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The History of Aspartame

Citation
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I. Introduction

Aspartame is everywhere. It is in our restaurants and in our homes. Mere mention of the word aspartame or its brand names, NutraSweet and Equal, engenders a vide variety of reactions amongst consumers. In America, where evidence of the war against obesity is omnipresent, consumers are not only sophisticated about low calorie alternatives to their favorite foods; they have begun to demand them. As the market desire for these products grows at an exponential rate, it becomes increasingly acceptable to order lower calorie meal options in restaurants. Indeed, many restaurants have begun to cater to a demographic that has money to spend and a desire to be thin. Correspondingly, the use of aspartame as an every day tabletop sweetener has blossomed. It has become unusual to be served a hot beverage such as coffee or tea in a restaurant without both sugar and NutraSweet or Equal, both brand names for aspartame. Furthermore, the use of non-sugar sweeteners has moved from a female-only habit to one generally embraced by more health-conscious men and women.

As drinking diet soda and using non-sugar sweeteners has become increasingly mainstream, such items have replaced sugar even in the diets of many people who do not consider themselves overweight or dieting. NutraSweet has provided one way of getting the flavor of sugar while saving on extra calories that can now be spent elsewhere. So, as Americans seem to be becoming in-

creasingly conscious of their health and weight, the market is promoting ways of having your cake and eating it too. Low-calorie sweeteners play an enormous role in this industry.

As the diet industry has grown, some consumers and consumer advocates have been waging a simultaneous war against what they feel is an industry that threatens the health of overly trusting and quick fix oriented American consumers. Paradoxically, as American's become increasingly concerned about their waistlines and their general health, these consumer advocates feel an increasing need to protect citizens from potentially harmful diet products and low-calorie substitutes for certain foods. Although the Food and Drug Administration (FDA) regulates the introduction of food additives into the market, some consumer advocates feel that the agency is not doing a sufficient job.[1]

These two opposing tensions, the market desire for low-calorie foods including sugar substitutes, and the fear of consumer manipulation by a burgeoning industry and a collusive FDA, drive the fascinating history of aspartame. This paper follows the important hurdles in aspartame's past, including the attempts of its promoters to gain regulatory acceptance, several safety scares, botched scientific research, scandals, lawsuits and investigations. It also seeks to illuminate how FDA has dealt with, and participated in the tenacious struggle surrounding aspartame's regulation, use and safety. Finally, this paper looks to the future in order to determine if the aspartame debate will soon come to a final end.

[1]The Food Additives Amendment, 72 Stat. 1784 (1958) was promulgated to close loopholes in existing law.

II. A Brief History of Sugar-Substitutes

In the United States, there has been a longstanding tension between market desire for a low calorie sugar substitute and fears about the safety of such substitutes. Despite the FDA's attempts to allay consumer fears about FDA approved additives and promote confidence in the ability of the agency to balance the market demands with safety concerns, some consumers have not been appeased. The two sides of the sugar substitute battle have illuminated real and fantastical concerns, and spawned a fiery regulatory battle that has lasted over 100 years. Ironically, the FDA has apparently remained fairly neutral in its role as regulator, despite the passionate protests of the pro-approval and anti-approval camps.

The sugar substitute industry inception occurred largely by accident in 1879 when two Johns Hopkins University scientists who were hoping to discover a wonder drug instead found saccharine - a non-nutritive coal-tar derivative that is 300 times sweeter than sugar.[2] By 1907, saccharine was widely used as a sweetener in canned foods, though just five years later it was banned from use as a food additive. With the onset of sugar shortages in World War I, however, saccharine was again declared safe. With that, saccharine use increased steadily until the 1950's while the potential adverse effects of the sugar substitute maintained a low profile. [3]

From the time of its invention, saccharine and the sugar-substitute industry has

[2]NY Times., March 29, 1997, at page 24; col.1.
[3]Id.

been driven by twin American desires: the desire for health and the desire for beauty. Throughout the centuries, sugar has been linked to many human ills from cavities and tooth decay, to gout, obesity and heart disease. Instead of correcting the real and imagined negative effects of sugar consumption, however, sugar-substitutes seem to have merely spawned more health related concerns while offering only less calories for more sweetness in the American diet. Recently, scientists have stated that no major health problems are in fact directly associated with eating sugar. Food scientists acknowledge that sugar consumption can contribute to excess calories which in turn may fuel the problems of obesity, though the introduction of sugar-substitutes has not had a significant impact in lowering rates of obesity amongst Americans.[4] Diabetics also must limit sugar consumption since their bodies do not properly metabolize it, but sugar has not been shown to cause the disease.[5]

Although health concerns have played a role in promoting the market demand for sugar-substitutes, the complicit role of American beauty ideals is also significant. In many ways the American ideals of health and beauty are linked. What is promoted as beautiful in our society has for the most part been linked to health. However, as slim and even emaciated bodies have increasingly become the pinnacles of beauty promoted by the fashion industry, health and beauty diverge in reality. Even so, companies that promote diet aids and low calorie substitutes to high calorie foods are careful to make the two ideals seem to be one and the same. This partially explains the American consumers' voracious

[4]NY Times, September 5, 1989, at page 1; col 3
[5]Id.

appetite for sugar substitutes that has propelled the sugar-substitute industry. The dynamic history of sugar-substitutes in America cannot be fully understood without an exploration of the element of fear that has plagued consumers and nearly tempered the sugar-substitute industry.

Concern over the safety of saccharine became widespread in the 1950's when the marketing of cyclamate, another sugar-substitute, prompted additional research on the effects of sweetening agents.[6] In 1950 Abbot laboratories introduced a sweetening tablet designed for diabetics, that contained cyclamate, a chemical isolated in 1937 when a student working with a fever-reducing drug, flicked some tobacco off his lips and wondered why his fingers tasted so sweet. In 1951 the FDA approved cyclamate for use in food. Then in 1953, Kirsch Beverages Corp. introduced the first diet soda, cyclamate-sweetened No-cal, and the diet-soda industry was born.[7]

The use of low-calorie sugar substitutes increased as the Cumberland Packing Corporation of Brooklyn, New York marketed cyclamate-based Sweet 'n Low in the bright pink individual-portion wrappers that are still recognizable today. By 1963, cyclamate, which was often used in combination with saccharine, was the country's most popular sugar substitute. It was used in canned goods, baked goods, bacon, toothpaste, mouthwash, lipstick and cereal as well as diet and non-diet beverages.[8] It is not clear whether the cyclamate's use was so pervasive because of its taste, its lower calorie content per sweetness or the fact

[6] supra note 2
[7] Id.
[8] Id.

that it was sold at one tenth the price of sugar.[9]

By 1967, diet soda sales were increasing at a fantastic pace. They had doubled since 1963 and would quintuple in the next two decades.[10] Seemingly in reaction to this explosion of artificial-sweetener sales and consumption, the FDA set forth a recommendation that adults use no more than 3,500 milligrams of cyclamate a day, the equivalent of ten cans of diet soda. A FDA report states that [N]one of the studies reported have established a useful role for non-nutritive sweeteners as weight-reducing aids...[11]

This cautionary momentum continued and in 1969 the FDA banned cyclamate when testing that was done on both saccharine and cyclamate suggested that large doses of cyclamate caused bladder tumors in laboratory rats. This was not enough to stifle the American desire for low-calorie sweeteners. However, in the wake of the ban on cyclamate, a saccharine-based table sweetener appeared on the market. Soon after that, a group of people sued the US Government on behalf of free and unindentured American citizens for banning cyclamate.[12] This suit is one of the first shots the pro-sweetener, anti-regulation camp took against government regulation. It marks the beginning of their heated struggle to keep sweeteners, despite potential health risks, on the market.

III. FDA Announces Proposed Ban on Saccharine

March 1977 brought mayhem to the soft-drink industry. When the FDA be-

[9] Id.
[10] Id.
[11] Id.
[12] Id.

came aware of a Canadian study that linked use of saccharin to bladder cancer in laboratory rats, speculation grew that saccharine would soon be banned.[13] The possibility that the widely used sugar substitute would be banned sent manufacturers scrambling for a way to keep their low-calorie beverages on the market. At that time, soft-drink manufacturers accounted for 75 percent of the estimated 5 million pounds of saccharin consumed in the U.S. annually. Despite the industry's considerable size and influence, however, it could not dissuade the FDA from its proposal.

A study that came from the Albany Medical College in Albany, N.Y., reporting that saccharin proved to be completely harmless also failed to prevent the ban.[14] Even accounts of numerous calls to the American Diabetes Association, whose switchboards were flooded with calls from concerned diabetics, could not persuade the FDA that the need for a sugar substitute was more important than the safety of consumers.

In fact, under the Delaney Amendment to the Pure Food and Drug Act, the FDA had little choice but to ban saccharine.[15] The amendment mandates that any product that produces any sign of cancer in test animals or humans is banned.[16] Dr. Sherwin Gardner, then acting commissioner of FDA, said the FDA had no evidence that saccharin has ever caused cancer in human beings, but that the Canadian tests show unequivocally that this substance can produce malignant bladder tumors in rats.[17] Ironically, despite the Commissioner's initial concerns

[13]Wash. Post., March 11, 1977, at D9
[14]Id.
[15]Supra note 1
[16]Id.
[17]Supra note 13

or the requirements of the Delaney Amendment, Congress overruled FDA's attempt to restrict the use of saccharine.[18] The damage to saccharin's reputation could not be repaired despite the fact that it remained on the market.

What was bad news for saccharine producers and marketers, was a boon to G. D. Searle (Searle) the manufacturer and patent owner for the sugar-substitute aspartame. The proposed saccharin ban's repercussions on Wall Street included a boost in sugar stock prices and $1 jump in Searle's stock which was the most actively traded stock of the day.[19] However, investor confidence in Searle, did not translate into immediate approval of aspartame for market purposes.

IV. Background on Aspartame

The tumultuous history of the food additive aspartame began serendipitously thirty-five years ago. On the day that James M. Schlatter, a chemist, unintentionally discovered it, he was working on an anti-ulcer drug. As Mr. Schlatter mixed asparatic acid and phenylalanine, two naturally occurring amino acids that are the building blocks of protein, he stuck his finger in the mixture and for some reason decided to taste it. I licked my finger and it tasted good. He later recalled. And with that, a new, low-calorie sweetener was born.[20] What has happened since that fateful day in 1965 comprises the additive's struggle from birth to maturity; not unlike a human being moving from inception to adulthood, aspartame has overcome many hurdles and incited much controversy on its path to a somewhat more stable maturity.

Once aspartame had been more thoroughly tested and successfully reproduced,

[18] Wash. Post., July 16, 1981, at A10
[19] Supra note 1
[20] Wash. Post., September 22, 1982, at E1

the Skokie, Illinois based pharmaceutical company by the name of G. D. Searle & Co., employer to Mr. Schlatter, resolved to manufacture it. In 1973, Searle filed a food additive petition for aspartame;[21] thus entering aspartame into the vigorous sugar-substitute competition and beginning a battle that would last for more than twenty-five years.

It seemed that the market was ripe for aspartame's introduction. Since the 1969 ban on cyclamate, saccharine manufacturers had held a virtual monopoly on the low calorie sweetener market. Searle executives saw the potential market for a new sugar substitute and decided to push for aspartame's approval. Despite the market demand for low calorie sugar substitutes, however, it would be another eight years before Searle would eventually receive final approval for aspartame in 1981.[22]

V. FDA Approval

As required by law, Searle petitioned the FDA for approval to market aspartame as a sweetening agent in certain foods.[23] Included in its petition, was extensive data from the research that had been performed on aspartame, all of which purported the safety of the additive. After reviewing the data included in the petition, FDA approved Searle's food additive petition for aspartame on July 26, 1974. The agency then issued a regulation authorizing the use of aspartame in certain foods and for certain technological purposes.[24]

[21] 38 Fed. Reg. 5921 (1973)

[22] 46 Fed. Reg. 3828 (1981). FDA's initial approval of aspartame came in 1974, but was quickly stayed.

[23] Supra note 21

[24] 39 Fed. Reg. 27317; correction 39 Fed. Reg. 34520 (1974).

The regulation that the FDA issued approved aspartame for use as a sweetener in the following foods:

a) Dry, free-flowing sugar substitutes for table use (not to include use in cooking) in package units, not to exceed the sweetening equivalent of 2 teaspoonfuls of sugar.
b) Sugar substitute tablets for sweetening hot beverages, including coffee and tea.
c) Cold breakfast cereals.
d) Chewing gum.
e) Dry bases for: i) beverages; ii) instant coffee and tea; iii) gelatins, puddings and fillings; and iv) dairy products and toppings. In chewing gum, aspartame was also approved for use as a flavor enhancer in addition to use as a sweetener.[25]

The Federal Register Notice concerning the regulation stated that of principal importance to the Commissioner's judgement of aspartame's safety were two long-term studies of aspartame using rats and dogs. The notice noted that these two studies revealed a no-effect level (the maximum level of exposure without a statistically significant adverse effect) for aspartame at least as high as two grams per kilogram of body weight. The notice also pointed out that by using a 100-fold safety factor and applying the no effect level to the average 60-kilogram (about 132 pounds) man, an acceptable intake level would be at least 1.2 grams of aspartame per day. The general regulation provides that a safety factor of 100 to 1 should be used when applying animal experimentation data to man.[26] Based on the restrictions imposed by its regulation on aspartame's use, the FDA calculated that an individual's daily consumption level would not likely exceed 1.3-1.7 grams per day. These calculations were based on the intake of the following foods sweetened with aspartame shown in the following table. Because

[25] 46 Fed. Reg. 38285; Codified in 21 CFR 172.804.
[26] 21 C.F.R. 121.5

of the conservative nature of the no-effect level derived from the animal tests and the 100-fold safety factor employed in relating the tests to man, the FDA believed that the uses approved by its regulation constituted an acceptable daily intake of aspartame with a sufficient margin of safety.[27]

Aspartame Approved Use	FDA's Estimate of Daily Intake (grams)	
	Low	High
As a table top sweetener in coffee or tea with an estimated.083 grams of aspartame per 8-ounce cup– drink 3 cups a day	.250	.250
In a dry beverage mix with .725 grams of aspartame per quart– drink 1 quart	a/.650	.725
In a gelatin dessert mix with 1.04 grams of aspartame per 2 cups dessert or.26 grams of aspartame per 1/2 cup serving –eat 1 to 2 servings	.260	.520
In a whipped topping with.15 grams of aspartame per 2 cups topping, or.038 grams of aspartame per 1/2 cup serving –eat 1 to 2 servings	.038	.075
In a presweetened breakfast cereal with.083 Grams of aspartame per 1-ounce cereal –eat 1 to 1-1/2 ounces	.083	.125
Total	1.281	1.695

a/ To arrive at the low estimate, FDA assumed there would be 1.3 grams of aspartame in 2 quarts of dry beverage mix or.650 per quart.

Despite the somewhat limited approval that was granted at this stage, the FDA's regulation included three conditions for the use of aspartame regarding final product labeling. First, the label of any food containing aspartame was re-

[27]GAO, Regulation of the Food Additive Aspartame, Rep. No. MWD-76-111 (April 8, 1976)

quired to bear the following statement: PHENYLKETONURICS: CONTAINS PHENYLALANINE. This requirement was designed to alert persons who, because of specific health reasons, need to restrict carefully their phenylalanine intake. Second, when aspartame was to be used as a tabletop sweetener, its label was required to bear instructions not to use aspartame in cooking or baking. This is because aspartame breaks down when exposed to prolonged heat, resulting in a loss of sweetness. Finally, the regulation required that if a food containing aspartame purported to be, or was represented, for special dietary uses, as might be expected of a low calorie product, it was required to be labeled in compliance with FDA's special dietary foods regulations.[28]

VI. The First Obstacle

Although the FDA approved Searle's food additive petition for aspartame in 1974, many hurdles lay ahead.[29] Once the Commissioner had publicly concluded that the evaluation of the data in the food additive petition for aspartame, which included approximately 150 studies and other relevant material, justified amending the food additive regulations to provide for the same use of aspartame under specified conditions, Searle's troubles began.

The first obstacle that Searle met came from Dr. John W. Olney, M.D., psychiatrist and Professor of Psychiatry at Washington University of St. Louis, and James S. Turner, author of The Chemical Feast, and co-founder of the Center for Study of Responsive Law.[30] Olney and Turner formally objected to the reg-

[28]Supra note 25
[29]39 Fed. Reg. 27,137 (1974)
[30]See Smyth, The FDA's Public Board of Inquiry and the Aspartame Decision, 1982-1983,

ulation that authorized the marketing of aspartame as a sweetener in foods.[31] Dr. Olney had performed research in animals regarding the toxic effects on the brain of certain Amino acids, including asparatic acid. Both parties objected to the use of aspartame in foods, especially those consumed by children. They asserted that aspartame might cause brain damage resulting in mental retardation, endocrine dysfunction, or both. Turner and Olney also argued that aspartame could be dangerous to persons with the genetic disorder phenylketonuria (PKU), a disorder that prevents the metabolism of phenylalanine, one of the amino acids in aspartame.[32]

These along with other concerns and allegations necessitated a FDA hearing provided for by 21 U. S. C. 348.[33] Instead of having a full evidentiary hearing, which was customary at the time, the parties waived their right and accepted a hearing before a public board of inquiry instead.[34] This was the first time that the FDA had ever used this type of hearing in place of a full evidentiary hearing. Searle agreed to delay marketing of aspartame temporarily, pending resolution of the safety questions.[35]

Dr. Olney, Searle and the Bureau of Foods all submitted lists of nominees for the public board.[36] The acting commissioner then selected a panel that included: Walle J. H. Nauta, M.D., Ph.D., Institute Professor, Department of

58 Ind. L.J.633.

[31]Supra note 24

[32][1981 New Matters] FOOD DRUG COSM. L. REP. (CCH) ([In the matter of] Aspartame) ¶38, 124; 46 Fed. Reg. 38,285 (1981) (Commissioner's Final Decision). [Hereinafter cited as Final Decision].

[33]Id.

[34]40 Fed. Reg. 56,907 (1975).

[35]Final Decision Supra note 3 at 38,285.

[36]Final Decision, supra note 3, at 38, 736; 46 Fed. Reg. 38,286.

Psychology and Brain Science, Massachusetts Institute of Technology; Peter J. Lampert, M.D., Professor and Chairman, Department of Pathology, University of California (San Diego); and Vernon R. Young, Ph.D. Professor of Nutritional Biochemistry, Department of Nutrition and Food Science, Massachusetts Institute of Technology. Dr. Nauta was the Chairman of the board.[37]

Before the board could hold a hearing regarding the safety of aspartame as a food additive in response to Olney and Turner's allegations, however, Searle's quest for aspartame approval hit another snag. Preliminary results from an audit of the records of certain animal studies conducted by or for Searle, including studies on aspartame, indicated a need for a comprehensive review of the authenticity of the aspartame research data. Apparently, the audit of Searle's clinical methods revealed sloppy research, including some research that was being done on aspartame.[38] The negative publicity that surrounded Searle's clinical methods bolstered consumer criticism of aspartame, and further clouded the safety issues that had not yet been addressed. Alexander Schmidt, then FDA commissioner, noted that the FDA audit revealed different discrepancies of different kinds.[39] Pursuant to 21 U. S. C. 348(e), FDA formally stayed the regulation authorizing the marketing of aspartame.[40]

Once the regulation that approved the use of aspartame was stayed, and a task force was convened, the FDA began to consider methods of authenticating the studies previously submitted by Searle.[41] The FDA decided to authenticate the

[37] Id.
[38] Wall St. J., July 21, 1975, at 4, col. 3.
[39] Id., Dec. 5, 1975, at 8, col. 3.
[40] 40 Fed. Reg. 56907.
[41] 131 Cong. Rec. S10800-01 (Publication page references not available).

study through the use of a non-government panel of experts that they required Searle to fund.[42] With the knowledge and approval of Searle, the aspartame data in fifteen pivotal studies was thoroughly audited to determine its authenticity. According to FDA records, the FDA audited three of these studies, and twelve of the studies were audited by the Universities Associated for Research and Education in Pathology, Inc. (UAREP). The audit took over two years to complete. Upon its conclusion, UAREP had determined that the studies were authentic. FDA agreed with UAREP that those twelve studies, as well as the three that were reviewed by the FDA were authentic.[43]

Former FDA official, M. Adrian Gross, a veterinarian and pathologist, led the task force set up by the FDA in July of 1975 to investigate the validity of Searle animal studies on aspartame and Aldactone. Aldactone was a widely prescribed drug for high a blood pressure and the only aforementioned Searle product that was eventually examined by the grand jury. Although the task force eventually concluded that the studies provided valid conclusions with regard to the safety of aspartame, the analysis of these studies was not an easy task and the results were not entirely clear.

VII. Analyzing the Data: The 52-Week Toxicity Study in the Infant Monkey

In 1969 Searle commenced a study of the side effects of aspartame as com-

[42] Id.
[43] 46 Fed. Reg. 38285 at 38286

pared with those of phenylalanine. Searle chose Dr. Harry A. Waisman, a leading researcher associated with the University of Wisconsin Regional Primate Center who had published extensively on the toxicity of phenylalanine, to lead the research effort. Dr. Waisman's earlier writings established that phenylalanine is capable of producing brain damage in Rhesus monkeys.[44] Although Dr. Waisman seemed to be quite capable of completing the proposed research, things did not turn out as expected. The study was initiated on January 15, 1971. Unfortunately, Dr. Waisman died a little over a year after the experiments began. The study was terminated about a month later on or about April 25, 1971. Searle then submitted its report to the FDA on October 10, 1972. Analysis seems to indicate that the results of the study were falsely deemed conclusive when in reality, many questions remained.

The study included seven newborn Rhesus monkeys who were fed a diet that included aspartame. The study did not have a control group of newborn monkeys who were not fed aspartame. According to a Searle document that was drafted after the initiation of the study, the monkeys were to be kept on a diet with aspartame for one year before being returned to a basal diet. They were then to be subjected to behavioral and learning tests; and finally sacrificed and necropsied for the preparation of tissue slides to be reviewed microscopically for alteration.[45] Of the seven test monkeys, one died after 300 days; four were continually fed a diet containing aspartame for 365 days as planned; and administration of aspartame for two others was ceased after 200 days. According

[44]Supra note 35
[45]Id.

to the records, no behavioral or learning tests were performed. Only the one monkey that died during the test was necropsied. It is clear that the test results are not conclusive as to the side effects of aspartame. Searle has since referred to the study as a pilot experiment, and acknowledged its evident shortcomings.[46] Despite Searle's subsequent disparagement of the study, according to the Department of Health, Education and Welfare, the company provided this inadequate study to the FDA in order to expedite the approval of aspartame. The Department's memoranda states that [t]he report to FDA is drafted in a manner which covers up the admitted inadequacy of the design, control and documentation of the study. However, when Searle is accused or (sic) representing this study for far more than it was (sic), it denies almost all knowledge of or involvement with its initiation, design or performance... [47] The Department goes on to accuse Searle of many deviations from standard research practice. The accusations include concealing the fact that the infant monkeys were not suitable for the study, and falsely stating that the necropsy data on the one non-surviving monkey was lost do to similar reasons, namely confusion after Dr. Waisman's death.[48] Whether or not these allegations proved to be true is unclear. It is quite apparent, however, that by the accounts of all parties, the study was in many ways inadequate and incomplete.

VIII. Analyzing the Data: the 46-Week Hamster Study

Another study that engendered severe criticism from the Department of

[46] Id.
[47] Id.
[48] Id.

Health Education and Welfare (the Department) was the 46- week toxicity study performed on the hamster. Although the data appears to be faulty and incomplete, Searle argues that any falsehood in the study is not material to the appraisal of the safety of aspartame.[49]

The Department's report provides a chronology of the numerous problems they allege that the study encountered. It seems that many of these contentions are uncontested by Searle though the company does not agree that the data is therefore useless. The hamster study was intended to be a 104 -week toxicity study on aspartame in the hamster. Unfortunately, the study was terminated after 46 weeks due to a high mortality rate in both control and treated animals that was not ascribed to aspartame.

In addition to criticizing the study as a whole, the Department alleges that Searle violated Title 18, Section 1001by falsifying data. The report alleges that the testing ran into problems and instead of correcting them, Searle covered the problem up. Blood from certain animals in the study was collected for hematology testing and blood chemistry at the scheduled 26 - week interval. At that time, samples were drawn and the appropriate testing was performed. The testing included six different tests. Out of the six, the results for the serum glucose (blood sugar) appear problematic. Apparently the technicians had methodological problems with that test. According to the Department, Searle did not correct this problem until about 12 weeks later and by that time approximately 30 percent of the hamsters had died.[50]

[49]Id. at 173
[50]Id.

At the 38^{th} week of the study, other hamsters were taken as substitutes from the same feeding groups and blood was collected from them. According to the Department, Searle substituted the glucose values of the new animals' blood as being those of tests run at 26 weeks on blood samples from the original animals. Hence, the Department concluded that glucose values presented in the study that were supposed to represent one set of animals really represented another.[51] Subsequently, Searle has admitted that the report contains this false information, but argues that the inclusion of false data did not result from willful conduct or any intentional act. Furthermore, Searle has argued that this inaccuracy is not material to the appraisal of the safety of aspartame and that there was no motive for any intentional misrepresentation regarding the glucose values of the hamsters.[52] It appears that the question of glucose levels was non-controversial with regard to the results of the study. Even the Department has acknowledged that the substituted data may not have been material to a determination of the ultimate safety of aspartame.[53]

IX. Task Force's Conclusions

After analyzing the data and conclusions of Searle's aspartame and Aldactone studies, the task force concluded that the data was inconclusive and more research was necessary. Adrian Gross, former FDA investigator and scientist, presented the comments of the task force. In his statement, Gross noted that the conclusions of the task force in fact represented an FDA institutional view

[51] Id.
[52] Id.
[53] Id. at 174.

which Commissioner Schmidt had agreed upon in 1976.[54] The comments made by Gross regarding the task force's conclusions centered around three main topics as articulated by Gross:

(a) The studies carried out by Searle to establish the safety of aspartame; this is a conclusion that would follow the FDA's own extensive investigations into the acceptability of experimental studies conducted by and for Searle...
(b) Their serious shortcomings notwithstanding, at least on of those studies has established beyond any reasonable doubt that aspartame is capable of inducing rain tumors in experimental animals and that this predisposition of it is of extremely high significance...
(c) I would view the Acceptable Daily Intake (ADI) set by the FDA for aspartame (5mgm/kgm body weight/day) as totally unwarranted and extremely high in that it can be associated with completely unacceptable risks as far as the induction of such tumors are concerned... [55]

In conclusion, Gross, in his statement on behalf of he task force said, At the heart of FDA's regulatory process is its ability to rely upon the basic safety data submitted by sponsors of regulated products. Our investigation clearly demonstrates that, in the G. D. Searle Co., we have no basis for such reliance now.[56] Furthermore, Gross later stated that Searle's own studies established beyond a reasonable doubt that aspartame is capable of inducing brain tumors in experimental animals.[57] In July of 1975, even the FDA Commissioner concluded that the integrity of certain animal studies conducted by Searle were questionable.[58]

Though it did not necessarily implicate the safety of aspartame as a food additive, the task force's audit renewed concern about the additive's safety. On January 10, 1977, the Department of Health, Education and Welfare submitted a

[54]Id at 180.
[55]Id.
[56]Wash. Post., Feb. 7, 1986, B9
[57]Id.
[58]Id.

detailed request to Samuel K. Skinner, U.S. Attorney for the Northern District of Illinois for a Grand Jury investigation. The Department urged Skinner to convene a Grand jury investigation based on apparent violation of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 331(e), and the False Reports to the Government Act, 18 U.S.C. 1001 by G. D. Searle and Company, including three of its responsible officers. The request alleged that these parties willfully and knowingly failed to make reports to the Food and Drug Administration required by the Act, 21 U. S. C. 355(I). Furthermore, it alleged that Searle concealed material facts and made false statements in reports of animal studies conducted to establish the safety of the drug Aldactone and the food additive Aspartame.[59]

X. Senator Metzenbaum's 1977 Report

Prior to the request for an investigation into the actions of Searle and its top officers, Senator Metzenbaum's staff had produced an extensive and somewhat similar request for further investigation of Searle and the safety of aspartame. In raising questions about the clinical methods that Searle employed to verify the safety of aspartame as a food additive, however, the report gets mired in accusations of fraud. The authors seem to lose sight of the important question of whether aspartame is indeed safe for human consumption. The report focuses on Searle's strategies with regard to marketing and seeking approval from the FDA instead of true safety concerns. For example, in discussing two of Searle's clinical studies, the 46-week toxicity study in the hamster and the 52-week toxicity study in the infant monkey, the report states:

[59] 131 Cong. Rec. S10800-01

In considering the extent to which the reports [of the monkey and hamster studies] were written to convey impressions more favorable than the underlying data would support, reference should be make to the memorandum of December 28, 1970, from Mr. Helling of Searle to, among others, Drs. — [omitted in original], entitled Food and Drug Sweetener Strategy. In that memorandum, Searle commits itself to obtaining favorable review by FDA personnel by seeking to develop in them a subconscious spirit of participation in the Searle studies.[60]

Although interesting, and possibly even relevant as to the moral character of Searle employees and company strategy, it is not of great importance with regard to the safety of aspartame.

XI. The Board's Inquiry

In response to Senator Metzenbaum's report and the request of the task force, in June of 1979, FDA announced a hearing and set up a public board of inquiry to look into the safety of aspartame as a food additive.[61] The board, which had been set up previously by FDA with the suggestions of Dr. John Olney, Searle, and the Bureau of foods, was to look into several issues, including:

1. Whether the ingestion of aspartame, whether alone or together with glutamate, poses a risk of contributing to mental retardation, brain damage, or undesirable effects on neuroendocrine regulatory systems.

2. Whether the ingestion of aspartame may induce brain neoplasms (tumors) in the rat, and

3. Based on the answers to the above questions, (a) should aspartame be allowed for use in foods, or instead should the approval of aspartame be withdrawn? (b) If aspartame is allowed for use in foods, i.e., if its approval is not

[60] Id. at 174.
[61] 45 Fed. Reg. 31716; 45 Fed. Reg. 2908.

withdrawn, what conditions of use and labeling and label statements should be required, if any?[62]

The notice specifies that the board's decision regarding these issues would become final unless the parties filed exceptions.[63] If exceptions were filed, the commissioner was to review the decision and make his own determinations.[64]

The board had its first meetings on January 30, 31 and February 1, 1980.[65] On the first question, whether the ingestion of aspartame poses a risk of contributing to mental retardation, brain damage, or undesirable effects on the neuroendocrine regulatory system, the board found that aspartame did not pose an increased risk of brain or endocrine dysfunction.[66]

On the second issue, however, the board ruled that aspartame might cause cancer.[67] In response to the multifaceted third issue, the board vacated the stay on the aspartame regulation and revoked the regulation. The board had concluded that aspartame should not be on the market until further safety testing had ruled out potentially dangerous side effects.[68]

The board's consideration had a decidedly narrow scope. It included only three studies dealing with aspartame's propensity to cause tumor formation. The reason for this was that these were the only relevant studies that Searle reported.[69] Out of the three studies the board reviewed, two were found to be

[62]Final Decision, supra note 13, at 38,737; 46 Fed. Reg. 38,286.
[63]44 Fed. Reg. 31, 716,31,718 (1979).
[64]Id.
[65]Final Decision, supra note 13, at 38,737, Fed. Reg. 38,286.
[66]Initial Decision, supra note 13 a 38,346.
[67]Id. at 38,349.
[68]Id.
[69]Id. at 38,346.

problematic. The first study raised questions because it indicated a high rate of death amongst young test rats and a possible dose-effect relationship that indicated aspartame may cause cancer.[70] The second study troubled the board for several reasons. First of all, it used an apparently insufficient number of experimental animals. And secondly, the control group had a higher incidence of brain tumors than the board though normal.[71]

In conclusion, the board determined that it was difficult, if not impossible, to judge aspartame's possible oncogenity on the basis of the data provided by Searle.[72] The board acknowledged that the results of the study might have been misleading because the test animals were fed enough aspartame to cause amino acid imbalance. Therefore the study could have produced results that would not have been reproduced as a symptom of human intake of aspartame. However, the board decided that on the record before it, an oncogenic effect from aspartame could not be ruled out entirely.[73]

Surprisingly, the FDA commissioner only differed significantly on the evidence pertaining to carcinogenicity.[74] He took issue with the way the board evaluated the data for the two aforementioned studies, however.[75] In the first study he found that the board had made an error in their calculation of the statistical analysis,[76] and had made factual errors in noting age at death for certain lab rats.[77] The commissioner noted that when the errors were corrected, the study

[70]Id. at 38,347.
[71]Id. at 38,348.
[72]Id.
[73]Id. at 38,348-49.
[74]Final Decision, supra note 13, at 38,752-64; 46 Fed. Reg. 38,294-301.
[75]Id. at 38,752-64
[76]Id. at 38,761; Fed. Reg. 38,299-300.
[77]Id. at 38,761; Fed. Reg. 38,300.

was found not to indicate carcinogenicity.[78] In the second study, the commissioner found that the board had set a normal rate of tumor incidence much too low,[79] thereby incorrectly dismissing concern over the study size.[80]

XII. The Commissioner's Reversal

The board's decision against aspartame approval and its call for more safety testing elicited numerous protests. All parties filed exceptions.[81] Since exceptions were filed, the Commissioner had the responsibility of reviewing the findings and making a decision that could contradict the task forces' conclusions. Searle immediately took further action by issuing press releases contesting the board's determinations.[82]

On July 24, 1981, FDA Commissioner, Arthur Hull Hayes Jr. ruled that the sweetener, aspartame, is safe.[83] Despite the board's finding Commissioner Hayes approved the additive's use in food. The FDA granted broad approval for aspartame's use as a tabletop sugar substitute, as a tablet or as an additive in cereals, drink mixes, instant coffee and tea, gelatins, puddings, fillings, dairy products and toppings.[84] However, it was not approved for use in soft drinks at that time because Searle had not sought such approval.

[78]Id. at 38,764; 46 Fed. Reg. 38,301.
[79]Id at 38,758; 46 Fed. Reg. 38,298.
[80]Id at 38,762-63; Fed. Reg. 38,300.
[81]Final Decision, supra note 13, at 38,737; 46 Fed. Reg. 38,286.
[82][1980 New Matters] FOOD DRUG COSM. L. REP. (CCH) ¶ 40,789.
[83]46 Fed. Reg. 3828; 46 Fed. Reg. 50947.
[84]Id.

In discussion of his decision to overrule the board that urged long-term study to make sure that aspartame did not cause brain tumors, the Commissioner noted what he believed to be errors that the board made in their inquiry which led them to conclude that more research was necessary. Commissioner Hayes also cited a study by Ajinomoto Co., Inc., the Japanese licensee of Searle's aspartame patent that affirmed aspartame's safety. The study was released after the board had published its decision against aspartame approval. Hayes justified including the study in his consideration of the evidence despite its late availability by noting that the proceeding was intended to be a scientific inquiry using all available evidence.[85]

One safety concern that FDA did address further was the issue of aspartame consumption by persons with the hereditary disease phenylketonuria or PKU. Individuals with PKU must avoid protein foods that contain phenylalanine, one of aspartame's principle components. Accordingly, FDA established a requirement that food makers put a warning label on packages of food containing aspartame to give notice to those with PKU. FDA also planned to require manufacturers to monitor aspartame consumption levels.[86] This safety requirement was present in the original regulation authorizing aspartame to be used as a sweetener in foods.[87]

XIII. FDA Continues Approving Aspartame for Additional Uses Despite Pressure from Consumer Groups

Once aspartame had been officially sanctioned for use as a sweetener in a

[85] Final Decision, supra note 13, at 38,753-54; 46 Fed. Reg. 38,295.
[86] 46 Fed. Reg. 3828; 46 Fed. Reg. 50947.
[87] 39 Fed. Reg. 27317; correction 39 Fed. Reg. 34520

limited number of foods, Searle began filing additional petitions for approval and the FDA responded by granting them despite the controversy that still surrounded aspartame. In 1983 the FDA proposed to declare aspartame suitable for use as an inactive ingredient in human drug products provided that the label and labeling of the drug products declared the presence and amount of the component phenylalanine that was contained in the drug product per dose unit.[88] The FDA made this proposal in response to inquiries from drug manufacturers. In 1987, the FDA issued a final rule declaring that aspartame, when used at a level no higher than reasonably required to perform its intended technical function, is safe for use as an inactive ingredient in human drug products.[89]

XIV. The Approval Process Continues and the Soft-Drink Industry Adjusts

Although aspartame would eventually prove to be a catalyst for major increases in diet soft-drink sales, at the time of its approval, the soft-drink industry was resistant to making the change from saccharine, which had been the dominant non-sugar sweetener, to the newer aspartame.[90] Ironically, the industry that has arguably benefited the most from the aspartame tried to convince the FDA to delay its use in diet sodas.[91] In the early eighties, after aspartame had been approved for use in food and pending its approval for soft drink use, the National Soft Drink Association (NSDA), which at the time represented the nation's major soft drink makers, raised health and quality control concerns about

[88] 48 Fed. Reg. 54993
[89] 52 Fed. Reg. 2108; 52 Fed. Reg. 12152
[90] Wash Post, July 14, 1983, at A1
[91] Id.

the sweetener.[92] The NSDA wrote a letter to the FDA requesting the delay of aspartame's approval. The letter expressed the industry's doubts about aspartame's ability to keep its sweetness in high temperatures and over extended periods of time.[93]

Industry sources and analysts saw different reasons for the NSDA objections. Some said that the industry was not financially prepared for the change and that the NSDA wanted to stall the FDA approval until there would be less risk of economic upheaval. Others speculated that the two major soft drink companies, Coca-Cola Co. and PepsiCo Inc., were afraid that rival 7-Up would use the new sweetener to its advantage in extending its successful no-artificial-ingredients, no-caffeine campaign before they were ready to put forth competing products.[94] There was also speculation that the industry wanted to postpone the approval of aspartame until the market-mayhem caused by the introduction of Diet Coke and numerous other caffeine-free soft drinks had settled down.[95]

Meanwhile, the same soft drink makers were scrambling to buy large quantities of aspartame in case its approval could not be delayed.[96] Since the sweetener was still in relatively short supply and only manufactured by Searle, a fear-driven competition for the additive began. Coca-Cola Co. and PepsiCo Inc. were apparently afraid that 7-Up would corner the aspartame-sweetened

[92] Id.
[93] Id.
[94] Id.
[95] Id.
[96] Id.

soft drink market unless Searle had produced enough aspartame to satisfy the demand.[97] Robert Shapiro, the then head of the Searle division that made aspartame for commercial use, stated that in his discussions with soft-drink companies there had been no reluctance on their part to put aspartame into their diet soft drinks. There had been anything but that, he said.[98] It seems likely that while none of the soft-drink companies wanted to be left behind if aspartame were to be a market hit, they were concerned about the trouble it could bring in light of the history of cyclamates and saccharin.

XV. Aspartame's Market Share of the Low Calorie Sweetener Industry Explodes

As predicted, the FDA approved aspartame for use in soft drinks in July of 1983.[99] In response to soft-drink industry's safety concerns, FDA said that it was satisfied that aspartame would not cause quality-control problems for soft-drink makers or health problems for users. According to one FDA official, aspartame was, at that time, the most extensively tested food additive FDA had ever approved.[100]

Aspartame's initial introduction to the market in the United States came in 1981; in 1984, the year after aspartame was approved for use in soft drinks, Searle sold $600 million worth of aspartame, on which it held the exclusive United States Patent.[101] Searle began using the trade names Equal and NutraSweet to market the product. Coca-Cola's consumer poling indicated that a

[97] Id.
[98] Id.
[99] 48 Fed. Reg. 31376
[100] Wash Post, July 14, 1983, at A1
[101] NY TIMES, July 3, 1985, A Sweetener's Effects: New Questions Raised by Marian Burros

significant number of diet soda drinkers and infrequent soda drinkers would be attracted to Coke's new product, Diet Coke with NutraSweet. This data turned out to be accurate as aspartame-sweetened Diet Coke became increasingly popular.[102] In addition to its wide consumer appeal, aspartame also received a positive response from government officials. Dr. Richard Ronk, then deputy director of the Bureau of Foods for the Food and Drug Administration called it [T]he ideal food additive, noting that aspartame has one-tenth of a calorie in the amount needed to replace one teaspoon of sugar (18 calories), does not cause cavities, and is supposedly safer than saccharine.[103]

XVI. Searle's Business (as Affected by the Market for Aspartame)

As market demand for aspartame grew, Searle had an increased need for the ingredients that make up the additive. In order to quickly and efficiently meet the demand, Searle had to adjust its business plan. Instead of continuing to rely on the Japanese supplier of L-Phenylalanine, one of the key components of aspartame, Searle officials began looking for new ways to obtain it. They also sought new ways to obtain L-asparatic acid, the amino acid that is mixed with L-Phenylalanine in roughly equal portions to produce aspartame. Searle sought a manufacturer of the ingredients that could avoid the relatively expensive fermenting process used by the Japanese company to create L-Phenylalanine.

In August of 1983, Searle entered into a contract with Genex Corp., a biotechnology company, to buy L-Phenylalanine produced through a new method. Genex

[102]Wash Post, August 28, 1983, at M1
[103]Wash Post, July 23, 1981, at E1

asserted that through an innovative bio-reactor technology, the company would be able to produce the chemical faster and at a lower cost than it had been produced in the past.[104] The agreement also granted Searle a license and rights of access to some areas of Genex technology that involved sweeteners other than aspartame.[105] It seemed that the contract would provide both companies with opportunities that they had eagerly sought out.

In 1993, NutraSweet accounted for 35 percent of Searle's sales. Projections for 1984 indicated that NutraSweet sales would provide 50 to 55 percent of total sales.[106] It was the middle of 1984 when the heirs of the founder of G. D. Searle & Co. decided that it would be in their best interests to diversify their holdings; even if this proposition would lead to the sale of the company.[107] In a statement for the press, the family members, who include Daniel Searle, William Searle, and Suzanne Dixon, said that they have been delighted at the progress that the company has made in recent years and recognize the potential for very substantial growth in the future. But they added that having such a large portion of the family's financial interests tied up in one enterprise prompted them to consider diversification.[108] It is unclear whether this sudden desire for diversification reflected concern over the fate of NutraSweet, or just cautious financial planning. Despite the phenomenal reported earnings of $151.2 million in 1983, the NutraSweet controversy was far from over.[109]

[104]Wash Post, August 16, 1983, at D7
[105]Id.
[106]Wash Post, September 28, 1984, at D1
[107]Id.
[108]Id.
[109]Id.

In June of 1985, Searle made headlines once more, though not directly on account of aspartame. In its search for corporate efficiency, Searle executives decided not to renew its contract with Genex Corp., the company that had produced a component of aspartame for Searle. At Genex's annual shareholder's meeting, which took place on October 31, Genex Chairman J. Leslie Glick announced that Searle was planning to let Genex's contract expire that year. The visceral reaction Genex had was due in part to its heavy investment in a manufacturing plant to produce the aspartame component, L-Phenylalanine in accordance with the Searle contract.

Although Genex spokeswoman, Shellie Roth said that Searle's decision was not a life-threatening blow, Genex's only other commercial product was an enzyme-based drain cleaner which, according to the company, produced negligible sales in 1984.[110] Furthermore, Genex had seen its revenue and losses both swell in 1984 with the success of its aspartame ingredient and the costs of starting up a manufacturing plant for the ingredient. The company's revenue tripled compared with the prior year, but reported losses increased to $7.4 million in 1984 from $5.4 million in 1983 due largely to start up costs of the manufacturing plant.[111] Searle provided little public response to Genex's complaints about the contract expiration.

Within a year, Genex had taken action against Searle by filing a $40 million suit alleging fraud, concealment and violations of federal securities, anti-trust and anti-racketeering laws. Though Searle remained mute in the press, its rep-

[110]Wash Post, June 14, 1985, at F1
[111]Id.

utation again took a beating. The plaintiffs argued that Genex should be paid $40 million in actual damages, in addition to punitive damages at least equal to the actual damages and treble damages because of violations of anti-trust and other federal laws.[112] Genex alleged that Searle's refusal to renew Genex's contract had a devastating impact on Genex after Genex had invested approximately $17.5 million in a new manufacturing plant designed for the production of L-Phenylalanine, a product Genex produced for Searle.[113] The lawsuit also alleged that Searle made material and false representations leading Genex to believe that Searle wanted a long-term supply relationship, and thereby induced Genex into dramatically increasing its production capabilities.[114]

Although the Genex suit was eventually settled out of court, Searle's reputation took another blow in the news. It is likely that Searle's negative reputation contributed in some way to consumer fears of aspartame. Despite reports that in the settlement, Searle only paid Genex a nominal amount, and Searle dropped a claim that Genex overcharged it $1.35 million, Searle's payment signaled an acceptance of wrongdoing.[115] It is difficult to tell what consumer reaction to this settlement was; it is doubtful that there was great consumer interest, but the settlement contributed in some way to Searle's increasingly dim reputation amongst consumers.

XVII. Senator Metzenbaum's 1985 Bill

[112]Wash Post, October 10, 1985, at E3
[113]Id.
[114]Id.
[115]Wash Post, July 24, 1987, at F2

The ongoing controversy surrounding Searle and the manufacture and sale of aspartame is apparent in a bill introduced in Congress in 1985. Senator Metzenbaum, a long time opponent to aspartame's approval, introduced a bill called the Aspartame Safety Act of 1985.[116] This bill was intended to provide consumers with information concerning the use of products containing aspartame, to provide for the conduct of studies to determine the health effects of using products containing aspartame, and for other purposes. In his address to Congress, Senator Metzenbaum stated that this bill contained the absolute minimum that Congress needs to do in order to protect the health and safety of the 100 million American consumers who are using this chemical sweetener under its better-known brand name of NutraSweet.[117]

Senator Metzenbaum's concerns seem to stem from what he referred to as the troubling circumstances under which the FDA approved aspartame.[118] That issue was in his mind exacerbated by the quantity of the product being consumed. The Senator noted that in 1984, Americans consumed over 7 million pounds of aspartame, which is equivalent to 1.4 billion pounds of sugar. He went on to predict that in 1985 Americans would consume over 20 billion cans of diet soft drinks, the vast majority of which are sweetened with 100 percent NutraSweet.[119] Despite the dubious accuracy of these statistics, it is clear that Senator Metzenbaum's desire to find answers to any safety questions about aspartame was echoed by a large number of American consumers.

[116] 131 Cong. Rec. S10800-01
[117] Id. at 134.
[118] Id.
[119] Id.

Senator Metzenbaum's bill centered on the problematic nature of Searle's research methods and the nature of the FDA, which he called a mere shadow of what that agency used to be.[120] His doubt about the accuracy of the aspartame safety tests and the ability of the FDA to sufficiently judge the safety of aspartame are highly apparent, but he does not provide any factual basis for doubt of the FDA's decision to approve the product. In fact, it seems that he is advocating the same kind of review of the tests that had already occurred by that time.

Just one year prior to the introduction of the Aspartame Safety Act of 1985, the federal Center for Disease Control (CDC) had completed a review of aspartame. After finishing the review, researchers concluded that there was no evidence of serious, widespread adverse health consequences among those who consumed the sweetener in diet soft drinks and other products.[121] The four-month long study included approximately 600 participants. It looked at complaints noted by consumers, many of whom reported more than one symptom. Two-thirds of the complaints involved nervous system or behavioral problems such as headaches, dizziness, and mood changes. One-fourth of the complaints reported included gastrointestinal symptoms, and 15 percent reported included allergic-type reactions.[122]

The CDC scientists concluded that there was no particular pattern in the reported symptoms. The analysis of nearly 600 complaints from people who consumed aspartame demonstrated that a wide variety of complaints... [were] gen-

[120] Id.
[121] Wash Post November 2, 1984, A18.
[122] Id.

erally of a mild nature.[123] The CDC review noted that most of the symptoms were so common that it was impossible to tell whether the complaints were unrelated to the sweetener or resulted, at least in part, from some individuals' unusual sensitivity to the product.[124]

The CDC's conclusions should have provided consumers with some re-assurance, but if they did, it was not widespread. Complaints of aspartame-related illness continued along with the controversy. In a letter to then FDA Commissioner, Frank Young, Community Nutrition Institute criticized the FDA and the CDC's report on aspartame.[125] The letter alleged that no serious effort had been made to determine the actual extent of consumer reactions to NutraSweet, or to analyze and categorize the complaints.[126] It also accused the FDA of not inviting physicians to send in reports of complaints and therefore making it easy for FDA to claim that the complaints about aspartame could be explained by the placebo effect. The placebo theory being that whenever any new product is introduced, the public seizes upon it as the source of their ailment.

Within a year of publication of the CDC's report, Senator Metzenbaum's bill, the Aspartame Safety Act of 1985, was discussed in the Senate. The bill included a number of mandates that the Senator felt would increase the likelihood that aspartame was being used safely. In addition to additional independent testing of aspartame, the bill required product labels with specific amounts of aspartame per serving products contained. This was intended to inform consumers

[123]Id.
[124]Id.
[125]131 Cong. Rec. S10800-01 at 198.
[126]Id.

how much aspartame they were consuming. This requirement was also intended for physicians who were treating individuals who felt that they had aspartame-related side effects since such side effects were thought to be dose related.

The proposed labeling requirements also included a statement regarding the maximum allowable daily intake established by the FDA. There was also a required advisory statement on the label that would inform consumers that aspartame is not intended for infant feeding.[127] Finally, Senator Metzenbaum's bill proposed to establish a Clinical Adverse Reaction Committee within the FDA. This committee was intended to address the problems of consumers who felt that they had experienced negative effects from aspartame and investigate their claims.[128] Despite the passionate attempt on the part of Senator Metzenbaum and a group of consumer advocates, the bill never became law; the controversy surrounding aspartame did not diminish.

XVIII. Community Nutrition Institute Files Suit

In fact, the controversy was again heating up. On the day that Senator Metzenbaum introduced the Aspartame Safety Act of 1985, a national organization, known as the Aspartame Victims and Their Friends, Inc. was launched at a Washington, D.C. press conference. The organization, which was affiliated with the Aspartame Resource Center of the Community Nutrition Institute, a Washington-based consumer group, set up headquarters in Ocala, Florida. At that press conference one of the founding members of the group announced that

[127]Supra note 115 at 137.
[128]Id.

a lawsuit would be filed against Searle with regard to the manufacture of aspartame. The group also announced that it would operate a national telephone hotline for victims of bad reactions to aspartame.[129] The Executive Director of the Community Nutrition Institute, Ron Leonard, said that the new organization would provide a link between aspartame users who have experienced adverse reactions and have suffered injury and economic loss.[130]

On December 23, 1983, Community Nutrition Institute (CNI) filed a complaint requesting that the Court enter an order directing the FDA to conduct public hearings to determine the safety of using the food additive aspartame in carbonated beverages.[131] CNI's complaint also sought an order staying the FDA's regulation permitting the addition of aspartame to carbonated beverages until such time as the FDA would convene and conclude the requested public hearings. On August 8, 1983, the plaintiffs had previously filed with the FDA similar requests for a hearing and a stay, along with objections on the merits to the approval of aspartame's use in carbonated beverages.

On January 24, 1984, CNI filed a motion for a temporary restraining order seeking relief on an emergency basis. The group also sought to broaden their request for a temporary stay to bar the addition of aspartame not only to carbonated beverages, but to all food products. The District Court denied CNI's motion for a temporary restraining order. In an Order entered on January 27, 1984, the Court noted several deficiencies with the group's motion. According to the Court, the affidavits submitted by CNI in support of the motion were largely

[129]Id. at 197.
[130]Id.
[131]583 F. Supp. 294

anecdotal, the conclusions advanced were unsubstantiated by direct scientific evidence and most of the factual assertions relied upon were in actuality inadmissible hearsay. The Court also noted in the order that the government had indicated, at the argument on the motion for a temporary restraining order, that a FDA ruling on the plaintiff's request for a public hearing was imminent.[132] On February 15, 1984, CNI filed a second motion for a temporary restraining order. Two days later, the FDA entered a final ruling on plaintiff's request for an oral hearing. Not surprisingly, the FDA denied CNI's request for a hearing.[133] Furthermore, in response to CNI's second motion for temporary injunctive relief, the FDA filed a motion to dismiss. In this motion, FDA asserted that the District Court lacked jurisdiction to make a determination on the matter and that judicial review was appropriate only in the court of appeals.[134]

On March 22, 1984 the United States District Court, in D. C. heard the case Community Nutrition Institute, et al., v. Dr. Mark Novitch, Acting Commissioner Food and Drug Admin District Judge Barrington D. Parker, writing for the District Court, held that under section of the Food, Drug, and Cosmetic Act governing judicial review of FDA orders relating to food additives, jurisdiction over FDA orders pertaining to aspartame lay in Court of Appeals, not district court. The Court determined that FDA's motion to dismiss should be granted and CNI's motion for a temporary restraining order should be denied.[136]

[132]Id.
[133]FDA Denial of CNI's hearing request Feb 17, 1984
[134]Supra note 122 at 295
[135]Id.
[136]Id.

The plaintiffs appealed, and on January 25, 1985 Community Nutrition Institute, et al., v. Dr. Frank Youn began.[137] The case was heard before a panel of three Circuit judges: Judge Mikva, Judge Edwards and Judge Starr. The underlying issue in that case, as the judges interpreted it, was the FDA's action in approving the use of aspartame in liquids. The judges therefore, reviewed the FDA's regulation approving the use of aspartame in liquids and the District Court's dismissal of a claim seeking to compel the FDA to conduct a hearing on aspartame, as well as a request to stay the approval pending the hearing, for lack of jurisdiction.[138]

Circuit Judge Abner Mikva, writing for the Court of Appeals, held that the district court lacked jurisdiction over the request for a stay of effective date of rules approving both wet and dry use of the artificial sweetener aspartame. The opinion notes that the exclusive grant of jurisdiction to the Court of Appeals meant that mandamus to obtain a stay was available only in the Court of Appeals. Secondly, the Court held that the FDA did not exceed its lawful discretion in denying requests for a hearing on possible dangers of aspartame in carbonated soft drinks and other wet uses. The Court's conclusion rested on the fact that the parties requesting a hearing failed to raise any material issue regarding the safety of wet use of aspartame.[139]

XIX. FDA Invites Consumer Participation

Before the Court of Appeals ruled in the case, Community Nutrition Institute v. Young, the FDA decided to invite consumer participation in an open meeting address-

[137] 773 F.2d 1356, 249 U.S. App. D.C. 150
[138] Id at 1357-58.
[139] Id.

ing aspartame, amongst other things. On October 3, 1984 the FDA announced this meeting which was chaired by Jack Dempster, Director of Compliance.[140] This meeting came as a surprise since the FDA's recent denials of requests for a hearing on aspartame safety issues had spawned the aforementioned litigation. This new invitation for consumer participation in an open meeting can be interpreted as a means of allaying consumer fears about the product. However, unlike the hearing that was initially requested, this open meeting was not set up to address safety issues related to the amendment to the food additive regulation concerning aspartame. That regulation is the one that provides for the safe use of the substance in carbonated beverages and carbonated beverage syrup bases. Consumer advocates were further thwarted by the fact that this meeting was scheduled to be only an hour long, and it took place in Detroit, MI.[141]

XX. The General Accounting Office's Report

Despite the Court's ruling in Community Nutrition Institute v. Young, opponents of aspartame continued their mission to ban the food additive. As per Senator Metzenbaum's request made in 1985, the General Accounting Office, (GAO) undertook a comprehensive study regarding whether the FDA followed proper procedures in approving the sale of aspartame and whether the FDA was conducting adequate follow up studies to monitor the safety of the product. On July 16, 1987, the GAO released its completed report. The GAO concluded that the FDA had indeed followed proper procedures in its approval

[140] 49 FR 39108
[141] Id.

of aspartame as well as its continuing efforts to monitor the safety of the popular sugar-substitute.[142] Throughout aspartame's approval history, GAO found that FDA addressed safety issues raised internally and by outside scientists and concerned citizens, the report stated.[143]

Despite the assurance of this respected body, who polled 69 medical researchers regarding their confidence in the safety of aspartame, some consumers concerns were not obviated. Because it had no medical expertise, the GAO made no recommendations in its report. The group found that the FDA adhered to proper procedures by approving the sweetener, but the GAO investigators said that they could not comment on whether important issues surrounding aspartame's safety remain unresolved.[144] One critic of the report, Dr. Louis Elsas, director of medical genetics at Emory University Medical School commented, They never asked the right questions about what [aspartame] does to brain function in humans. He continued, They decided without data that you had to have enormous amounts of phenylalanine in your blood before it becomes a problem. We don' t know that's the case (sic).[145] Furthermore, Senator Metzenbaum, an outspoken opponent to the approval of aspartame for use in food, said in a statement that more than half the researchers surveyed by the GAO said they had some concerns over safety.[146] The Senator, who was at the time chairman of the Labor subcommittee of the Labor and Human Resources Committee, said that he would convene a hearing of his subcommittee in September to consider,

[142]Supra note 27
[143]Id.
[144]Id.
[145]Wash Post, July 17, 1987, at A23
[146]NY Times, July 18, 1987, at page 50, column 2

once again, the safety of aspartame.[147]

Prior to Senator Metzenbaum's 1987 request for a GAO report, Senator Gaylord Nelson made a similar request for investigation in 1975.[148] In response to Senator Nelson's request, the GAO undertook a detailed analysis of three additives: Food, Drug, and Cosmetic Red No. 2; saccharine; and aspartame for use in food. The purpose of the first GAO investigation into aspartame for use in food focused on several general goals. First, the report was to look at the history of FDA's regulation of aspartame, including in-house and outside tests leading to change in regulated status. Second, the GAO was charged with investigating the current status of testing of aspartame and FDA activities affecting the status of aspartame. Thirdly, the report was to determine the extent to which FDA had examined alternatives to aspartame since its safety was questioned. Finally, the report was to examine whether based on the scientific evidence available, the regulatory action taken by the FDA on aspartame complied with the Federal Food, Drug, and Cosmetic Act, as amended.[149]

In the process of undertaking this investigation, the GAO reported that it concentrated on the period since 1973, when a petition for aspartame's use was submitted to FDA for approval. The Office reviewed pertinent legislation, regulations, and practices relating to FDA's regulation of food additives; examined FDA records relating to the regulatory status of aspartame; and reviewed documents submitted by its petitioner in support of the additive's safety. The GAO

[147] Id.
[148] Supra note 27
[149] 21 U.S.C. 301.

also purportedly interviewed officials of FDA; Canada's Food and Drug Directorate, Ottawa, Canada; and Searle officials. After completing the investigation in 1976, the GAO concluded that the FDA had followed proper procedures in approving the sale of aspartame and was conducting adequate follow up studies to monitor the safety of the product.[150]

The GAO's subsequent report on the safety of aspartame which was released over ten years later, in 1987, was similarly unsuccessful in allaying the fears of many consumer advocates and quieting the controversy that aspartame had stirred up. Although the GAO's report carried a significant amount of weight within the government and the legal community, the text of the report on aspartame did not add much additional information to what was already public knowledge. Because the GAO does not have any medical expertise, its role in this situation was limited to determining whether the FDA acted within the bounds of the law, and polling medical researchers for their thoughts on the safety of aspartame.

The GAO report did not discover much in terms of new data; its focus was on reviewing the FDA's process in approving aspartame. In determining whether a proposed use of a food additive is safe, the Food, Drug and Cosmetic Act requires FDA to consider several things:

1) The probable consumption of the additive and of any substance formed in or on food through use of the additive.
2) The cumulative effects of the additive in the diet of man or animals,

[150]Supra note 27

taken into account any chemically or pharmacologically related substance or substances in the diet; and

3) Safety factors generally recognized by qualified experts as appropriate for the use of animal experimentation data.[151]

The statute mandates that a food additive will be deemed unsafe and restricted from public use by FDA if available information fails to establish the safety of its proposed use or if it is found to induce cancer when ingested by man or animals.[152] The GAO reviewed the FDA's data and concluded that there was no wrongdoing, but because of the somewhat vague nature of these factors, it is easy to see why persistent fears of some anti-aspartame consumer rights groups remained. Even the opinions of the medical researchers who participated in the poll were varied enough to feed ongoing controversy despite the reassuring nature of the GAO's conclusions.

It is interesting to note, however, that both sides of the aspartame struggle claimed that the GAO report supported their beliefs about the safety, or lack thereof, of aspartame as a food additive. This was possible because the poll results were mixed. Although the majority of the sixty-seven participants who responded to the question regarding aspartame's safety as a food additive did not have major concerns about the product's safety, many of the respondents reported having some safety-related concerns regarding aspartame.

The GAO's poll results included the responses of sixty-seven medical researchers who rated their confidence in aspartame as a harmless food additive. Only twelve of the sixty-seven researchers who responded to the safety question

[151] 21 U.S.C. 348(c)(5)
[152] 21 U.S.C. 348 (c)(3)(A)

said that they had major concerns and little, if any, confidence in the safety of aspartame.[153] However, more than half of the researchers who responded said that they had some concerns over safety. Of the remaining respondents, twenty-nine said that they had few, if any, concerns and were very confident of the safety of aspartame. Twenty-six researchers said that they were somewhat concerned but generally confident about the safety of aspartame as a food additive.[154] Despite the generally positive results of the poll, room for doubt was not eliminated entirely.

During the next eight years, consumer use of aspartame increased dramatically as the FDA continued approving he substance for different uses.[155] Although the controversy was not the focus of much mainstream media attention for that period of time, the war was not over. As CNI continued to object to aspartame's approval, the FDA continued to overrule these objections and deny requests for additional public hearings regarding the safety of aspartame for use in food.[156] Research and related controversy continued on without much mass-media attention until 1996 when John Olney, a physician at the Washington University Medical School in St. Louis and a long time aspartame critic, completed a study connecting the use of aspartame to increased rates of brain tumors. Once Dr. Olney's study was complete, it was published in the Journal of Neuropathy and Experimental Neurology in November of 1996.[157] The Community Nutrition Institute, along with former senator Metzenbaum, the then head of the Con-

[153]Supra note 27
[154]Id.
[155]See Approval of Aspartame for Use in Food, 21 C.F.R. §172.804
[156]53 Fed. Reg. 6595 (March 2, 1988).
[157]Journal of Neuropathy and Experimental Neurology (Vol. 55, No. 11, Nov. 1996)

sumer Federation of America, took the opportunity to once again raise consumer awareness of their belief in the dangers of aspartame. CNI and Metzenbaum held a press conference in at which Metzenbaum said that the FDA had not done enough to ensure the safety of aspartame.[158] Olney's study immediately engendered media attention and once again heightened skepticism about the safety of aspartame and concerns about the role of the FDA.

The study preformed by Olney reviewed data on incidences of brain tumors compiled by the National Cancer Institute. Dr. Olney described his research:

> [W]e analyzed these (sic) data from 1975-1992 and found that the brain tumor incidences in the United States occurred in two distinct phases, an early modest increase that may primarily reflect improved diagnostic technology, and a more recent sustained increase in the incidence and shift toward greater malignancy that must be explained by some other factor(s). Compared to other environmental factors putatively linked to brain tumors, the artificial sweetener aspartame is a promising candidate to explain the recent increase... Evidence potentially implicating aspartame includes...the close temporal association (aspartame was introduced into U.S. food and beverage markets several years prior to the sharp increase in brain tumors and malignancy).[159]

What the media did not latch on to was the study's conclusion that more studies on the subject were necessary.

Within days of the issuance of Dr. Olney's study results the NutraSweet Kelco Co., then producer of aspartame, issued a rebuttal charging that the authors manipulated the National Cancer Institute's data to create an overly dramatized graph of the rate of increase in brain tumors.[160] According to the company, the increasing brain tumor and mortality rates in the United States and other countries began before aspartame had been introduced to the general public.

[158] 15 No. 6 Prod. Liab. L. & Strat. 4
[159] Supra note 157
[160] Supra note 158

Furthermore, the company argued, There is also no association between the amount of aspartame use and overall brain tumor rates... The use of aspartame increased dramatically starting in 1983-1984 and continued to increase while the increase in brain tumor rates decelerated... [161]

According to the NutraSweet Kelco Co., there were several problematic elements of Olney's study. First of all, although Olney used data from the National Cancer Institute (NCI) on the rate of brain cancer incidence in his study, he failed to state that it was unknown whether any of the individuals consumed aspartame. The NCI data shows that the greatest increase in brain tumor incidence was found in the elderly, while the most avid users of aspartame were the young and the middle aged. Furthermore the NCI data clearly shows that the rate of brain cancer incidence began leveling off in the mid-eighties, the same time that aspartame use expanded.[162]

Standing behind its original decision to approve the use of aspartame as a food additive, the FDA emphasized the problems with Olney's study. Prompted by the morass of media attention and consumer hype, the FDA prepared a talk paper disputing the study. The paper, which was released on November 8, 1996, asserted that the National Cancer Institute's database on cancer incidence did not support an association between the use of aspartame and increased incidence of brain tumors.[163] According to the FDA, the data from the National Cancer Institute show that overall incidence of brain and central nervous system cancers

[161]Supra note 154
[162]Supra note 155
[163]FDA No. T96-75, Nov. 8, 1996.

began increasing in 1973 and continued to increase through 1985.[164] The FDA argued further that since the 1985 trend line had flattened for these cancers, and decreased slightly in 1991-1993, Olney's study results were flawed.[165] Other members of the community were equally irate that this controversy had been revived by what many people felt was unsubstantiated data. Dr. Dimitrios Trichopoulous, professor of epidemiology and then director of the Harvard Center for Cancer Prevention, called the study preposterous.[166] Trichopoulous also said, [T]he arguments of Olney et al. implicitly require two biologically indefensible assumptions: that a certain factor (aspartame) could cause a solid tumor (brain cancer) with a latency period of less than four years and that subsequent widespread exposure to this factor would cause no further increase in the incidence of that cancer.[167] A harsher criticism of Olney and his study came from Michael Fumento in a Washington Times commentary discussing the amount of media attention the study had received. Fumento wrote, [T]his is a study that doesn't deserve the least bit of ink...Dr. Olney could just as easily have blamed the rise in brain tumors on Ronald Reagan becoming president, which also occurred in 1981.[168]

XXI. The Internet's Role in the Aspartame Controversy

Despite widespread agreement between members of the medical, scientific and government communities that Olney's study did not constitute a significant

[164]Id.
[165]Id.
[166]Supra Note 154
[167]Id.
[168]Wash Times, Dec. 5. at A14.

addition to the research on aspartame as a food additive, the study did succeed in re-fueling consumer interest in the possible dangers related to aspartame consumption. Olney provided additional fodder for the numerous aspartame-related Internet sites that have appeared in the last five years.

Today there are a wide variety of web sites that address aspartame related safety concerns. The site content ranges from panic-driven rhetoric and warnings addressed to all site visitors that tell of the horrors that will result from aspartame consumption, to the more standard consumer advocacy sites that tend to provide less myth-generation and hyperbolic information. Because the Internet is an easy-access forum for people to perform research and express their own views on different topics, it has become a brilliant forum for promoting the largely unsubstantiated fears regarding the consumption of aspartame. Not only are there no checks on the accuracy of information on the web, it provides people the space to voice their own (often irrational) fears about any topic. For example, one site temporarily proclaimed, EQUAL KILLS! Because the research that has been done on aspartame has not concluded that there is absolutely no possibility that the additive could cause any adverse reaction, there is enough room for the necessary doubt to keep this controversy alive.

XXII. Conclusion

Since James Schlatter discovered the sweet taste of aspartame in 1965, the food additive has become one of the most controversial and most consumed food additives in the United States. It has also been plagued by controversy de-

rived from myriad sources. From the beginning, aspartame had to enter into the already controversial low-calorie sweetener industry that was tarnished by concerns over the safety of saccharine. It then was the subject of poorly handled research that was supposed to determine whether or not aspartame was safe for human consumption. Even though the studies demonstrated that aspartame was safe, these conclusions were questioned because of the sloppy research methods employed. Once the FDA had finally reviewed all the data of the task force as well as some additional studies and concluded that aspartame was indeed safe for human consumption, the controversy that had attached to aspartame spread to the FDA as well.

FDA's approval of aspartame for human consumption, and the agency's tenacity in holding on to its position on this matter led to a heightened level of public scrutiny of the agency as well as increasingly virulent attacks on aspartame. It also led to the solidification of some extraordinarily passionate consumer advocates, such as Dr. John Olney, who made it their mission to remove aspartame from the shelves of American grocery stores. As a group, these people contributed to the attempts of CNI to have judges overrule the FDA's holdings on the aspartame issue, and to generally stir up negative publicity about aspartame and its supposed dangers.

Despite the impressive attempts of CNI and other consumer advocates to dampen consumer enthusiasm for aspartame, consumption of aspartame and other low-calorie sweeteners has continued to increase in the United States. Although it is not easy to determine whether this increasing use of aspartame can be at-

tributed to simple consumer desire for the product, or market demand combined with a certain level of widespread trust in the ability of the FDA to do its job. It seems likely that the high level of market demand for aspartame would not exist without a combination of trust in the FDA and desire for a low calorie sugar substitute.

The extensive research into the history of aspartame done for this paper has dispelled many of the myths that are commonly associated with the food additive and its potential dangerous side effects. Although there are merits to having forums such as Internet sites and public hearings in which consumers can express their thoughts and concerns about a wide range of topics including fears about aspartame side effects, there are damaging consequences to having these easy-access forums as well. As the controversy surrounding aspartame has petered out in governmental forums for example, it has once again flared through scare tactics amongst consumers. The Internet provides the public with access to enormous amounts of data, but that data is oftentimes one-sided and not entirely reliable. Hopefully, as the Internet develops and is increasingly used as a research tool, more accurate information about controversies, such as the history of aspartame, will be accessible. Once this goal is achieved, consumers will have access to a much more complicated, and much more accurate pool of information on which to base their personal decisions.