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United Press International

October 13, 1987, Tuesday, BC cycle

UPI investigative report: NutraSweet: Questions swirl

SECTION: Washington News

LENGTH: 1745 words

DATELINE: WASHINGTON

Poring over laboratory rat studies in the spring of 1981 in the government's final safety review of a new artificial sweetener, senior statistician **Satya Dubey** of the Food and Drug Administration was troubled.

Dubey, a member of a special FDA "commissioner's team" formed to help decide the fate of the product to be known as NutraSweet, wrote in an internal memo that brain tumor data from rat tests was so "worrisome" he could not recommend approval.

Two other statisticians on the six-member team agreed with **Dubey** that the Chicago-based G.D. Searle Co. had not proved with "reasonable certainty" the safety of the sweetener, known generically as aspartame. A 1980 Public Board of Inquiry had voted 3-0 to ban aspartame because of similar fears.

But a few weeks later, on July 18, 1981, new FDA Commissioner Arthur Hull Hayes Jr., a pharmacologist who had been in office less than three months and had little background in food additives, overturned the board and approved the use of aspartame in dry foods.

The ruling, one of the first regulatory actions of the Reagan presidency, came at a time of growing concern that the most widely used low-calorie sweetener, saccharin, was linked to cancer. Thus Hayes' approval of NutraSweet profoundly changed the eating habits of millions of Americans, handing Searle a financial bonanza.

It also climaxed a topsy-turvy, eight-year FDA review process in which the agency approved the sweetener, then banned it and demanded a grand jury investigation of its manufacturer, only to reverse course again after reexamining the issue at least five times.

Now six years after Hayes' ruling, its uses expanded, the sweetener is widely consumed in diet sodas, puddings, cereal, drink mixes and even chewing gum and vitamins. Yet NutraSweet and its FDA approval remain at the center of controversy, the sweetener's safety questioned by a small corps of independent scientists; defended by its manufacturer and the diet food and drink industry.

In a recently released report, the General Accounting Office concluded that the FDA "adequately followed" its food additive approval process on NutraSweet. Congress's investigative arm did not evaluate the sweetener's safety. A federal appeals court also has rejected court suits by consumer groups challenging the NutraSweet approval.

United Press International has learned that more than 10 federal officials involved in the NutraSweet review have taken private sector jobs linked to the industry -- among them Hayes, an acting FDA commissioner and former chiefs and acting chiefs of the agency's Bureau of Foods.

In addition, many of the scientists who have produced favorable studies or served as outspoken advocates of NutraSweet's safety have received grants or consulting fees from Searle and the industry.

Consumer lawyer James Turner, who has unsuccessfully pressed petitions for a NutraSweet ban as part of an 11-year campaign against the sweetener, asserted, "NutraSweet is an opportunity for the entire country to look in great detail at how we make food safety decisions. It is a rickety, 19th Century process."

G.D. Searle began to study the artificial sweetener aspartame soon after a company laboratory chemist, James Schlatter, stumbled on the compound when he licked it off his finger while conducting ulcer research in 1965.

In a memo on Dec. 28, 1970, a Searle official laid out a plan for winning FDA approval for the sweetener. "We must create an affirmative atmosphere in our dealing with them," Herbert Helling wrote senior company executives.

Helling suggested that Searle representatives carefully order proposals to the FDA to put Bureau of Foods officials "into a yes-saying habit." If FDA officials could be swayed to do Searle some favor, he asserted, it would "help bring them into a subconscious spirit of participation."

On July 26, 1974, just 15 months after Searle petitioned for approval, FDA commissioner Alexander Schmidt approved aspartame use in dry foods, allowing a 30-day period for public hearings and comment. He acted on a strong endorsement from the Bureau of Foods, now called the Center for Food Safety and Applied Nutrition.

At that point, consumer attorney Turner, author of a 1970 book about food additives, objected to the short comment period. Turner was joined in his protest by a now-defunct public interest group and by Dr. John Olney, a Washington University neuropathologist who had linked aspartame to brain lesions in mice.

Schmidt promptly froze the approval. In an action that was the first of its kind, he ordered that a Public Board of Inquiry be named to look into aspartame.

Schmidt also had been alerted to conflicts between Searle's research reports and conclusions from independent animal studies that the firm's anti-infective drug Flagyl and its cardiovascular drug Aldactone may cause cancer. He named a Bureau of Drugs task force to investigate. Philip Brodsky, the unit'

The task force assailed Searle's conduct of research on most of the products, including aspartame, in a searing, 84-page report.

"At the heart of the FDA's regulatory process," the report said, "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 Co., we have no basis for such reliance now."

The task force charged, for example, that the company removed tumors from live animals and stored animal tissues in formaldahyde for so long that they deteriorated. Instead of performing autopsies on rhesus monkeys that suffered seizures after being fed aspartame, the company had financed a new monkey seizure study with a different methadology that showed no problems.

For the next seven years, Searle's petition was tied up in reviews by the task force and other sharply critical FDA panels.

At the task force's request, Richard Merrill, the FDA's general counsel, demanded in a letter that Samuel Skinner, the U.S. attorney in Chicago, open a grand jury investigation of Searle and three of its employees.

One Searle official named by Merrill was Robert McConnell, who had been director of Searle's Department of Pathology and Toxicology and oversaw most of the company's aspartame research.

McConnell's Detroit lawyer, Gerald Wahl, said that as the inquiries heated up, his client suddenly was awarded a $15,000 bonus and asked to take a three-year sabbatical by director Wesley Dixon. Wahl said Dixon told McConnell he had become a "political liability," a remark Dixon later denied making.

McConnell received his annual salary of more than $60,000 during the sabbatical at the Massachusetts Institute of Technology, but he never got his job back and ended up suing the company, Wahl said.

"I've represented hundreds of executives, but I've never seen anybody get the deal that McConnell got," he said. "When you boil it all down, they were looking for continued support from McConnell" during the inquiries.

Wahl said McConnell had felt pressure to hurry his research because of the "profit motive," but that the company never ordered him to alter test results.

Chief investigator Brodsky said that "politicized" handling of the task force disclosures, at hearings chaired by Sen. Edward Kennedy, D-Mass., was one reason he retired in 1977. He said the main witnesses, Searle executives and top FDA officials uninvolved in the investigation, gave "the wrong answers to the wrong questions ... They didn't even let the experts answer the questions."

The FDA, rocked by the controversy, established a set of "good laboratory practices" -- minimum standards for future corporate research work.

Richard Ronk, deputy Bureau of Foods chief, stressed that Searle's practices were typical of the industry at the time, not "the worst on the block."

Searle's fortunes did not begin to change until 1977, when Donald Rumsfeld, White House chief of staff under Gerald Ford, was named its new president.

Turner alleged that Searle chose, with Rumsfeld's hiring, not to redo the questioned studies on the belief he could handle aspartame as "a legal problem rather than a scientific problem."

The company also hired another Ford White House official, William Timmons, as a Washington lobbyist.

Before deciding on Merrill's grand jury request, U.S. Attorney Skinner and an aide agreed in February 1977 to meet with lawyers for Searle, including Newton Minow, a partner in the law firm of Sidley & Austin.

A month later, Skinner, a Republican appointee who was looking for a job as a result of Jimmy Carter's election, informed aides in a memo that he had begun preliminary employment discussions with the law firm.

Withdrawing from the Searle matter, Skinner suggested his designated successor, Thomas Sullivan, be left to decide whether to open a grand jury inquiry -- a move that delayed action for at least four months. Sullivan took office just 12 weeks before expiration of the statute of limitations for prosecuting alleged false statements on aspartame. While a grand jury inquiry ultimately was convened, those allegations were not explored.

Skinner has denied any conflict of interest.

Assistant U.S. Attorney William Conlon worked with the grand jury until Oct. 12, 1977, two days after the statute of limitations expired on the aspartame allegations. No indictments were brought on the few matters investigated. Conlon, who declined comment, joined Sidley & Austin 15 months later.

Following issuance of the task force report in March 1976 and facing a dilemma as to how to proceed, the FDA sought new reviews of several "pivotal" studies -- long-term animal tests to see whether aspartame causes cancer.

A new, five-member internal FDA task force analyzed three of these studies, and Universities Associated for

Research and Education in Pathology, Inc., a consortium formed by 15 universities, was contracted to look at another dozen. Much like the earlier team, the five-member FDA task force, headed by veteran Chicago inspector Jerome Bressler, assailed the quality of animal tests into whether the substance might cause birth defects and tumors.

The report said Searle laboratory employee Raymond Schroeder, who worked on related research, first told investigators the feed in a study of the aspartame breakdown product DKP was so inadequately mixed it appeared the rats could "discriminate" and avoid eating the DKP.

LANGUAGE: ENGLISH

ADVANCED-DATE: October 12, 1987, Monday, BC cycle