ASPARTAME Chronology

December 1965 James Schlatter, G.D. Searle Company chemist, discovers aspartame (NutraSweet, Equal, Spoonful) while testing an anti-ulcer drug. Schlatter said he was "heating aspartame in a flask with methanol when the mixture bumped onto the outside of the flask...some of the powder got onto my fingers...when licking my finger to pick up a piece of paper, I noticed a very strong sweet taste...I felt that this dipeptide was not likely to be toxic." (1)

December 28, 1970 Confidential internal memo at Searle indicates concern or lack of complete toxicological data on diketopiperazine (DKP), an aspartame by-product. (2)

October-December 1972 The State of Limitations begins to run on two Nutrasweet tests cited by the FDA.

March 5, 1973 Searle petitions the Food and Drug Administration (FDA) for approval of aspartame for use in food. (3)

July 16, 1974 FDA Commissioner Alexander Schmidt, M.D., approves aspartame as a food additive for dry foods only, including chewing gum. (4)

August 1974 Consumer attorney James Turner and Dr. John Olney, Washington University researcher, file objections to FDA's approval of aspartame citing evidence of brain lesions and neuroendocrine disorders in animal studies and concerns that it may cause brain damage and mental retardation in humans. They request a hearing on the safety of aspartame. (5,6)

July 23, 1975 FDA Commissioner Schmidt appoints a task force to investigate Searle's animal studies on aspartame to determine if Searle submitted false information to FDA. (7)

December 5, 1975 Turner and Olney waive their right to a public hearing and agree to a Public Board of Inquiry to hear safety concerns. (8,9)

December 5, 1975 The FDA task force concludes that some of Searle's research practices were so severely flawed that tests results were unreliable. Based on this conclusion FDA stayed aspartame approval. The Public Board of Inquiry is delayed. (6,9)

March 24, 1976 The FDA's task force reports, "At the heart of the FDA's regulatory process is its ability to rely upon the integrity of the basic safety data submitted by sponsors of regulated products. Our investigation clearly demonstrates that, in the G.D. Searle Company, we have no basis for such reliance now." The task force further says, "Some of our findings suggest an attitude of disregard for FDA's mission of protection of the public health by selectively reporting the results of studies in a manner which allays the concerns of questions of an FDA reviewed." (10)

April 7, 1976 FDA notifies US Federal attorney in Chicargo, Sam Skinner, about impending Grand Jury request re. G D Searle. Skinner assigns Assistant US Attorneys William Conlon and Fred Branding to the Searle investigation.

July 1976 In response to the task force findings, FDA decides to investigate aspartame studies to determine whether FDA could rely on these studies to assess aspartame's safety. (11)

January 10, 1977 In a 33-page letter, FDA Chief Counsel Richard Merrill writes to U.S. Attorney Sam Skinner recommending that a grand jury investigate Searle for "apparent violations of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 331(3) and the False Reports to the Government Act, 18 U.S.C. 1001, for "their willful and knowing failure to make reports to the Food and Drug Administration required by the Act, 21 U.S.C. 355(I), and for concealing material facts and making false statements in reports of animal studies conducted to establish the safety of (aspartame)." The FDA calls special attention to studies investigating the effect NutraSweet on monkeys and hamsters. (12)

January 26, 1977 Searle's law firm, Sidley and Austin, request a meeting with Skinner prior to the submission of any matters relating to Searle to a grand jury. (13)

February 2, 1977 Skinner meets representatives of Sidley and Austin, concerning the Searle investigation, Newton Minow (partner in Sidley & Austin) attends.

February - March 1977 Newton Minow offers Skinner a job with Sidley and Austin. (7)

March 8, 1977 Skinner sends a confidential memo to his colleagues citing his preliminary employment discussions with the law firm of Sidley and Austin. He states it would be inappropriate for him to make any decision on the Searle investigation. He says a decision on the grand jury investigation should wait until a new U.S. attorney is appointed. (Note: The statutes of limitation on any prosecution against Searle regarding violations of the Food, Drug and Cosmetic Act regarding aspartame would expire for the monkey study on October 10, and on December 8, 1977 for the hamster study.) (14)

April 13, 1977 A Justice Department memo from US Attonry Charles Kocoras advised Skinner to proceed with the grand jury investigation as soon as possible, citing the statute of limitations deadline, and emphasising that '..any delay is inappropriate'. (15)

July 1, 1977 Skinner leaves his post with U.S. Attorney General's office and joins Searle's law firm, Sidley and Austin. (7)

July 20, 1997 FDA requests expeditious action of the Grand Jury's investigation of Searle, from Chicago Federal attonrey's office, and also flags possible fraud in test on 'DKP', a breakdown product of aspartame.

August 1977 The Bressler Report, compiled by FDA investigators and headed by Jerome Bressler, is released. The report found that 98 of the 196 animals died during one of Searle's studies and weren't autopsied until later dates, in some cases over one year after they died. Records for approximately 30 animals showed substantial differences between original observations on pathology sheets and the observations on pathology sheets submitted to the FDA. There were numerous other inconsistencies and errors noted. For example, a rat was reported alive, then dead, then alive, then dead again; a mass, a uterine polyp, and ovarian neoplasms were found in animals but not reported or diagnosed in Searle's reports. The FDA investigators found dose-related uterine polyps in 15% of 34 animals. (16)

August 18, 1977 Aspartame is dropped from the Department of Justice investigation of Searle. US Attorney Thomas Sullivan decides that the case will focus only on Aldactone. (7)

September 28, 1977 The FDA's Bureau of Foods Task Force reports that the studies concerning aspartame conducted by Searle "appear to be authentic." H.R. Roberts, the primary recipient of this paradoxical document, subsequently left the FDA and became the vice president of the U.S. National Soft Drink Association. (7,18,19)

October 10, 1977 The statute of limitations expires on Searle's longitudinal study of the effects of aspartame on monkeys which showed seizures in some primates that were never autopsied. (7)

October 12, 1997 US Assistant Attorney William Conlon reduces his involvement in the Searle case, in advance of his departure to Sidley & Austin.

December 8, 1977 The statute of limitations expires on the study of aspartame toxicity in hamsters. (7)

March 1979 The FDA's Center for Food Safety and Nutrition concludes that the deficiencies noted in the reviews by the FDA and by the Universities Associated for Research and Education in Pathology, Inc. were not significant enough to invalidate Searle's aspartame studies. The FDA decides to convene a Public Board of Inquiry. (11)

June 1, 1979 The FDA establishes a Public Board of Inquiry to rule on safety issues surrounding NutraSweet. (21)

January 15, 1980 The Public Board of Inquiry holds hearings on objections to aspartame approval. (6.22)

September 30, 1980 The Public Board of Inquiry concludes NutraSweet should not be approved pending further investigations of brain tumors in animals. The board states it "has not been presented with proof of reasonable certainty that aspartame is safe for use as a food additive." (6,8,23,24)

March 1981 An FDA commissioner's panel is established to review issues raised by the Public Board of Inquiry. (11)

May 19, 1981 Three of six in-house FDA scientists, Dr. Robert Condon, Dr. Satya Dubey, and Dr. Douglas Park, advise against approval of NutraSweet, saying the Searle tests are unreliable and not adequate to determine the safety of aspartame. (25)

July 15, 1981 Dr. Arthur Hull Hayes, Jr., FDA commissioner, overrules Public Board of Inquiry and approves NutraSweet for dry products saying that aspartame has been shown to be safe for its proposed uses. He says additional evidence, including a third long-term study, assessing aspartame's carcinogenic potential using a different strain of rat confirms that conclusion. The studies he cited were conducted by Ajinomoto, the Japanese manufacturer of aspartame. He says few compounds have withstood such detailed testing and repeated close scrutiny. (5,7,8,26,78)

October 22, 1981 The FDA approves aspartame for table-top sweetener, tablets, cold breakfast cereals, chewing gum, dry bases for beverages, instant coffee and tea, gelatins, puddings, fillings, dairy-product-analog toppings, and flavor enhancer for chewing gum. (24,28)

October 15, 1982 The FDA announces Searle has filed a petition that aspartame be approved as a sweetener in carbonated beverages and other liquids. (6,29)

July 1, 1983 The National Soft Drink Association urges the FDA to delay approval of aspartame for carbonated beverages pending further testing. The FDA responds that it is aware that temperature may affect carbonated liquids containing aspartame, "but believes proper shipping and marketing procedures should 'solve' the problems."(30)

July 8, 1983 Acting commissioner of the FDA, Mark Novitch, approves NutraSweet for use in carbonated beverages and carbonated beverage syrup bases, even though levels of aspartame remaining in beverages stored in eight weeks at 68 degrees F were between 84% and 89% of the original amount. "Lost" aspartame degrades to DKP, methanol (methyl alcohol), aspartic acid, and phenylalanine. (31)

July 28, 1983 The National Soft Drink Association drafts an objection to the final ruling, which permits the use of aspartame in carbonated beverages and carbonated beverage syrup bases and requests a hearing on the objections. The association says that Searle has not provided responsible certainty that aspartame and its degradation products are safe for use in soft drinks. The drafted document is not filed with the FDA. NSDA members feel the case was not strong enough. (32)

August 8, 1983 Consumer attorney James Turner of the Community Nutrition Institute and Dr. Woodrow Monte, Arizona State University's Director of Food Science and Nutritional Laboratories, filed suit with the FDA objecting to aspartame approval based on unresolved

safety issues. They request a stamp of approval and a public hearing to address aspartame's safety. (6)

September 1983 Searle files and FDA petition for approval of aspartame use in bulk amounts. (33)

September 1983 Commissioner Hayes of the FDA resigns and Buson-Marsteller, Searle's public relation firm hires him as senior scientific consultant. Hayes is unavailable to the press for the next ten years. (19) Fall 1983 The first carbonated beverages containing aspartame are sold for public consumption. (34)

November 16, 1983 The FDA denies Turner and Monte's request for stay of approval for aspartame use. (35)

December 8, 1983 The FDA proposes to declare aspartame suitable for use as a sweetener in drug products as long as the label warns phenylketonurics that phenylalanine is present. (8(

December 9, 1983 The Arizona Dietetic Association and the Central Arizona District Dietetic Association file a joinder of petition to request a public hearing and to add their objections to FDA's approval of aspartame.

December 23, 1983 The Arizona Dietetic Association and the Central Arizona District Dietetic Association file suit in district court seeking an order requiring FDA to hold a hearing. They cite consumer complaints of adverse effects and new medical evidence against aspartame. (6)

February 17, 1984 The FDA denies the request for a public hearing. The district court grants FDA's motion to dismiss the complaint on the ground the "jurisdiction was lacking."(6,36)

March 1984 The FDA and the Centers for Disease Control begin investigations of cases of adverse reactions to aspartame. (7)

May 30, 1984 The FDA approves aspartame for use in multivitamins. (37)

July 10, 1984 Florence Graves, vice president of publications and editor of COMMON CAUSE magazine, writes "NutraSweet has been touted as the most tested food additive in history, but our investigation reveals such serious flaws in the government's approval of NutraSweet that Congress should begin its own investigation immediately."(38)

November 1984 The Center for Disease Control reviews 213 of 592 cases of aspartame complaints. Ages of the complainants ranged from four months to 77 years: 77% were between the ages of 21 and 60 years, 75% were female, and 94% were white. Twenty-eight percent reported repeated episodes of symptoms, and 26 people experienced identical symptoms. Some of the reported symptoms included: aggressive behavior, disorientation, hyperactivity, extreme numbness, excitability, memory loss, loss of depth perception, liver

impairment, cardiac arrest, seizures, suicidal tendencies, severe mood swings, and death. The CDC recommends future investigations of aspartame investigate the neurological and behavioral problems, and focus on symptoms such as headaches, mood alterations, and behavioral changes. Frederick L. Trowbridge adds an executive summary to the report which conflicts with the information in the report. He states, "Currently available information, based on data with limitations as described in the report indicated a wide variety of complaints that are generally of a mild nature. Although it may be that certain individuals have an unusual sensitivity to the product, these data do not provide evidence for the existence of serious, widespread, adverse health consequences to the use of aspartame."(39)

July 17, 1985 An association called "Aspartame Victims and Their Friends" forms. (40)

July 13, 1985 EDITOR AND PUBLISHER magazine cites "The Food and Drug Administration NutraSweet cover-up" as one of the most under-reported stores of the year. (44)

August 1, 1985 U.S. Senator Howard Metzenbaum (D-OH) introduces The Aspartame Safety Act of 1985 to Congress. (44)

September 25, 1985 During a visit to the University of Tennessee, then President Ronald Reagan tells a student that he used to carry a vial of sweetener with him but recently quit using sugar substitutes because no one knows what's in them. (43)

October 1, 1985 Monsanto Company purchase G.D. Searle Company, including NutraSweet , for $2.7 billion. Searle's Pharmaceuticals and NutraSweet become separate subsidiaries. (44)

1986 George R. Verrilli, M.D., and Anne Marie Mueser publish WHILE WAITING: A PRENATAL GUIDEBOOK. The book says "aspartame is suspected of causing brain damage in sensitive individuals. A fetus may be at risk for these effects...some researchers have suggested that high doses of aspartame may be associated with problems ranging from dizziness and subtle brain changes to mental retardation."(45)

February 3, 1986 Sen. Metzenbaum's investigation reveals that "during a Searle sponsored monkey test, all the animals receiving medium or high dosages of NutraSweet experienced grand mal seizures."(7)

July 17, 1986 Turner files a petition on behalf of the Consumer Nutrition Institute to seek reconsideration of FDA's regulations about safe use of aspartame and to repeal the regulations. (46)

October 16, 1986 Turner files a citizen's petition regarding hazards of seizures and eye damage from aspartame. (27)

November 21, 1986 The FDA denies Turner's petition. (46)

November 28, 1986 The FDA approves aspartame for noncarbonated frozen or refrigerated concentrated and single-strength fruit juice, fruit drinks, fruit flavored drinks, imitation fruit flavored drinks, frozen stock-type confections and novelties, breath mints, and tea beverages. (37)

December 1986 The FDA declares aspartame safe for use as an inactive ingredient provided labeling meets certain specifications. (11)

December 16, 1986 The FDA lists 73 aspartame symptoms, including four deaths, by aspartame complainants. (47)

January 2, 1987 The FDA quarterly report on adverse reactions associated with aspartame reactions associated with aspartame states the majority of the complaints by 3,133 individuals refer to neurological effects. (48)

June 18, 1987 The General Accounting Office (GAO) report to Sen. Metzenbaum regarding the approval process for aspartame mentions that 12 of 69 scientists responding to a GAO questionnaire expressed major concerns about aspartame safety, and that during as examination of aspartame animal studies Olney found 12 brain tumors in 320 rats who had received aspartame and that none of the 120 control rats had brain tumors. (11)

August 1987 Mary Stoddard forms the Aspartame Consumer Safety Network in Dallas, Texas.

November 3, 1987 Dr. Jacqueline Verrett, FDA toxicologist and a member of the investigation task force, says the original aspartame studies were "built on a foundation of sand."(20)

February 2, 1988 Four hundred ninety-three U.S. consumer products and 18 over-the-counter pharmaceuticals contain NutraSweet. (49)

February 26, 1988 A letter from David Baine, associate director of the U.S. GAO, states methyl alcohol was not included in the initial description of aspartame because aspartame is only 10% methyl alcohol (by weight). (50)

April 14, 1988 The GAO assignment manager, Michelle L. Roman, admits that some definitions of methyl alcohol define it as a toxic substance. (51)

June 7, 1988 The FDA approves aspartame in yogurt products; frozen desserts; ready-to-serve non-refrigerated, pasteurized, aseptically packaged diluted fruit juice beverages; fruit wine beverages (wine coolers) with ethanol content below sever percent volume; and ready-to-serve gelatin. (37)

October 1, 1988 The FDA quarterly report on adverse reactions associated with aspartame includes 4,204 consumer complaints. (52)

October 19, 1988 The FDA approves aspartame for wafer cookies. (37)

December 21, 1988 Senator Metzenbaum issues a press release saying senators should not approve the appointment of Sam Skinner as Department of Transportation secretary without an inquiry concerning Skinner's failure, as U.S. District attorney in the Northern Illinois District, to pursue allegations about fraudulent testing of NutraSweet. Metzenbaum raises the issue of Skinner accepting a position with Searle's law Firm, Sidley and Austin, during the time the FDA asked Skinner to review allegations of fraudulent safety tests by Searle and urges the Senate to convene a grand jury to investigate the charges. (53) J

anuary 25, 1989 Senator Metzenbaum issues a press release saying that Skinner acknowledged he may have made mistakes in the NutraSweet investigation, but Metzenbaum says he supports Skinner's nomination as secretary of Department of Transportation. (54)

June 2, 1989 The FDA approves aspartame for frozen, ready-to-thaw-and-eat cheesecakes; fruit and fruit toppings; and dairy and non-dairy frostings, toppings and fillings. (55)

January 30, 1992 The FDA approves aspartame for malt beverages of less than seven percent ethanol by volume and containing fruit juice; dry, free-flowing sugar substitutes for table use in package unit not exceeding the sweetening equivalent of one pound of sugar; breakfast cereals; and refrigerated ready-to-serve puddings and fillings. (55)

April 16, 1993 The FDA approves aspartame for hard and soft candies. (55)

April 19, 1993 The FDA approves aspartame for all ready-to-serve non-alcoholic flavored beverages, tea beverages, fruit-juice based beverages and their concentrates, baked goods and baking mixes, and as a flavor enhancer in malt beverages containing less than three percent alcohol by volume. (55)

September 17, 1993 The FDA approves additional uses in frostings, toppings, and fillings for baked goods. (55)

February 28, 1994 The Department of Health and Human Services report on adverse reactions attributed to aspartame lists 6,888 complaints, including 649 reported by the Centers for Disease Control, and 1,305 reported by the FDA. Aspartame accounts for the majority (75.7%) of all the complaints in the Adverse Reaction Monitoring System. (56)

November 1996 John Olney of Washington University, St Louis and his colleagues published a paper in the *Journal of Neuropathology and Experimental Neurology*; they analysed the cancer statistics from the US National Cancer Institute for approximately 10% of the US population for the period from 1975 to 1995. They found that the introduction of aspartame into the USA, into dry goods in 1981 and soft drinks in 1983, was followed by an abrupt increase in the reported incidence of brain tumours. The change was most noticeable

between 1984 and 1985, and it corresponded to approximately 1,500 extra cases of brain cancer per year in the USA. (80)

July 2005, Soffritti and his colleagues publish a paper in the *European Journal of Oncology* reporting evidence that aspartame induced lymphomas and leukaemias in rats, in a consistent dose-related manner. (81)

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