Dr. Erik Millstone, Science Policy Research Unit, University of Sussex, October 1996. Report is posted on <http://web2.airmail.net/marystod/cancer.htm>, p. 2.

<sup>32</sup> "How Sweet Is It?", p.3.

for approval back in 1973. They argue that Commissioner Hays' decision to allow the sweetener into the homes and stomachs of consumers was both irresponsible and, indeed, a violation of the Federal Food, Drug, and Cosmetic Act.<sup>33</sup> Dr. Virginia Weldon of Monsanto, on the other hand, insists that "aspartame is one of the safest food ingredients ever approved by the Food and Drug Administration," a sentiment which FDA itself has echoed time and again.

When Searle initially applied for FDA approval in 1974, it submitted general information about aspartame's chemical composition and specifications along with summaries of 119 human and animal studies, in accordance with the broad guidelines then in effect for food additives.<sup>34</sup> Proposed uses included sweetening dry beverage mixes, gelatins, fillings, puddings, breakfast cereals, chewing gum, and soft drinks, as well as use as a free-flowing table sweetener. Searle amended the petition a month later to ask permission to include the water-soluble lubricant L-leucine in production of aspartame tablets. Without the help of L-leucine, which is a "generally recognized as safe"<sup>35</sup> substance, an unattractive film appeared on the surface of hot beverages in which aspartame was dissolved.

In making a determination of the safety of a proposed food additive,

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<sup>33</sup>21 U.S.C. 301, hereafter referred to as the FD&C Act.

<sup>34</sup>The Food, Drug, and Cosmetic Act does not indicate with any specificity the kinds of kind of scientific evidence required to prove the safety of a food additive. The FDA followed broad guidelines written by outside scientists until 1977, when FDA's Bureau of Foods (now called the Center for Food Safety and Applied Nutrition) published a memo of its own specifying what kinds of studies were required. In 1982, the Bureau published the "Red Book," which formally outlined the agency's standards and criteria for safety studies for food additives. A 1987 Report by the General Accounting Office found that the requirements for in effect when aspartame underwent evaluation were substantially similar to those late formalized by the Bureau.

<sup>35</sup>21 C.F.R. 121.101; 21 C.F.R. 121.1002

such as a sweetener, the 1958 Food Additives Amendment requires the FDA to consider the following factors<sup>36</sup>:

- a) the probable consumption of the additive and of any substance formed in or on food because of the use of the additive;
- b) the cumulative effect of such additive in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substance in the diet; and
- c) safety factors which in the opinion of experts qualified by scientific training and experience to evaluate the safety of food additives are generally recognized as appropriate for the use of animal experimentation data.

No additive will be deemed safe for consumption if the evidence “fails to establish that the proposed use of the food additive...will be safe” or if the additive is determined to cause cancer “when ingested by man or animal.”<sup>37</sup>

Having examined the studies and indications submitted by Searle, the FDA instructed them in September, 1973 that it would have to withdraw its petition unless the company could assuage certain concerns, namely<sup>38</sup>:

1. the potential of aspartame to combine with nitrates in the stomach to form carcinogens (nitrosation);
2. the adequacy of evidence to evaluate the significance of certain pathological findings, such as brain tumors, and liver and

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<sup>36</sup>21 U.S.C. 348(c)(5)

<sup>37</sup>21 U.S.C. 348 (c)(3)(A)

<sup>38</sup>Report from the Comptroller General of the United States: *Regulation of the Food Additive Aspartame*, April 8, 1976, p.4.

kidney changes observed in some test animals;

3. the significance of the increased incidence of hyperplasia (abnormal rise in the number of cells in a tissue) in mice administered aspartame and the significance of tumors noted in the urinary bladders of mice;
4. and, the sufficiency of data to determine the long-term effect of diketopiperazine (DKP), a byproduct of aspartame and a breakdown product occurring during prolonged storage or cooking.

The following January, Searle submitted additional studies and data addressing the aforementioned concerns. According to FDA's Division of Toxicology, the new evidence indicated that fears of nitrosation were unwarranted, that brain and kidney changes did not appear to be caused by exposure to aspartame, and that liver nodules found on some test animals were not statistically significant. Also, Searle's additional tests suggested that there was no causal link between bladder tumors and aspartame.

Two concerns nevertheless remained. First, the DKP which materialized as a breakdown product when aspartame is exposed to pronged heat posed uncertain health risks, as well as neutralized the sweet flavor. Second, the amino acid L-phenylalanine posed potential danger to a sub-group of the population suffering from a genetic metabolic disorder, phenylketonuria. Weighing the evidence before it, FDA issued a regulation in July, 1974, approving aspartame for use in certain foods and under certain labeling conditions. Searle would be permitted to market aspartame for use in cold breakfast cereals, chewing

gum, dry beverages and mixes, imitation whipped cream, as a chewing gum flavor-enhancer, and as a dry, free-flowing sweetener “in units not to exceed the sweetening equivalent of two teaspoonsful of sugar.”<sup>39</sup> To address lingering concerns about the product, FDA issued the following labeling requirements: First, aspartame of the free-flowing variety must indicate that it is not for use in cooking or baking. Second, any product containing aspartame must bear the warning: “PHENYLKETONURICS: CONTAINS PHENYLALANINE.”<sup>40</sup>

And so, with an excitement matched only by the anticipation of waist watchers and diabetics across the country, G.D. Searle prepared to introduce its delicious, safe sweetener into the American food supply.

Meanwhile, a small group of private individuals began to draft objections against the approval of aspartame, pursuant to § 348(f)(1) of the Act which provides that any person “adversely affected” by a food additive regulation may file objections within 30 days of the regulation’s publication requesting a public hearing. If the FDA deems such objections reasonable, it must convene a public hearing “as promptly as possible.” Objections were filed in August by Dr. John Olney and, jointly, by Washington attorney and former associate of Ralph Nader, James Turner, and the Washington consumer group Legal Action for Buyers’ Education and Labeling, Inc. (LABEL, Inc.).<sup>41</sup> Olney, Turner, and

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<sup>39</sup>Id., at 6.

<sup>40</sup>Aspartame was also required to be labeled in accordance with FDA’s dietary foods regulations, 21 C.F.R. 105.

<sup>41</sup>A third petition was filed by the Quaker Oats Company, which did not request a hearing but requested that its cereal boxes be permitted to omit the warning to phenylketonurics, on the grounds that amount of phenylalanine naturally occurring in their cereals was three times greater than would be contributed by the addition of aspartame. Therefore, they argued, the labeling would be “unnecessary and redundant.” FDA refused to grant the labeling exemption. See Comptroller General Report, 1976, p.9.



LABEL requested a hearing about aspartame's toxicity, especially in regard to infants and children. Olney also worried that the consumption of aspartame with monosodium glutamate might induce brain damage.<sup>42</sup> After negotiations with FDA, in November of 1975, the three opponents to waive their right to an evidentiary hearing before an administrative law judge (which in 1975 would have been at least a six month wait) and to allow a Public Board of Inquiry (PBOI) to evaluate the scientific evidence.<sup>43</sup>

It would be nearly five years, however, before the PBOI at last convened to adjudicate the safety of aspartame. Suspicions that Searle was guilty of laboratory misconduct and fraudulent data reporting with respect to two other products, the hypertension drug aldactone and the anti-infection drug flagyl, side-tracked FDA officials. In July of 1975, Commissioner Dr. Alexander Schmidt appointed a Searle Investigation Task Force to review the integrity of the manufacturer's studies. Though primarily focused on data from six drugs dating back to 1968, including flagyl and aldactone, the Task Force included aspartame studies as well because "1) of the additive's recent approval, 2) of its potential for wide use in foods, and 3) its inclusion would provide a broader

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<sup>42</sup>Olney had been a vocal critic of the FDA's approval of monosodium glutamate. See J. Verrett, J. Carper, *Eating May Be Hazardous to Your Health*, 1974, p.88-97.

<sup>43</sup>The Food, Drug, and Cosmetic Act provides that an evidentiary hearing be held when there is controversy about the safety of a proposed food additive (21 U.S.C. 348(f)), an adjudication pursuant to the Administrative Procedure Act (5 U.S.C. §§551-559, 701-706 (1982)). But the Commissioner may instead convene a Public Board of Inquiry when it "in the public interest" (21 C.F.R. §§13.1-.50(1985)). Many prefer the PBOI model of a roundtable of independent scientists analyzing data to the more adversarial administrative adjudications. Peter Barton Hutt, former Chief Counsel to the FDA, offers the following evaluation of the administrative hearing: "it has, of course, done one thing. It has employed hundreds of lawyers involved in these proceedings. But instead of advancing the scientific issue or the regulatory issue...I would argue that it has set us back." (Hutt, *Impact of Recent Court Decisions on the Future of FDA Regulations: An Impromptu Response to the Remarks of the Speakers*, 28 *Food, Drug, and Cosmetic Law Journal*, 707, 714 (1973))

product base to evaluate Searle's practices."<sup>44</sup> Schmidt charged the investigatory body to:

- 1) review the practices followed by Searle in conducting animal experiments, analyzing the experimental data, and submitting the data to FDA;
- 2) determine if there is evidence that any practices of Searle in carrying out the above functions violated the Federal Food, Drug, and Cosmetic Act or any other laws of the United States; and
- 3) recommend an appropriate course of action based on the investigation's findings.<sup>45</sup>

Faced with preliminary findings that Searle had engaged in dubious laboratory practice, in December of 1975 the Commissioner decided to stay approval of aspartame pending the completion of the investigation, pursuant to § 348(e) of the Act. Meanwhile, having invested an irretrievable \$29 million in its artificial sweetener, Searle was forced to pull the plug on production at its aspartame factory in Augusta, Georgia. The stay, coupled by the negative media attention, "lowered company morale and badly shook investor confidence in the drug manufacturer."<sup>46</sup>

The Searle Task Force concluded its investigation in March, 1976, declaring that "the results were so serious in some studies as to make it difficult, if not impossible, to draw conclusions regarding the full toxic potential of the products from the data."<sup>47</sup> FDA Toxicologist and Task Force member Dr.

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<sup>44</sup>Report of the Comptroller General, 1976, p.13.

<sup>45</sup>Id., at 12.

<sup>46</sup>*Wall Street Journal*, July 21, 1975, p.4, col. 3.

<sup>47</sup>General Accounting Office Report, 1987, p. 30.

Adrian Gross reported that in some of the aspartame studies he reviewed, Searle “lied and they didn’t submit the real nature of their observations because had they done that it is more than likely that a great number of these studies would have been rejected...they took great pains to camouflage these shortcomings.” For example, reports Gross, the Task Force found some instances of lab technicians cutting out tumors from live animals before the studies were finished. He comments that Searle “filter(ed) and just present(ed) to the FDA what they wished the FDA to know.”<sup>48</sup>

In conclusion, the Task Force identified “serious deficiencies in Searle’s operations and practices which undermine the basis for reliance on Searle’s integrity in conducting high-quality animal research to accurately determine or characterize the toxic potential of its products.”<sup>49</sup> The Task Force recommended that: 1) “the Department of Justice institute grand jury proceedings against Searle; 2) FDA establish regulations outlining good laboratory practice<sup>50</sup>; and 3) FDA determine whether to take administrative and/or regulatory actions on each of the Searle products investigated.”<sup>51</sup>

Turning back to the issue of aspartame, FDA now had to decide whether or not its initial conclusions about the product’s safety withstood the storm. Convening a PBOI, after all, would be a fruitless endeavor if the panel of scientists had no way of knowing if the studies before them were credible. No longer willing to trust Searle to authenticate its own data, CFSAN chose fifteen

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<sup>48</sup>Wilson, “Sweet Suspicions,” Congressional record, August, 1985, p.27.

<sup>49</sup>Id., p.83.

<sup>50</sup>On December 22, 1978, FDA did formalize good laboratory practice regulations, setting standards for scientific animal studies.

<sup>51</sup>Id., p.30.

aspartame studies and farmed out twelve to a consortium of nine independent universities (UAREP) and another three to an FDA team. Although Searle would pay for UAREP's investigation, a contract between them stipulated that the researchers work independently of either FDA or Searle influence.<sup>52</sup>

Between April and September of 1977, the FDA team undertook a thorough review of the laboratory procedures, observations, and data of each of the three studies, examining over 7,800 slides and 7,300 tissue blocks. In each study, the team identified "quality control problems" in each of the three studies it audited. For example, the investigators found that in one study the aspartame may not have been thoroughly distributed in the rat food, thereby allowing the animals to eat around the powder, a suspicion which was corroborated by photograph found in the notebook of a Searle employee.<sup>53</sup> The team also questioned some dubious claims about how many fetuses were examined in the two teratology studies. In particular, a report that 329 examinations were completed in two days by a single technician seemed infeasible. Despite these and other dubious findings, the team tentatively accepted the validity of the studies' results, pending the outcome of the UAREP investigation.

It took UAREP investigators two years to analyze the twelve studies at issue. They reviewed over 23,000 pages of clinical observations, background materials, and experimental data, examined 39,000 tissue samples from nearly 5,000 animals, reviewed laboratory protocols, and interviewed former and current Searle employees involved in aspartame research. Like the FDA team, and

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<sup>52</sup>Id., p.31.

<sup>53</sup>Id., p.32.

the Searle Task Force before it, UAREP located procedural flaw in Searle's animal studies; nevertheless, it found no evidence that "animals in any one group had been treated deliberately to produce biased results." Submitting a 1,062 page report to FDA on December 13, 1978, it concluded that it had identified no discrepancies "that are of sufficient magnitude or of a nature that would compromise the data as originally submitted by Searle."<sup>54</sup> It seemed the long-awaited aspartame hearing, which would be the first time FDA would test out its new PBOI format, could finally go forward.

Before the hearing could begin, however, the parties involved had to frame the relevant issues to be addressed by the panel. After much negotiation, they agreed to charge the scientific board with the following three questions:<sup>55</sup>

1) Whether ingestion of aspartame, either alone or together with the amino acid glutamate, poses a risk of contributing to mental retardation, brain damage, or undesirable effects on the neuroendocrine system.

2) Whether ingestion of aspartame may induce brain tumors in rats.

3) Based on answers to the above questions, (a) should aspartame be allowed for use in foods, or, instead, should approval be withdrawn?

(b) if allowed for use in foods, what conditions of use and labeling statements (if any) should be required?<sup>56</sup>

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<sup>54</sup>Id., Appendix IV, p.90.

<sup>55</sup>Mr. Turner requested that the PBOI review the evidence previously gathered indicating quality control problems in some of Searle's studies. Both the Commissioner and PBOI denied his request on the grounds that the integrity of the studies, however shabby, had already been affirmed by both the Searle Task Force and UAREP. Moreover, PBOI members explained their duty was to analyze the evidence, not the conduct of the studies.

<sup>56</sup>44 FR 31717

Who then should be entrusted with evaluating these issues?

As mentioned, the purpose of convening a PBOI was to provide a forum where experts could evaluate scientific evidence and resolve controversies insulated from political or professional pressures. To best expedite this goal, Acting Commissioner Sherwin Gardner asked Searle, FDA, and the objecting parties to each submit a list of five qualified candidates. After evaluating the nominees, Gardner selected one scientist from each list to create the following panel: from CFSAN's list, Walle Nauta, M.D., Ph.D, a neuroanatomist and professor at the Massachusetts Institute of Technology, who was named chairman; from the objectors' list, Peter Lambert, M.D., clinical pathologist and chairperson of the Department of Pathology at the University of California at San Diego; and, from Searle's list, Vernon Young, Ph.D., a nutritional biochemist and M.I.T. professor. Olney protested Dr. Young's selection, asserting that, as a nutrition and metabolism specialist, Young was not properly qualified to assess the neurotoxicity issue.<sup>57</sup> Furthermore, objected Olney, Young had written authors in conjunction with Searle in the past on nonaspartame-related issues and could therefore not be impartial. His objections, however, were overruled.

For three days the panel heard evidence on all three issues from all involved parties. Some presenters used slides to illustrate their points and, while the three board members raised questions throughout, the parties were not permitted to interrupt one another: "the proceeding resembled a roundtable discussion. These interchanges were almost always nonconfrontational and non-

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<sup>57</sup>Olney, John W. Letter to Senator Howard M. Metzenbaum, included in the record before the U.S. Senate Committee on Labor and Human Resources, November 3, 1987, regarding "NutraSweet Health and Safety Concerns," p.468-476.

adversarial in nature.<sup>58</sup> With the exception of Turner, no attorneys participated in the proceedings. After ten months of deliberation, the board issued its determinations in October of 1980, which would be final unless hearing participants later raised objections and the Commissioner chose to overrule the PBOI. First, it concluded that aspartame did not cause brain damage, mental retardation, or neuroendocrine dysfunction. Much to Searle's dismay, however, the board recommended that aspartame not be approved for use in foods based on "scientific data suggestive of aspartame's potential for causing brain tumors in laboratory rats."<sup>59</sup> More studies must be done, it commented, before aspartame's oncogenic tendency can be ruled out. The board vacated the stay of approval formerly issued and revoked the 1973 regulation which had first extended FDA approval.

Not surprisingly, Searle, faced with financial disaster, immediately filed objections to the PBOI determinations, thereby triggering Commissioner review and the possibility that he would overrule the earlier findings. Losing money with every passing hour, Searle also filed a lawsuit against the FDA in an attempt to hasten the Commissioner's review. In March of 1981, then FDA Commissioner Jere Goyan assembled a panel of five scientists to review the conclusions reached by the PBOI and to evaluate the objections filed. One month later, Ronald Reagan appointed a new Commissioner, Arthur Hull Hayes, Jr., to whom befell the unenviable task of resolving the aspartame controversy once

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<sup>58</sup>Sidney Shapiro, "Scientific Issues and the Function of Hearing Procedures: The FDA's Public Board of Inquiry," *Duke Law Journal*, April, 1986, p.309. From an interview with Robert Becker and Peter Safir, Counsel for Searle, Aspartame Hearing, in Washington, D.C. (June 24, 1985)

<sup>59</sup>45 FR 69558

and for all.

The panel Hayes inherited apprised him of the PBOI findings, reviewed the issues in controversy, summarized the arguments of both sides, and offered advice based on its own conclusions. Three of the five panelists tasked with assessing aspartame's role in causing brain tumors concluded that the Searle evidence did not sufficiently demonstrate aspartame's safety. Nevertheless, on July 24, 1981, Commissioner Hays decided "the available data establish that there is a reasonable certainty that human consumption of aspartame...will not cause brain tumors."<sup>60</sup> After a long, messy battle, Searle had finally gained approval for its artificial sweetener<sup>61</sup>.

What caused Commissioner Hays to contravene the conclusions of the PBOI and his own scientific panel? The answer essentially boils down to the frustrating, but inevitable conclusion that he simply interpreted the three rat studies available on carcinogenicity differently. As previously mentioned, in order to gain FDA approval for a food additive, the 1958 Amendment to the FD&C Act mandates that petitioners demonstrate "that the proposed use of the food additive, under conditions of use specified in the regulation, will be safe."<sup>62</sup> Of course, a petition must also satisfy the infamous Delaney Clause which stipulates that "no additive shall be deemed to be safe if it is found to indicate cancer when ingested by man or animal."<sup>63</sup> Views of certain aspar-

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<sup>60</sup>46 FR 38285

<sup>61</sup>In 1983, Searle requested, and Congress granted, an extension on its aspartame patent, to redress the nearly six years of marketing it lost due to the FDA stay of approval and subsequent hearings and investigations. The extension was added as a Senate floor amendment to the Orphan Drug Act of 1983. Pub.L. No. 97-414, § 11, 96 Stat. 2049, 2065-66 (1983). The patent for aspartame expired on December 14, 1992.

<sup>62</sup>21 U.S.C. 348(c)(3)(A)

<sup>63</sup>Ibid.



tame opponents notwithstanding, neither PBOI nor the three panelists argued that the Delaney Clause applied to the aspartame controversy<sup>64</sup>: this was not a case of a Commissioner approving a known carcinogen, but rather approving a substance whose safety had not been demonstrated conclusively.

The crux of the controversy between the Commissioner on the one hand, and the PBOI, majority of the advisory panel, and Olney on the other hand, was a difference in opinion about a causal relationship between exposure to aspartame and onset of brain tumors in test rats.<sup>65</sup> Evaluating the three brain tumor studies done on laboratory rats, the PBOI had concluded that one was “bizarre” because the control group had an unusually high incidence of tumors and “puzzling” because it contained an inadequate number of test animals<sup>66</sup>. Another study, according to the board, demonstrated the high mortality rate among the young rats exposed to aspartame, which suggested a biologically significant dose-effect.

Commissioner Hayes, however, contended that in the first study the number of test animals was experimentally sufficient and that the board was wrong to call the control group tumor rate “bizarre.” He believed the board was assuming a background rate (the rate at which tumors could be expected to “normally” develop) that was too low. The actual background rate for this species, he argued, is much higher and altogether consistent with that wit-

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<sup>64</sup>For an example of a Delaney Clause controversy, see 45 FR 61476 (Cyclamate Decision)

<sup>65</sup>In the interest of brevity, various arguments and counterarguments regarding aspartame’s connection to brain damage, exacerbation of phenylketonuria, hyperphenylalanemia, focal point brain lesions, and neuroendocrine disorders are excluded from this paper. In evaluating the wisdom of the Commissioner’s decision, I focus on the brain tumor debate because it was the issue about which FDA and outside scientists were most divided. For discussion of these issues, please see: 46 FR 38285, at 38287-38294.

<sup>66</sup>Final Decision, at 38295

nessed in the Searle study. To bolster his argument, he pointed to a long-term rat study conducted by the Japanese firm, Ajinomoto Co., Inc. which demonstrated a similarly high spontaneous rate.<sup>67</sup> Therefore, since the incidence of tumors among the exposed and unexposed were similar, the study with the high control group rate had demonstrated not an experimental oddity, but rather the non-carcinogenicity of aspartame. As for the board's conclusion about carcinogenicity causality among the young rats, Hayes argued that the board had made factual errors in computing the age of death for some of the young rats. He also contended that the board had erred in its statistical analysis of the dose-response relationship and that no statistically significant relationship in fact exists.<sup>68</sup>

In Hays' decision to permit aspartame into the food supply resides the classic conundrum of FDA regulatory power: how much evidence is sufficient to keep a much-desired additive from entering the marketplace? FDA decision-makers look to two main signposts as they navigate through a body of evidence to arrive at conclusions about safety. First, in enacting the 1958 Amendment, Congress intended to place the burden of proving safety squarely on the petitioner. Even if no evidence of *lack* of safety exists, a petition which fails affirmatively to establish safety may be rejected pending further testing.<sup>69</sup> Second, FDA assesses the meaning of the statutory language *safety* by applying the legal standard of a "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use."<sup>70</sup>

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<sup>67</sup>Searle and Ajinomoto Co., Inc. would enjoy a close professional friendship, opening up an aspartame manufacturing plant together in Gravelines, France in 1991.

<sup>68</sup>Final Decision, at 38,299.

<sup>69</sup>*Aspartame: Commissioner's Final Decision*, July 24, 1981, 46 FR 38285, at 38286.

<sup>70</sup>21 C.F.R. 170.3(i) (1983)

But what does “reasonable certainty” really mean, and how many competent scientists does it take to meet such a standard? A General Accounting Office survey of 69 scientists nationwide who either personally researched aspartame or had studied the research of colleagues revealed that ten believe aspartame should be withdrawn from the market; twelve expressed major concerns about its safety; and another twenty-six indicated they harbored some concerns about aspartame in the food supply. Dr. Adrian Gross, Senior Science Advisor at the Environmental Protection Agency and former Searle Task Force investigator, feels that “at least one of [the aspartame rat] studies has established beyond any reasonable doubt that aspartame is capable of inducing brain tumors.”<sup>71</sup> In the aspartame controversy, so-called reasonable scientists were divided; thus, to put it cynically, the reasonable scientist with the most power made the ultimate determination. Whereas those unsatisfied with Searle’s safety evidence demanded more testing before they felt they could achieve this elusive level of certainty, the Commissioner felt that the minimal evidentiary threshold *had been* met, remarking, “if [you] wait for unanimity...nothing is ever going to happen.”<sup>72</sup>

Epidemiologist Debra Davis makes the following observation about applying the food additive legal standard in a gray area such as aspartame: “the question of how much evidence is enough is not a scientific question. It’s a policy question. That’s what the FDA has to deal with.” Some aspartame critics worry, however, that when the FDA moves away from sheer scientific determina-

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<sup>71</sup>Statement from Adrian Gross, included in the Congressional record, August, 1985.

<sup>72</sup>United States General Accounting Office Report, 1987, p.57.

tions it becomes vulnerable to political and industry influence. Discovery of an internal memorandum entitled “Food and Drug Sweetener Strategy” furthered fueled these suspicion. The memo sets out tactics that Searle representatives should use to gain FDA approval of aspartame: “the basic philosophy of our approach...should be to try to get them to say “Yes,” to rank the things that we are going to ask for so we are putting first those questions we would like to get a “yes” to, even if we have to throw some in that have no significance to us, other than putting them in a yes saying habit.” The memo continued, “we must create an affirmative atmosphere in our dealing with them. It would help if we can get them or get their people involved to do us any such favors.” Finally, it urged the Searle representatives to bring FDA decision-makers “into a subconscious spirit of participation.”<sup>73</sup>

Even if one discounts the Searle memorandum as an innocent company pep-talk, there is legitimate concern that industries may be unduly influencing important FDA health decisions by conducting their own research tests. As revealed by the Searle Task Force, industries with heavily vested interests may be tempted to airbrush unattractive findings here and there. Dr. Ralph G. Walton, professor of psychiatry at Northeastern Ohio’s College of Medicine, recently completed a survey of the 164 aspartame studies conducted over the past three decades. Of the 90 independently funded studies, 83 “identified a problem,”;

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<sup>73</sup>Memorandum from Herbert Helling, G.D. Searle official, to other Searle officials, regarding “Food and Drug Sweetener Strategy,” December 28, 1970, included in the U.S. Senate Joint Hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare and the Subcommittee on Administrative Practice and Procedure of the Committee on the Judiciary, “Preclinical and Clinical Testing by the Pharmaceutical Industry,” 1976, Part 2, p.16-19.

of the 74 studies funded by the aspartame industry, “every single one of them attested to the safety of aspartame.<sup>74</sup>” What, however, would be a preferable alternative testing regime? Surely it is financially untenable to suggest the FDA itself conduct all studies on new foods, drugs, and medical devices. Disallowing industry tests on the grounds that they might be biased might result in deterring research and development of new products, surely not a desirable outcome. Occasionally auditing tests, as was done with Searle in the 1970’s, and professional accountability might be the optimal checking mechanisms for the FDA. As Monsanto’s Dr. Weldon remarked, “no scientist is going to sacrifice his or her reputation just because of where the sponsor is or where the money came from. That would be a very foolish thing to do.”<sup>75</sup>

Those concerned about the vulnerability of FDA to industry courtship also bemoan the “revolving door” between government agencies and private industry. Some argue that this cross fertilization may taint the regulatory process. Arthur Hull Hays, for example, left his post at FDA a few months after approving aspartame’s use in carbonated drinks to take job as senior scientific consultant at Burson-Marsteller, Searle’s public relations firm, earning \$1000 a day<sup>76</sup>. In April of 1976, presented with the Searle Task Force’s shocking findings, FDA Chief Counsel Richard Merrill informed Samuel Skinner, U.S. Attorney for the Northern District of Illinois, of an FDA investigation into Searle’s violations of the FD&C Act and the False Reports to the Government

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<sup>74</sup> “How Sweet Is It?” p. 7.

<sup>75</sup> Ibid.

<sup>76</sup> *Nutrition & Healing*, November, 1995, p. 3.

Act.<sup>77</sup> The following January, Merrill formally requested Skinner to initiate grand jury proceedings against Searle. In February, learning that President Carter would not reappoint him, Skinner entered into employment negotiations with the Chicago firm Sidley & Austin, who was representing Searle in its battle with the FDA. That summer, he left the U.S. Attorney's office to become a partner at Sidley. Skinner, who was later appointed Secretary of Transportation and Chief of Staff by President Bush, insists that he had recused himself from the grand jury investigation as soon as he contemplated going over the Sidley and that his professional judgment as U.S. Attorney was in no way compromised by his employment prospects<sup>78</sup>. Skinner turned the investigation over to assistant U.S. Attorney William Conlon who convened a grand jury, but under whose direction the statute of limitations for the aspartame charges ran out. Fifteen months later, Conlon too left the U.S.A.O. to work for Sidley.<sup>79</sup>

Nevertheless, the decision to approve aspartame has survived extra-agency scrutiny time and again. When Skinner, for example, presented himself as President Bush's nominee for Secretary of Transportation in 1989, Senator Howard Metzenbaum led an investigation into his contacts with Searle. Skinner was exonerated, and received confirmation. The United States General Accounting Office (GAO), also at the behest of Metzenbaum, undertook a thorough investigation of six former Health and Human Services and FDA employees involved in the aspartame decision, including former Commissioners Hayes and

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<sup>77</sup>18 U.S.C. 1001

<sup>78</sup>Senate Proceedings and Debates of the 101st Congress

<sup>79</sup>Gordon, Gregory, 1987. "NutraSweet: Question Swirl," UPI Investigative Report, October, 1987, reprinted in U.S. Senate Committee on Labor and Human Resources, "NutraSweet Health and Safety Concerns," November 3, 1987, p.497.

Sherwin Gardner.

The report, published in 1986, concluded that none of these officials had violated the federal postemployment statute, 18 U.S.C. 207, as amended by the Ethics in Government Act of 1978<sup>80</sup>. In 1987, GAO published the results of another investigation into FDA's approval of aspartame. The report "did not evaluate the scientific issues raised concerning the studies...nor did we determine aspartame's safety. We do not have such scientific expertise."<sup>81</sup> GAO did determine that FDA had followed the appropriate procedures and fulfilled its legal duties in endorsing the sweetener.

A final nod of approval emerged from the bench of the D.C. Court of Appeals, where Judge Abner Mikva wrote a unanimous opinion endorsing FDA's decision to grant both Searle's dry foods and carbonated beverage petitions<sup>82</sup>. With the caveat that it was not purporting to reinterpret the scientific data ("the judiciary is ill-equipped to conduct investigations and analyze facts of the type involved in this case. Because of the agency's expertise and broad discretion in ensuring the safety of food additives, we cannot substitute our judgment for the agency's.<sup>83</sup>"), the court held that the agency had not abused its discretion in approving aspartame for wet use on the basis of the studies

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<sup>80</sup>"Six Former HHS Employees' Involvement in Aspartame's Approval," a briefing report from the United States General Accounting Office to the Honorable Howard Metzenbaum, United States Senate, July, 1986.

<sup>81</sup>"Food Additive Approval Process Followed for Aspartame," United States General Accounting Office, June, 1987.

<sup>82</sup>*Community Nutrition Institute v Young*, 773 F.2d 1356 (1985). Court denied plaintiffs' request for a temporary restraining order barring aspartame and held that the FDA did not abuse its discretion in denying plaintiffs' request for a public hearing before approval of aspartame in carbonated beverages, on the grounds that the objectors (including James Tuner) had raised no new material evidence.

<sup>83</sup>*Id.*, at 1363

used to support the earlier approval for dry use.

Perhaps at the eye of the hurricane that is the aspartame controversy there dwells a simple risk-benefit analysis. The risks loom large but uncertain—a possibility, as yet unquantified, that aspartame has contributed to 1,500 cases of deadly brain cancer a year, a suspicion among some scientists that it induces brain damage and seizures, and thousands of reported adverse reactions. Even harder to assess are the benefits. After all, with the exception of diabetics for whom natural sugar is not an option, the benefit to having a low-calorie alternative to sugar are not comparable to the benefits of a life-saving drug, for example. Moreover, although Americans are consuming millions of pounds of aspartame each year, there is no evidence that this habit contributes to weight loss. In fact, Americans have never been more obese than we are today. However, availability of an artificial is an integral part of the diet industry and withdrawal of aspartame would force those unwilling to use sugar to consume saccharin instead. This would be an undesirable displacement, as saccharin's carcinogenic potential is probably greater than aspartame's. In the absence of clear proof of either safety or hazard, allowing aspartame to enter the market (and stay) is “a good example of one trade-off that has sometimes been made in risk management: acceptance of a compound with no use experience, but little animal evidence of toxicity, in preference to one with long use experience, but some evidence of toxicity.”<sup>84</sup>

Some who believe there is not enough scientific evidence to ban out-

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<sup>84</sup>Michael A. Kamrin, *Toxicology- A Primer on Toxicology Principles and Applications*, Lewis Publishers, Inc., 1988, p. 77.



right the highly valued sweetener propose more informative labeling. In 1985, former Senator Howard Metzenbaum introduced a bill entitled “the Aspartame Safety Act,” which would require manufacturer’s to indicate on the label how much aspartame is contained in the product. This would aid consumers and their physicians to better understand the relationship between aspartame consumption to adverse reactions. Most consumers do not know that the FDA has set an Acceptable Daily Intake limit of 50 mg/kg for the sweetener. Including the number of mgs of aspartame in food and beverages would allow individuals to monitor their intake so they don’t exceed this ADI and would impose a negligible burden on manufacturers.

But isn’t the daily tolerance high enough that consumers needn’t worry about approaching it? As Metzenbaum explained, “sure, if you weigh 130 pounds you would have to drink 4 or 5 liters of diet soft drink to hit the limit. But if you are a child that weighs 30 pounds, you hit that limit with 3 or 4 cans of diet soft drink. That’s even without the gum, pudding, breakfast cereal- all sweetened with aspartame.”<sup>85</sup> With the recent approval for use in all foods, aspartame will emerge in even more products, from loaves of bread to birthday cakes. Many consumers might not understand what a 50 mg/kg ADI really means; however, with simultaneous national education efforts, a labeling requirement would allow the consumer to conduct a private risk-benefit analysis of his own. With hysterical and confused consumers in one corner, diabetics and the weight-conscious unwilling to surrender their delicious sweetener in another,

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<sup>85</sup>Congressional Record, August 1985. Metzenbaum’s proposal for the Aspartame Safety Act was rejected by Congress.

and science hovering uncertain and splintered in the middle, shifting the information and responsibility to the individual might be the most pragmatic, and conscionable, step FDA could take.