

Position of the Academy of Nutrition and Dietetics: Use of Nutritive and Nonnutritive Sweeteners

ABSTRACT

It is the position of the Academy of Nutrition and Dietetics that consumers can safely enjoy a range of nutritive sweeteners and nonnutritive sweeteners (NNS) when consumed within an eating plan that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary Reference Intakes, as well as individual health goals and personal preference. A preference for sweet taste is innate and sweeteners can increase the pleasure of eating. Nutritive sweeteners contain carbohydrate and provide energy. They occur naturally in foods or may be added in food processing or by consumers before consumption. Higher intake of added sugars is associated with higher energy intake and lower diet quality, which can increase the risk for obesity, prediabetes, type 2 diabetes, and cardiovascular disease. On average, adults in the United States consume 14.6% of energy from added sugars. Polyols (also referred to as sugar alcohols) add sweetness with less energy and may reduce risk for dental caries. Foods containing polyols and/or no added sugars can, within food labeling guidelines, be labeled as sugar-free. NNS are those that sweeten with minimal or no carbohydrate or energy. They are regulated by the Food and Drug Administration as food additives or generally recognized as safe. The Food and Drug Administration approval process includes determination of probable intake, cumulative effect from all uses, and toxicology studies in animals. Seven NNS are approved for use in the United States: acesulfame K, aspartame, Luo Han Guo fruit extract, neotame, saccharin, stevia, and sucralose. They have different functional properties that may affect perceived taste or use in different food applications. All NNS approved for use in the United States are determined to be safe.

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POSITION STATEMENT

It is the position of the Academy of Nutrition and Dietetics that consumers can safely enjoy a range of nutritive and nonnutritive sweeteners when consumed within an eating plan that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary Reference Intakes, as well as individual health goals and personal preference.

SWEETENERS CAN BE GROUPED IN various ways. For the purpose of this article sweeteners will be grouped as nutritive and nonnutritive. Nutritive sweeteners contain carbohydrate and provide energy; they may be further classified into monosaccharides or disaccharides, which impart 4 kcal/g, or sugar alcohols (polyols), which provide an average of 2 kcal/g (1). Different terms are used to refer to nutritive sweeteners, including *sugars*, *sugar*, *caloric sweeteners*, and *added sugars*. Sugars occur naturally (intrinsic) in all fruit, vegetables, and dairy foods or are added (extrinsic) to foods during processing, or in preparation for consumption by an individual (2).

Sugars commonly found in foods include:

- **Glucose** A monosaccharide and the primary source of energy for body cells.
- **Fructose** A monosaccharide found in fruit, honey, and some vegetables. In nature, it is linked with glucose as the disaccharide sucrose. Fructose may be used as a nutritive sweetener.
- **Galactose** A monosaccharide that occurs in dairy products and some plants.
- **Sucrose** A disaccharide that occurs naturally in fruit and vegetables. It is composed of approximately equal parts glucose and fructose and is used as a nutritive sweetener and for its other functional properties.
- **Maltose** A disaccharide composed of two glucose units; it is found in molasses and is used for fermentation.
- **Corn-based sweetener** Refers to many products made from corn.

They may be composed primarily of glucose, fructose, or any combination of the two. High-fructose corn syrup (HFCS) is a mixture of glucose and fructose and is only available to food manufacturers.

- **Agave nectar** A nutritive sweetener that contains fructans, oligosaccharides of fructose and glucose, and monosaccharides of fructose and glucose.

Sugar often refers to sucrose, which is derived from sugar cane or sugar beets. The US Department of Agriculture (USDA) uses *added sugars* to refer to sugars and syrups added to foods during processing, preparation or before consumption. In addition to imparting a sweet taste, sugars have the following functions that are important to safety and quality in foods:

- Inhibit microbial growth by binding water in jams and jellies.

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- Add texture, flavor, and color to baked goods.
- Support the growth of yeast for leavening or fermentation.
- Contribute volume in ice cream, baked goods, and jams.
- Enhance the creamy consistency of frozen desserts.
- Enhance the crystallization of confectionary products.
- Balance acidity in salad dressings, sauces, and condiments.
- Help to maintain the natural color, texture, and shape of preserved fruits (3).

Nonnutritive sweeteners (NNS) offer little to no energy when ingested. They are referred to as high-intensity sweeteners because, as sweetening ingredients, they are many times sweeter than sucrose. NNS can replace the sweetness of sugar or energy-containing sweeteners. However, they do not have the same functional properties such as browning, crystallization, or microbial inhibition.

MECHANISM OF SWEET TASTE

Liking of sweet taste is innate, but perception of sweetness and preferred level of sweetness vary among individuals. Taste perception begins on the tongue and soft palate where taste receptors interact with food or beverages. Taste receptor cells are organized into taste buds, which are distributed throughout the tongue and on specialized structures called papillae (4). Sweet taste is elicited through interaction with a sweet receptor, identified as a dimeric G-protein coupled receptor composed of T1R2 and T1R3 subunits with multiple active sites (5). Li and colleagues (6) showed that these receptors (T1R2 and T1R3) responded to sugars (ie, sucrose, fructose, galactose, glucose, lactose, and maltose), amino acids (ie, glycine and D-tryptophan), sweet proteins (ie, monellin and thaumatin), and NNS (ie, acesulfame K, aspartame, cyclamate, dulcin, neotame, saccharin, and sucralose), although specific preferential binding sites may vary. Synergy among sweeteners is because they bind different subunits. Binding a single subunit activates the sweet response, whereas a second ligand binding another subunit enhances the response (7). A transduction mechanism translates the sweet chemical message through the nervous system to the per-

This Academy position paper includes the authors' independent review of the literature in addition to systematic review conducted using the Academy's evidence analysis process and information from the Academy's Evidence Analysis Library (EAL). Topics from the EAL are clearly delineated and references used in EAL sections can be found on the EAL Web site. The use of an evidence-based approach provides important added benefits to earlier review methods. The major advantage of the approach is the more rigorous standardization of review criteria, which minimizes the likelihood of reviewer bias and increases the ease with which disparate articles may be compared. For a detailed description of the methods used in the Academy's evidence analysis process, to www.andevidencelibrary.com/eaprocess.

Conclusion Statements are assigned a grade by an expert work group based on the systematic analysis and evaluation of the supporting research evidence. **Grade I=Good; Grade II=Fair; Grade III=Limited; Grade IV=Expert Opinion Only; and Grade V=Not Assignable (because there is no evidence to support or refute the conclusion).** Criteria for grades can be found at www.andevidencelibrary.com/grades.

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ception of sweet taste in the brain. The characteristics of this transduction pathway are not well defined (5). Margolski (8) hypothesized that the pathway for saccharide sweeteners uses cAMP as a second messenger and the pathway for nonsaccharide sweeteners uses inositol 1,4,5-triphosphate and diacylglycerol as second messengers. Both mechanisms work through regulation of Ca²⁺ and ion channels and are thought to exist in the same taste receptor cells. Some NNS compounds interfere with signal termination in the downstream elements of the transduction pathway, resulting in a lingering aftertaste (9,10).

Taste perception and food preference are complex and differences in concentration of papillae, number and type of taste receptors, or gene sequencing of signal transduction molecules contribute to individual variation (7). Although there is good evidence for the heredity of bitter taste, studies in twins and other family members have found few similarities in perception of sweet taste that could be attributed to genetics

(11). Preference for sweet taste may be genetic; variations in a taste receptor gene accounted for some differences in sweet preference among children, but not in adults (12). Differences in preference for sweet taste are most likely due to an interaction between genetics and environmental exposure (4).

REGULATION OF NNS IN THE UNITED STATES

In the United States, the responsibility for evaluating the safety of NNS was given to the Food and Drug Administration (FDA) in 1958 under the Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act. Throughout the world, nations have their own regulatory agencies or rely on other regional or international governing bodies and expert scientific committees, including the Bureau of Chemical Safety, in Health Canada's Food Directorate (13), the Scientific Committee on Food of the European Commission, the Joint Expert Committee on Food Additives of the United Nations Food and Agricultural Organization, and World Health Organization (WHO) to evaluate the safety of NNS.

The US Food Additives Amendment of 1958 required all new food additives to undergo a strict premarket approval process unless the substance is generally recognized as safe (GRAS) among experts qualified by training and experience to evaluate its safety under the conditions of its intended use. Common food ingredients that were used before 1958 were listed as GRAS and not included in the definition of a food additive (14), which is "any substance, the intended use of which results or may be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food" (15).

Some sweeteners in the United States are listed or affirmed as GRAS. The GRAS exemption requires the same standard of safety as food additives do, that is "the reasonable certainty of no harm." Before passage of the Food Additive Amendment in 1958, the FDA provided to Congress a list of substances that were considered GRAS and added to that list between 1958 and 1973. To be listed, the substance must have a history of consumption before 1958 by a significant number of people or there must be consensus among ex-

perts qualified to evaluate product safety that the use of the substance is safe. In 1973, FDA initiated a GRAS affirmation process, which encouraged manufacturers to submit their GRAS determinations to the agency for review. In 1997, FDA replaced the affirmation process with a GRAS notification process (14). Manufacturers may determine that use of a substance is GRAS and will notify FDA of that conclusion. FDA responds to the manufacturer with one of three responses: it has no questions about the petitioner's conclusion; the notice does not provide a sufficient basis for a GRAS determination; or the agency has, at the petitioner's request, ceased to evaluate the GRAS notice. The *Federal Register* provides a published explanation of the GRAS exemption (16). It is important to note that the GRAS exemption refers specifically to the intended use of a substance.

For approval of a food additive, the petitioner (the manufacturer, company, or interested partner that wants to market a sweetener) must assemble and present to FDA all required safety data relevant to the proposed use of the additive in accordance with safety guidelines published by the FDA (15). To determine safety of a food additive, FDA considers: probable intake, cumulative effect from all uses, and toxicological data required to establish safety. Guidelines for toxicology studies to document the safety of food additives are published by FDA in *Redbook 2000* (17) and are consistent with guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (18). Initial tests should include pharmacokinetics and metabolism to allow FDA scientists to evaluate:

- extent of absorption;
- tissue distribution;
- pathways and rates of metabolism; and
- rates of elimination of the substance and any metabolites.

Information from these studies, known collectively as absorption, distribution, metabolism, and excretion, is used to design toxicity studies and determine potential mechanisms of toxicity. Toxicity studies include short-term and subchronic toxicity tests with rodents, subchronic and long-term toxic-

ity tests with nonrodents, reproductive and developmental toxicity and tests of carcinogenicity (19). Some food additives may generate questions beyond the usual toxicology studies. These may include the potential for allergic reactions, interactions with medications, or effects on nutritional status, blood glucose control, or other clinical conditions. In these cases, FDA may require a more extensive evaluation procedure that includes clinical studies with human subjects. The safety evidence that must be established before studies in human subjects can be conducted may exceed that required for clinical trials of new drugs because there is no anticipated health benefit from food additives (17). If the use of the additive is safe for most consumers, but may present a risk for certain subpopulations such as those with an allergy or inborn error of metabolism, FDA can require that an informational label that alerts consumers to the presence of that additive be placed on all foods containing it. A detailed review of the FDA food additive approval and GRAS affirmation processes can be found in Rulis and Levitt (19).

Three safety concepts are integral to the FDA food additive approval process. The first concept is the highest no effect level (HNEL). Any petition brought to the FDA for use of a new food additive must include information that allows the FDA to determine the highest level or threshold of intake at which no adverse effect occurs. FDA scientists independently review the results of the animal toxicology studies to determine the exposure at which there were no adverse effects in the most sensitive of animal studies. The second safety concept is the acceptable daily intake (ADI). With the HNEL, the FDA will determine an ADI for human beings, generally with a 100-fold safety factor to account for the fact that the studies were conducted in animals (10-fold) and for normal, genetic variation (additional 10-fold). The HNEL, divided by 100, is consistent with the FDA standard "reasonable certainty of no harm" and is assigned as the ADI. The ADI represents an amount considered safe to consume every day over the course of a lifetime without adverse effects. An ADI for the food additive is communicated by the regulatory agency for that coun-

try. The FDA ADI may differ from the ADI from regulatory bodies in other countries. The third safety concept is the estimated daily intake (EDI), derived from the amount of the additive to be added to foods, assuming 100% replacement of sugars and other NNS and the typical consumption of those foods by people of different ages and health status. The EDI generally overestimates consumption because it assumes that the new additive will replace all sweeteners in the market (100% market penetration). It is based on a consumption level equal to the 90th percentile level for the foods that will contain the additive and the assumption that all population subgroups will consume the new additive. The ADI is compared with the EDI to confirm that the ADI is well in excess of human exposure. See the final rule on sucralose in *Federal Register* (20) for a good example of the process the FDA used to determine HNEL, EDI, and ADI.

Once a food additive receives final FDA approval, that approval is published in *Federal Register*. In the approval documentation, FDA may request that additional data on actual consumption or other safety data be collected by the petitioner during the post-approval period. If the EDI is determined to exceed the ADI, there may be limitations placed on the use of the additive. To date, this has not been documented with any NNS. An FDA ruling may be challenged after approval with new evidence. The FDA will examine the postmarket evidence with the same rigor that premarket studies received and will consider new data in context of the entire body of evidence to ensure appropriate risk analysis to protect the public health.

NUTRITIVE SWEETENERS

Sugars Added to Foods and Beverages

Added sugars, not naturally occurring sugars, when considered with solid fats and excess energy intake, have been linked to health concerns, including overweight and obesity, type 2 diabetes or prediabetes, inflammation, and cardiovascular disease (21). Added sugars in processed foods can be identified by reading the list of ingredients on the food label (Figure) (21,22). Other added sugars that can be found in foods but are not recognized by FDA as ingredients include cane juice, evaporated

Anhydrous dextrose	Lactose
Brown sugar	Malt syrup
Confectioner's powdered sugar	Maltose
Corn syrup	Maple syrup
Corn syrup solids	Molasses
Dextrose	Nectars (eg, peach nectar, pear nectar)
Fructose	Pancake syrup
High-fructose corn syrup	Raw sugar
Honey	Sucrose
Invert sugar	White granulated sugar

Figure. Ingredients on food labels consumers can use to identify added sugars.

corn sweetener, fruit juice concentrate, crystal dextrose, glucose, liquid fructose, sugar cane juice, and fruit nectar (21,22).

HFCS is produced from corn syrup, which is typically 100% glucose. This syrup undergoes enzymatic processing to increase fructose content and is then mixed with glucose (23). HFCS can range in percentage fructose from 42%, which is most often used in baked goods to 55%, which is used in beverages and has a similar composition as sucrose (2).

Agave nectar has received interest from consumers as a way to sweeten foods. Agave nectar is produced from the heart of the agave plant (*Agave tequilana* Weber var. azul.) (24), which is also the starting material for the production of tequila (25). Freshly extracted agave juice is composed of inulin, a fructan that is heated or treated enzymatically to convert this complex carbohydrate to monosaccharides (25,26). The amount of sugar (mostly fructose but with some glucose and dextrose), will vary depending on the pH, temperature, and length of heating time (27).

Digestion and Absorption

Sucrose is hydrolyzed to fructose and glucose by the α -glucosidase sucrase in the sucrase-isomaltase complex of the enterocytes in the small intestine. Lactose digestion is accomplished by the β -galactosidase, lactase-phlorizin hydrolase found in the brush-border of the small intestine and yields glucose and galactose (28).

Monosaccharides (ie, glucose, fructose, and galactose) need a transporter system for absorption. The systems are present on the apical border and basolateral cell membranes of the enterocytes and work in concert. Glucose and galactose use the same sodium-glucose cotransporter 1 on the apical membrane to pass into the enterocyte linked with two sodium molecules. Fructose absorption is facilitated by glucose-fructose transporter 5. Once in the enterocyte, all three monosaccharides pass into the portal capillaries by a glucose transporter, which is located on the basolateral membrane (28).

Consumption of Sucrose, Glucose, and Fructose

Different terms and methods used to estimate the intake or availability of sugars in the food supply complicate monitoring of sugar consumption. The National Health and Nutrition Examination Survey (NHANES) (released in 2-year waves since 1999-2000) uses self-report to estimate intake. Food availability data are provided by the USDA Economic Research Service (ERS).

Food Consumption Patterns of Added Sugars

The 2010 Dietary Guidelines for Americans (DGA) reported that added sugars contributed approximately 16% of total energy in the US population (21) or 21 tsp added sugars using NHANES 2005-2006 data (21,29) (Table 1). More re-

cently, Welsh and colleagues (30) found that added sugars provided 14.6% of total energy intake using 2007-2008 NHANES data. The main contributor of added sugar intake was soda and energy/sports drinks sweetened with nutritive sweeteners, providing 7.5 tsp/day (29) or 35.7% of total added sugars (31). The other top contributors were grain-based desserts, fruit drinks, dairy desserts, and candy (21,31). Based on these added sugars intakes and after adjusting the intake to 2,000 kcal, the usual added sugars intake for adults aged 19 years and older is 79 g or 20 tsp (2,29). The USDA pattern for 2,000 kcal recommends no more than 32 g (8 tsp added sugars/day) (2) or 6% of 2,000 kcal.

The consumption of added sugars of the US population decreased from 1999-2000 to 2007-2008 along with a decreasing trend in total energy intake of 76 kcal/day (*P* for trend=0.004) for the US population (30). There was a decreased added sugars intake of 100.1 g (95% confidence interval [CI]: 92.8 to 107.3 g; 401 kcal) in 1999-2000 to 76.7 g (95% CI: 71.6 to 81.9 g; 307 kcal) in 2007-2008 (*P* for trend <0.001). This was a significant decrease in percentage of total energy from added sugars of 18.1% (95% CI: 16.9%, 19.3%) to 14.6% (95% CI: 13.7%, 15.5%) (*P* for trend <0.001) during the same period for the US population. The rank order of food sources did not change and neither did population groups who consumed higher amounts of added sugars over this time period (data presented later in this article). Welsh and colleagues (30) concluded that although consumption of added sugars decreased between 1999-2000 and 2007-2008, intake of added sugars are still higher than recommended.

Intake by Different Population Groups

NHANES data from 2005-2006 indicated children aged 2 to 18 years consumed 23 tsp added sugar (29) or 365 kcal (32,33), which is 18% of total energy needs (2,027 kcal/day) (34) (Table 1). Teenagers aged 9 to 13 years compared with other life stages had the highest proportion who consumed more than 25% of total energy from

Table 1. Food sources of added sugar intake of total US population aged 2 to 18 years and 19 years or older, National Health and Nutrition Examination Survey, 2005-2006^a

Food group	All Persons		2-18 y		≥19 y	
	Tsp	% ^b	Tsp	%	Tsp	%
Mean intake of added sugars	21.0	100.0	23.0	100.0	20.0	100.0
Soda/energy/sports drinks	7.5	35.7	7.3	31.8	7.6	37.1
Grain-based desserts	2.7	12.9	2.5	10.9	2.8	13.7
Fruit drinks	2.2	10.5	3.4	15.0	1.8	8.9
Dairy desserts	1.4	6.6	1.8	7.9	1.2	6.1
Candy	1.3	6.1	1.6	6.8	1.2	5.8

^aAdapted from references 29 (tsp) and 31 (%).

^bPercentage of total added sugars from these various foods.

Table 2. Food sources of added sugar intake of total US population by racial groups and income, National Health and Nutrition Examination Survey, 2005-2006^a

Food group	Race/Ethnicity						Household Income					
	Non-Hispanic White		Non-Hispanic Black		Mexican American		≤130% Poverty Level		131% to 185% Poverty Level		≥186% Poverty Level	
	tsp	% ^b	tsp	%	tsp	%	tsp	%	tsp	%	tsp	%
Mean intake of added sugars	21.0	100.0	22.0	100.0	22.0	100.0	23.0	100.0	20.0	100.0	20.0	100.0
Soda/energy/sports drinks	7.6	36.3	7.2	32.3	8.6	39.0	9.4	40.8	8.1	40.6	6.7	32.9
Grain-based desserts	2.8	13.4	2.6	11.6	2.5	11.5	2.5	10.6	2.6	13.2	2.8	13.6
Fruit drinks	1.7	8.2	4.4	19.4	3.4	15.4	2.6	11.2	1.8	9.2	2.1	10.5
Dairy desserts	1.5	7.0	1.3	6.0	1.0	4.6	1.3	5.5	1.2	6.1	1.5	7.2
Candy	1.3	6.1	1.5	6.4	1.1	4.9	1.5	6.4	1.2	5.9	1.2	6.0

^aAdapted from references 37 (household income) and 38 (race/ethnicity).

^bPercentage of total added sugars from these various foods.

added sugars (boys 31.2%, girls 27.8%) (35).

Thompson and colleagues (36) examined the relation between race and socioeconomic status and added sugars intake, using 2005 US National Health Interview Survey Cancer Control Supplement and the NHANES 2003-2004 data. Added sugars intake was higher in men than in women. African-American women had the highest added sugars intake when compared with white or Hispanic women, but African Americans in general had the highest added sugars intake. Those who had the highest level of education (more than high school) had the lowest added sugars intake. As income decreased, added sug-

ars intake increased in men and women. Thompson and colleagues (36) concluded that adults with lower income and less education and those in ethnic minority groups are consuming diets higher in added sugars, which may put them at greater risk for chronic disease.

Sources of Added Sugars by Different Groups

Based on NHANES 2005-2006, rank order of food sources of added sugars differed by age and race/ethnic groups (Tables 1 and 2). Fruit drinks sweetened with nutritive sweeteners were ranked second for children and third

for adults (Table 1) (31). The rank order of foods that provide added sugars differed by race/ethnic group, but did not differ across income groups (≤130% poverty, 131% to 185% poverty, ≥186% poverty) (37,38) (Table 2). Soda/energy/sports drinks provided the most added sugars across all race/ethnic and income groups. Mexican Americans and non-Hispanic blacks both differed from non-Hispanic whites in that fruit drinks were the second ranked food and grain-based desserts was third.

Table 3 presents the top five sources of added sugars by age (34). Energy from added sugars increased from 197 kcal for those aged 2 to 3 years to 444

Table 3. Major sources of added sugars among children and adolescents in the United States (aged 2 to 18 years) by age and race, National Health and Nutrition Examination Survey, 2003-2004^a

	Top 5 Sources									
	First source	%	Second source	%	Third source	%	Fourth source	%	Fifth source	%
Age group										
All	Soda	31.8	Fruit drinks	15.0	Grain desserts	10.9	Dairy desserts	7.9	Candy	6.8
2-3 y	Fruit drinks	19.3	Soda	11.4	Grain desserts	11.3	Candy	8.5	Cold cereals	8.3
4-8 y	Soda	19.9	Fruit drinks	17.0	Grain desserts	11.2	Dairy desserts	10.4	Cold cereals	8.3
9-13 y	Soda	30.7	Fruit drinks	13.6	Grain desserts	12.4	Dairy desserts	8.8	Candy	7.8
14-18 y	Soda	44.5	Fruit drinks	14.1	Grain desserts	9.4	Candy	5.6	Dairy desserts	5.5
Race										
NHW ^b	Soda	34.7	Fruit drinks	12.2	Grain desserts	10.3	Dairy desserts	8.4	Candy	6.5
NHB ^c	Fruit drinks	24.3	Soda	21.8	Grain desserts	12.1	Candy	9.4	Dairy desserts	7.2
Mex Am ^d	Soda	31.5	Fruit drinks	19.0	Grain desserts	11.5	Candy	6.1	Dairy desserts	5.8

^aAdapted from reference 34.
^bNHW=non-Hispanic white.
^cNHB=non-Hispanic black.
^dMex Am=Mexican American.

kcal for those aged 14 to 18 years in 2003-2004 (32-34). Soda/energy drinks/sport drinks or fruit drinks were the top two sources of added sugars for all ages. Fox and colleagues (39) reported that 44% of children aged 19 to 24 months consumed either fruit drinks (38%) or sodas (11%) once per day in 2002. Intake of soda (nutritive sweeteners and NNS) increased as children aged, with the greatest increase happening at age 8 years (40).

Food Consumption Patterns of Fructose

Fructose consumption patterns over time are difficult to describe because fructose intake has not always been measured in large national surveys (41). Bray and colleagues (42) calculated fructose intake by taking half of sucrose as fructose and adding to this value fructose from HFCS. In more recent work (41-43), the fructose content of the foods was included in the nutrient data base. Bray and colleagues (42) estimated that fructose intake was 8.8% of total energy in 1977-1978 and increased to 11.5% in 1994-1998. Two other researchers estimated fructose intake was 10.2% (54.7 g) (41) or 9.1% (43) of total energy using NHANES III (1988-1994) or NHANES 1999-2004 data, respectively.

Food Availability Data and Changes Over Time

Food availability data are compiled by the ERS by estimating food supplies from production to marketing. Another term used for these data is food disappearance data because they describe how the food supply disappears as it moves through the food marketing system. The ERS takes the total annual available supply of a commodity and subtracts out measurable uses, such as farm inputs (feed and seed), exports, ending stocks, and industrial uses. This total supply is divided by the US population to get per capita availability. Food availability data exceed actual intake because not all waste or loss is estimated (44).

Based on ERS data, nutritive sweeteners available per capita were 119.1 lb in 1970, 141.1 lb in 2005 (45), and 130.7 lb in 2009 (46). There were no changes in availability of honey (1 lb) or edible syrups (0.5 lb) between 1970 and 2009. Refined cane and beet sugar decreased from 101.8 lb in 1970 to 63.6 lb in 2009. Dextrose decreased from 1970 to 2009 (4.6 lb to 2.7 lb, respectively). Availability of other energy-containing sweeteners increased. Between 1970 and 2005, the annual per capita availability of corn sweetener increased 387% with the HFCS share of corn sweeteners in-

creasing from 3% (0.5 lb) to 76% (59 lb), whereas the per capita availability of refined cane and beet sugar decreased 38% (from 102 lb to 63 lb) (45). Energy-containing sweeteners provided the following teaspoons per day and energy per day in 2009 when adjusted for loss (47): refined cane and beet sugar (13.4 tsp, 214.2 kcal) (48), HFCS (10.6 tsp, 168.9 kcal) (49), and other sweeteners (eg, glucose syrup, dextrose, honey, and edible syrups) (3.6 tsp, 57.4 kcal) (50).

HFCS availability increased between 1970 and 1999 then began to decrease, dropping by 59 lb by 2005 (51). HFCS availability was 50.1 lb in 2009 (49). Wells and Buzby (51) hypothesized that this trend may be a reflection of the increased availability of no-energy bottled water and diet sodas; increased cost of HFCS because of pressure to make ethanol from corn; or increasing use of sugar alcohols and NNS.

Guidance on Use of Nutritive Sweeteners

Dietary Reference Intakes from the Institute of Medicine. The Acceptable Macronutrient Distribution Ranges for carbohydrate is estimated at 45% to 65% of energy (52). The Recommended Dietary Allowance for carbohydrate is 130 g/day for adults and children. This

is based on the average minimum amount of glucose used by the brain. The Institute of Medicine recommended that the intake of added sugars not exceed 25% of energy to ensure adequate intake of essential micronutrients that are typically not present in foods high in added sugars.

American Heart Association. In 2006, the American Heart Association's Diet and Lifestyle Recommendations stated to minimize the intake of beverages and foods containing added sugars (53). That recommendation was expanded in 2009 to set an upper limit of added sugars intake at half of the discretionary energy allowance as determined by the USDA food intake patterns (54). The final statement of the American Heart Association reads: "Most American women should eat or drink no more than 100 calories/day (25 g or 6 tsp) from added sugars, and most American men should eat or drink no more than 150 calories/day (38 g or 10 tsp) from added sugars."

WHO Recommendations. The WHO Global Strategy on Diet, Physical Activity and Health, endorsed at the 57th World Health Assembly, includes limiting the intake of free or added sugars (55). In an earlier document, WHO recommended that $\leq 10\%$ of energy be provided by added sugars (56).

2010 DGA and ChooseMyPlate. The 2010 DGA recommend intake of foods to result in a more healthful diet (21). The guidelines acknowledge that the body metabolizes added sugars and natural sugars found in fruits and dairy foods the same, but typically foods high in added sugars are higher in energy and low in essential nutrients or dietary fiber (21). Recommendations related to added sugars include the following: reduce the calories from solid fats and added sugars (SoFAS); and limit the consumption of foods that contain refined grains, especially refined grain foods that contain SoFAS and sodium. The DGA advisory committee recognized the need to obtain adequate nutrients without overconsumption of energy to reduce risk of common chronic diseases such as obesity, cardiovascular disease, and some cancers (2).

Using the MyFood-a-pedia Web site (www.myfoodapedia.gov) one can

identify the SoFAS content of foods and beverages and choose those with fewer SoFAS, choose them less often, or choose a smaller portion. Recommendations include:

- Cut back on foods and drinks with added sugars or energy-containing sweeteners.
- Drink few or no regular sodas, sports drinks, and fruit drinks.
- Eat fewer grained-based or dairy-based desserts, other desserts, and candy or eat smaller portions less frequently.
- Drink water, fat-free milk, 100% fruit juice, or unsweetened tea or coffee instead of sugar-sweetened drinks.
- Drink 100% fruit juice instead of fruit-flavored drinks.
- Eat fruit for dessert.
- Use the Nutrition Facts label to choose breakfast cereals and other packaged foods with less sugar and use the ingredients list to choose foods with little or no added sugars.

ChooseMyPlate is part of a large communications initiative sponsored by the USDA to help consumers implement the 2010 DGA recommendations. The messages for consumers emphasize foods to eat less often, including foods that are high in SoFAS, and drinking water instead of sugary drinks. The plan presents a recommended daily limit for empty energy such as SoFAS that add energy to foods without adding nutrients.

Polyols (Sugar Alcohols) and Other Sweeteners

Polyols or sugar alcohols have been used in food products for many years to decrease the intake of carbohydrates that raise blood glucose levels. Polyols can be used alone but are more often used in combination with other polyols or NNS because of the bulking property of some polyols. Energy provided by polyols varies (Table 4) because of differences in digestibility and because polyols are typically absorbed slowly and incompletely by passive diffusion (57). Metabolism also varies (57). For example, erythritol is completely absorbed but is not metabolized. Many polyols are found in nature but may be manufactured from monosaccharides

or polysaccharides to be used as food ingredients. Foods containing polyols and no added sugars can be labeled as sugar-free (1). Table 4 presents regulatory status, EDI, and ADI for selected polyols and other sweeteners, sweetness compared with sucrose, and their use in foods.

Trehalose and D-tagatose are other sweeteners used in food (Table 4). Trehalose is found naturally in foods such as honey and unprocessed mushrooms. The enzyme trehalase is present in the brush-border membrane of the small intestine and hydrolyzes the α -1,1 bond of trehalose into two glucose molecules (58). D-tagatose is similar to fructose in structure other than an inversion of the hydroxyl and hydrogen groups at the fourth carbon and is found in many foods, including dairy products (59). Only 15% to 20% of D-tagatose is absorbed with much being fermented in the colon (60). The metabolism of absorbed D-tagatose is the same as that of fructose. Both of these other sweeteners are used with other nutritive sweeteners and NNS in foods.

NONNUTRITIVE SWEETENERS

Consumption Patterns

Since the discovery of saccharin in the late 1800s, NNS have been used by consumers to achieve a sweet taste, for reasons of economics, blood glucose control, or energy control. NNS approved for use in the US have been tested and determined to be safe at levels that are within the ADI. Intake of food additives, including NNS, is difficult to assess. Studies of NNS intake need to have an adequate number of subjects to include consumers at the 95th percentile of intake and should include groups who may have higher than normal intakes (eg, people with diabetes) or groups of people with special concerns (pregnant women or children) (61). Food products may contain a blend of different NNS, which further complicates estimation of intake. Mattes and Popkin (62) used existing data from US nutrient monitoring systems to locate items that contained NNS on food composition tables to estimate NNS consumption. Although consumption of NNS in foods and beverages has increased since 1965, only about 15% of the pop-

Table 4. Energy, regulatory status, and function in foods of polyols and other sweeteners

Type	kcal/g	Regulatory status	Use in foods
Monosaccharide polyols or other sweeteners			
Sorbitol (117)	2.6	GRAS ^a label must state risk of laxative effect	50%-70% as sweet as sucrose; bulk ingredient; humectant; texturizing agent; noncariogenic; some individuals may experience a laxative effect from a daily load of ≥ 50 g
Mannitol (118,119)	1.6	Approved food additive; label must state risk of laxative effect	50%-70% as sweet as sucrose; low-energy sweetener; cooling effect to mask bitter taste; non-cariogenic; used as dusting powder; some individuals may experience a laxative effect from a daily load of ≥ 20 g
Xylitol (120,121)	2.4	Approved as food additive for use in foods for special dietary uses	As sweet as sucrose; bulk ingredient; cariostatic and anticariogenic
Erythritol (122,123)	0.2	Independent GRAS determinations EDI ^b mean: 1 g/d; 90 th percentile: 4 g/d	60%-80% as sweet as sucrose; bulk ingredient; flavor enhancer, formulation aid, humectant, stabilizer and thickener, sequestrant, and texturizer
D-Tagatose (59,60)	1.5	Independent GRAS determinations EDI mean: 7.5 g/d; 90 th percentile: 15 g/d ADI ^c : 15 g/50 kg adult/d	75%-92% as sweet as sucrose; sweetness synergizer; functions as a texturizer, stabilizer, humectants, and formulation aid; flavor enhancer
Disaccharide polyols			
Isomalt (124)	2.0	GRAS affirmation petition filed	45%-65% as sweet as sucrose; bulk ingredient; flavor enhancer; when heated does not lose sweetness
Lactitol (125)	2.0	GRAS affirmation petition filed; September, 1993	30%-40% as sweet as sucrose; bulk ingredient; synergistic with NNS ^d ; does not contribute to tooth decay
Maltitol (126)	2.1	GRAS affirmation petition filed; December 23, 1986, Web site	90% as sweet as sucrose; bulk ingredient; can replace fat because of adding creaminess to mouth feel; does not contribute to tooth decay
Isomaltulose (127)	4.0	Independent GRAS determinations EDI mean: 3-6 g/d	50% as sweet as sucrose; used as a slow release carbohydrate source
Trehalose (58,128)	3.6	Independent GRAS determinations EDI mean: 34 g/d 90 th percentile: 68 g/d	45% as sweet as sucrose; coloring adjuvant; flavor enhancer; humectants; stabilizer; thickener; synergist; texturizer
Polysaccharide polyols			
Hydrogenated starch hydrolysates (HSH; maltitol syrup; sorbitol syrups) (129)	3.0	GRAS affirmation petition filed	25%-50% as sweet as sucrose (depending on the monosaccharide composition); bulk ingredient; viscosity or bodying agents; humectants; crystallization modifiers; cryoprotectants; rehydration aids; carrier for flavors, colors and enzymes; synergistic with NNS

^aGRAS=generally recognized as safe.

^bEDI=estimated daily intake.

^cADI=acceptable daily intake.

^dNNS=nonnutritive sweetener.

Table 5. Nonnutritive sweeteners (NNS) approved in the United States by the Food and Drug Administration

Name (chemical name)	Times sweeter than sucrose	ADI ^a and EDI ^b	Use in foods
Acesulfame K (5,6-dimethyl-1,2,3-oxathiazine-4(3H)-1,2,2-dioxide) (66)	200	ADI: 15 mg/kg BW ^c EDI: 0.2 to 1.7 mg/kg BW	Approved for general use, except in meat and poultry. Combines well with other NNS; stable at baking temperatures
Aspartame (L-aspartyl-L-phenylalanine methyl ester) (68)	160-220	ADI: 50 mg/kg BW EDI: 0.2-4.1 mg/kg BW	Approved for general use. Degrades during heating
Luo han guo extract (cucurbitane glycosides, mogroside II, III, IV, V, VI) (70)	150-300	ADI: No ADI determined EDI: 6.8 mg/kg BW	GRAS ^d . Intended for use as a tabletop sweetener, a food ingredient, and a component of other sweetener blends
Neotame (N-[N-3,3-dimethylbutyl]-L-aspartyl]-L-phenylalanine-1-methyl ester) (71)	7,000-13,000	ADI: 18 mg/kg BW EDI: 0.05-0.17 mg/kg BW	Approved for general use, except in meat and poultry. To date, little used in food processing
Saccharin (1,1-dioxo-1,2-benzothiazol-3-one) (14)	300	ADI: Prior sanctioned food ingredient; no ADI determined EDI: 0.1-2 mg/kg BW	Limited to <12 mg/fl oz in beverages, 20 mg/serving in individual packages, or 30 mg/serving in processed foods
Stevia (steviol glycosides, rebaudioside A, stevioside) (74)	250	ADI: (determined by JECFA ^e) 4 mg/kg BW EDI: 1.3-3.4 mg/kg BW	GRAS ^d . Intended for use as a sweetener in a variety of food products such as cereals, energy bars, and beverages and as a tabletop sweetener
Sucralose (trichlorogalactosucrose) (20)	600	ADI: 5 mg/kg BW EDI: 0.1-2.0 mg/kg BW	General use; heat stable for cooking and baking

^aADI=acceptable daily intake.

^bEDI=estimated daily intake.

^cBW=body weight.

^dGRAS=generally recognized as safe.

^eJECFA=Joint Expert Committee on Food Additives.

ulation reported consuming any foods or beverages with NNS in 2003-2004. A systematic review of NNS intake data indicated that average intakes by adults are consistently well below their ADIs (61).

Guidance on Use of NNS

2010 DGA. The DGA contains a minimal number of statements related to the use of NNS (21). A key recommendation related to the use of NNS is to control total energy intake and increase physical activity to manage body weight (21). Eating patterns that are low in energy density improve weight loss and weight maintenance, and may be associated with a lower risk of type 2 diabetes in adults. Substituting NNS for higher-energy foods and beverages can

decrease energy intake, but evidence of their effectiveness for weight management is limited.

American Diabetes Association. The American Diabetes Association position statement on nutrition recommendations, last revised in 2008, states that, "Sugar alcohols and nonnutritive sweeteners are safe when consumed within the daily intake levels established by the Food and Drug Administration" (63). Recommendations for management of diabetes include monitoring carbohydrates by carbohydrate counting, choices, or experience-based estimation to achieve glycemic control (64). Choosing NNS instead of nutritive sweeteners is one method to assist with moderating carbohydrate intake.

National Cancer Institute. The National Cancer Institute updated a fact sheet on NNS and cancer in 2009 and noted that there is no clear evidence that the NNS available commercially in the United States are associated with cancer risk in human beings (65).

NNS Approved in the United States

The following section contains information about the structure and use of NNS approved in the United States (Table 5). The section regarding the Academy's Evidence Analysis Library contains information about effects on dietary intake, energy balance, and human health.

Acesulfame K. Acesulfame K (5,6-dimethyl-1,2,3-oxathiazine-4(3H)-1,2,2-dioxide) is a combination of an organic

acid and potassium approved by the FDA in 1988 for use in foods and as a tabletop sweetener; in 1998 it was approved for use in beverages and in 2003 it was approved as a general use sweetener, which includes any food or beverage category (66). It is 95% excreted unchanged in the urine so it does not provide energy or influence potassium intake (67). It combines well with other NNS, which is the most common way it is currently used in the US food supply. It is stable at baking temperatures.

Aspartame. Aspartame (L-aspartyl-L-phenylalanine methyl ester) is a methyl ester of aspartic acid and phenylalanine dipeptide. It was discovered in 1965 and approved by the FDA in 1981 for use in specific foods and in 1983 for use in soft drinks. In 1996 it was approved as a general use sweetener. Although aspartame provides 4 kcal/g, the intensity of the sweet taste means that very small amounts are required to achieve desired sweetness levels. In the intestine, aspartame is hydrolyzed to aspartic acid, methanol, and phenylalanine (68). In the United States the largest use of aspartame is to sweeten low-energy beverages, but it is found in many products. Despite the numerous products containing aspartame, average consumption even for the highest users remains below the ADI (61,68). Because aspartame yields phenylalanine when it is hydrolyzed in the intestine, the FDA requires any foods containing aspartame to have an informational label with the statement: "Phenylketonurics: contains phenylalanine." Individuals with phenylketonuria had small but not clinically significant increases in phenylalanine after drinking 12 oz diet soda sweetened with aspartame (69). Aspartame is stable under dry conditions, but in solutions, it degrades during heating. The rate of degradation depends on pH and temperature (68).

Luo han guo. Luo han guo is the common name for *Siraitia grosvenorii*, or Swingle fruit extract, a sweetener recently approved as GRAS (70). Another common name is monk fruit extract. This product is a combination of several different cucurbitane glycosides, known as mogrosides. Mogroside V is predominate and makes up >30% of the product. Luo han guo is 150 to 300 times sweeter than sucrose depending

on the exact structure of the mogrosides and number of glucose units. It may have an aftertaste at high levels.

Neotame. Neotame (N-[N-3,3-dimethylbutyl]-L-a-aspartyl]-L-phenylalanine-1-methyl ester) is a derivative of the dipeptide phenylalanine and aspartic acid. The FDA approved neotame as a general use sweetener in 2002 (71). Neotame is partially absorbed in the small intestine and rapidly metabolized by esterases present throughout the body. The resulting products are de-esterified neotame, which is rapidly excreted in urine and feces, and an insignificant amount of methanol (72). Although neotame contains phenylalanine, the amount used is very low because of its high intensity sweetening property and the amount released in the body is negligible (72). To date, neotame is rarely used in foods. It is stable under dry storage conditions; stability varies with pH in aqueous solutions (72).

Saccharin. Saccharin (1,1-dioxo-1,2-benzothiazol-3-one) is the oldest NNS approved for food and beverage use (73). It is not metabolized in the body, and is heat stable. It is approved as a food additive for foods and beverages, a tabletop NNS, and for use in gums, cosmetics, and pharmaceuticals. Saccharin was originally listed as GRAS. In 1977, the FDA proposed a ban on saccharin under the Delaney Clause because of an association with bladder cancer in laboratory animals. The Delaney Clause was an amendment added by Congress to the Food Drug and Cosmetic Act of 1958. It stated that no food additive would "be deemed safe if it is found to induce cancer when ingested by man or animal" and prohibited the FDA from approving such food additives—a zero-risk standard. Congress imposed an 18-month moratorium on the FDA ban on saccharin but required products containing saccharin to carry a warning that saccharin has been determined to cause cancer in laboratory animals. Congress asked the National Academy of Sciences to lead a study on the safety of saccharin. The National Institute for Environmental Health Sciences determined that the mechanism by which saccharin caused bladder tumors in rats was not relevant to human beings and recommended that it be removed

from the list of human carcinogens. In 1996, the Delaney Clause was repealed and the zero-risk standard changed to one of "reasonable certainty of no harm." In 2000, Congress repealed the requirement for a warning label. Saccharin is widely used, often in combination with other sweeteners. EDI of saccharin is well below ADI for average and high users (61).

Stevia. Steviol glycosides-rebaudioside A and stevioside are extracted from leaves of the plant *Stevia rebaudiana Bertoni*. In 2008, the FDA allowed GRAS status for purified rebaudioside A followed by stevioside. These purified glycosides should not be confused with whole stevia leaves, which are sold as dietary supplements under the Dietary Supplement and Health Education Act of 1994. Whole stevia leaves contain a number of active components, not all of them sweet (74). Steviol glycosides are described as having a sweet, clean taste at usual amounts but may be bitter at higher amounts (75,76). They are shelf-stable in dry form and more stable than aspartame or acesulfame K in liquid form (75).

Sucralose. Sucralose (trichlorogalactosucrose) is a disaccharide in which three chlorine molecules replace three hydroxyl groups on the sucrose molecule. It was approved by the FDA for use as a tabletop sweetener and in a number of desserts and beverages in 1998 (20) and as a general use sweetener in 1999. Most sucralose (85%) is not absorbed and is excreted unchanged in feces. Sucralose that is absorbed is excreted unchanged in urine (77). Sucralose is heat stable in cooking and baking.

NNS Approved in Other Nations, but not in the United States

Alitame, cyclamate, neohesperidine, and thaumatin are approved as NNS in other nations, but not in the United States. In 1986, a petition was submitted to the FDA to approve alitame for use as a tabletop sweetener and in baked goods, beverages, and confections. The petition was reviewed and found to be deficient. Currently, the FDA is not reviewing alitame for use as a food additive. Cyclamate was banned by the FDA as a food additive in 1969 under the Delaney Clause because one

study found that a saccharin/cyclamate mixture caused cancer in laboratory rats. In 1982, the Cancer Assessment Committee of the FDA reviewed the scientific evidence and concluded that cyclamate was not carcinogenic. This was reaffirmed by the National Academy of Sciences in 1985. It is 30 times sweeter than sucrose and is used in more than 50 countries, including Canada. Neohesperidine and thaumatin are GRAS for use as flavor ingredients, but are not approved or currently being considered for use as NNS in the United States.

ACADEMY EVIDENCE ANALYSIS LIBRARY (EAL)

This section includes the results of a systematic review of literature conducted using the Academy's evidence analysis process and information from the Academy's EAL. In this process, an expert work group identified dietetic practice related questions, performed a systematic literature review, and developed and rated a conclusion statement for each question. The workgroup used the Academy's process to answer a total of 60 questions related to the use of nutritive sweeteners and NNS; one question each on HFCS, polyols, and steviol glycosides (stevia); and multiple questions on aspartame, neotame, saccharin, and sucralose. The workgroup was unable to write a conclusion statement on 34 questions because no studies were identified that met the search criteria (Grade V=Not Assignable). All of these questions, as well as the full list of references used, may be found on the EAL Web site (www.andevidencelibrary.com). Most pre-market approval research studies on the safety of NNS are animal studies that are reviewed by the FDA before granting approval or a GRAS determination. The Academy's EAL includes only NNS that have been approved by the FDA for use in the United States. The Academy's EAL does not evaluate safety; however, it does evaluate available human subjects research documenting adverse effects for each NNS which meets EAL criteria. Articles that were reviewed for this process were published in English, described human subjects research, were peer-reviewed and published in juried journals, and met other specific inclusion criteria documented in the Search Plan and also published in the EAL.

To identify and select articles for review, the National Library of Medicine's PubMed database was searched using the terms *obesity*, *appetite*, *metabolism*, *adverse effects*, and *safety*; the term *non-nutritive sweeteners* and the names of the specific NNS; specific terms for the nutritive sweeteners, *HFCS*, *fructose*, and *sugar-sweetened beverages*; and *polyols* and *sugar alcohols*. Articles reviewed were published within the past 10 years for HFCS, 20 years for polyols, or between 2002 and 2009 for NNS. Studies must have included at least 10 subjects in each treatment group and have a dropout rate <20%. Articles described clinical trials, randomized controlled trials, reviews, or meta-analyses.

Detailed search plans, including the search criteria, a list of the articles included and articles reviewed but excluded, and reasons for exclusion are linked to each conclusion statement on the EAL Web site. Conclusion statements, based on a synthesis of the findings of all relevant studies, are assigned grades through the use of predefined criteria evaluating the quality of studies, quantity of studies and subjects, consistency of findings across studies, the magnitude of effect, and the generalizability of findings. A table defining the criteria to determine each grade level can be found at www.andevidencelibrary.com/grades.

Nutritive Sweeteners

HFCS. *What is the evidence from human subject research that consumption of HFCS is associated with obesity and metabolic and/or adverse effects in adults?*

Conclusion Statement. Four short-term randomized controlled trials (Akhaven 2007, Melanson 2007, Soenen 2008, and Stanhope 2008), two longitudinal studies (Monsivais 2007 and Streigel-Moore 2006), two cross-sectional studies (Duffy 2008 and Mackenzie 2006), and five review articles (Angelopoulos 2009, Bray 2004, Forshee 2007, Melanson 2008, and White 2009) examined the effects of HFCS compared with other nutritive sweeteners. These studies consistently found little evidence that HFCS differs uniquely from sucrose and other nutritive sweeteners in metabolic effects (ie, circulating glucose, insulin, postprandial triglycerides, leptin, and ghrelin),

subjective effects (ie, hunger, satiety, and energy intake at subsequent meals) and adverse effect such as risk of weight gain. Randomized trials dealing specifically with HFCS were of limited numbers, short duration, and of small sample size; therefore, long-term data are needed. **Grade II=Fair.**

Polyols. *What is the evidence from human subject research that consumption of polyols/sugar alcohols is associated with metabolic and/or adverse effects in adults?*

Conclusion Statement. A total of six studies met inclusion criteria. Five of these were short-term randomized controlled trials (Finney 2007, Gostner 2005, Koutsou 1996, Madsen 2006, and Storey 2007) and one was a review article (Grabitske 2009). The five randomized controlled trials studied gastrointestinal effects of polyols/sugar alcohols and consistently found that in moderate doses of up to 10 to 15 g/day, polyols/sugar alcohols are tolerated. At high doses (≥ 30 g/day), consumption of some polyols/sugar alcohols (including lactitol, isomalt, and xylitol) may result in significant increases in flatulence, borborygmus, colic, defecation frequency and loose/watery stools. The review article (Grabitske 2009) examined the use of sugar alcohols and concluded that usual intake is below levels that would result in significant gastrointestinal side effects. One study (Gostner 2005) examined the effect of polyols/sugar alcohols on total cholesterol and triglycerides, and found no significant differences between subjects consuming isomalt or sucrose. None of the other studies examined metabolic effects of sugar alcohols, including glycaemia. **Grade III=Limited.**

NNS

Aspartame. *In adults, does using foods or beverages with aspartame in an energy-restricted or ad libitum diet affect energy balance (weight)?*

Conclusion Statement. Use of aspartame and aspartame-sweetened products as part of a comprehensive weight loss or maintenance program by individuals may be associated with greater weight loss and may assist individuals with weight maintenance over time. **Grade I=Good.**

In adults, does using foods or beverages with aspartame affect appetite or food intake?

Conclusion Statement. There is good evidence that aspartame does not affect appetite or food intake. **Grade I=Good.**

In children, does using foods or beverages with aspartame affect appetite or food intake?

Conclusion Statement. Limited evidence indicates that aspartame consumption affects appetite or food intake in children. The 2009 update did not find new studies meeting the inclusion criteria for this question and the Nutritive and Nonnutritive Sweeteners workgroup (2009) concurs with the conclusion above formulated by the aspartame workgroup (2008). **Grade III=Limited.**

What is the evidence from human subjects research that aspartame consumption is associated with adverse effects in the general population?

Conclusion Statement. Aspartame consumption is not associated with adverse effects in the general population. Studies have found no evidence of a wide range of adverse effects of aspartame, including hypersensitivity reactions, elevated blood methanol or formate levels, and hematopoietic or brain cancers. Neurologic changes tested included cognitive functions, seizures, headaches, and changes in memory or mood. The 2009 update did not find new studies meeting the inclusion criteria for this question and the Nutritive and Nonnutritive Sweeteners workgroup (2009) concurs with the conclusion above formulated by the aspartame workgroup (2008). **Grade I=Good.**

What is the evidence from human subjects research that aspartame consumption is associated with adverse effects in special populations, including children?

Conclusion Statement. A limited number of human studies published in peer-reviewed journals that involved children or special adult populations were available for this question. Limited evidence from human studies suggests that aspartame consumption is not associated with detrimental effect on blood methanol, eye problems, acne, blood pressure, seizure disorder, or at-

ention deficit disorder in children. There is limited evidence from human studies for three special adult populations. In people with diabetes, aspartame consumption is not associated with elevated plasma phenylalanine and tyrosine levels, fasting glucose control, intolerance to aspartame, ophthalmologic effects, heart rhythm, or weight. In people with chronic alcoholic liver disease, portal systemic encephalopathy index was unchanged. Levodopa levels were not significantly different in individuals with Parkinson disease. The 2009 update did not find new studies meeting the inclusion criteria for this question and the Nutritive and Nonnutritive Sweeteners workgroup (2009) concurs with the conclusion above formulated by the aspartame workgroup (2008). **Grade III=Limited.**

To date, adequately powered studies have not been conducted to evaluate the effect of aspartame on preference for sweet taste in adults and children or the effect on energy balance in children.

Neotame. To date, no studies meeting the inclusion criteria were identified to evaluate 14 EAL questions related to neotame consumption and appetite, energy balance, estimated and acceptable intake, nutrient quality, and health risks and benefits.

Saccharin. *In adults, does saccharin affect food intake?*

Conclusion Statement. Saccharin does not increase food intake in adults. Modest energy savings can result if saccharin-sweetened foods replace sugar-sweetened products in a form that is also lower in energy. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade III=Limited.**

In adults, does using foods or beverages with saccharin affect appetite?

Conclusion Statement. In short-term studies, saccharin does not affect appetite in adults. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive

and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade III=Limited.**

In adults, does using foods or beverages with saccharin in a calorie-restricted or ad libitum diet affect energy balance?

Conclusion Statement. Using saccharin in either an energy-restricted or ad libitum diet will affect overall energy balance, only if the saccharin-sweetened foods are substituted for higher-energy food or beverages. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade III=Limited.**

What is the estimated saccharin consumption level and is it within ADI limits?

Conclusion Statement. Cross-sectional research conducted outside the United States, is consistent in finding that saccharin intakes for adults and children are below the ADI of 5 mg/kg body weight set by the Joint Expert Committee on Food Additives, an international scientific expert committee administered jointly by the Food and Agriculture Organization of the United Nations. Persons with diabetes and young children had the highest saccharin intakes, when expressed as milligrams per kilogram body weight. Reported intakes ranged from a mean intake of 0.3 mg/kg body weight to a 95th percentile intake of 2.7 mg/kg body weight; therefore, intake at the 95th percentile is well within the Joint Expert Committee on Food Additives ADI. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade II=Fair.**

In adults, can saccharin be used to manage diabetes and glycemic response?

Conclusion Statement. In a limited number of human studies, saccharin had no effect on changes in lipid profiles and glycemic response in adults with diabetes. The Nutritive and Nonnutritive Sweeteners workgroup

(2009) reviewed and accepted the studies identified by the NNS workgroup (2006) and found one additional article (Skokan and colleagues, 2007) meeting the inclusion criteria for the update of this question. **Grade III=Limited.**

In children with diabetes, what is the intake of saccharin, and is this within the ADI of NNS?

Conclusion Statement. In one study conducted outside the United States, children with diabetes were found to have higher intakes of NNS, including saccharin, compared with controls, which did not exceed the ADI. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade III=Limited.**

In adults, can saccharin be used to prevent and manage hyperlipidemia?

Conclusion Statement. Saccharin has no significant effect on lipid profile in short-term dietary intervention studies in adults. The evidence to determine if saccharin can be used to prevent and manage hyperlipidemia is limited. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade III=Limited.**

What is the evidence from human subjects research that saccharin consumption is associated with adverse effects in the general population?

Conclusion Statement. Limited research in human beings, from peer reviewed journals, did not find an association between adverse effects and the intake of saccharin in the general population. No data from longitudinal cohort studies were available for review. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies identified by the NNS workgroup (2006). **Grade III=Limited.**

To date, no studies were identified to evaluate the effect of saccharin intake on energy density, nutrient quality, or behavior or cognitive changes in adults or to evaluate the effects of saccharin in children other than the acceptable daily intake for children with diabetes.

Steviol Glycosides (Stevia). *In adults, is there evidence regarding the influence of stevia on metabolic outcomes and/or weight?*

Conclusion Statement. Five randomized controlled trials (Barriocanal and colleagues, 2008, Maki and colleagues, 2008, Ferri and colleagues, 2006, Gregerson and colleagues, 2004, and Hsieh and colleagues, 2003) examined the effects of stevia compared with placebo on metabolic outcomes or weight and reported minimal, if any effects on blood glucose and insulin levels, hypertension, and weight. However, the majority of trials was of small sample size and used varying doses of stevia. One trial (Barriocanal 2008) in subjects with type 1 or type 2 diabetes or without diabetes reported no significant changes from baseline in serum glucose or hemoglobin A1c levels. However, one trial (Gregerson 2004) in subjects with type 2 diabetes reported a reduced postprandial blood glucose and glucagon response after a test meal of stevia vs placebo. In subjects without diabetes, one trial (Ferri 2006) reported both glucose and insulin reductions in both the stevia and placebo groups. Two trials (Berriocanal 2008, Maki 2008) in subjects with normal/low blood pressure detected no significant changes from baseline in blood pressure from stevioside compared with controls. In subjects with Stage 1 hypertension, no anti-hypertensive effects of stevioside compared with placebo were found (Ferri 2006). A third study (Gregerson 2004) also reported no changes in blood pressure from stevioside compared with placebo. However, a 2-year trial in Chinese subjects with mild hypertension reported decreases in blood pressure from stevia compared with placebo (Hsieh 2003). Only one trial studied weight change and reported no change (Hsieh 2003). **Grade II=Fair.**

Sucralose. *In adults, does sucralose affect food intake?*

Conclusion Statement. One randomized controlled trial (Rodearmel and colleagues, 2007) examined sucralose and food intake in adults. Sucralose does not increase food intake. Modest energy savings can result if sucralose replaces sugar-sweetened products in a form that is also lower energy. This conclusion statement developed by the Nutritive and Nonnutritive Sweeteners workgroup (2009) is consistent with the previous statement on food intake in adults developed by the NNS workgroup (2006). **Grade III=Limited.**

In children, does sucralose affect food intake?

Conclusion Statement. One randomized controlled trial (Rodearmel and colleagues, 2007) examined sucralose and food intake in children. Sucralose does not increase food intake. Short-term studies suggest that modest energy savings can result if sucralose replaces sugar-sweetened products in a form that is also lower energy. Long-term studies need to assess if use of sucralose in children helps to balance energy intakes with energy expenditures. This conclusion statement developed by the Nutritive and Nonnutritive Sweeteners workgroup (2009) is consistent with the previous statement on food intake in adults developed by the NNS workgroup (2006). **Grade III=Limited.**

In adults, does using foods or beverages with sucralose affect appetite?

Conclusion Statement. One cross-sectional study with a small sample size of only women (Frank and colleagues, 2008) indicates that sucralose does not affect appetite in adults. This conclusion statement developed by the Nutritive and Nonnutritive Sweeteners workgroup (2009) is consistent with the previous statement on food intake in adults developed by the NNS workgroup (2006). **Grade III=Limited.**

In adults, does using foods or beverages with sucralose in an energy-restricted or ad libitum diet affect energy balance?

Conclusion Statement. One randomized controlled trial (Rodearmel and colleagues, 2007) examined sucralose and energy balance in adults. Using sucralose in either an energy-restricted or ad libitum diet will affect overall en-

ergy balance only if the sucralose is substituted for higher-energy food or beverages. This conclusion statement developed by the Nutritive and Nonnutritive Sweeteners workgroup (2009) is consistent with the previous statement on food intake in adults developed by the NNS workgroup (2006). **Grade III=Limited.**

In children, does using beverages with sucralose in an energy-restricted or ad libitum diet affect energy balance (weight)?

Conclusion Statement. One randomized controlled trial (Rodearmel and colleagues, 2007) examined sucralose and energy balance in children. The study, using human subjects, supports that the use of sucralose does not cause weight gain among children and adolescents. If non-energy-containing beverages, including those containing sucralose, are substituted for sugar-sweetened beverages, there is a potential for energy savings in adolescents. This conclusion statement developed by the Nutritive and Nonnutritive Sweeteners workgroup (2009) is consistent with the previous statement on food intake in adults developed by the NNS workgroup (2006). **Grade III=Limited.**

In adults, can sucralose be used to manage diabetes and glycemic response?

Conclusion Statement. Limited evidence from three controlled trials (Mezitis and colleagues, 1996; Reyna and colleagues, 2003; and Grotz and colleagues, 2003) showed little or no effects of sucralose on metabolic effects, including blood glucose in adults; however, the trials were of small size and used varying doses of sucralose for different lengths of time. Two trials (Mezitis and colleagues, 1996; and Reyna and colleagues, 2003) found no difference in measures of glycemic response when sucralose was added to diets compared with control diets. One trial (Grotz and colleagues, 2003) found decreased Hb A1c levels and fasting plasma glucose levels from baseline in adults with diabetes after consuming sucralose for 3 months. The sucralose group also had a statistically significant decrease in fasting plasma glucose from baseline compared with the control group. The 2009 update did not find

new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted these studies identified by the NNS workgroup (2006). **Grade III=Limited.**

In adults, can sucralose be used to prevent and manage hyperlipidemia?

Conclusion Statement. One study of short duration and small sample size in men (Reyna and colleagues, 2003) indicated that sucralose has no significant effect on lipid profile in adults. The evidence to determine whether sucralose can be used to prevent and manage hyperlipidemia is limited. The 2009 update did not find new studies meeting the inclusion criteria for this question; the Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the above study identified by the NNS workgroup (2006). **Grade III=Limited.**

What is the evidence from human subjects research that sucralose consumption is associated with adverse effects in the general population?

Conclusion Statement. Limited research in human beings, from peer reviewed journals, did not find an association between adverse effect and the intake of sucralose in the general population. No data from longitudinal cohort studies were available for review. The Nutritive and Nonnutritive Sweeteners workgroup (2009) reviewed and accepted the studies (Grice and Goldsmith, 2000; and Weihrauch and colleagues, 2004) identified by the NNS workgroup (2006) and found one additional article (Grotz and Munro, 2009) meeting the inclusion criteria for the update of this question. **Grade III=Limited.**

To date, no studies meeting the EAL inclusion criteria were identified to evaluate the effect of sucralose intake on energy density, nutrient quality, or behavior or cognitive changes in adult or the ADI for persons with diabetes; and no studies were identified to evaluate the effects of sucralose on appetite in children.

SWEETENER USE AND HEALTH

Both nutritive and NNS have generated health concerns among health care providers (42,78) and the public for many

years. Concerns related to safety of NNS are addressed primarily in animal studies. This EAL addresses many of the common health concerns with sweetener use in children and adults. Others, specifically sweetener use during pregnancy and effects on dental caries and hyperactivity, are addressed in this section.

Nutritive and NNS Use during Pregnancy

Pregnancy is a time of special concern because the focus is on maternal and fetal health. All FDA-approved nutritive sweeteners and NNS are approved for use by the general public, which includes pregnant and lactating women. The position of the Academy is that use of nutritive sweeteners is acceptable during pregnancy (79). Safety of food additives, including NNS, is based on studies in animals as required by the FDA approval process. Using an appropriate animal model consistent with International Conference on Harmonisation protocols allows testing with large amounts of the food additive that would not be permitted in human subjects. This testing is carried out over several generations of the animal model and includes tests on the reproductive abilities in women and men and effects on the developing fetus. Any NNS that was found to be unsafe at any stage of life would not be approved for use (19).

One study on use of NNS during pregnancy has been published after the EAL on NNS was completed. In 2010, Hall-dorsson and colleagues (80) reported an association between intakes of NNS-sweetened carbonated and noncarbonated soft drinks and preterm birth among 59,334 Danish women in the Danish National Birth Cohort. They excluded women with gestational diabetes and controlled for maternal age, body mass index, smoking status, marital status, parity, and social status. Women who consumed one or more NNS-sweetened soft drinks per day were significantly more likely to deliver preterm. The association was stronger for carbonated than for noncarbonated drinks. At the time of the study, aspartame and acesulfame-K were used most often for carbonated drinks and saccharin and cyclamates were more often used for noncarbonated drinks. The authors concluded that daily intake

of beverages containing NNS may be associated with an increased risk of preterm delivery. It is important to point out that the incidence of preterm birth was low and the increased risk was due mostly to medically induced preterm birth. This finding has not been confirmed in other studies.

Dental Caries

Dental caries are the localized destruction of dental hard tissue by acidic material from bacterial fermentation of dietary carbohydrate (81). Factors that influence the development of dental caries include microbiological shifts in the biofilm, salivary flow, buffering capacity of saliva, frequency and kind of dietary sugars consumed, length of time oral bacteria have to ferment the fermentable carbohydrate and make organic acids, tooth susceptibility, preventive behaviors such as cleaning of teeth (82), and exposure to fluoride (83). The American Academy of Pediatric Dentistry recommends reducing between-meal snacks and prolonged exposures to any food, juice, or beverage containing fermentable carbohydrate during infancy, early childhood, and adolescents (84-86). A child who consumes more than three between meal nutritive sweetener-containing snacks or beverages per day is considered at increased risk for dental caries (84).

Xylitol is considered cariostatic and anticariogenic and aids in the prevention of dental caries (87,88). Milgrom and colleagues (89) concluded that a minimum of 5 to 6 g xylitol and three exposures per day are needed for clinical effect. Studies of chewing gum containing anticariogenic polyols and caries reduction are confounded by the fact that chewing gum stimulates salivary flow and salivary flow may be as important as the polyol in controlling mouth pH and levels of *Streptococcus mutans* to prevent caries (90). The FDA regulates health claims on food labels (91). The health claim that sweeteners do not promote dental caries has been approved for sugar alcohols (91), erythritol (92), D-tagatose (93), sucralose (94), and isomaltulose (95).

Behavior Disorders

The possible negative influence of added sugars on behavior has received attention over the years. Wolraich and colleagues (96) in a meta-analysis on

the effect of sugar on behavior of children concluded that sugar does not affect the behavior or cognition of children, including hyperactive children and children who were "sugar reactors" based on parent perception and normal children. More recent reviews have also stated that sugar does not affect behavior or cognition in children with or without attention-deficit hyperactivity disorder (ADHD) (97). Research testing the relation between refined sugars and behavior has several design flaws. Modifying the diet is one complementary approach used often by parents for their child with ADHD (98). Many sugar behavior studies used a dose of sugar that was lower than what children consume on a regular basis. Levels used in previous research included 1.75 to 2 g/kg body weight or 52.5g to 60 g (13 to 15 tsp) in a 30 kg child (99-102). Wolraich and colleagues (103) found no effect on behavior of 21.3 g (5 tsp) sucrose per day in preschool children and 120 g (30 tsp) sucrose per day in school-aged children without ADHD. Children (aged 2 to 18 years) today consume, on average, 23 tsp added sugars per day (29,34) with gram intake of added sugars being 52 g for 2- to 5-year-olds, 84 g for 6- to 11-year-olds, and 90 g for 12- to 17-year-olds (30).

Several researchers have concluded (96,104,105) that parental expectations and perception are major confounders in many short- and long-term studies of the effect of sugars on behavior of children. Clinicians should use caution when restricting the diet of children who have ADHD even though many parents believe diet affects their child's behavior (104). Clinical practice guidelines regarding the treatment of children with ADHD state there is a lack of evidence that removing sugar from the diet of a child with ADHD results in fewer symptoms (106,107). The American Academy of Child and Adolescent Psychiatry does not address diet or elimination diets in treatment of children with ADHD (108). Diet-oriented treatment is not appropriate for children with behavioral problems; the goal of diet treatment is to ensure a balanced healthy diet with adequate energy and nutrients for optimal growth and normal body weight (109).

Recent work has focused on whether or not refined sugars, even if part of foods, are addictive (110-113).

This is of interest to consumers and to scientists because of the linkage to cravings, binge eating, and obesity (110). The concept of addiction means a psychological dependence and is a cognitive as well as physical condition (114). Sweet foods per se are not substances as are drugs such as alcohol. The literature is complex. It does not always focus on added sugars alone but includes all foods and is often studied within the context of binge eating behaviors (112).

To be dependent on or addicted to a substance, any three of the following seven criteria must be met at any time in 1 year: tolerance, which means more substance is needed for the same effect; withdrawal; larger amount of the substance taken or taken for a longer period than intended; a persistent desire for the substance or an inability to reduce or control its use; much time spent seeking or consuming the substance or recovering from its effects; use of the substance interferes with important activities; and use of the substance continues despite adverse consequences (110,115). Corwin and Grigson (110) proposed that foods rich in sugar can promote addictive-like behavior and neuronal changes in certain situations. These high-sugar foods may not be addictive per se but may become addictive if consumed in a restrictive/binge-like pattern. This may lead to other chronic conditions such as obesity, depression, and anxiety.

Avena and colleagues (111,116) have done much of the work in refined sugar intake and addictive behavior using animal models. Studies using animal models to determine if sugar is addictive use an excessive binge-eating method and have found that sugar may meet some of the criteria for being a substance of abuse using these animal models (116). Changes in neurotransmitters of the limbic system were similar to changes seen when addictive drugs were provided but at a much smaller magnitude. It is hypothesized that when rats are bingeing on sugar there is an increase in extracellular dopamine that, when the sugar is removed, results in the addictive responses (111). Similar changes in neurotransmitters were observed in those with bulimia ner-

vosa that may indicate an addictive relation but it is not clear if this is based on sugar intake alone (116). Functional magnetic resonance imaging trials in subjects with obesity may indicate a craving situation in response to palatable foods that may be similar to a drug craving (116). That a sugar addiction is present in human beings has not been resolved based on these animal studies. Avena and colleagues (116) are hesitant to state that these results support a sugar or food addiction in human beings and more high quality well controlled research in human beings is needed.

Health and Added Sugars Intake from Dietary Guidelines

The 2010 DGA Committee conducted an evidence analysis to answer questions that pertain to added sugars and health (2):

- *In adults, what is the association between intake of sugar-sweetened beverages and energy intake?* **Conclusion:** Limited evidence shows that intake of sugar-sweetened beverages is linked to higher energy intake in adults.
- *In adults, what is the association between intake of sugar-sweetened beverages and body weight?* **Conclusion:** A moderate body of epidemiologic evidence suggests that greater consumption of sugar-sweetened beverages is associated with increased body weight in adults. A moderate body of evidence suggests that under isocaloric controlled conditions, added sugars, including sugar-sweetened beverages, are no more likely to cause weight gain than any other source of energy (2). **Implications:** Added sugars, as found in beverages with nutritive sweeteners, are not different than other extra energy in the diet for energy intake and body weight. Reducing intake of all added sugars, including sucrose, corn sweeteners, fructose, HFCS, and other forms of added sugars, is a recommended strategy to reduce energy intake in Americans. Intake of energy beverages, including beverages sweetened with nutritive sweeteners, sweetened coffee and tea, energy drinks, and other drinks high in energy and low in nutri-

ents should be reduced in consumers needing to lower body weight.

The 2010 DGA also asked:

- *How are NNSs related to energy intake and body weight (2)?* **Conclusion:** Moderate evidence shows that using a NNS will affect energy intake only if they are substituted for higher-energy foods and beverages. A few observational studies reported that individuals who use NNS are more likely to gain weight or be heavier. This does not mean that NNS cause weight gain; rather, that they are more likely to be consumed by individuals with overweight or obesity. **Implications:** The replacement of sugar-sweetened foods and beverages with sugar-free products should theoretically reduce body weight. Yet many questions remain, as epidemiologic studies show a positive link with use of NNS and body mass index (2).

Implications for Food and Nutrition Practitioners and Consumers

Consumers have a number of choices to satisfy their innate desire for sweet taste. Sugars occur naturally in foods or may be added during processing or preparation for consumption. The body does not differentiate between naturally occurring sugars and those added to foods, but those that are added to foods are most often associated with low nutrient-dense foods. Consumers should limit these empty sources of energy to help achieve or maintain a healthy weight. Consumers who want a sweet taste without added energy can choose from seven FDA-approved NNS based on their personal taste preference and the intended use (eg, for cooking or for tabletop use). NNS, when substituted for nutritive sweeteners, may help consumers limit carbohydrate and energy intake as a strategy to manage blood glucose or weight. Registered dietitians and dietetic technicians, registered, working under the supervision of a registered dietitian, can help consumers determine the energy allowance that meets their needs based on age, sex, physical activity, and nutritional status. They can provide education and

guidance on use of nutritive sweeteners and NNS within the ADI that give the desired results in food preparation and for use at the table. Registered dietitians and dietetic technicians, registered, have an important role in providing evidence-based information about the use of nutritive sweeteners and NNS.

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