Despite the popularity of low-calorie, sugar-free foods and beverages, some people have concerns or questions about the safety of the sugar substitutes that make these products possible. Misinformation about sugar substitutes abounds, especially on the Internet, and people may have difficulty distinguishing trustworthy sources of information on this topic from less reliable ones. This revised and updated report by the American Council on Science and Health summarizes the scientific facts about the safety of sugar substitutes.

This consumer-friendly publication is based on the manuscript "Low-Calorie Sweeteners and Other Sugar Substitutes: A Review of the Safety Issues," published in the journal *Comprehensive Reviews in Food Science and Food Safety*, by Dr. Manfred Kroger of Pennsylvania State University and Kathleen Meister and Dr. Ruth Kava of the American Council on Science and Health. This second edition was updated and revised by ACSH's Dr. Ruth Kava, and Ariel Savransky, M.S.

The American Council on Science and Health is a consumer education consortium concerned with issues related to food, nutrition, chemicals, pharmaceuticals, lifestyle, the environment and health. It was founded in 1978 by a group of scientists concerned that many important public policies related to health and the environment did not have a sound scientific basis. These scientists created the organization to add reason and balance to debates about public health issues and bring common sense views to the public.
SUGAR SUBSTITUTE

YOUR HEALTH

First Edition by
Kathleen Meister, M.S.

Second Edition
Revised and Updated by
Ruth Kava, Ph.D., R.D.
Ariel Savransky, M.S.

For
The American Council on Science and Health

Based on
“Low-Calorie Sweeteners and Other Sugar Substitutes: A Review of the Safety Issues,” by Manfred Kroger, Ph.D., Kathleen Meister, M.S., and Ruth Kava, Ph.D., R.D. Published in the online journal, Comprehensive Reviews in Food Science and Food Safety

March 2015

a publication of the
American Council on Science and Health
Science. Not Hype.
ACSH THANKS THE FOLLOWING INDIVIDUALS FOR THEIR REVIEWS OF THE 2006 ORIGINAL TECHNICAL VERSION OF THIS PAPER

JOSEPH F. BORZELLECA, PH.D.
Medical College of Virginia

FERGUS M. CLYDESDALE, PH.D.
University of Massachusetts, Amherst

NANCY COTUGNA, DR. P.H., R.D., C.D.N
University of Delaware

F.J. FRANCIS, PH.D.
University of Massachusetts, Amherst

KATHRYN KOLASA, PH.D., R.D. LD/N
East Carolina University

BILL D. ROEBUCK, PH.D., D.A.B.T.
Dartmouth Medical School

GILBERT L. ROSS, M.D.
ACSH

AUBREY N. STIMOLA
ACSH

ELIZABETH M. WHELAN, SC.D., M.P.H.
ACSH

CAROL A. WHITLOCK, PH.D., R.D.
Rochester Institute of Technology

ACSH accepts unrestricted grants on the condition that it is solely responsible for the conduct of its research and the dissemination of its work to the public. The organization does not perform proprietary research, nor does it accept support from individual corporations for specific research projects. All contributions to ACSH—a publicly funded organization under Section 501(c)(3) of the Internal Revenue Code—are tax deductible.

Individual copies of this report are available at Amazon.com.

Copyright © 2015 by American Council on Science and Health, Inc.

This book may not be reproduced in whole or in part, by mimeograph or any other means, without permission.
Sugar Substitutes and Your Health
EXECUTIVE SUMMARY

• Foods and beverages containing sugar substitutes are widely used in the United States and other countries; they offer attractive dietary options for people who are trying to limit calorie intake and/or reduce the risk of tooth decay.

• In the U.S., there are eight high intensity sweeteners that have been approved by the FDA. These are: acesulfame-K, advantame, aspartame, Luo Han Guo fruit extracts, neotame, saccharin, stevia and sucralose.

• In several instances, scientific studies have raised questions about the safety of specific sugar substitutes. Concerns about the possible cancer-causing potential of cyclamate and saccharin, raised during the 1960s and 1970s, respectively, have been resolved.

• Two sugar substitutes currently used in some other countries — alitame and cyclamate — are not approved as food ingredients in the United States. Alitame and cyclamate are under consideration for approval. Although the stevia plant itself is not considered to be GRAS by the FDA, certain purified preparations that are derived from the plant are.

• A variety of polyols (sugar alcohols) and other bulk sweeteners, including two naturally occurring rare sugars, trehalose and tagatose, are accepted for use in foods in the U.S. The only significant health issue pertaining to these sugar substitutes, most of which are incompletely digested, is the potential for gastrointestinal discomfort with excessive use.

• The availability of a variety of safe sugar substitutes is a benefit to consumers because it enables food manufacturers to formulate a variety of good-tasting sweet foods and beverages that are safe for the teeth and lower in calorie content than sugar-sweetened foods and beverages.

1. The term sugar substitutes includes both food ingredients with very strong sweetening power that provide zero or very few calories, which are used in very small amounts to sweeten foods, and bulk sweetening agents such as polyols, which can replace both the bulk of sugar and some of its sweetness. This booklet discusses both types of sweeteners, with an emphasis on the safety aspects of the eight high intensity sweeteners currently approved for use in the United States as well as Rebaudioside A from Stevia.
INTRODUCTION

If you enjoy diet soft drinks or other reduced-calorie or “light” products, you’re in good company. According to a recent survey, 180 million American adults use low-calorie, sugar-free foods and beverages. Despite the popularity of these products, though, some people have concerns or questions about the safety of the sugar substitutes that make the products possible. Misinformation about sugar substitutes abounds, especially on the Internet, and people may have difficulty distinguishing trustworthy sources of information on this topic from less reliable ones.

This report by the American Council on Science and Health summarizes the scientific facts about the safety of sugar substitutes. The principal source of information for this booklet was a technical manuscript entitled “Low-Calorie Sweeteners and Other Sugar Substitutes: A Review of the Safety Issues,” published in the journal Comprehensive Reviews in Food Science and Food Safety, by Dr. Manfred Kroger of Pennsylvania State University and Kathleen Meister and Dr. Ruth Kava of the American Council on Science and Health.
The sugar substitutes discussed in this section of this booklet, which may also be called alternative, artificial, high-intensity, or nonnutritive sweeteners, can replace the sweetness of sugar while providing few or no calories. In addition to the calorie savings, these sugar substitutes have the advantage of not promoting tooth decay, and they are useful in dietary planning for people who are coping with obesity or diabetes. Eight high intensity sweeteners of this type are currently approved for use in foods and beverages in the United States: acesulfame-K, advantame, aspartame, Luo Han Guo fruit extracts, neotame, saccharin, certain purified preparations of the stevia plant and sucralose (Table 1). Others, including alitame and cyclamate, are approved as sweeteners in some other countries but not in the United States. Each of these high intensity sweeteners is discussed individually below.

With the exception of saccharin, which was in use long before current procedures were adopted in the 1950s, each of the high intensity sweeteners discussed here had to earn approval as a new food additive in the United States. The Food and Drug Administration (FDA) approves new food additives based on reviews of extensive scientific research on safety. Before a new food additive can go on the market, the company that wishes to sell it must petition the FDA for its approval. The petition must provide convincing evidence that the new additive performs as intended and is safe, where “safe” means a reasonable certainty of no harm under the intended conditions of use. Demonstrating that an additive is safe is the manufacturer’s responsibility; it is the manufacturer, not the FDA, who conducts and pays for the necessary research. FDA’s roles are to assess the research results and to make decisions on the submitted petitions; FDA does not decide what substances will be considered as potential food additives, and it does not conduct safety studies. For additives that are likely to be widely used, such as sugar substitutes, the necessary research includes extensive studies in experimental animals, including studies in which high doses of the additive are administered to two species of animals for the greater part of the animals’ lifetime. In many instances, studies in human volunteers are also conducted.
### Table 1. High Intensity Sweeteners Currently Approved for Use in the United States

<table>
<thead>
<tr>
<th>Sugar Substitute</th>
<th>Caloric Value (Cal/g)</th>
<th>Date Approved</th>
<th>Regulatory Status</th>
<th>Potency (times sweeter than sucrose)</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acesulfame-K</td>
<td>0</td>
<td>1998</td>
<td>Approved as a food additive; ADI&lt;sup&gt;b&lt;/sup&gt; = 15 mg/kg bw/day</td>
<td>200</td>
<td>Sunett, Sweet One</td>
</tr>
<tr>
<td>Advantame</td>
<td>0</td>
<td>2014</td>
<td>Approved as a food additive; ADI = 32.8 mg/kg bw/day</td>
<td>20,000</td>
<td>Information not yet available</td>
</tr>
<tr>
<td>Aspartame</td>
<td>4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1981</td>
<td>Approved as a food additive; ADI = 50 mg/kg bw/day</td>
<td>180</td>
<td>NutraSweet, Equal, others</td>
</tr>
<tr>
<td>Mogrosides</td>
<td>0</td>
<td>2014</td>
<td>Approved as a GRAS food additive</td>
<td>100-250</td>
<td>Monk Fruit in the Raw, EZ Sweetz</td>
</tr>
<tr>
<td>Mogrosides</td>
<td>0</td>
<td>2014</td>
<td>Approved as a GRAS food additive</td>
<td>100-250</td>
<td>Monk Fruit in the Raw, EZ Sweetz</td>
</tr>
<tr>
<td>Saccharin</td>
<td>0</td>
<td>In use for decades prior to the Food Additives Amendment of 1958</td>
<td>Permitted for use under an interim regulation</td>
<td>300</td>
<td>Sweet’n Low, Sweet Twin, Sugar Twin, others</td>
</tr>
<tr>
<td>Sucralose</td>
<td>0</td>
<td>1998</td>
<td>Approved as a food additive; ADI = 5 mg/kg/day</td>
<td>600</td>
<td>Splenda</td>
</tr>
<tr>
<td>Purified Rebaudiosides from stevia</td>
<td>0</td>
<td>2008</td>
<td>Approved as a food additive; GRAS ADI=4 mg/kgm/day</td>
<td>200</td>
<td>Truvia, Pure Via, Rebiana</td>
</tr>
</tbody>
</table>
It can be difficult for people who are not involved in the testing of food additives to appreciate just how extensive their premarket testing must be. Most safety studies on prospective food additives are never published in the scientific literature because they do not make an important contribution to scientific knowledge. One exception, however, involves the sugar substitute sucralose. Many of the more than 100 studies conducted in support of the safety of this additive were published in a scientific journal in 2000 (see the Suggestions for Further Reading at the end of this report). They provide insight into the quantity and sophistication of the research required before a new food additive can be marketed in the United States.

2. Opponents of particular food additives sometimes attempt to cast aspersions on them by pointing out that the studies supporting their safety were conducted by the additives’ manufacturers. But there is nothing scandalous in this. It is inherent in the way the system for food additive approval works. The alternative (having a government agency or independent entity test food additives for safety) may sound good in theory, but it would require research on prospective new products to be paid for with the public’s tax dollars. Under the current system, the company that processes ensures that the studies were properly performed and interpreted.

a. Potency varies in different food applications. These values should be regarded as rough estimates.

b. ADI = acceptable daily intake, defined as the estimated amount that a person can safely consume on average every day over a lifetime without risk. The ADI values listed here are those established by the U.S. Food and Drug Administration; ADIs used in other countries may be slightly different. ADI values are usually expressed in milligrams per kilogram of body weight per day (mg/kg bw/day); however, FDA has expressed the ADI for neotame in terms of milligrams per person per day (mg/p/day).

c. Although aspartame provides 4 Cal/g, as many calories as an equivalent weight of protein or carbohydrate, the amount of aspartame used in foods and beverages is so small that its caloric contribution is negligible.
Acesulfame-K, sold under the brand name Sunett, is the most successful sugar substitute that you’ve probably never heard of. It is inconspicuous because it is almost always used in combination with other sweetening agents. When used in this way, it contributes to creating a sweet taste very close to that of sugar. However, if used alone, it can have a bitter aftertaste that consumers would find undesirable. Acesulfame-K is approximately 200 times as sweet as sugar, and it provides zero calories.

As with all new food additives, acesulfame-K underwent extensive safety testing before regulatory authorities in the U.S. and other countries approved its use. More than 50 studies of various aspects of safety were conducted before the FDA approved acesulfame-K for use in dry foods in 1988, and additional tests were conducted before FDA approved its use in beverages a few years later.

Over the years, concerns have been raised about several aspects of the safety of acesulfame-K. All of these issues have been resolved, as follows:

- Questions were raised about one of the animal experiments, a long-term study in rats, that was conducted during the safety testing of acesulfame-K. It has been claimed that this study was inadequate and that its results might have linked acesulfame-K to an increased risk of cancer. There was indeed a problem with this study; an illness had spread through the rat colony while the study was in progress. Because of this complication, it was necessary for the researchers to repeat the study. The second study was completed with no problems, and it did not link acesulfame-K to cancer or other harmful effects. It was this second study, not the first, that was used by regulatory authorities in their evaluation of acesulfame-K.

- It has been argued that a breakdown product, acetoacetamide, that may form during storage in beverages sweetened with acesulfame-K could have harmful effects. Regulatory authorities are aware of this breakdown product, and they took its formation into account before approving acesulfame-K for use in beverages. Because the amount of acetoacetamide...
that could form in beverages is extremely small, far too small to cause adverse health effects, the formation of this substance is not considered to be a cause for concern.

- In the late 1990s, researchers from India reported findings that seemed to indicate that acesulfame-K could cause mutations (genetic changes) in mouse bone marrow cells. However, when the same researchers and others attempted to replicate this finding, they were unable to do so. The later studies showed no evidence of mutations, indicating that the original finding was incorrect.

Recent reevaluations of the scientific evidence on acesulfame-K, including a comprehensive review by the food safety authorities of the European Union in 2000, have reaffirmed its safety. No human health problems associated with the consumption of acesulfame-K have been reported in the scientific literature, despite more than 15 years of extensive use in many countries.

**ADVANTAME**

Advantame is the “newest kid on the block.” Just approved by the FDA (May, 2014) for general use as a tabletop sweetener as well as for use in cooking and baking (it is heat-resistant), advantame is some 20,000 times sweeter than sugar, according to its producer Ajinomoto, making it the sweetest of the artificial sweeteners.

The FDA reviewed 37 animal and human safety studies before deciding on whether to approve the sweetener, and found no evidence indicating any toxic effects. The FDA set the safe daily consumption level of advantame at 32.8 milligrams per kilogram of body weight. This is the equivalent of 40,000 packets of advantame. This is compared to 165 packets for aspartame and sucralose (Equal, Splenda) and 250 packets for saccharine (Sweet N low).

The European Food Safety Authority (EFSA) also evaluated the safety of advantame as a food additive and on July 21, 2013 concluded that advantame is safe for use. However, they also point out that animal studies have demonstrated gastrointestinal disturbances as a result of consumption and therefore propose an ADI of 5 milligrams per kilogram of bodyweight, the equivalent of 6,000 packets.

The Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives also concluded that advantame is safe for the intended use and issued the same ADI recommendations as EFSA.

Advantame is composed of aspartame and vanillin. However, unlike aspartame, advantame does not break down under heat and can therefore be used to sweeten baked goods, although the FDA says advantame should not be used in meats or poultry.
Although, like its cousin, aspartame, advantame does contain the amino acid phenylalanine, the fact that the new sweetener is so sweet means that only tiny amounts are used. It is about 100 times sweeter than aspartame, so the amount needed for sweetening is far less than aspartame. Thus, even phenylketonurics, people with a genetic disorder that means they must avoid the amino acid phenylalanine, do not have to be concerned with advantame. The sweetener will not be required to carry a warning label, as does aspartame. Advantame is not yet in consumer products, but will surely appear in the near future.

**ASPARTAME**

Aspartame was discovered in 1965 and approved by the FDA in 1981. It is widely used in foods and beverages because its taste is very close to that of table sugar. During the first years after approval, when aspartame was sold exclusively by the patent holder, it was known primarily by the brand names NutraSweet and Equal (the latter is the popular table-top sugar substitute sold in blue packets). Since the expiration of the patent in December 1992, aspartame has also been sold under other brand names. Aspartame is approximately 180 times as sweet as sugar.

The aspartame molecule consists of two amino acids — phenylalanine and aspartic acid — linked to methanol (methyl alcohol). The two amino acids in aspartame occur naturally in foods as protein components. Methanol also occurs naturally in foods and is produced by the digestion of other food constituents. Aspartame itself does not occur naturally.

Unlike most other low-calorie sugar substitutes, aspartame is broken down in the human body. Enzymes in the digestive tract break it down into its components (phenylalanine, aspartic acid, and methanol), each of which is then metabolized just as it would be if derived from other dietary sources. Because aspartame is metabolized, it provides as many calories as an equivalent weight of protein or carbohydrate does. However, because aspartame is intensely sweet, the amount used in foods and beverages is so small that its caloric contribution is negligible.

As with all modern food additives, aspartame underwent extensive safety testing prior to approval. Many additional studies have been conducted in the decades since aspartame went on the market. On the basis of this scientific evidence, authorities in numerous countries have approved and repeatedly reapproved the use of aspartame. The most recent reevaluations, including a reassessment of aspartame by authorities in the European Union in 2002, have continued to support its safety.

To scientists, it has always seemed unlikely that the normal use of aspartame could cause adverse health effects. Aspartame breaks down in the digestive tract into ordinary food components, and it accounts for only a small
proportion of the total intake of these components. Thus, it is difficult to con-
ceive of a mechanism by which the use of normal amounts of aspartame could
cause an adverse effect.

Of course, any substance can be harmful if consumed in a large enough
quantity. This is true for the components of aspartame, just as it is true for
water, vitamins, and numerous other substances in foods and beverages.
However, the amounts of phenylalanine, aspartic acid, and methanol in
aspartame-sweetened foods and beverages are small — well below the levels
that could cause any harm.

It has been calculated that even a relatively heavy user of aspartame (a
person at the 90th percentile of aspartame consumption) would increase his
or her intake of the two amino acids in aspartame — aspartic acid and phe-
nylalanine — by only one to two percent. Such changes are within the range
of variation caused by day-to-day differences in food intake and are clearly not
harmful. A 90th-percentile consumer of aspartame-sweetened products would
increase his or her daily consumption of methanol by an amount only one
twenty-fifth of the maximum tolerable level established by the FDA; a small
increase of this sort would not cause harmful effects.

Even when aspartame is consumed in unusually large (but physically possi-
ble) amounts, adverse health effects do not occur. Aspartame has been tested
in human volunteers in single doses four times the acceptable daily intake (the
amount considered safe for daily consumption for a lifetime) and in studies
where volunteers consumed aspartame daily at a level 50% higher than the
acceptable daily intake for several months. Even at these high doses, the levels
of all three of aspartame’s components in the volunteers’ blood remained
within safe ranges, and no adverse effects occurred.

Consumers sometimes worry about the presence of methanol in aspartame
because they know that methanol, in large doses, is toxic. Many people do not
realize that methanol is a common constituent of foods and beverages and that
people routinely consume small amounts of it without ill effect. Methanol is
found in many fruits and vegetables. Fruit juices contain substantial amounts
of methanol; for example, apple juice has been reported to contain up to 88
milligrams per liter. This is not a reason to avoid apple juice, however. To
obtain a fatal dose of methanol from apple juice, an individual would have to
consume between 100 and 1000 quarts of the juice at a single sitting — an
obviously absurd scenario. All fermented foods and beverages, such as alco-
holic beverages and fermented milk products, can be expected to contain
methanol as well as other alcohols in trace amounts. Except in the case of
unprofessionally distilled alcoholic beverages, however, the amount of metha-

ol in fermented foods and beverages is too low to cause any health damage.
The same is true of the small amounts of methanol present in aspartame-
sweetened foods or beverages.
Foods and beverages that contain aspartame must carry a label statement indicating that the product contains phenylalanine. This statement is for the benefit of individuals with the disease phenylketonuria, who must strictly limit their intake of this amino acid.

Phenylketonuria is a rare disease, affecting approximately one in 15,000 people, that results from a hereditary lack of an enzyme necessary for the normal metabolism of phenylalanine. Unless the disorder is detected in early infancy and treated with a phenylalanine-restricted diet, it results in mental retardation and other severe, permanent effects. Newborn infants in the U.S. and many other countries are screened for phenylketonuria at birth. Because of screening and effective treatment, substantial numbers of people with phenylketonuria are living near-normal lives except for the need for dietary restriction.

The phenylalanine notice on aspartame-sweetened products is not relevant to the general public; it is meant only for people with phenylketonuria. It is much like the statements provided on food labels for the benefit of people with food allergies (e.g., “contains wheat and soy”). Such label statements are intended only for people with a specific problem; they do not imply that consumers in general need to avoid the food.

Aspartame is unstable if subjected to prolonged heating and therefore cannot be used in baking or cooking (unless added at the end of the cooking process). Aspartame also decomposes in liquids during prolonged storage (this is why diet soft drinks have a shelf life about half that of regular soft drinks). When aspartame decomposes, the breakdown products include its three components (the two amino acids and methanol), as well as the diketopiperazine derivative of aspartame, which has been tested for safety and is not regarded as hazardous. The relative instability of aspartame is a quality issue, not a safety issue. For example, if you drink a can of diet soft drink that has been left too long in a hot car, causing some of the aspartame in the beverage to break down, it will not make you sick. However, you may notice a deterioration in the quality of the beverage.

Despite the extensive evidence supporting the safety of aspartame and the very low likelihood that a substance of aspartame’s composition could cause adverse health effects, claims of such effects abound, especially on the Internet. Anyone who enters the term “aspartame” into an Internet search engine will find thousands of references to this substance, including hundreds of Web sites filled with anecdotal reports supposedly linking aspartame with a wide variety of effects — including neurological and behavior problems, multiple sclerosis, systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, Alzheimer’s disease, birth defects, and even the health problems experienced by some Gulf War veterans. The scientific evidence does not support any of these alleged associations. A lack of scientific support, however, does not prevent misinformation from being repeated, over and over, on the Internet.
Sugar Substitutes and Your Health

It is important to realize that anyone can publish anything on a Web site — including speculation, misconceptions, and unsupported allegations — and that in cyberspace, myths and rumors never die. People who use the Internet as a source of information on health-related issues would be well advised to visit the sites of trusted organizations or government agencies and search the collections of documents posted there rather than searching the Internet as a whole. Further advice on using the Internet as a health information source is given at the end of this report.

In 2005, a group of Italian researchers reported that a study they had conducted had linked aspartame exposure to an increased risk of cancer in rats. The study was performed using methodology that differs from the standard, well-verified techniques for evaluating the cancer-causing potential of substances in experimental animals, and its findings conflict with those of studies conducted using officially recognized methodology. In addition, the researchers did not follow the customary procedure of allowing a second group of scientists to examine all of the samples of the animals’ tissues that had been prepared for microscopic study. Moreover, the research was conducted at a laboratory whose previous work has been criticized as “unreliable” by the FDA.

Regulatory authorities in the United States and other countries have now reviewed the data from the study and have determined that the findings are not indicative of any real cause for concern about aspartame. The European Food Safety Authority (EFSA) noted substantial flaws in the study that make the study’s results invalid. EFSA points to a high background incidence of “chronic inflammatory changes in the lungs and other vital organs and tissues.” It is a known fact that lymphomas/leukemias can develop as a result of rapid growth of normal cells in the lungs of rats suffering from chronic respiratory disease. Therefore, the slight increase in incidence of these tumors was not related to consumption of aspartame. Next, preneoplastic and neoplastic lesions in the renal pelvis, ureter and bladder were most likely related to treatment and EFSA concludes that this development has no relevance for humans. Furthermore, malignant schwannomas (nerve sheath tumors) may have been misdiagnosed, and not only were these rare, but there was also a very flat dose-response relationship, which means that conclusions about cause and effect cannot be made. Due to these conclusions, as well as previous evaluations by the European Commission Scientific Committee on Food, negative results of carcinogenicity studies conducted by the US National Toxicology Program on aspartame in transgenic mice, and findings by the US National Cancer Institute reporting no association between brain-and-blood related cancers and aspartame, EFSA concludes that there is no need to revise the previously established ADI for aspartame.
The FDA completed a review of this study in 2007 and came to the same conclusions as EFSA. Because of shortcomings in the design, conduct, reporting and interpretation of this study, the study is not reliable and results are not valid. They found no reason to alter conclusions that aspartame is safe as a general purpose sweetener in food.

In 2013, EFSA re-evaluated the safety of aspartame as a food additive. The Panel on Food Additives and Nutrient Sources convened at the request of the European Commission. The panel reviewed original reports, previous evaluations, additional literature and data which included chronic toxicity and carcinogenicity studies in animals, reproductive and developmental toxicity studies, prospective cohort studies looking at consumption of artificially sweetened beverages during pregnancy and asthma in children and oral studies on chronic toxicity and carcinogenicity of methanol in mice and rats. They concluded, again, that aspartame is not a safety concern at the current exposure estimates and therefore, there is no reason to revise the ADI of aspartame.

**LUO HAN GUO (MONK FRUIT) EXTRACT**

The monk fruit plant is a vine that has been cultivated in China for centuries. Its fruit contains a number of sweet compounds, including glucose, fructose and a group of chemicals called mogrosides. By a process developed by Procter & Gamble in 1995, the mogrosides can be extracted, purified and used as sweeteners. In late 2014 the FDA allowed a GRAS (Generally Recognized as Safe) designation for monk fruit extract to be used as a table-top sweetener and as a sweetener in foods.

**NEOTAME**

Neotame was approved in 2002 and currently appears in a limited variety of commercial products in the United States. Like aspartame, neotame contains the amino acids phenylalanine and aspartic acid. The two amino acids, however, are combined in a way that is different from that in aspartame, giving neotame different properties. Neotame is extraordinarily sweet, with a sweetness potency at least 7,000 times that of sugar and at least 30 times that of aspartame. Unlike aspartame, neotame is heat stable and therefore can be used in cooking and baking.

Although neotame is chemically similar to aspartame, it is not the same substance. Therefore, neotame had to be comprehensively tested for safety, just as any other new food additive would, before it was approved by the FDA. The scientific evidence submitted to FDA by neotame’s manufacturer in support of its safety included the results of more than 110 scientific studies, including tests in
both experimental animals and human volunteers. This is typical of the amount of research that is necessary before a new food additive can be marketed.

When a person consumes neotame, most of it is broken down into a derivative and methanol, both of which are rapidly excreted from the body through either the digestive tract or the urinary tract. Because the amount of neotame used to sweeten a food or beverage is extremely small, the exposure to methanol from neotame is also extremely small in comparison to methanol exposure from other sources. The amount of methanol in a glass of fruit juice is about 100 times that in a glass of a neotame-sweetened soft drink.

Although neotame contains phenylalanine, products sweetened with neotame will not be required to bear a warning notice for people with phenylketonuria, in the way that aspartame-sweetened products do. The amount of phenylalanine in a neotame-sweetened product is so small that it is insignificant, even for people who must limit their phenylalanine intake. The FDA has calculated that the amount of phenylalanine that would be consumed by a person in the 90th percentile of predicted consumption for neotame is only about 0.4 percent of the amount that a child with phenylketonuria is permitted to consume daily. Thus, the effect of consumption of neotame-sweetened products on total phenylalanine intake is negligible.

Neotame is likely to receive increased public attention once products containing it begin to appear on the market. Consumers should be aware that neotame is a safe, well-tested food ingredient.

**SACCHARIN**

Saccharin, the oldest low-calorie sugar substitute, was discovered in 1878. It is 300 times sweeter than sugar and provides no calories. In the first half of the twentieth century, saccharin was popular as a sugar substitute in the diets of people with diabetes and other medical conditions. It was also used extensively as a replacement for strictly rationed sugar in Europe during both World Wars. Between 1970 and 1981, saccharin was the only low-calorie sugar substitute available in the United States. Saccharin is still widely used today, often in combination with other sugar substitutes, and owes much of its popularity to its low cost. Although saccharin can have a bitter aftertaste when used alone, it works well in blends with other sugar substitutes. Saccharin is perhaps most familiar to U.S. consumers as the sugar substitute sold in pink packets, under the brand name Sweet’n Low.

During the 1970s, concerns were raised about whether saccharin might be capable of causing human cancer. In several studies in which a particular chemical form of saccharin, sodium saccharin, was administered to rats in
extremely large doses for a lifetime, the male rats had an increased rate of bladder cancer. In 1977, on the basis of this evidence, the FDA attempted to ban saccharin. This decision met with an extremely negative reaction from the American public because saccharin was the only low-calorie sugar substitute on the market at that time, and banning it would have meant that diet soft drinks and other sweet low-calorie products would become unavailable. Acting in response to a massive public mandate, Congress passed a law that imposed a moratorium on the proposed FDA action, and saccharin was never banned, although a warning label was required on saccharin-sweetened products.

Since the 1970s, scientific research has shown that saccharin is not a cancer hazard in humans. Researchers have learned that the mechanism by which sodium saccharin causes bladder cancer in rats is not applicable to people. In rats fed high doses of sodium saccharin, crystals form in the urine. These crystals damage bladder tissues, leading to the proliferation of new cells, which increases the risk of cancer. This phenomenon does not occur in humans, whose bladder physiology is quite different from that of rats. Moreover, the effect in rats is not even attributable to saccharin per se — it is caused by the sodium component of sodium saccharin, not the saccharin component. Researchers have been able to produce bladder tumors in male rats by feeding them very high doses of other sodium compounds, too — including sodium chloride (table salt) and sodium ascorbate (one of the chemical forms of vitamin C) — neither of which poses a bladder cancer risk in humans.

The relationship between saccharin and bladder cancer has been evaluated in epidemiological studies (studies of the occurrence of disease in human populations), most of which used the case-control design (i.e., people diagnosed with bladder cancer were compared with people of the same age and sex who did not have the disease to see how their past experiences, including exposure to saccharin, differed). The combined evidence from the many case-control studies indicates that no detectable association exists between saccharin consumption and the risk of bladder cancer in humans.

Because the animal evidence indicates that the mechanism by which saccharin causes cancer in rats is not relevant to humans and because the human evidence does not demonstrate any cancer hazard from the use of saccharin, regulatory agencies and international organizations have removed saccharin from their lists of probable human carcinogens, and the requirement for a warning label on saccharin-sweetened products has been discontinued. There are no unresolved safety issues pertaining to saccharin at the present time. Saccharin is currently permitted for use in the U.S. under an interim regulation that specifies the amounts of saccharin permitted in beverages, processed foods, and table-top sweeteners and requires that the product label must state saccharin in the ingredient declaration and specify the amount used.
Sugar Substitutes and Your Health

STEVIA

Indigenous peoples of South America have used the leaves of the stevia plant, a shrub that grows wild in Brazil and Paraguay, as a sweetener for centuries. Stevia leaves contain at least ten sweet components, the most important of which are stevioside and rebaudioside A. An extract of stevia containing these components has been used as a food ingredient in Japan for more than 30 years and more recently in other countries including China, Russia, and Korea.

At this time, the FDA has not approved the use of whole leaf stevia or crude stevia extracts as sweeteners. However, this version can be sold as a “dietary supplement, as long as it is not promoted as a sugar substitute or used as an ingredient in foods.

Although the stevia plant itself is not considered to be GRAS by the FDA, certain purified preparations that are derived from the plant are. These refined products are sold by five companies that are listed on the FDA website. These include: Sweet Green Fields (Altesse SteviaTM 99 and Puresse SteviaTM 100), Blue California (Good & Sweet), McNeil Nutritionals (Sun Crystals All-Natural Sweetener), Cargill (Truvia) and Whole Earth Sweetener Company (Pure Via).

SUCRALOSE

Sucralose was discovered in 1976 and approved for use in the United States in 1998. It is made from sucrose (table sugar) by a process that substitutes three chlorine atoms for three hydrogen-oxygen (hydroxyl) groups on the sucrose molecule. Although sucralose is made from sugar, the human body does not recognize it as a sugar and does not obtain energy by breaking it down; in fact, almost all of it is excreted from the body unchanged. Sucralose is about 600 times sweeter than sugar, and it is heat-stable. Like the other low-calorie sugar substitutes, it does not promote tooth decay. It is perhaps most familiar to U.S. consumers as the sugar substitute that comes in yellow packets, under the brand name Splenda.

As is true for all new food additives introduced in recent decades, sucralose underwent extensive safety testing in both experimental animals and human volunteers before it was approved in the United States and other countries. Sucralose is considered safe for all segments of the population, including people with chronic health problems such as diabetes.

In the years since sucralose was approved, some popular products have been reformulated to contain it, often with considerable publicity. During this time, concerns about the safety of sucralose have been raised on various Internet sites, especially those that also express concerns about aspartame. Most of
these concerns seem to be based on a general distrust of synthetic food ingredients or a specific unease about any substance that contains chlorine, which is also a component of some pesticides. However, the presence of chlorine in the sucralose molecule is not a cause for concern. Many commonly consumed substances, including table salt (sodium chloride), contain chlorine; the presence of this element in a compound does not indicate that the compound is toxic. Sucralose is a safe, well-tested food additive. There are no unresolved scientific concerns about its use.

3. The 90th percentile of aspartame consumption is roughly 3.0 milligrams per kilogram of body weight per day. For a 150-lb adult, this would be about 210 milligrams of aspartame, which is approximately the amount in one 12-oz. can of aspartame-sweetened soft drink plus one packet of aspartame-based table-top sweetener. The acceptable daily intake of aspartame (the estimated amount that a person can safely consume on average every day over a lifetime without risk) is 50 milligrams per kilogram of body weight per day, or about 16 times the 90th percentile intake.

4. For some food ingredients, an alternative route to approval called GRAS notification is possible. In this instance, the sponsor of the food ingredient notifies FDA that it believes a substance to be generally recognized as safe (gras) and provides both technical evidence of its safety and evidence that a consensus exists among qualified experts as to the safety of the substance under the conditions of its intended use. FDA then reviews the notification and decides whether or not to object to it. In this procedure, as with the food additive approval procedure described above, the manufacturer of the proposed food ingredient must take the initiative. In both instances, FDA merely reviews evidence submitted to it; the agency does not choose which substances to evaluate.
The eight high intensity sweeteners described in detail above are the only ones currently approved in the United States. Several other compounds are in use in other countries, however.

One of these is **alitame**. Like aspartame and neotame, alitame is a sugar substitute made from amino acids. Like neotame, it is a very powerful sweetening agent; alitame is 2,000 times sweeter than sugar. Alitame has been approved in Mexico, Colombia, China, Australia, and New Zealand. In the United States, a petition for the approval of alitame as a food additive has been submitted to the FDA. As of March 2006, this petition was being “held in abeyance,” according to the FDA Web site. “Held in abeyance” indicates that FDA needs additional data in order to evaluate a substance and has deferred its evaluation until the data are submitted. Thus, there appears to be some scientific issue delaying the approval of this sugar substitute in the United States.

Cyclamate is in use in about 50 countries. Cyclamate is not a new product; it was discovered in 1937 and was used as a sugar substitute in the U.S. in the 1950s and 1960s, primarily in a very successful blend with saccharin. In 1970, however, cyclamate was banned in the U.S. in response to an animal experiment that seemed to indicate that it could cause bladder cancer. Later, extensive further studies in several animal species did not show any link between cyclamate and cancer. Thus, on the basis of the complete body of evidence, scientists have concluded that cyclamate is not a cancer-causing agent. The manufacturer of cyclamate has submitted a petition for its reapproval in the United States. This petition, like the one for alitame, is currently being “held in abeyance” (as of March 2006) while additional scientific data are developed.
GENERAL ISSUES PERTAINING TO LOW-CALORIE SUGAR SUBSTITUTE

Choice of Sugar Substitutes. Food manufacturers choose among the available sugar substitutes based on taste considerations, stability, and cost. In some instances, blends of sugar substitutes are used. The use of blends has a long history; a cyclamate/saccharin blend was widely used in diet soft drinks in the 1960s, aspartame/saccharin blends are commonly used in fountain soft drinks in the U.S. today, and aspartame/acesulfame-K blends are currently used in many foods and beverages. Blends may have taste or cost advantages over individual sugar substitutes. There are no health-related reasons for choosing one sugar substitute over the others; all are safe, well-tested products.

Acceptable Levels of Consumption. Estimated intakes of all the low-calorie sugar substitutes currently approved in the U.S. are well within the ranges that are considered acceptable. Therefore, people do not need to limit their intake of products made with these ingredients for reasons pertaining to the sugar substitutes themselves. However, since many of the products that contain sugar substitutes are foods of minimal nutritional value (e.g., carbonated beverages), people who are trying to eat healthfully may find it necessary to limit consumption of these foods to avoid displacement of more nutritious foods from the diet. This issue is especially important for children and adolescents, among whom displacement of milk by other beverages is a concern.

The use of low-calorie sugar substitutes could improve dietary quality if consumers use calorie savings for the consumption of more nutritious foods. For example, if a person drinks a zero-calorie diet soft drink rather than a 150-calorie regular soft drink, this provides the opportunity to include 150 calories from a more nutritious food in the diet. Some people may indeed be using reduced-calorie foods and beverages this way. A recent analysis of data from two national diet surveys indicates that American adults who use reduced-sugar products have better diets and higher vitamin and mineral intakes than those who use the full-sugar versions of the same foods and beverages.

Effect on Weight Control. The effect of low-calorie sugar substitutes on weight control has been a subject of controversy. It has been claimed that the use of these products could hamper weight loss efforts by promoting increased food intake. However, the overall scientific evidence does not support this concern.
Sugar Substitutes and Your Health

The idea that sugar substitutes might promote weight gain originated with a 1986 British study in which self-rated appetite was found to be higher in people who drank aspartame-sweetened water as compared to those who drank plain water. In several other studies, however, consumption of aspartame or other sugar substitutes did not lead to increases in self-rated appetite. In addition, several studies have assessed the effect of sugar substitute consumption on actual food intake, and none has shown an increase.

The use of sugar substitutes may be helpful for individuals who are trying to control their weight by providing palatable low-calorie food choices. A study from Harvard Medical School supports this idea. The study involved overweight women who participated in a four-month multidisciplinary weight-reduction program. The women were divided into two groups; one group was encouraged to consume aspartame-sweetened products, while the other group was asked to avoid them. The two groups of women lost similar amounts of weight during the program. However, during the three years after the program ended, the women in the aspartame group were more successful than those in the other group in maintaining their weight loss.

Recently, some researchers have suggested that intense sweeteners (including aspartame) can actually provoke obesity and metabolic syndrome via mechanisms that have not been substantiated in humans. Their theories are based upon either animal studies, or use only small groups of people. Moreover, there are no valid biological hypotheses to support such theories. At the least, large studies involving humans would be required to lend any semblance of validity to such theories.

The American Heart Association embraces non-nutritive sweeteners (NNSs) as a way to “limit calories and achieve or maintain a healthy weight. ...Foods and beverages that contain NNSs can be included in a healthy diet, as long as the calories they save you are not added back by adding more foods as a reward later in the day.”
OTHER TYPES OF SUGAR SUBSTITUTE

The sugar substitutes discussed earlier in this booklet substitute only for the sweetness of sugar, not its physical bulk. When bulk is important, for example in chewing gums, candies, ice cream, baked goods, and fruit spreads, other types of sugar substitutes, such as sugar alcohols (polyols), may be used. Polyols usually replace sugar on a one-to-one basis (that is, one ounce of polyol substitutes for one ounce of sugar). Since some polyols are not as sweet as sugar, a low-calorie sugar substitute may also be included in the product to provide additional sweetness. Polyols used in foods in the U.S. include sorbitol, mannitol, xylitol, isomalt, erythritol, lactitol, maltitol, hydrogenated starch hydrolysates, and hydrogenated glucose syrups.

Polyols and other bulk sugar substitutes have three potential advantages over sugar as food ingredients:

1. Unlike sugars, they do not promote tooth decay. The bacteria in dental plaque, which produce substantial amounts of decay-promoting acid from sugars and starches, produce little or no acid from polyols. In the United States, FDA allows a health claim on foods made with polyols stating that the food does not promote tooth decay, provided that the food also meets other requirements (such as not containing decay-promoting sugars). Label claims of this type are often found on sugarless chewing gums made with polyols.

2. Polyols produce a lower glycemic response (i.e., a lower rise in blood sugar levels after consumption) than most sugars and starches do. Thus, their use may have advantages for people with diabetes.

3. Polyols are lower in calories than sugar is — usually by about half — because they are incompletely digested.

Incomplete digestion, however, is a mixed blessing. Although it helps with calorie reduction, it can also lead to gastrointestinal effects such as looser stools and gas production (flatulence). These effects are similar to those associated with foods that contain carbohydrates of low digestibility, such as bran cereals. Gastrointestinal effects of polyols increase with the amount consumed, and some people are more sensitive than others to these effects. In the United States, some products containing substantial amounts of polyols are required to carry a label notice stating that “excess consumption may have a laxative effect.”
Two new sugar substitutes that are functionally similar to polyols, trehalose and tagatose, have recently come onto the market. These substances are actually sugars, but their properties are more similar to those of sugar alcohols than those of table sugar. Tagatose is used in foods much as the polyols are. Although it is a sugar, it does not promote tooth decay, and products sweetened with it are permitted to carry a “does not cause tooth decay” label claim. Trehalose is used in foods primarily because it helps to stabilize them during freezing or dehydration, rather than as a sweetening agent. Both trehalose and tagatose have been evaluated for safety and accepted as “generally recognized as safe” (GRAS).
CONCLUSIONS

Extensive scientific research supports the safety of the eight high intensity sweeteners currently approved for use in foods in the U.S. (acesulfame-K, advantame, aspartame, neotame, saccharin, and sucralose). In addition, some substances derived from the stevia plant are approved for use as food additives. The polyols and similar substances used as bulk sugar substitutes in the U.S. are also safe, but consumers need to be aware of their presence in food products so that they can limit their intake sufficiently to avoid gastrointestinal discomfort. The availability of a variety of safe sugar substitutes is of benefit to consumers because it enables food manufacturers to formulate a variety of good-tasting sweet foods and beverages that are safe for the teeth and lower in calorie content than sugar-sweetened foods.

The proliferation of myths and misinformation on the Internet about the safety of sugar substitutes should serve as a reminder that all sources of health-related information are not created equal. Distinguishing between reliable and unreliable information sources on the World Wide Web can be challenging. Simply entering a topic into an Internet search engine is not the best way to obtain science-based advice.

A better approach is to visit trustworthy health-related Web sites, such as the National Library of Medicine site (http://www.nlm.nih.gov/medlineplus/), the U.S. government’s health clearinghouse site (http://www.healthfinder.gov/), the sites of government agencies such as the Food and Drug Administration (www.fda.gov) or the U.S. Department of Agriculture (www.usda.gov), or the sites of trusted professional organizations or voluntary groups such as the American Dietetic Association (www.eatright.org), the American Heart Association (www.americanheart.org), or the American Cancer Society (www.cancer.org), and then search within the collections of documents at these sites for information on a specific topic.

In instances where something sounds too good — or too horrible — to be true, it’s also a good idea to see whether the topic in question is discussed on the Urban Legends Reference Pages (www.snopes.com) and/or Quackwatch (www.quackwatch.com). Both sites are reliable, and they are frequently updated with new information about various health myths and misinformation.
A good basic source of information on all types of sugar substitutes is an article by John Henkel called “Sugar Substitutes: Americans Opt for Sweetness and Lite,” published in the Food and Drug Administration’s magazine FDA Consumer in 1999 and updated in some respects in 2006 (its discussion of neo-tame is still outdated, however). It is available on the FDA Web site at www.cfsan.fda.gov/~dms/fdsugar.html

The American Dietetic Association publishes and regularly updates a position paper on the use of nutritive and nonnutritive sweeteners. The current version, updated in 2004, is available online at www.eatright.org/cps/rde/xchg/ada/hs.xsl/advocacy_adap0598_ENU_HTML.htm

The Association also has an informative fact sheet about aspartame, which you can find at www.eatright.org/cps/rde/xchg/SID-5303FFE3-32E724A8/ada/hs.xsl/nutrition_1030_ENU_HTML.htm

Another good basic source of information on all types of sugar substitutes is the Calorie Control Council. Information is available on their website, http://www.caloriecontrol.org/sweeteners-and-lite/sugar-substitutes

The International Food Information Council has a brief but informative summary of information on sugars and sugar substitutes on its Web site at ific.org/nutrition/sugars/index.cfm

The National Cancer Institute has a fact sheet about sugar substitutes and cancer, with a link to additional information on the cancer testing of saccharin, on its Web site at www.cancer.gov/cancertopics/factsheet/Risk/artificial-sweeteners.

Readers who are interested in finding out about the research necessary before a new food additive can be approved may wish to browse supplement 2 of volume 38 of the journal Food and Chemical Toxicology, published in 2000. This 129-page report, devoted entirely to the safety testing of sucralose, can be found in many university libraries.
BOAROF OF TRUSTEES

CHAIRMAN
Nigel Bark, M.D.
Albert Einstein College of Medicine

VICE CHAIRMAN
Stephen Modzelewski
Maple Engine LLC

ACTING PRESIDENT
Gilbert Ross, M.D.
Executive and Medical Director, ACSH

MEMBERS

James E. Enstrom, Ph.D., M.P.H.
University of California, Los Angeles

Thom Golab
Media Research Center

Fred L. Smith, Jr.
Competitive Enterprise Institute

Jack C. Fisher, M.D., F.A.C.S.
University of California, San Diego, Emeritus

Herbert I. London, Ph.D.
London Center for Policy Research

Daniel T. Stein, M.D.
Albert Einstein College of Medicine

Paul A. Offit, M.D.
Children’s Hospital of Philadelphia

FOUNDERS CIRCLE

Norman E. Borlaug, Ph.D.
(1914-2009)
(Years of Service to ACSH: 1978-2009)
Father of the “Green Revolution” Nobel Laureate

Fredrick J. Stare, M.D., Ph.D.
(1910-2002)
(Years of Service to ACSH: 1978-2002)
Founder, Harvard Department of Nutrition

Elizabeth M. Whelan, Sc.D., M.P.H.
(1943-2014)
(Years of Service to ACSH: 1978-2014)
Founder and President, ACSH

ACSH STAFF

Madhukar (Mike) Balsara
Accountant

Josh Bloom, Ph.D.
Director of Chemical and Pharmaceutical Sciences

Meredith Coulis
Research Intern

Ruth Kava, Ph.D., R.D.
Senior Fellow in Nutrition

Erik Lief
Director of Communications

Ana Marcelo
Executive Assistant

Cheryl Martin
Associate Director and Director of Development

William McCain
Development Associate

Gilbert Ross, M.D.
Executive and Medical Director

Ariel Savransky
Associate Director of Public Health

Ana Simovska
Director of Video Productions
Ernest L. Abel, Ph.D.  
C.S. Mott Center  

Gary R. Acuff, Ph.D. 
Texas A&M University  

Casimir C. Akoh, Ph.D. 
University of Georgia  

Peter C. Albersen, M.D. 
University of Connecticut  

Julie A. Albrecht, Ph.D.  
University of Nebraska, Lincoln  

Philip Alcabes, Ph.D.  
Hunter College, CUNY  

James E. Alcock, Ph.D.  
Glendon College,  
York University (Canada)  

Thomas S. Alllems, M.D., M.P.H.  
San Francisco, CA  

Richard G. Allison, Ph.D.  
Federation of American Societies for  
Experimental Biology  

John B. Allred, Ph.D.  
Ohio State University  

Karl E. Anderson, M.D.  
University of Texas, Medical Branch  

Jerome C. Arnet, Jr., M.D.  
Helvetia, WV  

Dennis T. Avery  
Hudson Institute  

Ronald Bachman, M.D.  
Kaiser Permanente Medical Center  

Robert S. Baratz, D.D.S., Ph.D., M.D.  
International Medical Consultation Services  

Stephen Barrett, M.D.  
Pittsboro, NC  

Thomas G. Baumgartner, Pharm.D., M.Ed.  
Consultant Pharmacists of America  

W. Lawrence Beeson, Dr.P.H.  
Loma Linda University  

Elissa P. Benedek, M.D.  
University of Michigan Medical School  

Alex B. Beregow, Ph.D.  
RealClearScience  

Sir Colin Berry, D.Sc., Ph.D., M.D.  
Pathological Institute, Royal London Hospital (United Kingdom)  

William S. Bickel, Ph.D.  
University of Arizona  

Steven Black, M.D.  
Cincinnati Children’s Health Medical Center  

Blaine L. Blad, Ph.D.  
Kanosh, UT  

Hinrich L. Bohn, Ph.D.  
University of Arizona  

Ben Bolch, Ph.D.  
Rhodes College  

Joseph F. Borzelleca, Ph.D.  
Medical College of Virginia  

Michael K. Botts, Esq.  
Alexandria, VA  

George A. Bray, M.D.  
Pennington Biomedical Research Center  

Ronald W. Brecher, Ph.D.,  
C. Chem., DABT, QPRA  
MTE/GlobalTox (Canada)  

Allan Brett, M.D.  
University of South Carolina  

Kenneth G. Brown, Ph.D.  
Kbinc  

Christine M. Bruhn, Ph.D.  
University of Georgia  

Gale A. Buchanan, Ph.D.  
University of Georgia  

George M. Burditt, J.D.  
Bell, Boyd & Lloyd LLC  

Edward E. Burns, Ph.D.  
Texas A&M University  

Francis F. Busta, Ph.D.  
University of Minnesota  

Elwood F. Caldwell, Ph.D., M.B.A.  
University of Minnesota  

Zerle L. Carpenter, Ph.D.  
Texas A&M University System  

Robert G. Cassens, Ph.D.  
University of Wisconsin, Madison  

Ercole L. Cavalieri, D.Sc.  
University of Nebraska Medical Center  

Russell N. A. Cecil, M.D., Ph.D.  
Albany Medical College  

Rino Cerio, M.D.  
Barts and The London Hospital Institute of Pathology (United Kingdom)  

Sam K. C. Chang, Ph.D.  
Mississippi State University  

Bruce M. Chassy, Ph.D.  
University of Illinois, Urbana-Champaign  

David A. Christopher, Ph.D.  
University of Hawaii at Mānoa  

Emil William Chynn, M.D.  
New York Eye and Ear Infirmary  

F. M. Clydesdale, Ph.D.  
University of Massachusetts  

Donald G. Cochran, Ph.D.  
Virginia Polytechnic Institute and State University  

W. Ronnie Coffman, Ph.D.  
Cornell University  

Gerald F. Combs, Jr., Ph.D.  
USDA Grand Forks Human Nutrition Center  

Gregory Conko, J.D.  
Competitive Enterprise Institute  

Michael D. Corbett, Ph.D.  
Omaha, NE  

Morton Corn, Ph.D.  
Johns Hopkins University  

Nancy Cotugna, Dr.Ph., R.D., C.D.N.  
University of Delaware  

H. Russell Cross, Ph.D.  
Texas A&M University  

William J. Crowley, Jr., M.D., M.B.A.  
Spicewood, TX  

James W. Curran, M.D., M.P.H.  
Rollins School of Public Health, Emory University  

Charles R. Curtis, Ph.D.  
Ohio State University  

Jerry M. Cuttler, D.Sc, PEng  
Cuttler & Associates  

Taiwo K. Danmola, C.P.A.  
Ernst & Young  

Ilene R. Danse, M.D.  
Bolinas, CA  

Sherrill Davison, V.M.D., M.D., M.B.A.  
University of Pennsylvania  

Peter C. Dedon, M.D., Ph.D.  
Massachusetts Institute of Technology  

Thomas R. DeGregori, Ph.D.  
University of Houston  

Elvira G. de Mejia, Ph.D.  
University of Illinois, Urbana-Champaign  

Merle L. Diamond, M.D.  
Diamond Headache Clinic  

Seymour Diamond, M.D.  
Diamond Headache Clinic  

Donald C. Dickson, M.S.E.E.  
Gilbert, AZ
Ralph Dittman, M.D., M.P.H.  
Houston, TX

John E. Dodes, D.D.S.  
National Council Against Health Fraud

John Doull, M.D., Ph.D.  
University of Kansas

Theron W. Downes, Ph.D.  
Seneca, SC

Michael P. Doyle, Ph.D.  
University of Georgia

Adam Drewnowski, Ph.D.  
University of Washington

Michael A. Dubick, Ph.D.  
U.S. Army Institute of Surgical Research

Greg Dubord, M.D., M.P.H.  
Toronto Center for Cognitive Therapy (Canada)

Edward R. Duffie, Jr., M.D.  
Savannah, GA

Leonard J. Duhl, M.D.  
University of California, Berkeley

David F. Duncan, Dr.Ps.  
Duncan & Associates

James R. Dunn, Ph.D.  
Averill Park, NY

John Dale Dunn, M.D., J.D.  
Carl R. Darnall Hospital, Fort Hood, TX

Herbert L. DuPont, M.D.  
St. Luke’s Episcopal Hospital

Robert L. DuPont, M.D.  
Institute for Behavior and Health, Inc.

Michael W. Easley, D.D.S., M.P.H.  
International Health Management & Research Associates

Michael P. Elston, M.D., M.S.  
Rapid City, SD

William N. Elwood, Ph.D.  
NIH/Center for Scientific Review

Edward A. Emken, Ph.D.  
Midwest Research Consultants

Nicki J. Engeseth, Ph.D.  
University of Illinois

Stephen K. Epstein, M.D., M.P.P., FACEP  
Beth Israel Deaconess Medical Center

Terry D. Etherton, Ph.D.  
Pennsylvania State University

R. Gregory Evans, Ph.D., M.P.H.  
St. Louis University Center for the Study of Bioterrorism and Emerging Infections

Daniel F. Farkas, Ph.D., M.S., P.E.  
Oregon State University

Richard S. Fawcett, Ph.D.  
Huxley, IA

Frederick L. Ferris III, M.D.  
National Eye Institute

David N. Ferro, Ph.D.  
University of Massachusetts

Madelon L. Finkel, Ph.D.  
Cornell University Medical College

Harry Fisch, M.D.  
Weill-Cornell Medical College

Leonard T. Flynn, Ph.D., M.B.A.  
Morganville, NJ

William H. Foege, M.D., M.P.H.  
Seattle, WA

Christopher H. Foreman, Jr., Ph.D.  
University of Maryland

Shawn N. Fraser, Ph.D.  
Athabasca University (Canada)

Glenn W. Froning, Ph.D.  
University of Nebraska, Lincoln

Vincent A. Fulginiti, M.D.  
Tucson, AZ

Robert S. Gable, Ed.D., Ph.D., J.D.  
Claremont Graduate University

Shayne C. Gad, Ph.D., D.A.B.T., A.T.S.  
Gad Consulting Services

William G. Gaines, Jr., M.D., M.P.H.  
Scott & White Clinic

J. Bernard L. Gee, M.D.  
Yale University School of Medicine

K. H. Ginzel, M.D.  
University of Arkansas for Medical Sciences

Robert Glatter, M.D.  
Lenox Hill Hospital, North Shore LI

William Paul Glezen, M.D.  
Baylor College of Medicine

Jay A. Gold, M.D., J.D., M.P.H.  
Medical College of Wisconsin

Roger E. Gold, Ph.D.  
Texas A&M University

Reneé M. Goodrich, Ph.D.  
University of Florida

Frederick K. Goodwin, M.D.  
The George Washington University Medical Center

Timothy N. Gorski, M.D., F.A.C.O.G.  
University of North Texas

Ronald E. Gots, M.D., Ph.D.  
International Center for Toxicology and Medicine

Henry G. Grabowski, Ph.D.  
Duke University

James Ian Gray, Ph.D.  
Michigan State University

William W. Greaves, M.D., M.S.P.H.  
Medical College of Wisconsin

Laura C. Green, Ph.D., D.A.B.T.  
Cambridge Environmental, Inc.

Gordon W. Gribble, Ph.D.  
Dartmouth College

F. Peter Guengerich, Ph.D.  
Vanderbilt University School of Medicine

Caryl J. Guth, M.D.  
Advance, NC

Philip S. Guzelian, M.D.  
University of Colorado

David J. Hanson, Ph.D.  
State University of New York, Potsdam

Terral J. Hartman, Ph.D., M.P.H., R.D.  
Pennsylvania State University

Clare M. Hasler, Ph.D.  
The Robert Mondavi Institute of Wine and Food Science, University of California, Davis

Virgil W. Hays, Ph.D.  
University of Kentucky

Clark W. Heath, Jr., M.D.  
American Cancer Society

Dwight B. Heath, Ph.D.  
Brown University

Robert Heimer, Ph.D.  
Yale School of Public Health

Robert B. Helms, Ph.D.  
American Enterprise Institute

Zane R. Helsel, Ph.D.  
Rutgers University, Cook College

James D. Herbert, Ph.D.  
Drexel University
BOARD OF SCIENTIFIC AND POLICY ADVISORS
(CONTINUED)

Theodore R. Holford, Ph.D.
Yale University School of Medicine

Robert M. Hollingworth, Ph.D.
Michigan State University

Edward S. Horton, M.D.
Joslin Diabetes Center/Harvard Medical School

Joseph H. Hotchkiss, Ph.D.
Cornell University

Clifford A. Hudis, MD.
Memorial Sloan-Kettering Cancer Center

Peter Barton Hutt, Esq.
Covington & Burling, LLP

Susanne L. Huttner, Ph.D.
KE Squared

Lucien R. Jacobs, M.D.
University of California, Los Angeles

Alejandro R. Jadad, M.D., D.Phil., F.R.C.P.
University of Toronto (Canada)

Rudolph J. Jaeger, Ph.D.
Environmental Medicine, Inc.

William T. Jarvis, Ph.D.
Loma Linda University

Michele Jay-Russell, D.V.M., M.P.V.M., Ph.D.
University of California, Davis

Elizabeth H. Jeffery, P.h.D.
University of Illinois, Urbana-Champaign

Geoffrey C. Kabat, Ph.D.
Albert Einstein College of Medicine

Michael Kamrin, Ph.D.
Michigan State University

John B. Kaneene, Ph.D., M.P.H., D.V.M.
Michigan State University

P. Andrew Karam, Ph.D., CHP
MJW Corporation

Mark A. Katcher, M.S., M.B.A., C.I.H.
The Pihlmar Group

David L. Katz, M.D., M.P.H., FACP, FACP
Yale University Prevention Research Center

Kathryn E. Kelly, Dr.P.H.
Delta Toxicology

Robert D. Kerns, Ph.D.
Yale University School of Medicine

George R. Kerr, M.D.
University of Texas, Houston

George A. Keyworth II, Ph.D.
Carmel, CA

Michael Kirsch, M.D.
Highland Heights, OH

John C. Kirschman, Ph.D.
Allentown, PA

William M. P. Klein, Ph.D.
University of Pittsburgh

Ronald E. Kleinman, M.D.
Massachusetts General Hospital/ Harvard Medical School

Leslie M. Klevay, M.D., S.D. in Hyg.
University of North Dakota School of Medicine and Health Sciences

David M. Klurfeld, Ph.D.
U.S. Department of Agriculture

Kathryn M. Kolasa, Ph.D., R.D.
East Carolina University

James S. Koopman, M.D., M.P.H.
University of Michigan School of Public Health

Alan R. Kristal, Dr.P.H.
Fred Hutchinson Cancer Research Center

Manfred Kroger, Ph.D.
Pennsylvania State University

Sanford F. Kuvin, M.D.
University of Miami School of Medicine/Hebrew University of Jerusalem

Carolyn J. Lackey, Ph.D., R.D.
North Carolina State University

J. Clayburn LaForce, Ph.D.
University of California, Los Angeles

Robert G. Lahita, M.D., Ph.D.
Mount Sinai School of Medicine

James C. Lamb, IV, Ph.D., J.D.
Exponent

Lawrence E. Lamb, M.D.
San Antonio, TX

William E. M. Lands, Ph.D.
College Park, MD

Brian A. Larkins, Ph.D.
University of Arizona

Larry Laudan, Ph.D.
National Autonomous University of Mexico (Mexico)

Tom B. Leamon, Ph.D.
Liberty Mutual Insurance Company

Jay H. Lehr, Ph.D.
Environmental Education Enterprises, Inc.

Brian C. Lentle, M.D., FRCPC, DMRD
University of British Columbia (Canada)

Scott O. Lilienfeld, Ph.D.
Emory University

Floy Lilley, J.D.
Fernandina Beach, FL

Paul J. Lioy, Ph.D.
UMDNJ-Robert Wood Johnson Medical School

California State University, Los Angeles

William M. Lynch, Ph.D.
Oregon State University

Daryl Lund, Ph.D.
University of Wisconsin, Madison

John Lupien, M.Sc.
University of Massachusetts

Howard D. Maccabee, Ph.D., M.D.
Alamo, CA

Janet E. Macheledt, M.D., M.S., M.P.H.
Houston, TX

Henry G. Manne, J.S.D.
George Mason University Law School

Karl Maramorosch, Ph.D.
Rutgers University, Cook College

Judith A. Marlett, Ph.D., R.D.
University of Wisconsin, Madison

Lawrence J., Marnett, Ph.D.
Vanderbilt University

James R. Marshall, Ph.D.
Roswell Park Cancer Institute

Albuquerque, NM

Mary H. McGrath, M.D., M.P.H.
University of California, San Francisco

Alan G. McHughen, D.Phil.
University of California, Riverside

James D. McKean, D.V.M., J.D.
Iowa State University

Joseph P. McMenamin, M.D., J.D.
McGuireWoods, LLP

Patrick J. Michaels, Ph.D.
Cato Institute
THOMAS H. MILBY, M.D., M.P.H.
Boise, ID

J OSEPH M. MILLER, M.D., M.P.H.
Durham, NH

RICHARD A. MILLER, M.D.
Principia Biopharma, Inc.

RICHARD K. MILLER, PH.D.
University of Rochester

WILLIAM J. MILLER, PH.D.
University of Georgia

A. ALAN MOGHISSI, PH.D.
Institute for Regulatory Science

G RACE P. MONACO, J.D.
Medical Care Ombudsman Program

BRIAN E. MONDELL, M.D.
Baltimore Headache Institute

JOHN W. MORGAN, DR.P.H.
California Cancer Registry

S TEPHEN J. MOSS, D.D.S., M.S.
New York University College of Dentistry

BROOKE T. MOSSMAN, PH.D.
University of Vermont College of Medicine

PETER W. MULLEN, PH.D, FCSFS
Kemic Bioresearch

ALICIA A. MULLER, PHARM.D.
Institute for Continuing Healthcare Education

HARRIS M. NAGLER, M.D.
Beth Israel Medical Center/Albert Einstein College of Medicine

DANIEL J. NCAIYIANA, M.D.
Benguela Health (South Africa)

PHILIP E. NELSON, PH.D.
Purdue University

JOYCE A. NETTLINGTON, D.S.C., R.D.
Denver, CO

JOHN S. NEUBERGER, DR.P.H.
University of Kansas

THOMAS NICHOLSON, PH.D., M.P.H.
Western Kentucky University

ALBERT G. NICKEL
LyonHeart (ret.)

THERESA NICKLAS, DR.P.H.
Baylor College of Medicine

ROBERT J. NICOLOSI, PH.D.
University of Massachusetts, Lowell

JAMES L. OBLINGER, PH.D.
North Carolina State University

JOHN PATRICK O’GRADY, M.D.
Tufts University School of Medicine

JAMES E. OLDFIELD, PH.D.
Oregon State University

STANLEY T. OMAYE, PH.D., F.A.T.S., F.ACN, C.N.S.
University of Nevada, Reno

MICHAEL W. PARIZA, PH.D.
University of Wisconsin, Madison

STUART PATTON, PH.D.
Pennsylvania State University

JAMES MARC PERRIN, M.D.
Mass General Hospital for Children

JAY PHELAN, M.D.
Wyle Integrated Science and Engineering Group

TIMOTHY DUKES PHILLIPS, PH.D.
Texas A&M University

DAVID R. PIKE, PH.D.
Champaign, IL

HENRY C. PITOT, M.D., PH.D.
University of Wisconsin, Madison

THOMAS T. POLEMAN, PH.D.
Cornell University

GARY P. POSNER, M.D.
Plant City, FL

JOHN J. POWERS, PH.D.
University of Georgia

WILLIAM D. POWRIE, PH.D.
University of British Columbia (Canada)

C.S. PRakash, PH.D.
Tuskegee University

MARVIN P. Pritts, PH.D.
Cornell University

DANIEL J. RAITEN, PH.D.
National Institutes of Health

DAVID W. RAMEY, D.V.M.
Ramey Equine Group

R.T. RAVENHOLT, M.D., M.P.H.
Population Health Imperatives

RUSSEL J. REITER, PH.D.
University of Texas, San Antonio

WILLIAM REVILLE, PH.D.
University College Cork (Ireland)

DONALD R. ROBERTS, PH.D.
The Uniformed Services University of the Health Sciences

J. D. ROBINSON, M.D.
Georgetown University School of Medicine

B RAD RODU, D.D.S.
University of Louisville

B ILL D. ROEBUCK, PH.D., D.A.B.T.
Dartmouth Medical School

D AVID B. ROLL, PH.D.
Colleyville, TX

D ALE R. ROMSO, PH.D.
Michigan State University

J OSEPH D. ROSEN, PH.D.
Cook College, Rutgers University

S TEVEN T. ROSEN, M.D.
Northwestern University Medical School

S TANLEY ROTHMAN, PH.D.
Smith College

S TEPHEN H. SAFE, D.PHIL.
Texas A&M University

W ALLACE I. SAMPSON, M.D.
Stanford University School of Medicine

M ARK “JASON” SANDERS, M.D.
University of Texas Medical School

H AROLD H. SANDSTEAD, M.D.
University of Texas Medical Branch

C HARLES R. SANTERRE, PH.D.
Purdue University

L O WELL D. SATTERLEE, PH.D.
Vergas, MN

M ARK V. SAUER, M.D.
Columbia University

J EFFREY W. SAYELL, PH.D.
Texas A&M University

M ARVIN J. SCHISSEL, D.D.S.
Roslyn Heights, NY

D AVID SCHOTTENFELD, M.D., M.Sc.
University of Michigan

J OEL M. SCHWARTZ, M.S.
Reason Public Policy Institute

D AVID E. SEIDEMANN, PH.D.
Brooklyn College/Yale University

D AVID A. SHAYWITZ, M.D., PH.D.
Theravance, Inc.

P ATRICK J. SHEA, PH.D.
University of Nebraska, Lincoln

B OARD OF SCIENTIFIC AND POLICY ADVISORS
(continued)
The opinions expressed in ACSH publications do not necessarily represent the views of all members of the ACSH Board of Trustees, Founders Circle and Board of Scientific and Policy Advisors, who all serve without compensation.
Despite the popularity of low-calorie, sugar-free foods and beverages, some people have concerns or questions about the safety of the sugar substitutes that make these products possible. Misinformation about sugar substitutes abounds, especially on the Internet, and people may have difficulty distinguishing trustworthy sources of information on this topic from less reliable ones. This revised and updated report by the American Council on Science and Health summarizes the scientific facts about the safety of sugar substitutes.

This consumer-friendly publication is based on the manuscript “Low-Calorie Sweeteners and Other Sugar Substitutes: A Review of the Safety Issues,” published in the journal Comprehensive Reviews in Food Science and Food Safety, by Dr. Manfred Kroger of Pennsylvania State University and Kathleen Meister and Dr. Ruth Kava of the American Council on Science and Health. This second edition was updated and revised by ACSH’s Dr. Ruth Kava, and Ariel Savransky, M.S.

The American Council on Science and Health is a consumer education consortium concerned with issues related to food, nutrition, chemicals, pharmaceuticals, lifestyle, the environment and health. It was founded in 1978 by a group of scientists concerned that many important public policies related to health and the environment did not have a sound scientific basis. These scientists created the organization to add reason and balance to debates about public health issues and bring common sense views to the public.