

this article referred to in Ch'ch Press as acknowledging that this proves Asp. to be safe !!

I couldn't do my job as a nutritionist without a scientific background. But I know that a lot of my clients are outside their comfort zone when they hear scientific terms like "aspartic acid" and "phenylalanine".

Contrary to what you might believe, they are not the creations of some mad scientist in a chemistry laboratory. Irresponsible scare-mongering has frightened many people away from using foods containing aspartame – so let me reassure you of its safety.

Aspartic acid and phenylalanine are amino acids. They occur naturally in many high-protein foods we eat daily like meat, cereal and dairy foods.

Aspartame is the most common sweetener used in sugar-free, low-calorie foods and drinks. You'll find it in some carbonated soft drinks, chewing gum, diet and diabetic foods, and table sweeteners. It has 200 times the sweetness of sugar, yet has none of the calories.

Hundreds of valid scientific studies have been done on aspartame around the world, and they've all agreed that it's absolutely fine.

That's why food safety authorities in New Zealand, as well as in Australia,

the United Kingdom, Canada and the United States, among many others, are confident of its safety.

Aspartame is not only safe, but it can be good for you.

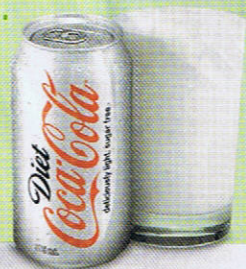
Thanks to aspartame, diabetics can enjoy a little sweetness in their food and drink with no damaging impact to their blood sugar levels. There are 115,000 Kiwis who've been diagnosed with diabetes, and the number is tipped to jump to 160,000 by 2021. Anything that helps people with diabetes control their blood sugar levels while allowing a healthy and varied diet has got to be good news.

And for people trying to lose or manage their weight using foods that contain aspartame can 'liven-up' a potentially boring diet.

The only group that should avoid aspartame is the tiny number of New Zealanders (around 200) who suffer from an inherited disease called phenylketonuria (PKU for

Did you know?

A glass of non-fat milk has six times as much phenylalanine and thirteen times as much aspartic acid as the same amount of diet drink sweetened with 100% aspartame. These amino acids are vital to our health.



short). These people cannot digest phenylalanine. But for the rest of us, the ingredients of aspartame are not only harmless but vital to our health.

So don't be spooked by the long scientific names. Although you may not be able to get your tongue round them, they're perfectly safe to put in your mouth!

"That's why food safety authorities in New Zealand, as well as in Australia, the United Kingdom, Canada and the United States, among many others, are confident of its safety."

For more insights into the make-up of a balanced diet and lifestyle, visit www.nikkihartnutrition.co.nz

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21 January, 2009

Dear Tania

Re: *The research behind aspartame* letter published in issue 40 of Fitness life

The extensive and independent review process on the safety of aspartame, which was chaired by Dr Magnuson and published in *Critical Reviews in Toxicology* cited over 500 studies, including both industry funded and non-industry funded research. The conclusions of this review clearly state that aspartame is shown to be safe to consume at current levels of consumption.

The point not made clear perhaps in her *Close Up* interview, was that regardless of the funding source, the most important factor with regards to research on aspartame safety is the *quality* of the research undertaken. Adequate safety testing of food ingredients must follow strict quality guidelines set by independent authorities, and all industry-funded studies follow these strict guidelines. It is in their interest to do so, so as to avoid bias and subjectivity. This is not always the case for non-industry funded research.

You may find it helpful to listen to Dr Magnuson objectively answer some commonly asked questions on aspartame at the following link, as it addresses other misconceptions about aspartame also covered in your magazine during the past year.

http://www.gettherealfacts.co.nz/bernadene_qanda.html

I act as a consultant dietitian to Coca-Cola Oceania. As a NZ Registered Dietitian I have a professional and ethical obligation to uphold what is scientifically accepted as fact, and to correct misinformation regarding dietary matters. I'm therefore not defending aspartame simply because I advise Coca-Cola. Obviously Coca-Cola use aspartame in some of their products and they take the health of their consumers and all New Zealanders extremely seriously. If there was even a trace of scientific evidence to show any ingredient to be unsafe, they would not use it. The converse is actually true for aspartame. It is not only shown to be safe as a result of hundreds of studies, but it is also shown to be beneficial – especially for weight management and management of diabetes.

Yours sincerely



Donnell Alexander
NZ Registered Dietitian

F.D.A. TO APPROVE A NEW SWEETENER

Low-Calorie Synthetic 180
Times as Strong as Sugar

By HAROLD M. SCHMECK Jr.
Special to The New York Times

WASHINGTON, July 25 — The Food and Drug Administration will announce tomorrow its approval of a high-intensity sweetener that is expected to be the first real competitor to saccharine since cyclamates were banned about three years ago.

The new sweetener is called aspartame. Weight for weight, it is 180 times sweeter than sugar.

It is a synthetic product made from two of the natural building blocks of protein — the amino acids aspartic acid and phenylalanine — and therefore is metabolized by the body as a protein. That means it could be used by diabetics.

It will provide the same number of calories, weight for weight, as either sugar or protein, but since aspartame is so intensely sweet its caloric contribution would ordinarily be insignificant.

Minute Fraction

"If aspartame is employed as a sweetener in place of sugar it will provide only about 1/180th of the calories that would be provided by the use of quantity of sugar yielding equivalent sweetness," said the preamble to the F.D.A. approval notice that will be published tomorrow in the Federal Register.

The document says, "The appearance of this new sweetener is expected to elicit considerable interest." The food industry is believed to be interested in the substance, which was developed by G. D. Searle & Co., a drug concern.

The F.D.A. calculations indicate that no one would be likely to use enough aspartame as a sugar substitute to accumulate as much as eight calories a day.

The approval permits use of the substance in a wide variety of products such as breakfast cereals, gelatins, puddings, fillings, dessert toppings, dry bases for mix-it-yourself beverages or as a substitute for sugar in coffee and tea.

Breaks Down Under Heat

For the time being, it will not be approved as an ingredient in bottled soft drinks, nor for use in cooking. The heat required for frying or baking foods tends to break aspartame down into a substance called diketopiperazine with a consequent loss of sweetness.

The F.D.A. approval followed submission by the drug company of safety studies in which the substance was fed to rats and dogs for two-year periods and another study in which rats were fed it during their natural lifetimes after being exposed to it in the uterus.

There was no detectable effect on the animals even when fed daily doses as high as 1/500th of the individual's total body weight, according to the food and drug agency.

In settings and acceptable level of use for humans, the agency reduced that one-to-500 ratio by an additional safety factor of 100. This amount—something less than a 15th of an ounce a day—came out in rough agreement with calculations of the probably maximum daily use by a human.

No Safety Problems Found

The F.D.A. announcement said the agency was not aware of any safety problems with diketopiperazine, the breakdown product that appears when aspartame is heated, but that additional studies will have to be done before the sweetener can be approved for any uses beyond those cited in the current approval.

A spokesman for the drug firm said the substance did not give a bitter after taste like that of saccharine when used in large amounts.

The safety status of saccharine is being restudied by a panel of the National Academy of Sciences. A petition to put cyclamates back on the market is in the hands of the drug agency. Cyclamates were taken off the market more than three years ago because

animal studies raised questions about their safety.

The F.D.A. said aspartame is changed, in the digestive tract, into the two naturally occurring amino acids, aspartic acid and phenylalanine.

"Both of these amino acids have previously been approved as safe for addition to food so as to improve the biological quality of the protein," said the F.D.A. document.

It noted that packages containing aspartame will have to be labeled to warn persons suffering from the inborn metabolic defect called phenylketonuria. Such persons must maintain a strict diet extremely low in phenylalanine.

F.D.A. Hearing Set To Resolve Dispute Over a Sweetener

WASHINGTON, Sept. 23 (AP)—The Food and Drug Administration said today that it would hold a public hearing to "resolve the issues raised" by a professor's contention on Aug. 16 that the sugar substitute Aspartame can cause brain damage to children when combined with a common food additive.

The agency approved Aspartame as a sweetener and sugar substitute in certain foods two months ago. It is not yet on the market.

The scientist, Dr. John W. Olney, associate professor of psychiatry at the Washington University School of Medicine in St. Louis, wrote a memorandum of protest and requested a re-hearing on the matter.

An F.D.A. spokesman announced the decision to hold a hearing in response to queries about a Senate speech planned for tomorrow by Senator William Proxmire, Democrat of Wisconsin. No date was set for the hearing.

Mr. Proxmire urged the agency to withdraw temporarily its approval of Aspartame.

F.D.A. Chief Is Criticized Over a Sugar Substitute

WASHINGTON, Oct. 21. (AP) — Senator William Proxmire, Democrat of Wisconsin, has criticized Food and Drug Commissioner Alexander M. Schmidt for allowing the sugar substitute Aspartame to be manufactured and distributed before holding a public hearing on it.

Mr. Proxmire said yesterday that Mr. Schmidt was guilty of misfeasance—performance of a legal act that causes harm.

There have been charges by Dr. John W. Olney, associate professor of psychiatry at the Washington University School of Medicine in St. Louis, that the new product can cause brain damage to children when combined with monosodium

glutamate, a common food additive.

Responding to Mr. Proxmire, Mr. Schmidt said the Food and Drug Administration had spent 16 months reviewing the safety of Aspartame before approving it.

F.D.A. BARS SALES OF A SWEETENER

Acts After Audit of Tests on Safety of the Drug

Special to The New York Times

WASHINGTON, Dec. 4—The Food and Drug Administration ordered today the immediate stay of a regulation it issued more than a year ago that approved the sale of an artificial sweetener called Aspartame, manufactured by G. D. Searle and Company.

The action, which would prevent the company from marketing the product, resulted from an audit of records of animal experiments done by or for the drug company to show that the drug was safe.

An F.D.A. spokesman said the 'audit indicates the need for a more comprehensive review' of the data submitted by the company and relied upon by the drug agency in determining that the product was safe.

The drug agency is conducting an over-all audit of animal research done on behalf of the company. Questions concerning some of the studies and the research reports were raised earlier this year by agency inspectors, the F.D.A. spokesman said.

In a statement today on the agency's action, Senator Edward M. Kennedy said that serious questions had been raised concerning the integrity of some of the company's research data at hearings before a Senate Health subcommittee of which he is chairman.

The questions concerned two other Searle products, Flagyl and Aldactone. The first is an antiparasite drug; the other a drug used in treating high blood pressure.

Senator Kennedy, Democrat of Massachusetts, said that the "extraordinary" regulatory action taken today by the drug agency was apparently based on similar concerns over "discrepancies in the scientific data for that product."

In a brief statement today, Searle said that the F.D.A. action did not alter the current status of Aspartame, since it had never been made available to the public. The statement said that the company had voluntarily withheld marketing pending "resolution of certain questions about the product."

DRUG RESEARCH UNDER QUESTION

New York Times (1857-Current file); Jan 21, 1976; ProQuest Historical Newspapers The New York Times (1851 - 2005)
pg. 25

DRUG RESEARCH UNDER QUESTION

**F.D.A. Sees Doubt Raised
in Study of Searle Data**

WASHINGTON, Jan. 20 (AP)

—A six-month Federal investigation of G. D. Searle & Company has turned up widespread evidence of "sloppy" research studies that call into question the safety of drugs taken by millions of Americans, the Commissioner of the Food and Drug Administration testified today at a Senate hearing.

Because of the initial findings in the Searle investigation, Dr. Alexander M. Schmidt, the Commissioner, said, drug inspectors are expanding their review of similar data submitted by other major pharmaceutical companies.

Dr. Schmidt said that he expected the review to show that Searle was "the exception rather than the norm in industry," but that problems were frequent in laboratories conducting studies with animals.

The Searle data are being turned over to the Justice Department and, because of the possibility of prosecution, some

of the findings must remain confidential, the Commissioner said.

Senator Edward M. Kennedy, Democrat of Massachusetts, chairman of the hearing of the Senate subcommittees on health and administrative practices and procedures, said the fact that some of the Searle research data were false was of greater concern than whether the falsity was intentional or accidental.

"Inaccurate science, sloppy science, fraudulent science—these are the greatest threats to the health and safety of the American people," Mr. Kennedy said. "Whether the science is wrong because of clerical error, or because of poor technique, or because of incompetence or because of criminal negligence, is less important than the fact that it is wrong."

Dr. Schmidt said that as a result of the F.D.A. investigation of Searle, new warning labels would be required for Flagyl, a drug used to treat a common vaginal infection, and Aldactone, a widely prescribed antihypertensive drug. The artificial sweetener Aspartame will be kept off the market until all safety questions are resolved; the cardiovascular drug Norpace probably will

have marketing approval delayed a year; and a Searle oral contraceptive and an intrauterine contraceptive device, both new on the market, are being studied anew.

F.D.A. Urges Grand Jury Study Of G. D. Searle's Drug Reports

Special to The New York Times

WASHINGTON, April 7—The Food and Drug Administration has recommended to the Justice Department that a grand jury be convened in Illinois to investigate charges that a major drug firm, G. D. Searle & Company, has falsified data and reports submitted in connection with new drug applications.

Charges that the company was giving the Government false information were made last summer by a medical officer of the drug agency. Since these disclosures the drug agency has mobilized to investigate in detail some 16 studies conducted by or for the drug company in its applications for drug approvals.

Because the drug agency does not have subpoena power, it has asked for the grand jury investigation to obtain additional facts in the case, an officer of the agency indicated tonight.

Testimony concerning the agency's action is to be given here tomorrow by Dr. Alexander M. Schmidt, Commissioner of Food and Drugs, at a Senate subcommittee hearing.

The testimony is expected to say that animal studies related to several drugs were involved in the F.D.A. task force's investigation, but that safety of the drugs on the market was not called into question by the task force findings. Before a drug is approved for marketing tests in humans as well as animals are required. It is understood that the case against G. D. Searle and Company is related to animal tests only.

Among the drugs under scrutiny were Aldactone, a diuretic designed to help the body remove excess fluid, and Flagyl, used against vaginal infections. In both cases, the drug agency plans to require that the labeling of the drug changed, presumably in the light of some of the the findings that have

been made during the investigation.

Also investigated were studies done for the company in support of applications to market an artificial sweetener called Aspartame.

The task force analysis of the studies submitted by Searle was described as extremely thorough and involved talking to animal handlers and others involved in the work, reviewing the raw data and all but recreating the studies. Altogether several million items of information were said to have been analyzed.

The investigation reportedly revealed practices such as the withholding of information and the deliberate manipulation of data to give impressions favorable to the drugs under study.

It is known that Dr. Schmidt believes there is a widespread problem of quality of animal research related to drug approvals in the drug industry. An investigation much more widespread than that involving the Illinois company is expected.

F.D.A. Broadens Inquiry on Testing of New Drugs

By RICHARD D. LYONS Special to The New York Times

New York Times (1857-Current file); Nov 17, 1976; ProQuest Historical Newspapers The New York Times (1851 - 20 pg. 24

F.D.A. Broadens Inquiry on Testing of New Drugs

By RICHARD D. LYONS

Special to The New York Times

WASHINGTON, Nov. 16.—Four years ago, Dr. Mario Rustia, an animal pathologist at the Eppley Cancer Institute in Omaha, published the results of tests that he had conducted on mice with Flagyl, a commonly prescribed drug used to treat parasitic infections.

When printed in The Journal of the National Cancer Institute here, the account aroused concern at the Food and Drug Administration because it asserted that the drug might cause cancer in the animals, although it had been generally assumed that the compound was safe for use in humans.

The drug had been widely used for nine years to treat a type of vaginal infection and a companion infection in men and had been described by one pharmaceutical handbook as "a good drug with a low incidence of serious adverse side effects."

Dr. M. Adrian Gross, a veterinary medical officer at the F.D.A., noted an apparent discrepancy between the results of Dr. Rustia's studies with mice and those conducted on rats by the manufacturer of the compound, G.D. Searle & Company of Skokie, Ill.

"Gee, isn't that odd; we have a study

on file saying that Flagyl is safe," Dr. Gross recalled today of his reaction in 1972.

From the seemingly obscure research of Dr. Rustia and the private suspicions of Dr. Gross have stemmed scientific and legal developments that have led to the following:

¶A widening investigation into the whole area of the safety of new drugs

¶A \$16.4 million increase in the F.D.A.'s budget to, in part, hire 600 more specialists to oversee animal drug testing.

¶Reviews of the animal testing procedures routinely conducted by 40 contract research laboratories throughout the country.

¶Preparation of the first proposed Federal regulations for the animal testing of drugs, which will be made public Friday.

¶Possible Federal grand jury investigations of Searle and another pharmaceutical house, Syntex, as well as three contract research laboratories, because of discrepancies in animal testing data for four other compounds.

Before these events were set in motion it had been assumed by the Federal drug agency and the public that animal studies

had been properly performed and the results properly reported.

But now there is a growing suspicion that some part of the proof with which drug companies have buttressed the claims of safety for their products may be erroneous. The problems that have been uncovered include poorly conceived and carelessly executed experiments, a lack of supervision and training of personnel, and inadequate record-keeping.

The developments also underscore the laborious process by which drug safety is monitored, and the possibility that the long delays that have been encountered may postpone, sometimes for years, the withdrawal from the market of pharmaceuticals that harm.

Flagyl, as an example, was first approved in 1963 for the treatment of infections in the genital tract by one-celled creatures called trichomonads. But the F.D.A. approved only short-term use of the medication.

Gave Results of Study

In 1970, according to agency officials, the Searle company, seeking approval of the drug for prolonged use, submitted the results of a study done on mice that had demonstrated no toxicity after 80 weeks of feedings.

The account by Dr. Rustia, which was co-authored by Dr. Philippe Shukrik, the director of the Eppley Institute, led Dr. Gross to take a fresh look at the 80-week study.

"It turned out that the Searle study had been inaccurately reviewed by our people," Dr. Gross said, "and I concluded that the Searle study did not agree with the rat data, and it was pointed out to Searle."

"They didn't do anything for two years. In 1974 they submitted their revised report on that study and guess what they did: They brought the data to agree with the summary."

"We knew that this can't happen so we inspected, and at each inspection we found more and more damaging things."

The problems were reported to higher F.D.A. officials by Dr. Gross, a 53-year-old veterinary pathologist who has served with the agency for 14 years.

During the next year the agency expanded its investigation of the Flagyl test results, and eventually extended the inquiry into another Searle drug, Aldactone, a diuretic used with other compounds to lower blood pressure.

In August 1975, the agency formed a 30-member force of investigators to conduct an extensive study of Searle's animal testing operations, which in turn led to a report last March urging tighter controls on tests.

As a result of the investigation, both Flagyl and Aldactone, while not withdrawn from the market, were given new labels pointing out that animal studies had raised questions of safety and that "unnecessary use of this drug should be avoided."

F.D.A. officials have also disclosed that the testing records for two other Searle products, a drug named Norpace, and an artificial sweetener named Aspartame, have also come into question.

F.D.A. officials have testified at Congressional hearings that they are continuing investigations into two other contract laboratories, Biometric Testing Inc. of Englewood Cliffs, N.J., and Hazleton Laboratories of Vienna, Va.

F.D.A. Is Sued By G.D. Searle
New York Times (1857-Current file); Oct 2, 1980; ProQuest Historical Newspapers The New York Times (1851 - 2005)
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F.D.A. Is Sued By G.D. Searle

SKOKIE, Ill., Oct. 1 (Reuters) — G.D. Searle & Company said today it had filed suit to require the Food and Drug Administration to render a final decision in its seven-year administrative proceeding involving aspartame, the company's low-calorie sweetener.

The suit was filed in United States District Court in Washington, D.C., Searle said, after its many requests for expedited handling of the proceeding had been unavailing.

It added that during the years of delay it has incurred tremendous costs and seen its patent protection eroded. The F.D.A. granted a food additive petition in 1974 for the use of aspartame, but stayed the order in December 1975 for further review.

[Also today, the Associated Press reported that a scientific panel of inquiry convened by the F.D.A. to investigate the safety of aspartame has recommended that the Government keep the sweetener off the market. In a 51-page report, the panel concluded that the sweetener "should be withheld at least until the questions concerning its possible oncogenic potential has been solved by further experiments."

[The term oncogenic refers to a substance's potential to cause tumors.

[The A.P. reported that Searle, which has estimated that it would lose \$10,000 for every day that it could not market aspartame, said it would have no immediate comment on the report.]

PERSONAL HEALTH

Judging Safety Of Aspartame In Soft Drinks

By JANE E. BRODY

A SIGNIFICANT move was made this month in the checkered career of artificial sweeteners. Aspartame, approved two years ago as a low-calorie sweetener for such dry foods as drink mixes, breakfast cereals and chewing gum, was released for use in by far the largest market for sugar substitutes: diet carbonated soft drinks.

The investment in this product by its developer, G. D. Searle & Company, has been great, but the potential return on the investment is much, much greater. Searle's tabletop aspartame sweetener, Equal, has already surpassed in dollar sales its leading competitor, Sweet 'n Low, a saccharin-based product that had had the field to itself since the banning of cyclamates 13 years ago. With a taste that is indistinguishable from sugar but without the bitter aftertaste left by saccharin, aspartame is expected to win a large share of the soft-drink market.

And a huge market it is. Every year, Americans consume 40 gallons (the equivalent of more than 400 12-ounce cans) of soda pop for every man, woman and child in the country. For teenagers, average consumption is more than double that figure. About \$4 billion of this \$25 billion market is now taken by diet sodas, and if aspartame wins the public acceptance its manufacturers anticipate, the diet-soda market could easily double its present size, as it seems to have done in Canada.

Although Searle could not say when the first aspartame-sweetened diet soda will appear on grocery shelves, the prospect of all this aspartame's being consumed by Americans naturally raises an important question: How safe is it? Is it safer than saccharin, its only rival in the soft-drink field, which since 1952 has been linked in animal studies to an increased risk of cancer?

The approval of aspartame as a soft-drink additive culminates a decadelong effort marked by scientific uncertainty and controversy over its potential risks and extreme caution on the part of the Food and Drug Administration, which has already been burned twice by artificial sweeteners. The banning of cyclamates as a possible cancer risk was followed by an attempted ban on saccharin for the same reason. However, in the case of saccha-

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Personal Health

Continued From Page C1

rin, the agency's hand was stayed by an act of Congress ostensibly protecting the interests of a sweets-loving but calorie-conscious public.

Ironically, despite the public outcry in saccharin's behalf and the fact that it has been in use as a food additive since 1938, neither it nor any other sugar substitute has ever been shown to help people lose weight nor to help diabetics control their disease. There is even some doubt that it makes any difference in tooth decay, since the most common decay-promoting foods are not the ones sweetened with low-calorie sugar substitutes.

What is aspartame? Aspartame was discovered serendipitously in 1965 by James M. Schlatter, a Searle research chemist who was developing possible new drugs to treat ulcers. One day while working in the lab, he licked his fingers and was struck by their very sweet taste. He soon deduced that it resulted from a combination of chemicals, neither of which was itself sweet: L-aspartic acid and the methyl ester of L-phenylalanine. Both aspartic acid and phenylalanine are natural amino acids (the building blocks of protein) and are normally present in rather large amounts in many ordinary protein-containing foods.

Searle spent the next seven years exploring aspartame's properties and commercial possibilities and testing it for safety in animals to satisfy F.D.A. requirements for approval of a new food additive. In 1973, Searle asked for the agency's approval to use aspartame in dry foods; there were serious doubts at the time about the compound's stability in liquids that might be stored for months. Approval was granted a year and a half later, only to be quickly rescinded when a scientist, Dr. John Olney, and an attorney, James Turner, raised questions about its safety.

The validity of the Searle studies was reviewed by independent university scientists and by an F.D.A. Public Board of Inquiry, which recommended additional studies. Finally, in July 1981, after 112 studies and with aspartame already approved for use in more than half a dozen other countries, the F.D.A. approved it as a dry food additive (under the brand name NutraSweet) and tabletop sweetener (brand name Equal). Now, two years later, after experience in Canada and England helped to convince the American agency of its safety and effectiveness in soft drinks, aspartame will be allowed to enter the soft-drink market here.

Searle showed that aspartame was digested and metabolized by animals as a protein, breaking down into its component amino acids and methyl alcohol. These substances are present in much higher concentrations in a

Judging safety of aspartame, low-calorie sweetener just approved for diet soft drinks.

number of other foods, such as tomato juice, cherries, bananas, meat, milk and beans.

Aspartame has calories — 4 per gram, the same as any other protein or the sugar that aspartame is meant to replace — but because it is about 180 times sweeter than sugar, only a tenth of a calorie's worth of aspartame is needed to provide the sweetening power of 1 teaspoon (18 calories' worth) of sugar. It is easy to see why it might be a dieter's delight, at least in foods that do not require cooking (it breaks down, losing its sweetness, under high temperatures, as well as in very acidic substances). And since it is a protein, it does not require insulin to be metabolized, making it useful for diabetics as well.

Is it safe? The answer is generally yes for most people, based on data gathered thus far, but there are some caveats. Aspartame is not safe for people with an inherited metabolic abnormality called phenylketonuria, which leads to brain damage and mental retardation if the developing brain is exposed to phenylalanine. A warning to phenylketonurics appears on packages of Equal and foods manufactured with aspartame, but who would warn them about foods sold in restaurants that may be so prepared? And what about pregnant women who might already have high levels of phenylalanine in their blood and not know it? Will their unborn babies be harmed?

Dr. Olney, of the Washington University School of Medicine in St. Louis, did studies in laboratory rats and mice indicating that aspartame might cause brain damage, and other studies hinted at an increased risk of brain tumors. But other researchers have not duplicated these findings. Dr. Richard Wurtman, a neuroendocrinologist at the Massachusetts Institute of Technology, has suggested that the combination of aspartame's amino acids with other foods might lead to changes in the levels of brain chemicals that affect behavior. Thus far, no one has studied possible behavioral effects thoroughly in animals or at all in people consuming aspartame.

As for the most frightening prospect — cancer — there is as yet no evidence

in animals of any possible harm. One concern is a breakdown product of aspartame called diketopiperazine (DKP), which is formed when aspartame is heated or liquids containing it are stored for months. DKP, a secondary amine, might result in the formation of cancer-causing nitrosamines in the body.

Still, according to Dr. Michael Jacobson, director of the Center for Science in the Public Interest, the lack of any known cancer risk makes aspartame a far preferable alternative to saccharin "if you must use an artificial sweetener." But, Dr. Jacobson warns, experience with aspartame in people is limited, "and we just don't know if there might be some people who are unusually sensitive to it in some way." As with nearly all other food additives, little or nothing is known about its possible interactions with other food chemicals, drugs, metabolic abnormalities or allergic sensitivities.

Nutritional benefits and risks. As its manufacturer correctly points out, aspartame, as a very low-calorie sweetener, has the potential of increasing the "nutrient density" of foods. This refers to the amount of essential nutrients (such as protein, vitamins and minerals) provided relative to the number of calories in a food. If sugar calories are reduced, the reasoning goes, the ratio of nutrients per calorie increases, assuming the food starts out with any nutrients in it besides sugar.

Unfortunately, for the most popular uses of artificial sweeteners — in soft drinks and other beverages — there is little or nothing nutritionally worthwhile to begin with. For the diet as a whole, however, there may be some benefit. Added sugar now represents about 18 percent of the calories consumed each day by the average American (that's 500 or more sweet calories a day), and if even half those calories were eliminated, the nutrient density of the overall diet would theoretically increase (not, of course, if the savings in sugar were made up for by an increase in fats, but only if nutritious foods were consumed in place of the reduced sugar calories).

On the debit side, however, there are concerns about encouraging the consumption of soft drinks, many of which contain other additives of questionable safety, such as artificial colorings, caffeine and quinine. Some nutrition and weight-control experts are worried about the effects of artificial sweeteners on the insatiable American sweet tooth. As they see it, substituting a low-calorie sweetener for sugar does nothing to curb the passion for sweets and simply perpetuates the likelihood that a person will succumb to very sweet high-calorie foods that are made with sugar (and probably also lots of fat), such as pies, cakes, cookies, candy and ice cream.

Aspartame may also increase the cost of some foods. It is much more expensive than saccharin, which costs about \$4 a pound in contrast to \$30 a pound for aspartame, more of which is needed to provide saccharin's sweetening power. In fact, the soft-drink industry is not all that eager to use aspartame because it will seriously cut into the enormous profits now being made on saccharin-sweetened drinks (unless, of course, a premium price is charged for drinks with aspartame or the market for them expands greatly). Dr. Jacobson estimates that consumers have paid more than \$300 million extra for saccharin-sweetened sodas, which are priced the same as those made with sugar, which is more costly.

FUTURES/OPTIONS

Suit Against Aspartame Spurs Rally in Sugar

By Reuters

Sugar futures rallied in New York yesterday on news that a lobbying group, seeking to ban the use of the artificial sweetener aspartame from soft drinks, said it would file a lawsuit in Federal court contending that the low-calorie product could be harmful.

Sugar futures closed 0.18 to 0.24 cent a pound higher after touching the lowest levels for the year on Tuesday. The growing use of aspartame and other sugar substitutes has contributed to a drastic decline in sugar consumption.

A ban on aspartame would increase sugar consumption and "help producers work down a burdensome world stock surplus of 10 million tons," said Erik Dunlaevy of Balfour MacLaine International.

Also in New York, cocoa futures closed \$88 to \$57 a metric ton higher. The volume of trade has lightened as traders have become uncomfortable with the market's seesaw action.

In Chicago, grain and soybean futures declined, reversing Tuesday's sharp advances. The setback reflected trade uncertainty over the disparity between recent Department of Agriculture crop estimates.

Interest-rate futures closed mixed, with Treasury bond futures declining despite a seemingly bullish report of a decline in December durable goods orders. When the report failed to spark a rally, "everybody who bought going into the report had to bail out afterwards," said Mike Jackson of ACLI International.

Livestock futures fell sharply early in the day, with most contracts down the maximum daily permissible limit. Live cattle futures recouped part of their slide, but all livestock futures ended lower.

U.S. Denies Hearing On Sweetener Safety

WASHINGTON, Feb. 17 (UPI) — The Food and Drug Administration today rejected a request by a consumer group and a food scientist to hold a public hearing on the safety of the low-calorie sweetener aspartame.

The agency said concerns raised last summer by the Community Nutrition Institute and Dr. Woodrow Monte of Arizona State University had been thoroughly explored before the agency approved the sweetener in July for use in carbonated drinks.

Jim Green of the Food and Drug Administration said, however, that the agency was still reviewing about 260 complaints of adverse reaction to aspartame.

Judge Rejects New Bid To Remove Sweetener

New York Times (1857-Current file); Mar 25, 1984; ProQuest Historical Newspapers The New York Times (1851 - 2005)
pg. 18

Judge Rejects New Bid To Remove Sweetener

WASHINGTON, March 24 (UPI) — For the second time in three months, a Federal district judge has rejected a request by a consumer group to remove the low-calorie sweetener aspartame from the market.

Without ruling on the Community Nutrition Institute's assertion that the sugar substitute might be a health hazard, Judge Barrington Parker agreed Friday with the Food and Drug Administration that he lacked jurisdiction in the case. The Washington-based consumer group said it would appeal the rejection.

The F.D.A., which approved aspartame for dry foods in 1982 and carbonated drinks last summer, has repeatedly maintained that the sweetener is safe and has been one of the most thoroughly tested food additives.

Judge Parker rejected the institute's first request for a temporary restraining order on Jan. 28.

Diet Sweetener Risk Is Being Reassessed After New Research

By PHILIP M. BOFFEY

LOW-CALORIE sweeteners, perhaps the most thoroughly studied of all food additives, are undergoing a new scientific evaluation that already seems to be changing judgments about their relative value and safety.

Studies have now confirmed beyond any doubt that saccharin, the most widely used artificial sweetener in the country, is a weak carcinogen that causes bladder tumors in rats, even at levels in the diet somewhat lower than previously realized.

Thus saccharin, the only artificial sweetener allowed on the American market in the 1970's, is turning out to have the most thoroughly documented health risk of any sweetener, although the risk appears very small.

In contrast, cyclamate, which was once the most feared of the sweeteners and was banned as a possible carcinogen in 1970, may be headed for at least partial rehabilitation. The Food and Drug Administration's cancer assessment committee concluded in April that cyclamate is not a carcinogen after all, and the National Research Council has been commissioned to issue an independent judgment.

If the F.D.A. ultimately allows cyclamate back on the market, it would be the sharpest turnabout in the agency's recent history.

Meanwhile, aspartame, a fast-rising challenger to saccharin that was approved for food uses in 1981 and for carbonated beverage use in 1983, has provoked hundreds of complaints from consumers who contend that they became dizzy, nauseous or otherwise ill after consuming the substance. Their complaints are being investigated by the Federal Centers for Disease Control to determine whether the sweetener was at fault or whether the alleged illnesses are coincidental.

None of the latest studies or assessments suggest that any of the sweeteners pose a major health hazard. Officials of the American Diabetes Association, who monitor the sweeteners because diabetics are heavy users of them, give saccharin and aspartame, and probably cyclamate as well, a clean bill of health if taken in moderation. "We feel that the benefits in terms of use outweigh any potential risk," said Karl

Comparing the Sweeteners

	Calories Sweetening equivalent of one teaspoon of sugar	Sweetness Compared with sugar	F.D.A. Status
SUGAR	16		No approval needed
SACCHARIN	1.5 (powder) 0 (tablet)	300X sweetener	Ban overruled by Congress until April 1985
CYCLAMATE	2 (powder) 0 (tablet)	30X sweetener	Banned, but now being reconsidered
ASPARTAME	2 (powder) 0.5 (tablet)	180X sweetener	Approved

Sources: Calorie Control Council, FDA, USDA,
Cumberland Packing Corp., G. D. Searle & Co.

The New York Times/Aug. 21, 1984

Sussmann, the president of the association, who is a professor of medicine at the University of Colorado Medical School. "We're counseling patients to use these agents in limited amounts, although we really haven't honed in on what the limits should be."

On the issue that most frightens the public — the possibility that some sweeteners may cause cancer — the risks appear relatively low.

"Sweeteners as used in the past are not responsible for any major increase in cancer risk," says Robert Hoover, an epidemiologist at the National Cancer Institute who has directed major studies of the sweeteners.

Nevertheless, the safety of the sweeteners is a matter of continuing concern because their use is spreading rapidly. The Calorie Control Council, a trade group representing more than 60 manufacturers and suppliers of dietary foods and beverages, estimated in April that more than 68 million adult Americans, or 40 percent of the adult population, consume saccharin or aspartame on a regular basis, an increase of more than 60 percent over the past six years. The Council defined regular usage as at least

Continued on Page C9

Diet Sweeteners Found Of Low Risk to Health

Continued From Page C1

once every two weeks, but many people use the substances in substantial amounts every day, gulping diet sodas or low-calorie foods and using the sweeteners in tablet or powdered form to flavor their coffee. Per capita consumption of saccharin increased more than 40 percent over the past decade, and per capita consumption of aspartame has soared even more rapidly in the past two years, according to figures compiled by the Federal Department of Agriculture.

Health experts appear to have no consistent set of recommendations regarding who should be concerned about particular levels of intake of the artificial sweeteners. Some authorities warn against heavy, long-term use by children, who often receive much higher doses per unit of body weight than adults and who will have decades ahead in which cancer or other damage can develop. Others express concern about women of childbearing age, whose intake might conceivably affect nursing infants, just as heavy intake by female rats seems to increase cancer among their offspring.

Dr. Hoover, of the National Cancer Institute, says he personally gets concerned about people who regularly drink more than four or five saccharin-sweetened diet sodas a day. But others believe it is safe to ingest far higher quantities. One Federal toxicologist calculated, unofficially, that consumers could drink more than eight 12-ounce aspartame-sweetened diet drinks every day for a lifetime without danger. Even that level has a very large safety factor built in, he said.

Here are the latest findings on the health risks of each of the major sweeteners:

Saccharin

The F.D.A. tried unsuccessfully to ban saccharin in 1977 after studies found that high doses caused bladder tumors in rats. But sharp public protest against removing the only low-calorie sweetener then available led Congress to impose a moratorium on the ban and to extend it repeatedly. Since then, according to the F.D.A., further animal studies have confirmed "unequivocally" that saccharin is a carcinogen in rats.

Perhaps the largest and most sophisticated animal study of all, sponsored by the Calorie Control Council and completed last year, found that a diet containing 3 percent saccharin clearly caused bladder tumors in rats while a 1 percent dose level also showed an increase in tumors, although not to a "statistically significant" extent. These dose levels were below those that produced bladder tumors in previous tests but still far above normal human usage. The 1 percent dose level in rats is equivalent to a human drinking 250 cans of diet soda daily for a lifetime, the industry council contends.

Virtually all experts now agree that saccharin is a "weak" carcinogen in rats, but it has not been shown to cause cancer in other animals or at sites other than the bladder. Moreover, the vast majority of epidemiological studies have found little or no evidence that humans have been adversely affected. The latest, a Danish study published last year, found it "highly unlikely that the consumption of artificial sweeteners has contributed to current bladder cancer rates in man."

However, one weakness of the epidemiological studies is that they focus heavily on bladder cancer, the kind found in rats that eat saccharin.

"Practically speaking, there is no evidence one way or the other on other types of cancer," said Steven Stellman, assistant vice president for epidemiology at the American Cancer Society.

The current moratorium on banning saccharin doesn't expire until next spring, but Senator Alfonse M. D'Amato, Republican of New York, and other lawmakers, coming to the defense of the food industry, sought to push through a three-year extension in the legislative confusion preceding the Democratic National Convention. They were blocked by Senator Howard M. Metzenbaum, Democrat of Ohio, who is seeking hearings on the whole sweetener situation.

Cyclamate

The chief factor spurring a review and possible rehabilitation of cyclamate is not so much any new evidence as a new way of looking at the old evidence. As recently as 1980, the F.D.A. rejected a petition to reinstate cyclamate. Now it appears on the verge of changing its mind. The agency's cancer assessment committee has concluded that the animal tests that previously disturbed regulators were oddities whose positive findings of cancer were overwhelmed by an array of negative findings. The committee has also challenged the statistical techniques previously used to determine risk.

This sharp about-face is viewed by industry supporters as a long overdue rejection of a previous mistake that was caused by pressure from the news media and consumer concerned about toxic chemicals. But some consumer groups fear that the reversal may simply reflect the antiregulation philosophy of the Reagan Administration.

"This is the most extreme divergence of views on a single set of evidence that I've ever seen," said one neutral scientist who has reviewed the data.

Cancer is not the only issue raised by cyclamate. The F.D.A. must also evaluate evidence that the substance can cause chromosome breakage, thus conceivably posing a mutagenic hazard, and that it can atrophy the testicles. In fact, some F.D.A. toxicologists expect testicular atrophy to

be the limiting factor in determining how much cyclamate is safe to use.

Aspartame

According to the F.D.A. and many scientists, aspartame is one of the most thoroughly tested food additives ever approved. Even so, a few scientists continue to warn that aspartame might cause brain damage or changes in brain chemistry and behavior.

Moreover, Common Cause, a citizens organization, charged last month that the F.D.A.'s decade-long review of aspartame was so deficient that Congress should conduct its own investigation. However, Common Cause stopped short of calling aspartame dangerous, and the F.D.A. retorted that it had already considered and rejected all the health issues raised by the citizens' group and the complaining scientists.

The food industry contends that all three major artificial sweeteners are safe and that the more sweeteners available the better, so that food manufacturers can capitalize on the advantages of each.

Comparing 3 Sweeteners

Saccharin is the cheapest of the sweeteners but leaves a bitter aftertaste. Cyclamate tastes better and is relatively cheap but has less sweetening power than saccharin. Aspartame also tastes better but is by far the most expensive; it also tends to deteriorate after long storage or when heated.

Most diet sodas today contain a blend of saccharin and aspartame, with saccharin being the primary sweetener. That enables manufacturers to combine the cheapness and stability of saccharin with the good taste and better safety reputation of aspartame.

The industry says that sweeteners used in combination enhance each other's sweetness, and that a variety of sweeteners makes it less likely that individual consumers will exceed acceptable daily intake for any single sweetener.

Although the diet drinks and sweeteners are often consumed in the belief that they will help people to lose weight, there is very little evidence that they are effective for this purpose. Dr. William Bennett, acting editor of the Harvard Medical School Health Letter, wrote last year that "there is no solid evidence that artificial sweeteners have any value at all

'We feel that the benefits outweigh any potential risk'

in weight control, the main reason people give for using them."

Although the use of low-calorie sweeteners has boomed over the past two decades, he noted, Americans have not lost weight as a result but have actually, on average, gained a few pounds. Instead of replacing sugar in the diet, he said, the artificial sweeteners are simply added to the diet, and people continue to eat sugared foods as well.

Nor is there any solid evidence that artificial sweeteners reduce the dental cavities that are caused by sugar or have therapeutic value in managing diabetes.

The only thorough laboratory studies came up with some hints, but no firm evidence, that low-calorie sweeteners might be effective dietary tools to reduce caloric intake. Dr. Katherine P. Forkos and her colleagues at St. Luke's-Roosevelt Hospital Center in New York City allowed healthy volunteers to eat a varied, normal diet, then surreptitiously substituted foods sweetened with aspartame rather than sugar and watched to see if the volunteers would increase their food intake to make up for the lost calories. The subjects ate a bit more food but nevertheless reduced their caloric intake by about 15 percent. That persuaded the scientists that there is no physiological drive to replace all the lost calories.

A Possible Psychological Factor

But in a book chapter just published, the scientists acknowledge that there may be psychological drives at work — that people may use low-calorie products as an excuse to eat more of other foods.

"Given the stable role that low-calorie foods have in the American diet, it is surprising how little information exists concerning their effectiveness in promoting weight loss," they wrote.

The lack of proven benefit from sweeteners, and their relatively low health risk, leaves most people to make up their minds on philosophical grounds.

"I wouldn't drink or eat any of them," said Dr. Sidney Wolfe, head of Ralph Nader's Health Research Group. "Saccharin is clearly a carcinogen, although a very weak one. Cyclamate causes chromosomal damage and may be a carcinogen. People complain of dizziness after eating aspartame. If you combine this with the fact that there is no evidence the sweeteners work, who needs them?"

But Elizabeth Whelan, director of the American Council on Science and Health, contends that the sweeteners pose so infinitesimal risk and are beneficial in allowing "freedom of choice in juggling calories."

"Why not drink three diet drinks and save a few hundred calories so that you can have dessert or wine with dinner?" she asks.

Manufacturer Assails Criticism of Sweetener
New York Times (1857-Current file); Sep 16, 1984; ProQuest Historical Newspapers The New York Times (1851 -
pg. 30

Manufacturer Assails Criticism of Sweetener

WASHINGTON, Sept. 15 (AP) — The Food and Drug Administration and the manufacturer of aspartame have discredited a new study by California researchers that questions whether the low-calorie sweetener is safe for use in cooking and hot beverages.

The study, conducted by Marcus F. Boehm and Jeffrey L. Bada at the University of California at San Diego, noted changes in the chemical components of aspartame when it was boiled for a long time.

They concluded in a report released Thursday that the health effects of this

molecular change were unknown but should have been investigated before aspartame was approved for sale to the public.

Denise Ertell, a representative for G. D. Searle, which manufactures Nutrasweet, the brand name for aspartame, said her company had evaluated the study in detail and concluded that the fears it raised were groundless.

Previous research shows that even when amino acids break down because of high temperatures, they are not toxic, she said, adding: "His experiment consisted of boiling solutions of Nutrasweet for periods ranging from five to 120 hours. There is no situation now where exposure to heat for that period of time is likely to occur for any of Nutrasweet's uses."

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Federal Agency Sees Little Risk in Sweetener

New York Times (1857-Current file); Nov 2, 1984; ProQuest Historical Newspapers The New York Times (1851 - 2005) pg. A22

Federal Agency Sees Little Risk in Sweetener

ATLANTA, Nov. 1 (AP) — The national Centers for Disease Control said today that it had found no evidence of "serious, widespread" side effects from aspartame, the low-calorie sweetener also known as "NutraSweet" that is used in many diet soft drinks.

At the request of the Food and Drug Administration, the Federal health agency evaluated 592 complaints from aspartame users, ranging from headaches to gastrointestinal disorders and rashes.

The agency conceded it was "unlikely" that interviews with people who had complained about aspartame could establish a relationship between the sweetener and illnesses. Only blind clinical tests could do that, scientists said.

But the study found no consistent pattern in either the complainers or their symptoms, although the agency found that "certain individuals" might "have an unusual sensitivity to the product."

Also today, Pepsico Inc. announced it would begin using NutraSweet instead of saccharine in its bottled and canned drinks. [Page D9.]

Groups Cite Complaints

Dr. Frederick Trowbridge, director of the health agency's nutrition division, said the drug agency performed clinical tests before it licensed aspartame in July 1983. Consumer groups citing users' complaints have demanded a ban on aspartame, pending more tests and public hearings on the sweetener's safety. The drug agency, soft drink companies and NutraSweet's maker, G.D. Searle and Company, have maintained it is safe.

The data collected by the Centers for Disease Control indicated no "evidence of serious, widespread, adverse health consequences" from the sweetener, the agency said.

Of the persons who complained, 67 percent told of "neurological" or

"behavioral symptoms," including headaches, dizziness and mood changes, the health agency said, adding that 24 percent complained of gastrointestinal symptoms, 15 percent of allergic-type reactions and 6 percent of changes in menstrual cycles. Some of those who complained about the product said they suffered more than one kind of symptom.

Had the symptoms been similar or more clear cut, Dr. Trowbridge said, "it would have raised more concern that there was a recognizable pattern associated with aspartame." He added, "That would not have been conclusive, but it would have been more suggestive."

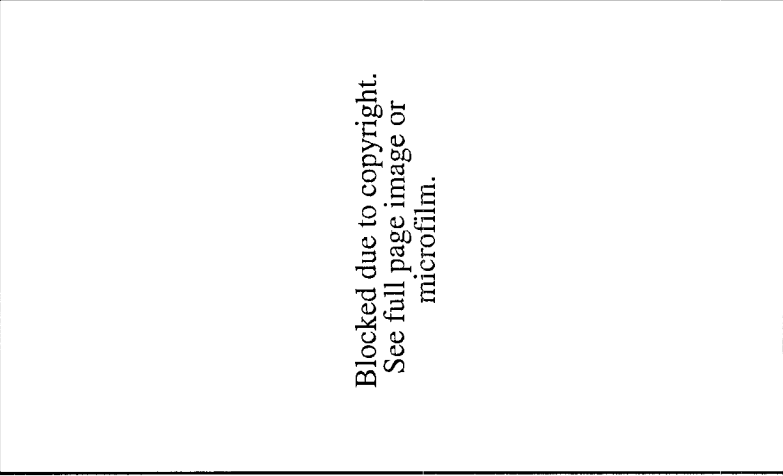
He noted that the symptoms — headache, fatigue and the like — were "generally of a mild nature" and "mostly the kinds of things that happen to people every day."

The health agency interviewed 517 people who had complained about aspartame; 96 percent of them were white, 76 percent were women and 79 percent were 21 to 60 years old. The health agency had no marketing data about aspartame, but Dr. Trowbridge said one "logical explanation" for the pattern of complaints was that white adult women bought more diet soft drinks than other segments of the population.

Sweetener Worries Some Scientists

By JANE E. BRODY

New York Times (1857-Current file): Feb 5, 1985; ProQuest Historical Newspapers The New York Times (1851 - 2005)
pg. C1



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Sweetener Worries Some Scientists

As use of aspartame grows, so does concern about people who may be sensitive to it.

By JANE E. BRODY

AS sales of aspartame, the nation's newest artificial sweetener, expand rapidly among millions of users, scientific concern is also growing among some researchers about its safety.

The researchers are alarmed by recent reports that a small percentage of users, including at least two young children, may have suffered severe adverse reactions to aspartame. Especially worrisome are reactions involving the brain, including seizures, incapacitating headaches, dizziness, behavioral changes and depression.

Although there is at present no evidence, there is concern, too, over the possibility that in some consumers, aspartame may cause subtle disruptions in the balance of brain chemicals that influence mood, alertness and hunger for certain nutrients. Animal studies have raised the issue but its investigation is only just beginning.

Two scientists, Dr. C. Keith Connors of Children's Hospital in Washington and Dr. Richard Wurtman of the Massachusetts Institute of Technology, believe that the Food and Drug Administration misled the public on aspartame's safety by understating the concern voiced in a recent official scientific analysis of consumer complaints.

"If you read the C.D.C. report," Dr. Wurtman said in an interview, referring to the national Centers for Disease Control, "it doesn't sound nearly so complicated as the F.D.A. Talk Paper that interpreted the findings for the public."

According to the C.D.C., its detailed investigation of 200 consumer complaints, out of more than 600 received, suggests the need for a systematic study of adverse effects, especially neurological and

behavioral effects, which accounted for 67 percent of the complaints received.

"The number of instances of persons challenging themselves several times with aspartame-containing products and reporting symptoms with each challenge suggests that some individuals may be sensitive," the report states. "The only way to clearly determine this is through focused clinical studies." Citing the "subtlety and potential seriousness of some of the manifestations" reported by consumers, the disease control centers said the studies should concentrate on such symptoms as "headaches, mood alterations and behavior changes."

The manufacturer of aspartame, G.D. Searle & Company, said a proposal for a clinical study has been submitted to the F.D.A., but there are as yet no plans to actively monitor the effects of aspartame in the general population.

Searle says the C.D.C. findings are not surprising, given the fact that more than 100 million people now use aspartame. Dr. Gerald E. Gaull, vice president for nutrition and medical affairs for aspartame at Searle, said it is possible that "a

Continued on Page C5

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Artificial Sweetener Worries Some Scientists

Continued From Page C1

few people may be allergic or sensitive to it." He added that "for these few people, the issue is not one of safety but rather of food selection."

Both the drug agency and Searle say aspartame is the most extensively studied food additive in history and that the studies clearly establish its safety. Dr. Gaull added, "It's not just the F.D.A. that has viewed the tests as adequate, but also the World Health Organization and comparable regulatory agencies in Canada, the United Kingdom, Japan and about 37 other countries."

Dr. Sanford Miller, head of the F.D.A.'s Bureau of Foods, said: "I don't know of any substance in recent years that's been looked at with the intensity of aspartame. No one had yet come up with the slightest evidence to show we were wrong in approving it."

However, some researchers and consumer organizations assert that the studies have not been careful or far-reaching enough to establish the safety of aspartame, which is now entering the food supply at an unprecedented rate following its approval in 1983 for use in soft drinks.

For example, Dr. Wallis Nauta, a Massachusetts Institute of Technology psychologist who heads a public board of inquiry that was asked by the F.D.A. in 1980 to review safety concerns about aspartame, has said that had the panel known how widely aspartame would be used, it would have issued stronger recommendations. He told Common Cause, a public affairs organization that completed a nine-month investigation of aspartame last year, that use of aspartame in soft drinks "never figured in our decision making."

Dr. Nauta's panel was also limited in its assessment to interpreting the results of safety tests. Whether the tests were properly conducted in the first place was not considered, he said.

Found in Wide Variety of Foods

Aspartame, marketed as Nutra-Sweet (when used as a food additive) and Equal (the table-top version), is now found in such foods as soft drinks, gum, breakfast cereals, mixes for hot chocolate and cold drinks and pudding mixes. Although in most products it is combined with either sugar or saccharin, a trend is already evident toward the use of aspartame as the sole sweetener in processed foods. Coca-Cola and Pepsi-Cola, for example, announced they would be using it alone in diet soft drinks, and Ralston-Purina has just introduced a new cereal, Sunflakes, sweetened only with aspartame. Several food processors have filed proposals to use the sweetener in yogurt, ice cream and flavored drinks.

Since it was approved for use in this country in 1981, worldwide sales of aspartame have grown from \$74 million in 1982 to \$600 million last year. It has been an enormous financial boost for a company that a decade ago was embroiled in costly controversy over the quality of its safety tests on several major drugs and aspartame.

Aspartame was originally approved for marketing in 1974, but the approval was quickly stayed when a scientist, Dr. John Olney of Washington University, and an attorney, James S. Turner, objected on the basis of Dr. Olney's findings in animals that aspartame might cause cancerous brain tumors. Dr. Olney remains a strong critic of aspartame approval. Mr. Turner, a consumer advocate with the Community Nutrition Institute in Washington, said the studies needed to clarify this risk had not yet been properly done. The institute recently petitioned the United States Court of Appeals for the District of Columbia to halt further marketing of aspartame products pending the outcome of a requested public hearing on aspartame's safety.

Nor were a number of key studies that had been called into question as scientifically lacking in design and execution ever redone, according to Common Cause and Mr. Turner. Nonetheless, in 1981, Arthur Hull Hayes, then Commissioner of Food and Drugs, approved aspartame for use in dry foods and as a table-top sweetener. Two years later Mark Novich, as acting commissioner, approved aspartame for use in soft drinks. Soon after Dr. Hayes left the agency and took a job as senior medical consultant for Burson-Marsteller, a public relations agency that represents Searle. The company says Dr. Hayes, who is also dean of New York Medical College, has never consulted on anything having to do with aspartame or any other product he ruled on at the drug agency.

Many Factors in Popularity

Among the reasons aspartame is so popular are that it provides the sweetening power of sugar at one-tenth the caloric cost; unlike products made with saccharin, it does not carry a warning about cancer risk and it tastes very much like sugar but, unlike saccharin, has no unpleasant aftertaste.

The drug agency has set an allowable daily intake of 50 milligrams of aspartame per kilogram of body weight, and the agency predicted that

actual average use would run around eight to ten milligrams. According to Dr. Gaull of Searle, levels of use found in a national survey last spring showed that the average was then already twice that — 19 milligrams — and the maximum level consumed by "aspartame abusers" was 28 milligrams. A United States attorney representing the F.D.A. said in court last month that average consumption is now 30 milligrams and that many consumers are above the 50 milligram maximum suggested.

According to Dr. Wurtman, some consumers can easily reach consumption levels that have been linked in animal studies to adverse effects on brain chemicals. Ironically, he added, those using the sweetener to control calories may be defeating their purpose, since his studies show high levels of aspartame may trigger a craving for carbohydrates by depleting the brain of a chemical that registers carbohydrate satiety.

Dr. Connors is worried about aspartame's effects on certain highly sensitive individuals. He has studied two young children who suffer extreme agitation following doses of aspartame equivalent to the amount found in a six-ounce serving of Kool-Aid sweetened with NutraSweet. One of the children becomes so agitated he has to be restrained, Dr. Connors said. The other, who is sensitive to sugar, becomes even more aggressive when given aspartame, he said.

Aspartame is the product of two amino acids (the chemical building blocks of protein), aspartic acid and phenylalanine, which are found in rather large amounts in ordinary protein-rich foods. When digested and metabolized, aspartame breaks down into its component amino acids and methyl alcohol.

Scientific concern has focused on phenylalanine, since some people are unable to process it properly, causing a buildup in the body that can damage

the developing brain. A phenylalanine buildup, should it occur in response to aspartame, could endanger an unborn child whose mother has high levels of phenylalanine in her blood in pregnancy, some scientists say. Dr. William Pardridge of the University of California at Los Angeles, for one, is worried about possible detrimental effects on I.Q. in the children of phenylalanine-intolerant women who consume large amounts of aspartame in pregnancy.

Phenylalanine is also the precursor to tyrosine, a neurotransmitter in the brain. A recent study in rats by researchers in Dr. Wurtman's laboratory showed that aspartame can cause large buildups of phenylalanine and tyrosine in the brain. However, Dr. Wurtman has noted that rats process phenylalanine differently from people. He added that a federally financed study of the behavioral effects of aspartame in animals and people was now under way in his laboratory.

Probe asked in charge that Searle rigged test
Chicago Tribune (1963-Current file); Jan 27, 1977; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
pg. B9

Probe asked in charge that Searle rigged test

WASHINGTON [AP]—The Food and Drug Administration is recommending a federal grand jury investigation into allegations that a major drug company withheld selected test results to win approval for two drugs and a food additive.

FDA officials said a 33-page letter sent to the Justice Department alleged that G.D. Searle & Co. of Skokie, Ill., decided which tests it wanted the FDA to see. The agency recommended that the grand jury investigate whether the company or its officers committed any criminal offense, the officials said.

FDA sources said the allegations involved data submitted by Searle in asking agency approval to market at least three substances: aspartame, an artificial sweetener for foods; aldactone, a diuretic; and flagyl, a treatment for vaginitis.

THE FDA approved aspartame but withdrew approval after it began suspecting the test data. Aspartame has not gone on the market. Aldactone and fla-

gyl are still in use but are labeled with safety warnings.

Justice Department spokesman Mark Sheehan confirmed receipt of the letter but said no decision has been made on the convening of a grand jury.

Both the FDA and the Justice Department declined to release the Jan. 10 letter, but FDA sources said the allegations made in the document were similar to those made by an FDA task force last year.

The task force also had recommended that federal prosecutors call a grand jury investigation.

A spokesman for the company said it could not comment on the specific allegations in the FDA letter "because we don't know what they are. We have maintained from the beginning that if this does go to a grand jury we will vigorously defend our position and we feel we can do so."

Searle has strongly disputed the conclusions of the earlier task force report, calling it "incomplete, biased, and distorted."

Aspartame locked up in classic case of FDA inaction

Janet Key

Chicago Tribune (1963-Current file); Oct 7, 1979; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986 pg. W1

Aspartame locked up in classic case of FDA inaction

By Janet Key

FOURTEEN YEARS, "significantly more than \$55 million, and thousands of man-hours after its discovery, G. D. Searle & Co.'s Aspartame—a low-calorie sugar substitute that could replace the controversial saccharin—remains locked in a logjam of federal Food and Drug Administration bureaucracy.

"It's a classic case of government by inaction, one of the great examples of regulatory paralysis," said John E. Robson, Searle's executive vice president for planning, development, and administration and a former chairman of the Civil Aeronautics Board.

Robson was complaining about the fact that Aspartame, a nutritive sweetener roughly 200 times sweeter than sugar, has been hanging in regulatory limbo since December, 1978. At that time, questions on the validity of Searle's test data—questions that in 1975 stayed the original FDA go-ahead given the year before—were resolved by an FDA-appointed group of independent university pathologists.

BUT ASPARTAME'S regulatory problems plague new drugs as well as food additives introduced in the U.S., causing many to be available in other countries years before they are available here. "The regulatory process has contributed materially to the lag in drug introductions in this country," said O. B. Parrish, president of Searle's Pharmaceutical and Consumer Products Division.

In a strongly worded letter to the FDA this spring, Searle began battling that lag in earnest, contending that the pathologists' report removed the need for Aspartame's continued suspension and resolved the safety questions that were to come before a public board of inquiry.

Searle argued that even if the FDA decided to go ahead with the hearing—originally scheduled for September but now postponed at least until late November—"we can't perceive any reason why the stay shouldn't be lifted immediately, rather than await the conclusion of a hearing that to date hasn't been scheduled."

THE PUBLIC BOARD of inquiry will be held, the FDA insists. But in August, France approved the use of Aspartame as a general purpose sweetener, and in September Canada announced its intent to approve the sweetener at the end of a 90-day objection period. In announcing its decision, Canada's department of health and welfare called the safety data on Aspartame "the most comprehensive ever received by the health protection branch in support of a food additive."

"The FDA is afraid that any mistake (in approving a drug or additive), however slight, will be a political disaster," Parrish said.

"Their tendency is to look for the riskless drug, and that drug doesn't exist," he said.

Indeed, the regulatory maze has contributed significantly to what many in the drug industry see as a two-fold "drug lag"—a delay in the introduction of new drugs in this country and a serious difference between availability in other countries and the U.S.

A SOON-TO-BE-released General Accounting Office (GAO) report found that of 14 drugs classified as "important" by the FDA from July, 1975, through February, 1978, thirteen were available in other countries two months to 12 years before they were available in the U.S.

In the report, the GAO cited the example of sodium valproate, a drug used to treat epilepsy, which won FDA approval in February, 1978, only after enormous public pressure was put on the agency and its manufacturer, Abbott Laboratories. The drug had been approved 11 years earlier in France.

A drug used in treatment of chronic asthma, which is called beclomethasone dipropionate, was submitted for FDA approval in February, 1974, and finally cleared in May, 1977—27 months later. According to the GAO report, approval time in Norway, Sweden, Switzerland, and Great Britain ranged from four months in Britain to 18 months in Sweden.

IN TESTIMONY before a House subcommittee on science research and technology, the University of Rochester's Dr.

Continued on page 3

Aspartame locked up

Continued from page 1

William Wardell, the leading chronicler of the U.S. drug lag, pointed out that the U.S. drug approvals ranged from 15th on endomethacin (an anti-arthritis drug) to 106th on co-trimoxazole (an anti-bacterial drug). The U.S. was the 40th country to recognize the anti-tuberculosis drug capreomycin, the 65th to approve the anti-allergy drug chomolyn sodium, and the 32d to approve the anti-cancer drug andreomycin, he said.

Drugs to prevent death after heart attack, an anti-coagulant to prevent blood clots, and a drug to dissolve gallstones—all available in other countries—are still awaiting FDA approval, according to the GAO report.

"Scientific concerns are basically the same between countries," Dr. Jean Di-Raddo, Wardell's associate, said. "But concern with safety is more politicized in this country than in others, and there are more consumer pressures.

"THE APPROVAL of any new drug is based on an evaluation of its risks and benefits—you're not going to get a riskless one," she continued. "But because the FDA can be called before Congress over any drug that has problems, their safest bet politically is to lie low and—if they have any doubt at all—to just not approve the drug."

In fact, the Pharmaceutical Manufacturers Association estimates that it costs a company on an average of \$54 million and eight to nine years itself, discounting efforts that failed, is a hefty \$11 million.

For a food additive such as Aspartame, where only its safety must be proved. Searle's head of research and development, Dr. Daniel L. Azarnoff, estimates an approximate price tag of \$2 million and three to four years of work.

BUT DR. JOHN T. Curran, an analyst with Wood Gundy, Inc., and a pharmacologist as well, points out that though drug companies make enormous outlays to develop new products, the rewards can be equally large.

"The relevant question is: 'Is it (the new drug) worth spending \$50 million on?' If it isn't, then these men should lose their jobs," Curran said. "But obviously it is because the returns could be enormous."

Curran is betting that Aspartame will replace Saccharin, which he expects to be banned within the next two years, as an artificial sweetener. The Searle Aspartame plant will be in production in 1983 and contributing from \$1.15 to \$1.90 a share to Searle's earnings, he said.

BUT SEARLE SEES itself in a race with the clock to get Aspartame on the market with a significant stake before its patent runs out in 1987—and disagrees with Curran's prediction that they can recoup their investment by 1983.

"I would be very surprised if Aspartame were approved by the end of the year," Azarnoff said. Parrish added: "It's conceivable we could recoup our losses (before the patent runs out). Conceivable, but not likely."

Searle files suit

Janet Key

Chicago Tribune (1963-Current file); Oct 2, 1980; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
pg. C8

Searle files suit

Aspartame opposed by FDA

By Janet Key

THE FEDERAL FOOD and Drug Administration (FDA) Wednesday released a report recommending that the artificial sweetener aspartame, developed by G.D. Searle & Co., not be approved for general use until additional questions on its safety are resolved.

The report by a special three-man board of inquiry said questions about the controversial artificial sweetener being a possible cause of brain tumors in rats should be evaluated before aspartame goes on the market. The board was convened in January.

The report was released just hours after the Skokie-based pharmaceutical company filed suit in federal court in Washington, D.C., to require the FDA

to make a final decision on aspartame.

FDA officials said the scientific board's recommendation to commissioner Jere E. Goyan is a preliminary finding. Searle may file an appeal if it wishes and await the commissioner's final decision, they said.

THERE WAS NO indication whether Searle would file an appeal. A company spokesman said the firm had not yet seen the FDA report.

Aspartame, a nutritive sweetener roughly 200 times sweeter than sugar, has been hanging in regulatory limbo since December, 1978. At that time, questions on the validity of Searle's test data were resolved by an FDA-appointed group of independent university pathologists. In 1975, those questions resulted in a stay of the

FDA's 1974 go-ahead for the sweetener.

Despite Searle's objections, the FDA in 1978 insisted that the company submit its data to another board of inquiry composed of three FDA-appointed university scientists. Aspartame's suspension was continued pending the board's findings.

FOURTEEN YEARS after aspartame's discovery, Searle executives estimate the company has spent more than \$55 million on its development as a substitute for saccharin.

"Over the years of delay and nondecision [by the FDA], the company has incurred tremendous costs and seen the patent protection for its invention eroded by the passage of time," said Searle's announcement of its suit.

Searle's patent on aspartame runs out in 1987.

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New aspartame plea
Chicago Tribune 1963-Current file; Dec. 18, 1980; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
pg. C8

New aspartame plea

G.D. Searle & Co., the Skokie-based pharmaceutical firm, asked the Food & Drug Administration to allow the marketing of its artificial sweetener, aspartame, contending it is safe. Searle made the plea in a scientific response to a Board of Inquiry's recommendation that the sweetener be barred until further research is done. The board's verdict was made public in October.

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Soft drink makers ask FDA to delay aspartame use
Michael L. Millenson
Chicago Tribune (1963-Current file); Jun 29, 1983; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
pg. C16

Soft drink makers ask FDA to delay aspartame use

By Michael L. Millenson
Chicago Tribune

WASHINGTON—The National Soft Drink Association is asking the Food and Drug Administration to delay approving the low-calorie sweetener aspartame for use in carbonated beverages because of possible safety questions related to aspartame's instability under high temperatures.

In a letter June 24 to FDA Commissioner Arthur H. Hayes Jr., the association also cites questions raised recently by Dr. Richard Wurtman of Massachusetts Institute of Technology about possible behavioral changes that high

doses of aspartame may cause.

The letter is the latest development in a continuing controversy about expanded use of aspartame, a low-calorie sweetener made by G.D. Searle & Co., Skokie. At stake is which sweetener will be used in the nearly \$4 billion worth of diet soft drinks Americans consume each year.

THE ASSOCIATION said it was concerned about the instability of aspartame in soft drinks when the temperature reaches 86 degrees Fahrenheit, noting that Searle had been unable to identify what happens to as much as 30 percent of aspartame after it breaks down at that temperature.

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Senate Rejects Labels On Aspartame Volume

WASHINGTON, May 7 (AP) — The Senate today defeated a proposal that would have required bottlers of soft drinks to tell consumers how much of the artificial sweetener aspartame is contained in their product.

The Senate voted 68 to 27 against the proposal, which Senator Howard M. Metzenbaum, Democrat of Ohio, said would allow consumers to judge for themselves how much of the sweetener they would consume.

Some scientists say aspartame, sold under the trade name NutraSweet, may be dangerous.

The amendment faced heavy opposition from the soft drink industry, which asserts that the sweetener is not harmful.

Mr. Metzenbaum predicted before the vote that it would be defeated, saying, "My guess is that the lobbyists have done their job and done it well."

The proposal was offered as an amendment to a pending bill extending for two more years the special exemption that allows saccharin to be used in foods despite animal tests linking that sweetener to bladder cancer.

The Senate passed the overall bill by a vote of 94 to 1 and sent it to the House, where quick approval was expected. Senator William Proxmire, Democrat of Wisconsin, cast the negative vote.

The Taste of Congressional Fudge

New York Times (1857-Current file); May 17, 1985; ProQuest Historical Newspapers The New York Times (1851 - 2005) pg. A30

The Taste of Congressional Fudge

Some 68 million Americans consume diet soda and other low-calorie products. In place of sugar those foods contain saccharin or aspartame, artificial chemicals that tickle the sense of sweetness. Shadows lie over both substances. It's far from proved that they really help people lose weight. And despite years of tests, doubts remain as to whether either is wholly safe.

Congress nonetheless seems quite unperturbed that so many people are exposed daily to sweeteners of imperfect safety. Its only concern is to keep serving a fudge it first cooked up in 1977.

At that time the Food and Drug Administration proposed to ban saccharin, having found it to be a weak carcinogen. The agency had no option, since the law known as the Delaney amendment requires the banning of any substance found by appropriate tests to cause cancer in animals. But an outcry from the consumers and makers of diet soft drinks made Congress postpone the ban by granting saccharin a two-year exemption from the Delaney law.

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One two-year exemption might be understandable, during which Congress rewrote the Delaney law to its liking, yet Congress has now given saccharin its fifth. Why should saccharin, an outlaw but for the repeated exemptions, remain as popular on Capitol Hill as apple pie? Why in all Congress should only two members, Senators William Proxmire and Howard Metzenbaum, be troubled by the contradiction of repeatedly instructing the F.D.A. to ignore a law that Congress has written and for eight years has been unable to change?

Because once you start fudging, it's hard to stop. Congress cannot in practice vote to weaken the

Delaney law because maybe nothing, including the doubtful advantages of artificial sweeteners, outweighs the risk of adding carcinogens to food. At first Congress extended saccharin's life because there was no alternative product.

Then aspartame — popularly known as Equal and NutraSweet — was approved for sale, eroding that justification. Still, even aspartame's continued safety is far from clear, and Congress fears the wrath of its constituents if the diet-soda industry should be left high and dry. No wonder the industry is pushing for reevaluation of a third sweetener, cyclamate, banned in 1969.

Each substance has its problems. Saccharin is a weak cause of bladder tumors, though only in male rats. A recent study by Common Cause fiercely criticized the F.D.A.'s approval of aspartame over the doubts of some of its own scientists. After investigating consumer complaints, the Centers for Disease Control this year recommended a systematic study of aspartame's effects on brain and behavior, though noting that such effects are neither serious nor widespread. Cyclamates, it now turns out, may have been banned on faulty evidence of carcinogenicity, but there are new worries about other possible effects.

On present evidence, the risks of both saccharin and aspartame seem extremely small at the worst. But their benefits appear also limited, except to diabetics. Substances consumed by 68 million people should surely command a very high certainty of safety. Congress, if it fears rewriting the Delaney law, should let it apply to saccharin. If it has doubts about aspartame, let it direct the F.D.A. to resolve them. To keep fudging the issue, year after year, is to shirk responsibility.

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A Sweetener's Effects: New Questions Raised

By MARIAN BURROS

New York Times (1857-Current file); Jul 3, 1985; ProQuest Historical Newspapers The New York Times (1851 - 2005)
pg. C1

A Sweetener's Effects: New Questions Raised

By MARIAN BURROS

IN 1984 G. D. Searle & Company of Skokie, Ill. sold \$600 million worth of the artificial sweetener aspartame, on which it holds the exclusive United States patent. Produced under the trademark NutraSweet as a food additive and Equal as a table-top sweetener, aspartame is found in a wide variety of products — from puddings, bubble gum and breakfast cereals to some of the best known diet soft drinks marketed by Coca-Cola, Pepsi and Seven-Up.

Recently, however, aspartame has been the target of criticism from several scientists conducting studies of the sweetener or its components. While their findings are not conclusive, preliminary data have indicated that aspartame may be responsible for a range of problems from temporary dizziness to mental retardation.

Their contentions are strongly denied by Searle, which has done its own studies on aspartame in the past and is conducting new ones. "When any new product is marketed and attention is called to it, people tend to ascribe any adverse experience to that new product," said Dr. Frank M. Sturtevant, a pharmacologist who is director of the office

of scientific affairs at Searle. "We expected a lot more in the way of complaints than we got: only 600 out of 70 million people who have used it."

Aspartame has been controversial since Searle first sought to market it in 1974. After considerable debate about its safety, the sweetener was approved by the United States Food and Drug Administration in 1981. But this spring questions about its effects began to surface again.

In May, the Senate Committee on Labor and Human Resources received testimony from two researchers favoring quantitative labeling of products containing aspartame. In accordance with Federal law, it is now listed on labels as an ingredient; no amount is specified. Dr. William Pardridge, an associate professor of medicine at the University of California at Los Angeles, said that too much of the artificial sweetener might cause subtle brain changes in young children. Dr. Richard J. Wurtman, director of the clinical research center at the Massachusetts Institute of Technology, said that consuming aspartame with carbohydrates might double aspartame's effect on the brain.

On June 17, Dr. Louis Elsas, director of the

Continued on Page C7

A Sweetener's Effects: New Questions

Continued From Page C1

division of medical genetics at Emory University in Atlanta, said that neither pregnant women nor infants under the age of 6 months should consume aspartame because of the chance of brain damage to the fetus or infant.

Dr. Sturtevant, who calls these conclusions "at best, highly speculative," says dozens of tests done by Searle prove the safety of aspartame. Dr. Sanford Miller, director of the F.D.A.'s Center for Food Safety and Applied Nutrition, says that the claims against aspartame are unfounded. And the American Diabetics Association has reaffirmed its faith in aspartame, saying that F.D.A.'s studies "appear sufficient to demonstrate its safety."

Since the marketing of aspartame four years ago, the Centers for Disease Control in Atlanta has received over 600 complaints from people who said they suffered dizziness, headaches, blurred vision or grand mal seizures (a type of epilepsy) after consuming aspartame. The centers called for studies to determine individual sensitivity to the sweetener.

On May 23, a \$2 million lawsuit was filed against Searle in United States District Court in Washington on behalf of a 5-year-old boy in Olney, Md. The suit charged that consumption of NutraSweet caused irreversible brain damage, but it did not specify the amount consumed.

In granting approval of aspartame — which is 180 to 200 times sweeter than sugar with only one-tenth of the calories — Dr. Arthur Hull Hayes Jr., the F.D.A. Commissioner in 1981, overruled several of the agency's scientists and an independent public board of inquiry set up to evaluate the Searle studies of aspartame's effect on animals. These scientists said that the company's research did not adequately answer the safety questions about carcinogenicity. According to

Congressional testimony from Dr. Alexander M. Schmidt, a former F.D.A. Commissioner, some of the experiments were "poorly conceived, carelessly executed or inaccurately analyzed or reported."

After a recent review of the Searle studies, Dr. M. Adrian Gross, a senior science adviser at the Environmental Protection Agency and a former pathologist at the F.D.A., wrote to the office of Senator Howard M. Metzenbaum, a member of the Committee on Labor and Human Resources. His letter said that despite the shortcomings of the experiments, "at least one of those studies has established beyond any reasonable doubt that aspartame is capable of inducing brain tumors in experimental animals."

In a telephone interview, Dr. Sturtevant asserted that some of the data presented to Dr. Gross for review were incorrect. The correct tabulations, he contended, were contained in a document that he wrote for the board of inquiry impaneled by the F.D.A. The document showed, he said, "that there is no statistically significant increase in brain tumors in experimental animals."

Aspartame-sweetened foods now carry a warning directed at phenylketonurics — people who are unable to metabolize phenylalanine, one of the two amino acids that make up aspartame. Victims of phenylketonuria, or PKU, will become permanently retarded if the condition is not diagnosed at birth and consumption of phenylalanine strictly controlled.

According to Dr. Elsas, about 2 percent of the population are carriers of the PKU gene and are unaware of the condition. He has expressed concern about the effects of phenylalanine on unborn children of PKU carriers.

"A small change in the phenylalanine level in a pregnant woman's blood is magnified by the placenta into the fetal blood, and the fetal brain will concentrate that further," Dr. Elsas explained. "High levels of

phenylalanine in unformed or forming brains could cause irreversible damage. No one knows what degree of elevation in the mother's blood may cause brain damage in the fetus."

Dr. Elsas's concern is based on two studies of the effects of phenylalanine on two groups of people — 10 in each group ranging in age from 8 to 24 — who have PKU but have developed normally. In these studies, the first of which was published in the *Journal of Clinical Investigation* in January, Dr. Elsas observed that the patients' reaction time was affected and the production of adrenalinlike chemicals in the brain was reduced.

The second study, just completed, confirms the first, he said, adding, "All of the brain changes were reversible within a three-week period, but it took longer for full mental functions to return."

Dr. Elsas said that anybody over the age of 6 months should consume "aspartame in moderation, and if they have symptoms, they should get their phenylalanine blood level checked."

Dr. Sturtevant says that Dr. Elsas "is scaring people unnecessarily." "It is not physically possible for an unknown PKU carrier to maintain a phenylalanine blood level in the unsafe range by means of consuming products containing NutraSweet," he said. "There is no experimental evidence to suggest a risk to the fetus." Searle has eight studies of its own under way exploring the effects of aspartame on the brain.

Dr. Wurtman of M.I.T. does not believe that moderate amounts of aspartame are a hazard to normal people. "But," he said in a recent interview, "I think there are some numbers of people who are at risk." Dr. Wurtman, who is a consultant to Searle on products other than aspartame, said that when he and Searle "talk about aspartame we tend not to agree."

Dr. Wurtman's own animal studies show that "you double the effect of the phenylalanine in the brain when you have aspartame and carbohydrates together, and no one knows what a safe amount is," he said. "There are several groups of people who might be especially susceptible to high doses. These include people who are taking drugs that act on the brain like antihypertensives, people with a history of seizures, young people and pregnant women." For adults who do not fall into the above categories, Dr. Wurtman said half a gram to one gram of aspartame a day should be safe.

"But," he added, "if a 7-year-old, weighing about 45 or 50 pounds, drinks a 2-liter bottle of Diet Coke, which contains about 1,200 milligrams, he is already exceeding the allowable daily limit for aspartame suggested by F.D.A."

Dr. Wurtman said he knew of a dozen patients "with first-time seizures confirmed in university hospitals who were consuming very large amounts of aspartame." "It is very important," he said, "that such people be subjects in controlled studies."

Dr. Wurtman also said all foods containing aspartame should state the amount on the label.

But Searle and soft-drink manufacturers disagreed. "We have no objection to F.D.A. requiring quantitative labeling for food ingredients in general," Dr. Sturtevant said, "but we do object to F.D.A. singling out aspartame, because there is no scientific evidence suggesting that it need be."

"Aspartame is safe," said Dr. Miller of the F.D.A., but he added: "We are not moving very rapidly to approve new uses. If there is another segment of the population besides phenylketonurics who are sensitive, we will do whatever we have to do — from putting something on the label up to banning it if the population is large enough."

Nutrasweet Faces A Senate Hearing

WASHINGTON, July 16 (Reuters) — Senator Howard M. Metzenbaum, Democrat of Ohio, said he would hold a hearing in September on health concerns about aspartame, the popular artificial sweetener marketed under the brand name Nutrasweet by the Monsanto Company. The hearing will be held by the Senate Labor and Human Resources Committee, which has jurisdiction over the Food and Drug Administration.

Despite the news, Monsanto's shares gained 12.5 cents a share, to close at \$87.625, on the New York Stock Exchange.

F.D.A. Cites Other Findings
New York Times (1857-Current file); Aug 16, 1987; ProQuest Historical Newspapers The New York Times (1851 - 2005)
pg. 30

F.D.A. Cites Other Findings

WASHINGTON, Aug. 15 (AP) — An expert with the Food and Drug Administration said the study simply confirmed the need for aspartame tests on humans.

The expert, Dave Hattian, chief of regulatory affairs for the agency's Food Safety Center, said other laboratories "have models in which there appears to be an enhancement of seizure expression."

He said testing under way on humans might end the debate.

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Aspartame hits a snag
Carol Rasmussen
Chicago Tribune (1963-Current file): Dec 11, 1975; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
Pg. S_B4

Aspartame hits a snag

By Carol Rasmussen
Tribune Staff Writer

A CHARMED LIFE nonsugar sweeteners do not lead. Aspartame, a sweetener 180 times as powerful as sugar has been removed from the Food and Drug Administration's list of approved food additives. Not long ago, aspartame held promise of filling the void left among nonsugar sweeteners when cyclamates were withdrawn from use by the FDA.

HOWEVER, SERIOUS questions were raised about the adequacy of research by aspartame's makers, G.D. Searle & Co., by Dr. John W. Olney of Washington University in St. Louis, a well-known research scientist. Olney questioned Searle's research during the usual comment period after the FDA published a proposal to make aspartame a legal

food additive in July, 1974.

Just recently, the FDA announced suspension of permission to market the nonsugar sweetener because, according to Ruth Weishelt, consumer affairs officer for the Chicago district FDA office, they need more comprehensive review of Searle's data, as well as the way in which the company conducted its research.

If the FDA concludes the research is adequate, it will file another petition in the federal register, which automatically allows for another comment period. But for the time being, use of the sweetener is at a "standstill," said Weishelt.

G.D. Searle & Co. spokesman, Sarah Bangser, said the company had voluntarily withheld aspartame from the market since the original objections were raised over a year ago.

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FDA disputes doctor's charge alleging dangers of aspartame

Michael L. Millenson

Chicago Tribune (1963-Current file); Aug 19, 1983; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
pg. B1

FDA disputes doctor's charge alleging dangers of aspartame

By Michael L. Millenson

THE SUCCESS of G.D. Searle & Co.'s artificial sweetener aspartame hit an air pocket Thursday after publication of a letter in a prestigious medical journal alleging that high doses of the compound could cause dizziness and a variety of mental problems.

The Food and Drug Administration said data presented in the letter didn't support the theory and reiterated its position that there is no evidence aspartame causes behavioral changes.

Nevertheless, the letter, which appeared in Thursday's issue of the New England Journal of Medicine, prompted a \$1.25-per-share drop, to \$53.75, in the price of Searle stock. The shares remained comfortably above the \$44.37 level at which they traded the day before the FDA decision announcing approval of the use of aspartame in soft drinks.

COCA-COLA CO., which began distributing an aspartame-sweetened cola Wednesday, saw the price of its stock drop \$1 to \$50.63 a share in composite trading.

On the other hand, Royal Crown Cos., which said Wednesday it is distributing a salt-free, aspartame-sweetened soft drink, recorded a 50 cent gain in the price of its stock to \$19.37 a share.

Squirt & CO. OF Holland, Mich., the third company to have announced the introduction of an aspartame-sweetened soft drink, is privately held.

DR. RICHARD J. Wurtman, a physician and professor of neuroendocrine regulation at Massachusetts Institute of Technology, warned in the letter that heavy doses of aspartame might change levels of chemicals in the brain that affect behavior.

He said pilot studies by his laboratory

showed that the effects would be more likely to be triggered if the aspartame-sweetened beverage was consumed with a carbohydrate, such as a sandwich, cake or cookie, because of the cumulative effect on the insulin level in the blood.

He wrote that "the dose of aspartame used in these studies was consistent with the amount that an 8-year-old child might consume during a hot afternoon" by drinking three cans of soda pop completely sweetened with aspartame, then eating a sandwich or other carbohydrate-rich food.

Others most likely to be affected include those with underlying brain disorders, such as insomnia, hyperactivity and Parkinson's disease, Wurtman wrote.

WURTMAN'S HYPOTHESIS was disputed by Sanford Miller, director of the FDA's Bureau of Foods and a former MIT professor of nutritional biochemistry. Wurtman, who opposed the FDA's decision last month to approve aspartame's use in carbonated beverages, had previously submitted results of his tests to the FDA.

"Based on the data I have seen so far, there is no evidence anybody should have any concern," said Miller. "The evidence does not support his hypothesis."

Miller noted that soft drinks sweetened completely with aspartame have been used in Canada for two years without any reports of unusual problems. Both Coca-Cola and Royal Crown have sold aspartame-sweetened soft drinks in Canada since 1981, when saccharin was banned after being linked to cancer in rats.

Both companies have said they will use a mixture of saccharin and aspartame in this country, while Squirt has said it will sell a 100

Continued on page 4

Aspartame

Continued from 1st Business page

percent aspartame-sweetened drink.

Miller said the FDA supports continuing studies of the substance. By law, the FDA presently is considering whether to hold a special hearing on its decision to permit aspartame use in carbonated beverages.

IN AN INTERVIEW with The Tribune, Wurtman called on Searle and the soft-drink industry to sponsor "reputable scientific research" at different laboratories on the possible behavior effects of aspartame.

Aspartame is composed of two naturally occurring amino acids, L-phenylalanine and L-aspartic acid. The concern is over the way high levels of phenylalanine might affect behavior.

At Searle, Dr. Daniel Azarnoff, head of the company's research and development division, pointed to the FDA decision on aspartame safety and said the Skokie-based firm is supporting continuing studies on the sweetener.

MEANWHILE, The Tribune learned that Wurtman presented his information on aspartame's possible link to behavioral changes to representatives of major soft-drink makers—including Coca-Cola, PepsiCo, Royal Crown and Seven-Up—at a July 18 meeting of a scientific committee of the National Soft Drink Association.

A spokesman for Coke said Thursday that "we basically adopt the FDA position that the [Wurtman] study is not conclusive."

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FDA reviews 200 complaints on aspartame

WASHINGTON [UPI]—Federal researchers are examining 200 allegations of adverse reactions to the low-caloric sweetener aspartame, which a consumer group wants taken off the market.

A spokesman for the Food and Drug Administration said a preliminary review last week of 50 complaints, ranging from headaches to seizures, found no causal relationship between the problems and the sweetener.

"We're now examining all 200 cases with the assistance of the Centers for Disease Control," the spokesman said Wednesday.

THE FDA told U.S. District Judge Barrington Parker last month that it would decide by Feb. 21 whether to hold public hearings on the safety of aspartame, approved in July for use in carbonated drinks.

The Community Nutrition Institute, a local consumer group, filed a suit Wednesday asking Parker to require the hearings and to order the sweetener off store shelves until health questions are resolved.

Parker rejected a similar request from the group Jan. 24, saying it had insufficient evidence.

The institute returned to court with letters from researchers and users that cited 100 cases of suspected adverse reactions.

DENISE ERTELL, an official at G.D. Searle & Co. of Skokie, maker of the sweetener, said: "We don't believe there is legal or scientific merit to their allegations. Aspartame is safe. It has been thoroughly tested. It has been approved not only by the FDA but by the health regulatory agencies of more than 30 countries." The first approval came in 1979.

Aspartame has been permitted in the United States since 1981 as a sugar substitute for table use, in powdered beverages, dessert toppings and chewing gum.

About 10 percent of the 100 complaints of suspected adverse reactions cited in the suit involve seizures, none fatal, the consumer group said. Others included headaches, dizziness, blurred vision and one miscarriage.

Almost 200 times as sweet as sugar, aspartame is composed of aspartic acid and phenylalanine. In extremely high levels, phenylalanine can be toxic to the brain.

Amino acids in aspartame cause for concern

By G. Timothy Johnson, M.D.

DEAR DR. JOHNSON: If aspartame, the artificial sweetener, is composed of naturally occurring chemicals, why do some scientists think it might be dangerous?

Even though aspartame is composed of two amino acids [the building blocks of protein], it does not contain those substances in the same balance and combination they are found—combined with other amino acids—in naturally occurring proteins.

Therefore, some scientists are concerned these amino acids, consumed in the form they appear in aspartame, may have a far different effect than when consumed as part of normal protein.

Scientists are most concerned about phenylketonuria—a condition in which the body cannot handle or metabolize phenylalanine. Because aspartame is composed of phenylalanine and aspartic acid, there is concern people with the problem in metabolizing this particular amino acid might have



How to keep well

problems from consuming large amounts of it via the artificial sweetener.

DEAR DR. JOHNSON: My young daughter recently had an infection in her urine and the doctor gave her antibiotics for only three days. I can remember from my childhood always having to take penicillin for at least two weeks and the doctor stressing it. Is three days enough?

For uncomplicated infections of the urine, three days of antibiotics turns out to be good as the usual 10 days to two weeks. Indeed, sometimes only a single day's worth of antibiotics seems to work.

However, this rule applies only for uncomplicated infections of the

urine and does not easily translate to other kinds of infection. Thus, a sore throat caused by bacteria, for example, usually does require the 10-days-to-two-weeks formula.

DEAR DR. JOHNSON: If you are bitten by a dog or cat should you bother to take antibiotics even if the cut is very minor?

There is a lot of controversy over whether antibiotics should be used on a preventive basis in the treatment of dog and cat bites. In general, many physicians believe cat bites are more dangerous than dog bites and so are more likely to use preventive antibiotics in treating a cat bite.

However, each case must be assessed individually in terms of the exact nature of the bite, its severity, its location and any other medical factors that might compromise the individual's ability to fight infection.

I also should point out that a person is at risk for tetanus from animal bites and, therefore, must make sure he or she is up to date on tetanus shots at the time of a bite injury.

Study says sweetener alters some brain functions of mice
Chicago Tribune (1963-Current file); Sep 7, 1985; ProQuest Historical Newspapers Chicago Tribune (1849 - 1986)
pg. 3

Study says sweetener alters some brain functions of mice

LOGAN, Utah [AP]—An ingredient in the artificial sweetener NutraSweet has caused irregularities in some brain functions of laboratory mice, Utah State University researchers said Friday.

The report sent the stock of Monsanto Co., which is acquiring NutraSweet's maker, G.D. Searle & Co. of Skokie, down sharply on Wall Street, even though Searle discounted the research.

Roger Coulombe, a researcher in the USU Food Science Department, said aspartame—the generic name for NutraSweet—induced changes in brain neurotransmitter levels controlling the pituitary gland.

Dissected brain tissue of the mice showed that most of those given aspartame had more nervous-system irregularities than those not given the sweetener, he said.

"We feel these changes explain some of the complaints associated with aspartame, such as mood alterations, nausea and menstrual irregularities," Coulombe said. He said consumers of NutraSweet should not be alarmed, but he called for more research.

Thym Smith, Searle's vice president of public affairs for Nu-

traSweet, criticized the research.

"It's our understanding that this was done with very high doses, which are not necessarily applicable to humans because a human being would never consume that much, either in one sitting or in a lifetime," Smith said.

"This issue is not a new issue. It's part of all the scientific data that was reviewed prior to the approval of aspartame," he said. "As always before, we stand by the safety of our product."

Coulombe said the mice "were fed aspartame at realistic human equivalent levels of low, high and abusive consumption levels."

One study sought to determine the effects that would be felt by a child who drinks four liters of soft drink containing aspartame in one day, he said.

That dose would cause a significant increase in the neurotransmitter levels of the child's brain, Coulombe said, but he could not predict how that would affect the child.

Searle recently agreed to be acquired by Monsanto, the St. Louis-based chemical company. Word of the report sent the stock price of Monsanto down \$2.25 a share,

Hearings sought on aspartame

Pamela Sherrod

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Hearings sought on aspartame

By Pamela Sherrod

A U.S. senator Thursday called on two Senate committees to hold formal hearings on the failure of the U.S. attorney's office in Chicago to investigate the effects of G.D. Searle & Co.'s artificial sweetener aspartame.

Sen. Howard Metzenbaum (D., Ohio) released more than 110 pages of documents from a year-long investigation by his staff into the government's probe of the artificial sweetener, claiming no follow-up procedures have been taken since 1978 when the investigation was closed.

The documents released by Metzen-

baum claim two key Chicago prosecutors, then-U.S. Atty. Samuel Skinner and Assistant U.S. Atty. William Conlon, failed to move on a 1977 request for a grand jury inquiry into Searle's handling of NutraSweet test results, and then joined the law firm that represented Searle, Sidley & Austin.

"I have not seen Mr. Metzenbaum's statement and I don't have any comment," Conlon said. Skinner, whose secretary said he would be out of town until Monday, was unavailable for comment.

Metzenbaum also released copies of letters he sent to Sen. Strom Thurmond

[R., S.C.], chairman of the Judiciary Committee, and to Sen. Orrin Hatch [R., Utah], chairman of the Labor and Human Resources Committee.

Citing concerns from the Food and Drug Administration and reports from doctors on possible adverse effects of aspartame, which is marketed under the names NutraSweet and Equal, Metzenbaum said 100 million Americans are using the product under the belief its safety has been confirmed.

In letters to both Thurmond and Hatch, Metzenbaum asked that "oversight hearings be held on how the

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Aspartame

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investigation was handled" by the U.S. attorney's office in Chicago. He also urged that the matter be reopened "to dispel the cloud hanging over a food additive presently being consumed in massive quantities by the American people."

"What we hope for is for congressional hearings with full subpoena power to get to the bottom of the controversy surrounding NutraSweet," said Drew Von Bergen, a spokesman for Metzenbaum in Washington. "I believe the documents that were released today really speak for themselves."

Metzenbaum said a year-long investigation by his staff into the government's handling of aspartame's tests "raises serious questions" as to whether all safety questions surrounding the sweetener have been resolved.

Metzenbaum claims in-house FDA memos showing credibility of key tumor tests were questioned by FDA scientists before NutraSweet's approval and that problems with the credibility of Searle's tests continued until the food additive's approval in 1981.

In addition to naming Skinner and Conlon among his "who's who" in the aspartame investigation, Metzenbaum listed U.S. Atty. Anton Valukas, who had previously worked with the U.S. attorney's office.

Valukas left the U.S. attorney's office May 2, 1976, to join the law firm of Jenner & Block before he became U.S. attorney last year.

"Despite at least three requests from the Food and Drug Administration, the U.S. attorney's office never opened the grand jury inquiry into allegations Searle failed to report or concealed unfavorable test results on aspartame," Metzenbaum wrote.

In commenting on Metzenbaum's charges, Valukas said, "We have no comment. I can say the investigation is not ongoing."

Searle has insisted the food additive has been fully tested, but some doctors who worked with the FDA and researchers have linked the sweetener to seizures, brain tumors and birth defects, Metzen-

baum said.

Searle, which is based in Skokie, was sold for \$2.8 billion last summer to Monsanto Co., which now sells the sweetener through a separate subsidiary—NutraSweet Co.

Revenues in 1985 for the sweetener came to \$700 million.

Bill Vaughn, a spokesman for NutraSweet, said that while Chicago prosecutors subpoenaed company records in 1977 "there was nothing in the subpoena requesting any information on NutraSweet."

Describing Metzenbaum's charges as "old stuff," Vaughn said to his knowledge Searle had no involvement in approaching anyone from the U.S. attorney's office to join the firm.

Although NutraSweet was first approved by the FDA in July, 1974, Metzenbaum said concerns about the credibility of Searle's tests led the FDA to stay that approval in December, 1975.

In 1976, however, an FDA Investigation Task Force published a report on the testing practices of Searle and concluded:

"At the heart of FDA's regulatory process is its ability to rely upon the integrity of the basic safety data submitted by sponsors or regulated products. Our investigation clearly demonstrates that, in the G.D. Searle Co., we have no basis for such reliance now."

Metzenbaum said one of the recommendations of the FDA's 1976 task force report was that the agency ask the U.S. attorney in the Northern District of Illinois to institute grand jury proceedings against Searle.

Metzenbaum said it's a matter of public record that in January, 1977, the FDA formally requested the U.S. attorney to conduct a grand jury investigation of tests on two Searle products—NutraSweet and Aldactone, a drug to test hypertension.

Metzenbaum charged that it is also known that Skinner, the first U.S. attorney in charge of the sweetener case, recused himself, citing preliminary employment discussions with the law firm of Sidley and Austin, which was then defending Searle. Skinner joined the firm in July, 1977.

Thomas Sullivan filled the post, but Metzenbaum claims Sullivan closed the investigation in December, 1978, despite the FDA's insistence that problems still existed.

Study links seizures to NutraSweet

From Chicago Tribune wires

CAMBRIDGE, Mass.—A scientist said Monday he has identified 82 people who say they suffered epileptic-like seizures after consuming a popular artificial sweetener.

A spokesman for the manufacturer of the sweetener, which is marketed as NutraSweet, said the additive has been proved safe.

In a separate development, the Supreme Court Monday refused to force the Food and Drug Administration to hold public hearings on the use of NutraSweet in soft drinks.

The high court, without comment, rejected an appeal by nutrition groups that said the additive, also known as aspartame, was approved by the FDA without adequate study of potential health hazards.

In the study of seizures, Dr. Richard Wurtman, a neuroscientist at the Massachusetts Institute of Technology, said the subjects suffered the attacks after ingesting foods or beverages containing NutraSweet.

The subjects were examined after the seizures and found to have no brain abnormalities that would explain the attacks, said Wurtman, who said the findings were turned over to the FDA.

The typical patient was a young woman between 20 and 40 with no history of neurological problems, he said. Many said they suffered moodiness, headaches, numbness, tingling or *deja vu*—a feeling of having experienced something before—for days or weeks before the seizures.

Wurtman accused the G.D. Searle Division of Monsanto Chemical Co., which makes NutraSweet, of failing to refer complaints about the seizures to the FDA.

"The companies are obligated by law to inform the Food and Drug Administration whenever they receive reports of adverse reactions like seizures," he said.

"But some of our patients tell us that when they contacted the manufacturer to tell about their seizures, instead of being given instructions to tell the FDA, they were sent letters denying the existence of the seizure problem," he said.

In a telephone interview, a spokesman for the Skokie, Ill., company dismissed Wurtman's criticism.

"He's been a longtime critic. We feel as a very responsible company that we're doing what needs to be done in this area," said spokesman Bill Vaughn.

Vaughn said no problems were found in more than 100 studies conducted before NutraSweet was approved by the FDA.

"There's been all kinds of studies done and there's been no evidence of seizures," said Vaughn.

He said two company-funded studies are investigating the seizure complaints.

But Wurtman, claiming the company has delayed the studies, said he plans to conduct his own research involving 10 people who said they experienced seizures after consuming NutraSweet.

The volunteers will be monitored at MIT's Clinical Research Center for 18 days while they consume NutraSweet in quantities similar to those they were taking when they said they had the seizures.

About 100 million people in the United States consume NutraSweet in a large number of foods and beverages, said Wurtman, who is conducting his study with Dr. Donald Schomer of Harvard Medical School.

Wurtman, who first brought attention to the possible seizure problem in a letter to the British journal *Lancet* in November, said the substance is made with an amino acid known as phenylalanine, which can be toxic to the brain.