Position of the American Dietetic Association: Use of Nutritive and Nonnutritive Sweeteners

ABSTRACT
Sweeteners elicit pleasurable sensations with (nutritive) or without (nonnutritive) energy. Nutritive sweeteners (eg, sucrose, fructose) are generally recognized as safe (GRAS) by the Food and Drug Administration (FDA), yet concern exists about increasing sweetener intakes relative to optimal nutrition and health. Dietary quality suffers at intakes above 25% of total energy (the Institutes of Medicine's suggested maximal intake level). In the United States, estimated intakes of nutritive sweeteners fall below this, although one in four children (ages 9 to 18 years) can surpass this level. Polyols (sugar alcohols), GRAS-affirmed or petitions filed for GRAS, add sweetness with reduced energy and functional properties to foods/beverages and promote dental health. Five nonnutritive sweeteners with intense sweetening power have FDA approval (acesulfame-K, aspartame, neotame, saccharin, sucralose) and estimated intakes below the Acceptable Daily Intake (level that a person can safely consume everyday over a lifetime without risk). By increasing palatability of nutrient-dense foods/beverages, sweeteners can promote diet healthfulness. Scientific evidence supports neither that intakes of nutritive sweeteners *by themselves* increase the risk of obesity nor that nutritive or nonnutritive sweeteners cause behavioral disorders. However, nutritive sweeteners increase risk of dental caries. High fructose intakes may cause hypertriglyceridemia and gastrointestinal symptoms in susceptible individuals. Thus, it is the position of The American Dietetic Association that consumers can safely enjoy a range of nutritive and nonnutritive sweeteners when consumed in a diet that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary References Intakes, as well as individual health goals. Dietetics professionals should provide consumers with science-based information about sweeteners and support research on the use of sweeteners to promote eating enjoyment, optimal nutrition, and health.
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People are born liking the sensation of sweetness (1). Sweetness can be a sensory cue for energy to fuel metabolic needs and physical activity. Foods that are naturally sweet, such as fruit and breast milk, contain important nutrients to support health. Sweet foods and beverages offer a pleasurable addition to a meal or snack. Sweet-tasting compounds help mask unpleasant tastes, thereby enabling the development of more palatable foods, health care products, and medicines.

Sweet taste is stimulated by a wide variety of compounds including sugars, sugar alcohols, and dipeptides. The properties of foods and beverages affect the sweetening power of these compounds, including physical state, temperature, and the presence of other flavors. Compounds stimulate the sweet sensation by interacting with taste receptors in the mouth and throat. Through a transduction mechanism, the sweet chemical message is changed to a nerve signal for the perception of sweet taste. Models of sweet transduction are being tested under speculation that nutritive sweeteners have different mechanisms than nonnutritive sweeteners (2). Sweet taste perception and liking for sweetness varies across individuals. One source is genetic. A phenotypical marker of genetic variation in taste is the bitterness of 6-*n*-propylthiouracil (PROP) (3). Those who taste PROP as very strongly bitter also taste a range of nutritive and nonnutritive sweeteners as sweeter than those who taste PROP as weakly bitter (4). Sweet taste can be altered in conditions that influence the integrity of the taste system (5). These conditions may elevate sweet threshold (ie, lower sensitivity) but may depress perceived sweet intensity at concentrations usual to eating. The aged population can show elevated sweet thresholds (depressed sensitivity) but report the sweetness of concentrated sweeteners equal to younger cohorts (6). Even though liking for sweet taste is innate, the preferred level of sweetness varies with a number of factors, some of which include taste genetics (7), exposure during childhood (8), diabetes (9), being fed or fasted (10), and addiction (11).

The food supply offers consumers a wide range of choice in sweeteners. One distinguishing characteristic of sweeteners is the provision of energy. Nutritive sweeteners provide a sweet taste and a source of energy; nonnutritive sweeteners are sweet without energy. Because obesity rates have increased globally (12), there is great interest in dietary factors that cause energy intake to exceed energy expenditure (13). Existing evidence does not support the claim that diets high in nutritive sweeteners *by themselves* have caused an increase in obesity rates or other chronic conditions (eg, hyperlipidemia, diabetes, dental caries, behavioral disorders) (14). Nonetheless, consumers who want the taste of sweetness without added energy may select nonnutritive sweeteners to assist in the management of weight, diabetes, and other chronic diseases. Nonnutritive sweeteners also have the potential to assist in dental health and dietary quality.

Added sugars	Food Guide Pyramid (US Departments of Agriculture and Health and Human Services)[1]	Eaten separately or used as ingredients in processed or prepared foods (such as white sugar, brown sugar, raw sugar, corn syrup, corn syrup solids, high fructose corn syrup, malt syrup, maple syrup, pancake syrup, fructose sweetener, liquid fructose, honey, molasses, anhydrous dextrose, crystal dextrose.) May contain oligosaccharides.
Caloric sweeteners	Food Availability Data (Economic Research Service, USDA)[2]	Sweeteners consumed directly and as food ingredients (such as sucrose [from refined cane and beet sugars]), honey, dextrose, edible syrups, and corn sweeteners (primarily high fructose corn syrup). Contains oligosaccharides.
Sugars	Food Label, in the Nutrition Facts Panel (FDA)[3]	All monosaccharides and disaccharides (includes naturally occurring sugars as well as those added to a food or drink, such as sucrose, fructose, maltose, lactose, honey, syrup, corn syrup, high fructose corn syrup, molasses, and fruit juice concentrate). Any oligosaccharides present in these compounds are not counted.
Sugar	Food Label, in the Ingredients Statement (FDA)[3]	Indicates sucrose in ingredients statement.

[1]Reference (54).
[2]Reference (35).
[3]Reference (57).

Figure 1. Commonly used definitions to describe nutritive sweeteners in food. (Adapted with permission by the *American Journal of Clinical Nutrition*. © Am. J. Clin. Nutr. American Society for Clinical Nutrition [32].)

Scientists have responded to consumer demand by developing, researching, and producing a number of energy-reduced or nonnutritive sweeteners.

POSITION STATEMENT

It is the position of The American Dietetic Association that consumers can safely enjoy a range of nutritive and nonnutritive sweeteners when consumed in a diet that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary References Intakes, as well as individual health goals.

TYPES OF SWEETENERS

Although sweeteners can be grouped a number of different ways, the grouping "nutritive" and "nonnutritive" acknowledges a difference in the amount of energy provided. A variety of ingredients impart sweetness with an energy value that equals 4 kcal/g (Figure 1). Sugar alcohols or polyols sweeten with less energy per gram (averaging 2 kcal/g); because they are not fully absorbed from the gut, polyols are less available for energy metabolism (Table 1). Nonnutritive sweeteners offer no energy (or insignificant energy in the case of aspartame), and, because they sweeten with little volume, they can also be referred to as high-intensity sweeteners (Table 2). Both polyols and nonnutritive sweeteners can replace sugar sweeteners and are thus termed *macronutrient substitutes*, *sugar substitutes*, *sugar replacers*, or *alternative sweeteners*.

The use of nutritive and nonnutritive sweeteners is evaluated by governing bodies throughout the world; these include the Food and Drug Administration (FDA) of the United States and expert scientific committees such as the Scientific Committee on Food (SCF) of the European Commission, the Joint Expert Committee of Food Additions (JECFA) of the United Nations Food and Agricultural Organization, and the World Health Organization (WHO).

In the United States, some sweeteners are considered generally recognized as safe (GRAS) ingredients, and others are food additives as defined by the 1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act. The procedures for premarket approval and procedures for GRAS status evaluation are found in the Code of Federal Regulations (21 CFR 170) (see FDA [15] for on-line access). GRAS sweeteners have scientific consensus on their safety based on a history of use prior to 1958 or on well-known scientific information (21 CFR, parts 182 and 184). Some, but not all, GRAS substances are listed in 21 CFR 182 and 184. Manufacturers often determine that use of a substance is GRAS and sometimes will notify FDA of their conclusions. Because substances whose use is GRAS are not subject to FDA approval, manufacturers may market on the basis of their own determination, provided that such a determination is correct. To GRAS notifications, FDA's response falls in one of three categories (16): "1. The agency does not question the basis for the notifier's GRAS determination; 2. The agency concludes that the notice does not provide a sufficient basis for a GRAS determination (eg, because the notice does not include appropriate data and information or because the available data and information raise questions about the safety of the notified substance); or 3. The agency has, at the notifier's request, ceased to evaluate the GRAS notice." A summary of GRAS notices received by FDA since 1998 can be found on the Internet (17).

In the United States, the FDA must approve the safety of all food additives. The Code of Federal Regulations (21 CFR 171), revised April 1, 2002, defines food additives and outlines the procedures for evaluating the safety of these substances (see US Department of Agriculture (18) for on-line access). During review of potential sweeteners as food additives, the FDA asks these basic questions: (a) How is it made? (b) What are the properties of the sweetener in food and beverage systems (ie, product specifications)? (c) How much of the sweetener will be consumed and will certain groups be particularly susceptible to the food additive? And (d) is

Table 1. Polyols and novel sugar sweeteners

Type	kcal/g	Regulatory status	Other names	Estimated Daily Intake (EDI) or Acceptable Daily Intake (ADI)	Description
Monosaccharide polyols or novel sugars					
Sorbitol	2.6	GRAS[a]—Label must warn about a laxative effect	Same as chemical name		50%-70% as sweet as sucrose; some individuals experience a laxative effect from a load of ≥50 g.
Mannitol	1.6	Approved food additive; the label must warn about a laxative effect	Same as chemical name		50%-70% as sweet as sucrose; some individuals experience a laxative effect from a load of ≥20 g
Xylitol	2.4	Approved food additive for use in foods for special dietary uses	Same as chemical name		As sweet as sucrose; new forms have better free-flowing abilities.
Erythritol	0.2	Independent GRAS determinations; no questions from FDA	Same as chemical name	EDI mean: 1 g/p/d; 90th percentile: 4 g/p/d	60%-80% as sweet as sucrose; also acts as a flavor enhancer, formulation aid, humectant, stabilizer and thickener, sequestrant, and texturizer
D-Tagatose	1.5	Independent GRAS determinations; no questions from FDA	Same as chemical name	EDI mean: 7.5 g/p/d; 90th percentile: 15 g/p/d ADI 15 grams/60 kg adult/d	75%-92% as sweet as sucrose; sweetness synergizer; functions also as a texturizer, stabilizer, humectant, and formulation aid
Disaccharide polyols or novel sugars					
Isomalt	2	GRAS affirmation petition filed	Same as chemical name		45%-65% as sweet as sucrose; used as a bulking agent.
Lactitol	2	GRAS affirmation petition filed	Same as chemical name		30%-40% as sweet as sucrose; used as a bulking agent.
Maltitol	2.1	GRAS affirmation petition filed	Same as chemical name		90% as sweet as sucrose; used as a bulking agent.
Trehalose	4	Independent GRAS determinations; no questions from FDA	Same as chemical name	EDI mean: 34 g/p/d; 90th percentile: 68 g/p/d	45% as sweet as sucrose; functions also as a texturizer, stabilizer, and humectant
Polysaccharide polyols					
HSH	3	GRAS affirmation petition filed	Hydrogenated starch hydrolysates; maltitol syrup		25%-50% as sweet as sucrose (depending on the monosaccharide composition)

[a]GRAS=Generally recognized as safe.

Table 2. Approved nonnutritive sweeteners

Type	kcal/g	Regulatory status	Other names	Description
Saccharin	0	Approved as a sweetener for beverages and as a tabletop sweetener in foods with specific maximum amounts allowed	Sweet and Low, Sweet Twin, Sweet 'N Low Brown, Necta Sweet	200-700 times sweeter than sucrose; noncariogenic and produces no glycemic response; synergizes the sweetening power of nutritive and nonnutritive sweeteners; sweetening power is not reduced with heating
Aspartame	4[a]	Approved as a general-purpose sweetener	Nutrasweet, Equal, Sugar Twin (Blue box)	160-220 times sweeter than sucrose; noncariogenic and produces limited glycemic response
Acesulfame-K	0	Approved as a general-purpose sweetener	Sunett, Sweet & Safe, Sweet One	200 times sweeter than sucrose; noncariogenic and produces no glycemic response; synergizes the sweetening power of nutritive and nonnutritive sweeteners; sweetening power is not reduced with heating.
Sucralose	0	Approved as a general-purpose sweetener	Splenda	600 times sweeter than sucrose; noncariogenic and produces no glycemic response; sweetening power is not reduced with heating
Neotame	0	Approved as general-purpose sweetener	Not available at time of publication	8,000 times sweeter than sucrose; noncariogenic and produces no glycemic response; sweetening power is not reduced with heating

[a]This sweetener does provide energy; however, because of the intense sweetness, the amount of energy derived from it is negligible.

the sweetener safe and does it cause adverse effects to the individual or offspring, including cancer, or chronic toxicity? Figure 2 shows routine procedures for testing the safety of food additive sweeteners. For sweeteners, this testing may be augmented to address specific end points (eg, neurotoxicity testing) and effects on humans with relevant conditions (eg, testing sweetener effects on glucose homeostasis in those with diabetes). This testing establishes a safety limit of food additives or conditions of use that are expressed as the Acceptable Daily Intake (ADI)—the estimated amount (usually milligrams) per kilogram of body weight that a person can safely consume on average every day over a lifetime without risk (hereafter abbreviated as mg/kg bw/day). ADI is a conservative level: it usually reflects an amount 100 times less than the maximum level at which no observed effect occurs in animal (or very occasionally human) studies. The ADI concept is communicated by the FDA and expert scientific committees including JECFA and SCF. Use levels are set to assure that intakes are below the ADI. These bodies monitor estimated daily intakes vs ADI. If estimated daily intakes exceed the ADI, there may be limitations on use of the sweetener. A recent evaluation of nonnutritive sweeteners intake worldwide reveals that intakes of nonnutritive sweeteners are well below acceptable levels (19).

Tables 1 and 2 provide a summary of the energy and regulatory status and descriptions of approved polyols and nonnutritive sweeteners. Health professionals and consumers can see a listing of food ingredients by visiting the FDA "Everything" Added to Food in the United States (EAFUS): Food Additive Database (20); they can also view sweetener additive reports on the Internet from the JECFA (21) and the SCF (22).

Toxicity Test	Outputs
Acute toxicity (single dose)	Nature of acute effects (overdose); median lethal dose
Subacute/subchronic toxicity (28-90 d)	Nature of toxicity; target organ(s); dose-response; NOEL (no adverse effect level); maximum tolerated dose
Mutagenicity/clastogenicity	Evidence of potential genotoxocity
Chronic toxicity (long-term dietary administration, eg, 6 months to 2 years)	Nature of chronic toxicity; target organ(s); cumulative effects; dose-response characteristics; NOEL
Carcinogenicity (long-term administration at maximum tolerated dose)	Carcinogenic potential; potency
Reproductive toxicity (single/multiple dose studies during pregnancy; multigenerational studies with dietary administration prior to and during mating, gestation, and suckling)	Effects on male and female fertility; fetotoxicity; teratogenic potential; effects on lactation and postnatal development
Metabolism and pharmacokinetic studies	Degree of absorption, distribution in the body, route of metabolism and metabolites, degree and mode of elimination

Figure 2. Summary of toxicology testing for food additives, based on reference (177): Walker R. Natural versus "Artificial" Sweeteners: Regulatory Aspects. In: Corti A, ed. Low-calorie Sweeteners: Present and Future. *World Rev Nutr Diet.* 1999;85:117-124. S. Karger AG, Basel, Switzerland.

NUTRITIVE SWEETENERS

As Components of Food and Beverages

Sucrose and fructose, which are GRAS substances, are primary sugar sweeteners that occur naturally or are added to foods. However, a host of other ingredients are included in the nutritive sweetener category (Figure 1). As can be seen, nutritive sweeteners are described differently by regulatory agencies. In addition to their sensory qualities, nutritive sweeteners add functional properties to foods through their effects on physical (eg, crystallization, viscosity), microbial (eg, preservation, fermentation), and chemical (eg, caramelization, antioxidation) characteristics (23).

Sucrose is a disaccharide composed of glucose and fructose that provides 4 kcal/g (approximately 16 kcal/tsp). Commercially, sucrose comes from processing sugar cane or sugar beets. Refinement removes the yellow-brown pigments of unrefined sugar to produce the white crystal form of table sugar. Molasses is the least refined form of sucrose.

The monosaccharide fructose also provides 4 kcal/g. Fructose is a component of sucrose (50% fructose), is present in fruit (also known as fruit sugar or levulose), and is added to foods and beverages as high fructose corn syrup (HFCS; 42% to 55% fructose) or in the crystalline form. Fructose has replaced sucrose in many foods and beverages because of its sweetening power, lower cost, and functional properties that enhance flavor, color, and product stability (24). Fructose also synergizes the sweetness potential of sucrose and certain nonnutritive sweeteners (24).

Digestion and Absorption

Nutritive sweeteners are easily digestible except in the cases of rare genetic abnormalities of carbohydrate metabolism (eg, galactosemia, inherited fructose intolerance) (25). The absorption of sweeteners occurs independent of other dietary sources. The brush border surface of the small intestine contains the enzymes maltase, sucrase, trehalase, and lactase that break down maltose, sucrose, trehalose, and lactose, respectively, into their constituent monosaccharides (26). Absorption rates differ in that fructose is absorbed slower than glucose and galactose but faster than polyols (27). Fructose is better absorbed when consumed as sucrose (28) than in products where the amount of free fructose exceeds the amount of glucose (eg, honey, prunes, apples, apple juice, some HFCS, or crystalline fructose) (25).

Glucose and galactose are actively absorbed through the ATP-sodium-potassium ion pump. Fructose, however, is absorbed by either facilitated diffusion or active transport, with both transport mechanisms being saturable (29), leaving unabsorbed fructose free to travel down the intestines. Through use of hydrogen breath tests, malabsorption of fructose can be detected in 37% to 80% of otherwise healthy adults in response to a 50-g fructose load (29) and in over 70% of children to a 2-g/kg bw/day load (30) (12 oz sweetened soda or fruit drink has between 14 and 22 g fructose; 1 cup of apple juice has 14 g fructose). Malabsorption symptoms may vary among individuals who show high levels of breath hydrogen after fructose loads because of an adaptive response of the intestinal bacterial flora (29). Nonetheless, nonspecific diarrhea can result in young children with fructose intakes that exceed these loads (especially if fructose is ingested with other indigestible carbohydrates and sorbitol); this diarrhea should not occur at recommended intake levels (29).

Although some unrefined nutritive sweeteners provide minerals (eg, molasses contains calcium, iron, magnesium, and potassium), the amount per teaspoon of these minerals is practically negligible compared with the Dietary Reference Intakes (31). Thus, consumers should base their selection of nutritive sweeteners on sensory or functional properties, not on misconceptions of differences in nutrient value.

Consumption

Human metabolism does not distinguish between sugars found in a food and those added to the food; however, scientists, economists, health professionals, and the public make these distinctions. For example, a common belief is that fructose in fruit juices is different from fructose added to produce fruit drinks. Fructose is absorbed, digested, and metabolized in an identical manner no matter what the source. Misconceptions such as this have led to confusion regarding consumption patterns (32). Adding more confusion is the variety of terms used to describe "sweet" foods and ingredients (Figure 1).

Food consumption patterns are monitored in two ways: food intake (self-reported survey data) and food availability (economic estimates). Food intake data tend to underestimate whereas food availability data overestimate consumption (32).

Food intake information has been based on two nationwide monitoring surveys: the Continuing Survey of Food Intakes by Individuals (CSFII) and the National Health and Nutrition Examination Survey (NHANES). These two surveys have been combined for future US nutrition surveillance. The 1994-1996 CSFII provides several different nutritive sweetener intake measures (33) and reports average population intakes of 25 g/day of sugars and sweets as well as intakes of foods containing nutritive sweeteners (eg, 95 g/day of fruit drinks and ades; 253 g/day regular carbonated beverages; 60 g/day of citrus juice; and 27 g/day noncitrus and nectars). The median daily intake of added sugar, according to the NHANES III data, varies widely across population groups, ranging from 10 to 30 teaspoons (40 to 120 g/day) (34).

Food availability data, according to the Economic Research Service (ERS), showed a per capita daily intake of 31.1 teaspoons of added sugars (124.4 g) in 2001, which represented a decline in daily consumption from 31.9 teaspoons in 1992 (35). Corn sweeteners make up more than half of this estimated intake. Consumption of HFCS has increased 4,000%, from 1.5 pounds (dry weight equivalent) per capita yearly intakes in 1970 to 1974 to 62.7 pounds in 2000 (35). Concomitantly, estimated yearly per capita intake of dextrose corn sweeteners declined 26%, from 4.6 to 3.4 pounds, and refined cane and beet sugars decreased 35%, from 100.5 to 65.6 pounds, while glucose intakes remained virtually unchanged. The increase in consumption of this corn syrup could have implications for absorption and lipid profiles in susceptible individuals (see sections on Di-

Table 3. Distribution of individuals consuming varying levels of added sugars as a percentage of energy

Population group	Percentage of Energy as Added Sugars							
	0% to ≤5%	5% to ≤10%	10% to ≤15%	15% to ≤20%	20% to ≤25%	25% to ≤30%[a]	30% to ≤35%[a]	≥35%[a]
	← *n* →							
Children, 4-8 y	7	18	25	21	15	9	4	
Males								
9-13 y	7	14	23	19	16	10	5	5
14-18 y	6	13	18	23	20	12	8	
19-50 y	15	18	21	18	13	7	4	4
50+ y	22	23	22	15	9	5	3	2
Females								
9-13 y	6	14	20	21	17	10	6	5
14-18 y	6	13	15	21	15	13	8	10
19-50 y	13	16	19	17	13	9	5	7
50+ y	23	25	21	14	9	4	2	2

[a]Indicates individuals consuming over the 25% recommended maximal level of added sugars intake.
NOTE. Data from: National Academy of Sciences, Institute of Medicine. *Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids.* Washington, DC; 2002. Tables J1-9.

gestion and Absorption as well as Hyperlipidemias, respectively).

The ability to monitor estimated consumption of nutritive sweeteners is influenced by a number of factors. For intake data from the CSFII and NHANES, intakes are self reported and, thus, not always accurate (36-40). The USDA nutrient database is used to translate what is self reported into sweetener intake; the accuracy of this database affects the accuracy of the estimated intake. The database uses ingredient amounts rather than actual amounts measured after processing and cooking; it is unknown how these two amounts differ. For food availability, data from ERS reflect an economic estimate of the amount of nutritive sweeteners within the food supply available to every US consumer. The ERS does adjust the estimated total sweetener supply for plate waste and some other losses but not for nonfood and nonbeverage uses (41). The lack of accounting for all losses may explain the discrepancy between food availability and intake estimates of nutritive sweetener consumption. Adjustments for these nonfood uses are made in the evaluation of the nonnutritive sweeteners.

Nationwide monitoring surveys reveal currently available estimates of average intake of energy from nutritive sweeteners ranging between 15% and 21%. Using the Food Guide Pyramid definition for sweeteners (Figure 1), the 2-day average for percentage of energy from added sugars is 15.7% (11.6% for 65+-year-old men and 20% for all adolescents) (42). Krebs-Smith (43) calculated an average population intake of 15.8%±0.17% SEM added sugars with a range of 18.6%±0.17% for children and 14.8%±0.21% for adults (>20 years). Kant (44) analyzed NHANES III data (adults only) for energy-dense, nutrient-poor food intakes (defined as desserts and sweeteners including sugar, candy, syrup, and sweetened carbonated and noncarbonated beverages). Desserts accounted for 8.6% of energy and sweeteners for 9.4%. Using the ERS per capita caloric intake (approximately 2,750 calories), added sugars would account for approximately 18.1% of total calories. The mean percentage for usual daily intake of added sugar derived from the NHANES III (1988-1994) data is 21.1% of total energy.

Of particular interest is the amount of added sugars in the American diet (45,46). The highest average daily intake is during adolescence (about 20% energy) and declines as age increases (33,34). Men 19 to 50 years of age are most likely to be in the highest category of added sugar intake (>95th percentile or 55 tsp/day) (34). The distribution of added sugars as a percentage of energy varies across the population according to Tables J1-9 from the National Academy of Sciences, Institutes of Medicine (Table 3) (34). Less than 10% of adults age 50+ years consume greater than 25% of energy from added sugar, the maximal intake value established by the IOM, whereas nearly one-third of adolescent females (14 to 18 years) exceed this level. Intakes of energy from added sugars show age-related declines; as males and females age, a greater proportion are consuming 10% or less of added sugars as expressed as percentage of energy.

For the entire population using CSFII databases, sweetened soft drinks account for almost one-third of the added sugars intake (42); these drinks are sweetened primarily with HFCS. Girls ages 6 to 11 years increased intakes of these beverages by 94 g from 1977-1978 to 1994-1996, 1998 (106 to 200 g), while the increase for boys rose 105 g over the same time period (112 to 217 g) (47). Examining CSFII data by ounces of beverage consumed per day, sweetened carbonated soft drink consumption shows a steep rise across childhood with the peak at 16 years (2.1 oz for 1 to 3 year olds, 4.5 oz for 4 to 8 year olds, 9.7 oz for 9 to 13 year olds, and 18 oz for 14 to 18 year olds), while fluid milk consumption and 100% fruit juice intake declined or remained the same, respectively (48). Consumption of 100% fruit juices by American children fell within the recommendations made by the American Academy of Pediatrics (49). These guidelines are the following: no juice for infants 0 to 6 months old; from 6 to 12 months, there is no

written recommendation; from 1 to 6 years, 4 to 6 oz of juice per day; and for ages 7 to 18 years, 8 to 12 oz daily. For children ages 1 to 4 years, daily 100% fruit juice intakes exceeded intake of fruit drinks/ades (3.6 oz) but was less than milk consumption (12.6 oz). For those 14 to 18 years of age, carbonated soft drink intake exceeded consumption of fluid milk (7.8 oz) and fruit drinks/ades (5.7 oz) (49). Hypothetically, approximating consumption of the sugar sweetened drinks by the 50th percentile kilograms body weight per age (50), intake of 100% fruit juice, fruit drinks/ades, and carbonated soft drinks is estimated to be highest in children up to the age of 8 years. For example, according to average intake of these drinks (48), a 27-month-old boy who weighs 13.6 kg would consume 0.82 oz/kg, a 6-year-old boy who weighs 21 kg would consume 0.61 oz/kg, an 11-year-old boy who weighs 36 kg would consume 0.49 oz/kg, and a 16-year-old boy who weighs 61 kg would consume 0.45 oz/kg.

The CSFII data also show that non-Hispanic white and non-Hispanic black preschoolers had higher added sugars and energy intakes than Hispanic preschoolers (51). Furthermore, those low-income preschoolers enrolled in the Women, Infants and Children Nutrition Program (WIC program) consumed less added sugar than nonparticipating low-income children (51). To put these intakes in perspective, both consumption and availability data indicate that the average population intakes do not exceed the recently established Recommended Maximal Intake of 25% of energy from added sugars (34). This level was chosen because it represented the highest point of sugar intake (based on NHANES III data) before a reduction in micronutrient intake is observed.

Guidance

In the United States, the USDA, the Institute of Medicine, and the USDA in conjunction with the Department of Health and Human Services (DHHS) have made recommendations regarding use of sweeteners added to food and beverages. These are the Food Guide Pyramid, the Dietary Reference Intakes, and the Dietary Guidelines, respectively. The USDA Food Guide Pyramid statement reads as follows: "Use sugars sparingly" (52). The Institute of Medicine's Dietary Reference Intakes suggests a maximal intake of 25% of energy in the form of added sugars (34). In 2002, Dietary Guidelines released by the USDA and DHHS do not state a numerical value but state "choose a diet moderate in sugars," with the additional suggestion to eat less sugar and fewer sweets (such as candy, cookies, cakes, and soda) (53).

In describing the Food Guide Pyramid, USDA suggested intakes ranging from 6% to 10% of energy (a range of 6 to 18 teaspoons depending on the total energy intake) from added sugars (54). As described in that publication, this range was not intended as a recommendation of an optimal amount of added sugars but rather as a goal to meet nutritional needs and balance calories while not exceeding the consumption levels of added sugars reported at that time. A series of calculations were made to determine this range. Using the number of servings for each nutrient-containing food group, three levels of energy were established to meet the needs of most Americans (1,600, 2,200, and 2,800 kcal). Estimates of energy from fat (using 30% as the goal) were then calculated. Using foods representing the lowest fat level (eg, fat-free milk), an intake pattern representing the lowest number of servings from each food group resulted in energy ranges from 1,220 to 1,990 kcal. The energy difference between the estimated total energy needs and that for the food pattern developed was obtained. This amount could be used to determine additional foods to add to the diet, including foods with added sugars. Thus, the suggestion of 6% to 10% of energy from added sugars was not based on any scientific evidence regarding health impacts but was calculated using the Food Guide Pyramid.

The Dietary Reference Intakes recommendations on added sugar intake represent a synthesis of scientific evidence and analysis of data from nutrition surveillance. During the Committee's deliberations, only recommendations based on available scientific evidence (primarily derived from clinical studies) were considered. To determine a recommended intake level, the Institute analyzed the NHANES III data for various micronutrient intakes at every fifth percentile of added sugars intake as a percentage of energy (from 0% to 35%) (34). Micronutrients examined were vitamins A and E, calcium, magnesium, iron, and zinc. Additionally, determinations of the prevalence of those not meeting the Estimated Average Requirement or exceeding Adequate Intake for these micronutrients were made for gender and age groups. Although there was some age inconsistency, as intakes of added sugars increased, intakes of calcium, vitamin A, iron, and zinc declined. On the basis of this analysis, and other evidence-based information, the committee concluded that a maximal intake of 25% of energy from added sugars would ensure that dietary quality could be maintained. Any higher level could result in diets of poorer quality.

The WHO is currently in the process of designing a global strategy for making recommendations regarding diet, physical activity, and health (55). On the basis of the opinions of a joint consultation report, the WHO recommended 10% of energy from added sugars (defined as "free sugars"). The strategies used in the panel's deliberations encompass their interpretation of a range of epidemiologic, economic, social, and political impacts on the prevention and control of noncommunicable diseases. Thus, the proposed 10% intake recommendation may not be based solely on scientific evidence.

Dietetics professionals should communicate science-based messages about recommendations for added sugar intake with the understanding that all foods can fit into healthful diets, even those high in added sugars (56). For individual recommendations on intakes of added sugars, dietetics professionals should assess food intake within the context of the entire diet and by considering personal health and nutrition goals. Consumers can monitor their intake of *total* sugars (but not added sugars) through the labels on foods and beverages. The Nutrition Labeling and Education Act of 1990 (57) required the labeling of total sugars. Through public rule making, the FDA defined labeling of total sugars (ie, any monosaccharide or disaccharide) and sugar alcohols. The FDA regulates la-

beling a product as "sugar-free" (less than 0.5 g sugar), "reduced sugar" or "less sugar" (a reduction of sugar by 25%), and "no added sugar" (no sugars added during processing).

Polyols (Sugar Alcohols) and Novel Sugar Sweeteners

Foods containing polyols can be labeled as sugar-free because they replace sugar sweeteners. They also contain less energy than sugars and have other potential health benefits (eg, reduced glycemic response, decreased caries risk, prebiotic effects). Polyols can have a chemical structure that is monosaccharide-derived (eg, sorbitol, mannitol, xylitol, erythritol), disaccharide-derived (eg, isomalt, lactitol, maltitol), or polysaccharide-derived mixtures (eg, maltitol syrup, hydrogenated starch hydrolysates [HSH]). Although many polyol sweeteners occur naturally in plants, they are produced for commercial usage. *D*-tagatose and trehalose are two novel sugars that offer sweetening power and functional properties in foods and beverages, as well as potential health benefits. *D*-tagatose has a chemical structure similar to fructose, and trehalose is a disaccharide found in mushrooms. Products containing these sweeteners cannot be labeled as sugar free (58).

Polyols (sugar alcohols) and sugar-derived sweeteners are regulated as either GRAS or food additives. In nutrition labeling, declaration is required when a claim is made about sugar alcohols or sugars (ie, sugar free) when sugar alcohols are present in the food. For voluntary and required declarations on the Nutrition Facts panel, "sugar alcohols" and gram weight are listed under total carbohydrate. If only one sugar alcohol is used, the specific name may be substituted for "sugar alcohol" (eg, xylitol) (21 CFR 101.9(c)(6)(iii)). *D*-tagatose and trehalose would appear on the food label in the ingredient declaration.

The polyols offering reduced-calorie sweetening are absorbed slowly and incompletely from the intestine by passive diffusion. An excessive load (eg, greater than 50 g/day of sorbitol; greater than 20 g/day of mannitol) may cause diarrhea. If polyols were completely absorbed, direct metabolism could provide the usual 4 kcal/g. However, incomplete absorption causes indirect metabolism via fermentive degradation by the intestinal flora. The energy return from indirect metabolism is less than the direct route. The FDA allows polyols to be labeled with less energy per gram than other nutritive sweeteners (see Table 1). *D*-tagatose is a low-energy bulk sweetener; only 15% to 20% of *D*-tagatose ingested is absorbed from the small intestine to provide 1.5 kcal/g (59). The majority ingested is available for fermentation by colonic bacteria. Trehalose is absorbed completely and metabolized directly to provide 4 kcal/g.

Products with sorbitol and mannitol may have the following label because high intakes increase the risk of malabsorption: "Excess consumption may have a laxative effect." Sorbitol is on the GRAS list for use in candies, chewing gum, jams/jellies, baked goods, and frozen confections. Mannitol is permitted for use on an interim basis pending further study of health effects, including potential laxative effects. This status is provided to food ingredients that have a history of use but whose safety has been brought into question by new information, even if it is not conclusive (60). Mannitol is used as a dusting agent for chewing gum and a bulking agent in powdered foods. Xylitol is approved as a food additive for use in foods for special dietary use. The FDA has filed GRAS affirmation petitions for isomalt, lactitol, maltitol, HSH, erythritol, tagatose, and trehalose. Recent GRAS notifications for erythritol, tagatose, and trehalose report comparison between ADI and estimated intakes as reported in Table 1. Health professionals and consumers can review WHO safety evaluations on-line, including those for trehalose (61) and *D*-tagatose (62).

Glycemic responses are lower for sweeteners that undergo incomplete absorption. Although trehalose provides 4 kcal/g, it can produce a lower glycemic response than glucose or galactose (63). The potential for prebiotic effects of sweeteners that undergo incomplete absorption is being explored. The aim in this research is to use these dietary components (ie, prebiotics) to modulate the colonic microflora to promote colon health and control disease conditions (64). These prebiotics are short-chain carbohydrates that are resistant to human digestive enzymes and reach the cecum to exert effects on the colonic bacteria (65). Because of their chemical structure, polyols could serve as a substrate for these bacteria (66). The sugar *D*-Tagatose has been shown through in vitro studies to stimulate colonic bacteria fermentation and production of short-chain fatty acids (eg, butyrate) and may have the potential to have prebiotic effects (59).

NONNUTRITIVE SWEETENERS

Up to nine in 10 consumers in the United States buy or use low-calorie products, including sugar-free and reduced-fat foods and beverages (67). Nonnutritive sweeteners have also seen increased use in European countries (due to the growing interest in health and an aging population) as well as in developing countries (with interest in making limited diets more palatable) (67).

High-intensity sweeteners can offer consumers a way to enjoy the taste of sweetness with little or no energy and or glycemic response. Nonnutritive sweeteners may assist in weight management, control of blood glucose, and prevention of dental caries. Scientists evaluate these sweeteners for many attributes including sensory qualities (eg, clean sweet taste, no bitterness, odorless), safety, compatibility with other food ingredients, and stability in different food environments. Because nonnutritive sweeteners provide sweet taste with little volume, manufacturers combine the sweetener with a bulking agent (eg, polydextrose, maltodextrin, polysaccharide polyols) to replace some of the functional properties of the nutritive sweeteners. The trend is to blend high-intensity sweeteners with other nonnutritive and nutritive sweeteners to create new sweet taste profiles. Blending can cause sweetness synergy (ie, the combination is sweeter than the individual components), which can decrease the amount of sweetener needed and can improve the overall sweet taste profile.

The FDA has approved five nonnutritive sweeteners and regulates them as food additives: saccharin, aspartame, acesulfame potassium (or acesulfame K), sucralose, and most recently neotame (Table 2). Nonnutri-

tive sweeteners, like other food ingredients, appear on the food label in the ingredient declaration. Aspartame appears to receive more attention in the media about its safety than other nonnutritive sweeteners. Accordingly, more information is in the text to provide dietetics professionals with science-based information to be able to respond to consumer questions about the use of aspartame as well as other nonnutritive sweeteners.

Acesulfame-K (5,6-dimethyl-1,2,3-oxathiazine-4(3H)-one-2,2-dioxide) is approximately 200 times sweeter than sucrose. The "K" refers to potassium. Pharmacokinetic studies show that 95% of consumed sweetener is excreted unchanged in the urine (68) and thus does not provide any energy. Thus, consumption of acesulfame-K does not influence intake of potassium. Acesulfame-K can withstand high cooking/baking temperatures. Acesulfame-K is available in granular forms to blend with other nutritive and nonnutritive sweeteners, which provides sweetness synergy while masking unpleasant flavors (69).

This sweetener was evaluated for safety by JECFA in 1983 (70,71). The FDA first approved acesulfame-K in 1988, and it is currently approved as a general-purpose sweetener, not including meat and poultry (72). Both FDA and JECFA have set an ADI of up to 15 mg/kg bw/day. The European Commission's SCF reevaluated this sweetener and supported its safety but recommended an ADI at 9 mg/kg of bw/day (73). The amount of acesulfame-K added to food products is very small because of its intense sweetening power and because it is often used in combination with other sweeteners. The EDI is estimated at 20% of the ADI because of its intense sweetening power. Estimated intakes in children are below the ADI (ranges from 3 to 9 mg/kg bw/day).

Aspartame, a dipeptide (L-α-aspartyl-L-phenylalanine methyl ester), is 160 to 220 times sweeter than sucrose. Intestinal esterases hydrolyze aspartame to aspartic acid, methanol, and phenylalanine (74). These components are found in much greater amounts in the normal diet in fruits, vegetables, meat, and milk. For example, a serving of nonfat milk provides about six times more phenylalanine and 13 times more aspartic acid, whereas a serving of tomato juice has about six times more methanol than an equal volume beverage sweetened 100% with aspartame (75). The amino acids are metabolized to provide 4 kcal/g. Thus, this sweetener does provide energy; however, because of the intense sweetness of aspartame, only minute amounts need to be added, and the amount of energy derived is negligible.

In 1981, the FDA approved aspartame as a sweetener for a number of dry uses (eg, tabletop sweetener, cold breakfast cereal, gelatins and puddings) and in chewing gum. This approval was expanded in 1983 to include carbonated beverages. The Council on Scientific Affairs of The American Medical Association in 1985 concluded that "Available evidence suggests that consumption of aspartame by normal humans is safe and is not associated with serious adverse health effects" (76). In 1996, the FDA approved aspartame as a "general purpose sweetener" for use in all foods and beverages. Aspartame is also approved for use in over 100 nations.

The United States leads the world in demand for aspartame, accounting for up to 75% of sales. Although soft drinks account for above 70% of aspartame consumption, this sweetener is added to more than 6,000 foods, personal care products, and pharmaceuticals. Aspartame is available in liquid, granular, encapsulated, and powder forms to extend use in food and beverage products. Aspartame decomposes during excessive heating and loses its sweetening power. However, appropriate cooking methods can minimize losses of aspartame sweetness (77).

Detailed studies have been conducted to determine how ingestion influences plasma levels of aspartic acid, phenylalanine, and methanol (or the byproduct formate). In studies with healthy adults (78), levels of plasma aspartate concentrations or blood levels of formate did not change with a bolus load up to four times the ADI for aspartame (ie, 200 mg/kg). Plasma phenylalanine response to aspartame (as well as to other dietary sources of phenylalanine) varies in persons with phenylketonuria (PKU), a homozygous recessive inborn error of metabolism of which affected individuals cannot metabolize phenylalanine. In persons with this rare (frequency is approximately one in 10,000 whites) inborn error, excess intake of this amino acid can cause higher plasma phenylalanine levels and its adverse effects (79). MNT involves the control of dietary sources of phenylalanine, including aspartame. The FDA requires that foods that contain aspartame have the prominent display of the following label: "PHENYLKETONURICS: CONTAINS PHENYLALANINE" (80).

Untreated individuals with PKU appear to tolerate the amount of phenylalanine in a diet soda sweetened with aspartame (approximately 104 mg/12 oz) (81). Heterozygotes for PKU do not show changes in cognitive performance or in electroencephalograms after 12 weeks of consuming either 15 or 45 mg/kg bw/day of aspartame (82). In non-PKU individuals, single-bolus studies of aspartame (up to 50 mg/kg bw) or repeat dose studies show a plasma phenylalanine response near the normal postprandial range and considerably lower than that observed in PKU individuals or those with mild hyperphenylalanemia (78).

Aspartame breaks down to diketopiperazine in liquid systems with excessive heat exposure. Animal toxicity studies show that, even if all aspartame were converted to diketopiperazine in beverages, the amount would be well below the FDA-established ADI of 3,000 mg/kg bw/day for this compound (83).

Some individuals report allergic reactions to aspartame, including edema of the lips, tongue, and throat; dermatologic reactions; and respiratory problems (84). However, two double-blinded challenge studies report difficulty in recruiting individuals who claim an allergic response to aspartame and a failure to reproduce the allergic reaction in controlled experimental conditions (85,86).

The FDA increased the ADI for aspartame to its present level of 50 mg/kg bw/day when it was approved for use in carbonated beverages in 1983 (87). This ADI would approximate a 60-kg individual consuming 500 to 600 grams of sucrose per day over a lifetime based on sweetness of aspartame compared with that of sucrose (75). Postmarket assessment of

aspartame conducted between July 1991 and June 1992 shows that daily intake of aspartame is below this ADI (88): Aspartame eaters (at least 90th percentile of consumption) in the general population consume 6% of the ADI (3.0 mg/kg bw/day), those 0 to 5 years of age consume 10.4% (5.2 mg/kg bw/day), people with diabetes consume 6.6% (3.3 mg/kg bw/day), and women of childbearing age consume 8.4% (4.2 mg/kg bw/day). As a tabletop sweetener, packets contain 35 to 40 mg of aspartame and are equivalent to the sweetness of 2 teaspoons of sugar. In the granular form, 1 teaspoon contains 16 mg and equals the sweetening of 1 teaspoon of sugar. Consumers would need to contact individual companies to determine the amount of aspartame in each product. The amount in some common foods is as follows: up to 225 mg in a 12-oz diet soda, 100 mg in an 8-oz drink made from powder, 80 mg in an 8-oz yogurt or a 4-oz gelatin dessert, up to 32 mg in ¾ cup of sweetened cereal, and up to 47 mg in frozen dairy desserts. To reach the ADI, an 18-kg (nearly 40 pound) child would need to consume 900 mg of aspartame per day, which translates to 24 packets of sweetener (equivalent to 48 teaspoons of sugar), four 12-oz cans of diet soda, or nine 8-oz glasses of fruit drink made from a powder.

A comprehensive review of the safety of aspartame has recently been published (75). The review covers previous publications as well as new information that support the safety of aspartame as a food additive and negates claims of its association with a range of health problems including brain tumors. The SCF (89) has also recently evaluated new scientific evidence. They conclude that current intakes in European countries are well below the ADI set by JECFA and SCF (40 mg/kg bw/day), that aspartame is not a carcinogen and is not associated with neurobehavioral disorders, and thus that there is no need to revise the risk assessment of, or ADI for, aspartame.

Neotame is a derivative of the dipeptide phenylalanine and aspartic acid (chemical name is (*N*-[*N*-3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine-1-methyl ester) with a sweetness potency approximately 7,000 to 13,000 times sweeter than sucrose. It is partially absorbed in the small intestine, rapidly metabolized by esterases, and excreted in urine and feces. Methanol is released during the deesterfication; the amount released is insignificant even at the 90th percentile of estimated daily intake of neotame. A small percentage (<20%) of the phenylalanine from the ingested neotame may be released into the plasma. If the 90th percentile EDI of neotame were consumed for adults or children, this would result in a phenylalanine intake of 2.6 and 1.5 mg, respectively. This amount is not clinically significant for individuals with PKU (ie, estimated at 0.3% to 0.4% of phenylalanine intake per day at the 90th EDI intake of neotame). Thus, the label for products with neotame does not need to alert phenylketonurics that the produce contains phenylalanine. Furthermore, no organs were found to concentrate neotame or its metabolites. Neotame consumed at 100 times the ADI in animals did not produce neurotoxic or behavioral or reproductive toxicity effects. In human studies, there were no significant treatment effects of neotame ingestion vs those with controls (90). Neotame ingestion also did not have a significant effect on fasting plasma glucose or insulin levels in those with type 2 diabetes (91).

On the basis of a review of 113 preclinical, clinical, and special studies and an additional 32 exploratory and screening studies, the FDA approved neotame as a general-purpose sweetener on July 5, 2002 (90). These studies followed toxicology testing outlined in Figure 2, including short-term, subchronic, and chronic dietary toxicity; multigenerational reproductive and developmental toxicity; carcinogenicity; and pharmacokinetic studies in animals. Human testing included short-term and longer term studies and pharmacokinetic measures. In 2002, the FDA set the ADI at 18 mg/day (90). The EDI as a general-purpose sweetener for consumers is 0.04 mg/kg bw/day at the mean and 0.10 mg/kg bw/day at the 90th percentile for adults and 0.05 mg/kg bw/day and 0.17 mg/kg bw/day for 2- to 5-year-old infants. Globally, neotame is approved for use in multiple countries in North America, South American, Europe, Africa, Asia, and Australia (92). In June 2003, the JECFA confirmed the safety of neotame and granted an ADI of 2 mg/kg bw/day (93).

Neotame is marketed as a sweetener with a clean sweet taste without bitter, metallic, or off flavors (94), as well as an enhancer to other flavors within a food or beverage. The functionality of this sweetener has been tested for beverages; for use as a tabletop sweetener; and for frozen desserts, chewing gum, confections, baked goods, sauces, and cereals.

Saccharin exceeds the sweetness of sugar by 200 to 700 times (95). It provides no energy because it is not metabolized by humans (95) and is not cariogenic. In the United States, 8 million pounds of saccharin disappear each year into food (2 to 3 million as tabletop sweetener), beverages (1 to 2 million pounds), and personal care products (3 million pounds). The JECFA has set the ADI for saccharin to 5 mg/kg bw/day (96). Despite the decline in usage since a peak in 1982, saccharin is the largest volume, lowest cost, high-intensity sweetener used in the world (nearly 62 million pounds in 1995) (97). It is approved for use in over 100 countries and has shown increased popularity in China (98).

Saccharin is approved as a food additive to foods and beverages, tabletop sugar substitutes, and gum and can be used in cosmetics and pharmaceuticals. Based on US Federal legislation in 2001, products with saccharin no longer need to carry a warning of its use associated with causing cancer in laboratory animals. Saccharin was originally included on the GRAS listing. In 1977, the FDA proposed a ban on use of saccharin because it was reported to be a carcinogen in rats. In the same year, Congress, through the Saccharin Study and Labeling Act, imposed an 18-month moratorium on any FDA ban and required products containing saccharin to bear the following warning: "Use of this product may be hazardous to your health. This product contains saccharin which has been determined to cause cancer in laboratory animals." In 2000, the National Toxicology Program of the National Institutes of Health concluded in its Report on Carcinogens, 9th edition, that saccharin should be removed from the list of potential carcinogens

(99). The Reproductive and Cancer Hazard Assessment Section of the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency also removed sodium saccharin from its Proposition 65 list of carcinogens (100).

As a sweetener, the FDA has approved saccharin (in the ammonium saccharin, calcium saccharin, and sodium saccharin forms) as a sweetener in beverages in amounts not to exceed 12 mg/fluid ounce, as a sugar substitute packaged in amounts not to exceed the sweetening power of 1 teaspoon of sugar (20 mg) for use in cooking or at the table, and in processed foods in amounts not to exceed 30 mg per serving. The label must state saccharin in the ingredient declaration, the amount of saccharin listed per fluid ounce for beverages, milligrams in the dispensing unit for cooking or tabletop use, and milligrams per serving for processed goods (101).

Sucralose is 600 times sweeter than sucrose; it has a disaccharide structure in which three chlorine molecules replace three hydroxyl groups (chemical name *trichlorogalactosucrose*). Sucralose provides essentially no energy: it is poorly absorbed (range 11% to 27%) and excreted unchanged in the feces. Any absorbed sucralose is excreted in the urine unchanged. This sweetener is heat stable in cooking and baking. Stability testing suggests insignificant formation of compounds from sucralose degradation (4-chloro-4-deoxy-galactose and 1,6-dichloro-1,6-dideoxyfructose); these products are formed under prolonged storage at elevated temperatures and in a highly acidic environment.

Sucralose was approved in April 1998 as a tabletop sweetener and for use in a number of desserts, confections, and nonalcoholic beverages. In 1999, sucralose was approved as a general-purpose sweetener. FDA concluded from a review of more than 110 studies in human beings and animals that this sweetener did not pose carcinogenic, reproductive, or neurologic risk to human beings (102). At this time, the FDA determined that the EDI at the 90th percentile for consumers 2 years of age and older was 1.6 mg/kg bw/day. The ADI for sucralose is 5 mg/kg bw/day (103). The EDI at the 90th percentile has a sweetness that would be equivalent to the total amount of nutritive sweetener commonly added to the diet.

In a multicenter, double-blind, placebo-controlled, randomized study, sucralose at 3 times the maximum EDI for 3 months had no significant effect on glucose homeostasis in individuals with type 2 diabetes (104).

Consumers can use sucralose in granular form for measuring and pouring like table sugar and in packets in powder form. The bulking agents used in these consumer products are in such small quantity that sucralose meets the FDA labeling requirements as a "no calorie" sweetener with an insignificant energy value per serving. For example, the sweetening equivalent of 2 pounds of sugar (770 kcal) is 3.8 oz of sucralose plus the bulking agent (96 kcal). Sucralose is heat stable and thus can be the sweetening agent in desserts and baked goods.

NONNUTRITIVE SWEETENERS NOT YET APPROVED IN THE UNITED STATES

Alitame is composed of L-aspartic acid, D-alanine, and a novel C-terminal amide moiety and is 2,000 times sweeter than sucrose without the bitter or metallic qualities of high-intensity sweeteners (105). This sweetener blends with other high-intensity sweeteners to maximize the quality of sweetness. From an oral load of alitame, 7% to 22% is unchanged and excreted in the feces. The remaining amount (77% to 96%) is hydrolyzed to aspartic acid and alanine amide. The aspartic acid is metabolized normally to yield 1.4 kcal/g. The alanine amide is not hydrolyzed further and is excreted in the urine as a sulfoxide isomer, sulfone, or conjugated with glucuronic acid. There was a petition submitted to the FDA in 1986 for alitame's use as a tabletop sweetener and in a range of products including baked goods, beverages, and confections. According to a January 2003 listing, this petition is in the abeyance category: the petition was fully reviewed, found to be deficient, and, when all information requested to address deficiency is submitted, it will be refiled and assigned a new filing date (106).

A number of toxicity studies on alitame were reviewed by the JEFCA and reported in 1995 (107). The committee concluded that available studies did not indicate that alitame was carcinogenic or showed reproductive toxicity. In 1996, JECFA set an ADI for alitame at 1 mg/kg bw/day. These reports are available on-line for review (108,109). In its 59th meeting occurring in June 2002, JECFA postponed making ADI or other toxicology recommendations about alitame until findings of a 90-day tolerance study were made available. In the FDA petition, the estimated daily intake as a sole sweetener in all products is 0.34 mg/kg bw/day. The level at which no observed adverse effects occurred in animals was 100 mg/kg (105). Alitame is approved for use in food and beverages in Australia, New Zealand, Mexico, People's Republic of China, and Columbia.

Cyclamates were banned by the FDA as a food ingredient in 1969 because the saccharin/cyclamate mixture was shown to cause cancer in experimental laboratory rats (110). The primary concern was that it could be toxic to some individuals who appear to metabolize cyclamate to cyclohexylamine (111). To support a petition for use of cyclamate in 1982, the Cancer Assessment Committee of FDA reviewed the scientific evidence and concluded that cyclamate was not carcinogenic. This was reaffirmed in 1985 by the National Academy of Sciences with the conclusion that "the weight of the experimental and epidemiological evidence does not indicate that cyclamate by itself is carcinogenic" (112). The petition to reapprove cyclamate in the United States is still under review by the FDA. According to a January 2003 listing, this petition is in the abeyance category as described above. This sweetener is more than 30 times sweeter than sucrose. It is approved by the JECFA and SCF and is in use by more than 50 countries worldwide. The JECFA set an ADI for cyclamate at 11 mg/kg bw/day (113).

Neohesperidine dihydrochalcone is 1,500 times sweeter than sucrose. It offers foods and beverages a licorice flavor and can enhance the mouthfeel of beverages. In the United States, neohesperidine dihydrochalcone is GRAS as a flavor ingredient but not as a sweetener. EU countries have authorized the use of this sweetener in a range of energy-controlled

products (114). JECFA has established no ADI for this sweetener at present.

Stevia (Steveoside), derived from a South American shrub, imparts a sweet taste but cannot be marketed or sold as a sweetener in the United States. The FDA has not received sufficient scientific evidence to assure that this substance can be safely used as a food additive. JECFA evaluated steveoside in 1998 (115); no ADI was set because insufficient data and specifications were available. Stevia can be sold as a "dietary supplement" and may be available in packets that resemble tabletop sweeteners. Consumers should be informed that Stevia is not approved as a nonnutritive sweetener.

Thaumatin is a mixture of proteins with tight disulfide bonds, imparts an intensely sweet taste, and acts as a flavor enhancer. In the United States, thaumatin is GRAS as a flavor adjunct for a number of categories. A JECFA review of the biologic, toxicologic, teratogenic, allergenic, short-term testing and some studies of this sweetener in humans suggest that thaumatin is not toxic (116). JECFA set an AID of "not specified" (ie, no need for a tolerance level).

SWEETENER USE AND HEALTH

Over the years, the effects of nutritive and nonnutritive sweetener use on health have been a concern among health professionals as well as the public for a variety of reasons (13,117). One area involves the safety of sweeteners for use by children, when sweetener intakes are high relative to body weight, and pregnant women, when the goal of the diet is to support maternal and fetal health (118). Concern about sweetener intakes has shifted from diabetes in the 1960s, to hyperactivity and behavior issues in children in the 1990s, and to the etiology of obesity in the 2000s. Taken as a whole, nutritive and FDA-approved nonnutritive sweeteners are safe for children and pregnant women. There is little direct clinical evidence showing negative long-term effects of these sweeteners (both nutritive and nonnutritive) on overall health. Two noted exceptions are the impact of nutritive sweeteners on the development of dental caries and, in specific conditions, the hypertriglyceridemic effect of fructose. Support for this conclusion can be found below and in several recent reports (34,119,120).

Sweetener Use During Childhood

Because of their size and relatively high food and fluid intakes compared with adults, children will have the highest intake of nutritive and nonnutritive sweeteners as calculated by milligram intake/kg bw/day. Children can safely consume nutritive sweeteners. Nonetheless, healthy young children (6 to 18 months) can exhibit malabsorption because of incomplete digestion of fructose found naturally in fruit juices or added to fruit drinks and carbonated sodas. For example, one cup of apple juice can contain 14 g of fructose, and a 12-oz sweetened soda or fruit drink has between 14 and 22 g of fructose. This is of concern because there has been a substantial rise in intake by children of all fruit juices and drinks, as well as other sweetened beverages (48). For example, the majority of children consume some type of fruit juice by 1 year of age. In addition to the effects of fructose, an excessive load of polyols (eg, $>$50 g/day of sorbitol; $>$20 g/day of mannitol) may cause diarrhea. The same cup of apple juice contains 2.5 g sorbitol. Therefore, children exhibiting nonspecific diarrhea may benefit from a reduction in fructose and products containing polyols. It should be noted that adults vary in their abilities to absorb fructose, with some also experiencing symptoms of malabsorption with a 20- to 50-g load (25).

The estimated intakes of nonnutritive sweeteners in children are below the established acceptable daily intakes for all approved sweeteners. As a percentage of EDI to ADI, they are as low as 10.4% for aspartame to as high as 60% for acesulfame-K. It has been suggested that caregivers may want to limit intake of saccharin by young children because of the limited amount of data available for its use in children (121). The wide range of nutritive and nonnutritive sweeteners available in the food supply, as well as blending these sweeteners in food and beverage systems, should continue to keep estimated intakes of nonnutritive sweeteners in children well below the acceptable daily intakes.

Sweetener Use During Pregnancy

Use of nutritive sweeteners is acceptable during pregnancy. Recommendations for nonnutritive sweeteners use during pregnancy must be based on well-designed and approved clinical investigations to ensure healthy pregnancy outcomes. As shown in Figure 2, tests on reproductive toxicity are part of the toxicology testing required for approval of sweeteners by regulatory agencies. These toxicology tests examine effects of the nonnutritive sweetener on reproductive abilities in females and males as well as effects on the developing fetus.

Some concern has been raised about saccharin consumption during pregnancy. Saccharin can cross the placenta and may remain in fetal tissues because of slow fetal clearance (122). It is uncertain how the combined exposure in utero and in the diet may influence cancer risk. Animal studies suggest that neonatal exposure showed the strongest relationship to bladder cancer risk (100). One ecologic study in humans (123) did not find a relationship between early-life exposure to saccharin and bladder cancer but may not have followed the offspring long enough for the cancer to show (100). Although it has been suggested that women consider careful use of saccharin during pregnancy (121), this suggestion was made prior to recommendations to remove saccharin from the list of potential carcinogens (99,100).

The safety of acesulfame-K, aspartame, sucralose, and neotame in pregnancy has been determined with rat studies; the scientific community accepts rats and some other animals as appropriate models for reproductive toxicology testing that is applicable to human beings. At high doses, there was no change observed in fertility, size of litter, body weight, growth, or mortality for acesulfame-K (124), sucralose (102), or neotame (90). In the case of aspartame, further evaluation of safety in pregnancy relates to fetal exposure to aspartic acid, phenylalanine, or methanol. Amino acids normally cross the placenta to nourish the fetus. In animals, an aspartame load does not change fetal exposure to aspartic acid (125). Fetal circulation levels of phenylalanine exceed maternal levels because of concentration across the placental barrier (126). A

bolus of aspartame (34 mg/kg or the 99th percentile of estimated daily intake) results in a peak plasma level of phenylalanine in normal subjects (1.85 mg/dL) and phenylketonuric heterozygotes (2.67 mg/dL) below the level that would cause neurologic problems in the fetus (18 mg/dL) (127). Plasma response of methanol and formate were not significant after an aspartame load. Thus, if placental transport of these compounds occurs, the amount is not clinically harmful (128). Use of aspartame within the FDA guidelines appears safe for pregnant women. Thus, consumption of these sweeteners within the acceptable daily intakes appears safe during pregnancy.

In summary, the studies on the effects of nonnutritive sweeteners on reproductive abilities in females and males as well as on the developing fetus have been reviewed and these sweeteners deemed safe by numerous regulatory bodies and expert communities around the world. Thus, the consumption of acesulfame potassium, aspartame, saccharin, sucralose, and neotame within acceptable daily intakes is safe during pregnancy.

Dietary Quality and Sweetener Intake

As reported by the Institute of Medicine, many foods and beverages consumed by Americans that contain added sugars have lower micronutrient contents than foods and beverages containing naturally occurring sugars (34). Several reports have linked high intakes of *added* sugars (sweeteners) with low intakes of some micronutrients (43,45,46,129,130). As indicated previously, the Institute of Medicine did suggest a maximal level of intake of added sugars at 25% of energy, after which dietary quality might be reduced. Moreover, the Institute decided that "it is not possible to determine a defined intake level at which inadequate macronutrient intakes can exist or define an intake level at which micronutrient deficiencies can occur. Furthermore, at very low or very high intakes, unusual eating habits most likely exist that allow for other attributing factors to low micronutrient intakes" (34).

To date, no published literature exists on the relationship between nonnutritive sweetener use and dietary quality. Nonnutritive sweeteners could improve dietary quality if consumers were to use energy savings for consumption of nutrient-dense foods. This might be especially important for the aging population who need to emphasize fluid intake while balancing low energy intakes with declining energy needs because of sedentary lifestyles (131). Nonnutritive sweeteners could offer consumers choice in beverages and savings in energy that they could use on nutrient-dense foods. Nonnutritive sweeteners could also increase the palatability of fruits and vegetables that have less desirable sour or bitter qualities.

Obesity

Excess body fat (132) arises from the energy imbalance caused by taking in too much energy and expending too little energy. Recent concerns have been expressed regarding high intakes of sweetened foods and beverages and the possible association with the increasing prevalence of overweight and obesity across the population, including children (35,42-46,133,134). Of particular interest is consumption of high-sugar, low-nutrient dense foods (44,45), specifically sweetened sodas and drinks (44,45,48,134-136). Although an association can be shown between intakes of sweeteners and body weight, there is no current evidence supporting a "direct link" between increasing obesity and increasing sweetener intakes independent of energy intakes (34).

Nonetheless, there is speculation that high intakes of fructose (particularly in the form of sweetened liquids) increase energy intake and obesity risk through the blunting of circulating insulin and leptin levels (137). The blunted insulin and leptin response results in a diminished ability of the body to inhibit food intake and feelings of satiety, which might result in increased energy consumption (137). This area deserves attention in that there has been a dramatic increase in *HFCS consumption since 1970. Consumption of sucrose and fructose in the forms of sweetened beverages may also promote weight gain because liquid forms of energy may be less satiating (138,139).

Obesity is a complex problem, and its cause cannot simply be attributed to any one component of the food supply such as sweeteners. Troiano and colleagues (135) found higher intakes of energy from sweetened soft drinks among overweight than nonoverweight youths, yet they suggest that physical inactivity may be more significant to the secular increase in weight within this population. Recent analyses by the National Bureau of Economic Research identify increases in total energy because of more frequent eating of all foods (especially those during snacking) (140) and less physical activity because of technologic advances (141) as causes of higher rates of obesity. These findings would support the review by the Institute of Medicine that concluded, "the effects of increased intakes of total sugars on energy intake is mixed and the increased intake of added sugars are most often associated with increased energy intake" (34).

Nonnutritive sweeteners have the potential to promote weight loss in overweight and obese individuals. The original motivation for their development was based on the goal of providing a sweet taste without energy to persons with diabetes and those wanting to control energy intakes. Nonnutritive sweeteners have the potential to save the consumer up to 16 kcal/tsp of sweetening. Replacing intake of added sugars with nonnutritive sweeteners could result in a deficit of 380 cal/day or 1 pound of weight loss in 9 to 10 days, if intake was at 95 g (24 tsp) daily. The energy savings could be substantial for those individuals who consume higher levels of total energy from added sugars. Nonnutritive sweeteners added to the diet have been shown to promote modest loss of weight (138) and, within a multidisciplinary weight-control program, may facilitate long-term maintenance of reduction in body weight (142). Nonnutritive sweeteners can enhance the palatability of low-energy foods (143) to aid in reducing total energy intake. Further research is required to assess the role of nonnutritive sweeteners to promote weight loss in overweight and obese and weight management, particularly over the long term (144).

The prevalence of obesity has increased substantially at the same time as the consumption of nonnutritive sweeteners has increased. The question is, do these sweeteners

*HFCS was put in place of the original wording of fructose.

maintain a highly sweet food environment to increase risk of obesity through appetite, intake, and energy regulation mechanisms? Some evidence primarily from studies with animals suggests that high intakes of sweets (nutritive sweeteners alone or in mixtures with fat) promotes weight gain through changes in neuropeptide control of appetite, intake, and energy expenditure (145). The application of this research to understanding the rise in rates of obesity is speculative at this time. Additionally, most of the research associating sweet and ingestive behaviors has involved nutritive sweeteners; according to a previous review (146), nonnutritive sweeteners do not have a paradoxical effect to increase appetite and food intake. Thus, the rise in prevalence clearly relates to all factors that cause an energy imbalance. Individuals who wish to lose weight may choose to use nonnutritive sweeteners but should do so within the context of a sensible weight management program including a balanced diet and exercise.

Diabetes and Glycemic Response

It is well recognized that sweeteners do not cause diabetes. Increasing intakes of sugars are not associated with increasing risk of diabetes (147,148), with the latest affirmation from a prospective study of over 39,000 women (149). Furthermore, current evidence does not indicate that, in isocaloric amounts, the glycemic response to nutritive sweeteners differs from dietary starch (150,151). Intakes as high as 60 g fructose or sucrose per day may not adversely affect glycemic or lipid response in persons with type 2 diabetes (152). However, because there exists concern for increased blood lipid levels with high intakes of fructose (see hyperlipidemia section), addition of fructose as a sweetening agent is not recommended for people with diabetes (151). Polyols, including trehalose, produce a lower glycemic response than fructose, glucose, or sucrose, most likely because of their incomplete absorption (63). Therefore, these substances can be used safely in the diets of people with diabetes; however, because of its laxative effect, the amount of polyols consumed may need to be limited (especially in children). The nonnutritive sweeteners do not affect glycemic response and can be safely used by those with diabetes.

Given that the primary goal for medical nutrition therapy of diabetes is to maintain near-normal blood glucose levels, the American Diabetes Association suggests that attention be given to the total amount of carbohydrates in meals and snacks rather than to glycemic responses resulting from their consumption (151). Nutritive sweeteners need not necessarily be restricted, but, if consumed, they should be substituted for other carbohydrate sources rather than added. Nonnutritive sweeteners also are appropriate in medical nutrition therapy for people with diabetes and may help control energy intake. Dietetics professionals can help persons with diabetes incorporate nutritive and nonnutritive sweeteners into their individual meal plans.

Hyperlipidemias

Nutritive sweeteners containing fructose and sucrose are of primary interest related to hyperlipidemia. Diets high in these sweeteners have been shown to increase serum triacylglycerol (TAG) and low-density lipoprotein (LDL) cholesterol levels in short-term studies, particularly if the diet is low in fat (34,153), with fructose being more hyperlipidemic than sucrose. It should be emphasized that not all studies show a positive association. LDL concentrations have been shown to rise with increases in sugar intake (34). Effects on high-density lipoprotein (HDL) levels are inversely related to sugar intake (34).

Parks and Hellerstein (153) concluded that the hyperlipidemic effects are more pronounced when the carbohydrate content of a high-carbohydrate diet is from monosaccharides rather than oligo- and polysaccharides. In addition, there is considerable genetic variability in TAG responses to high-sucrose diets as well as influences by absolute amounts of other dietary components present (eg, fiber, total carbohydrates, and fat) (119). Furthermore, few studies have been conducted to evaluate the long-term effects of high-sucrose diets.

Fried and Rao (119) conclude that there is insufficient clinical data to determine the amount of sucrose or fructose that can be incorporated into recommended dietary nutrient patterns that will not raise TAG levels. Current evidence does not indicate any negative effects with consumption of a moderately low-fat (30% of energy), high-carbohydrate (sweeteners or starch) diet on fasting TAG profiles in free-living Americans.

Dental Caries

Risk of dental caries increases with intake of nutritive sweeteners; this risk, however, does not work independently of factors such as oral hygiene and fluoridation (154,155). Development of caries is multifactorial: sweetener intake along with frequency of meals and snacks, frequency of tooth brushing, fluoridation of water, direct application of fluoride, and fluoridated toothpaste play a role (156,157). Use of polyol-based gum can reduce the risk of dental caries in children, with the greatest benefit in xylitol-based gums (158). The FDA authorizes use of the health claim in food labeling that sugar alcohols and some novel sugars (xylitol, sorbitol, erythritol, tagatose, mannitol, maltitol, isomalt, lactitol, hydrogenated starch hydrolysates, hydrogenated glucose syrups, or a combination of these) do not promote tooth decay (58,159). Nonnutritive sweeteners do not promote dental caries.

Behavioral Disorders

Claims of an association between sugar and hyperactivity have not been supported, even in those children who, by report, are sensitive to sugar (160-163). During the early 1990s, theories of the effect of sweeteners and sweetener-containing foods in relation to mood were proposed (164). It was suggested that states of anxiety, frustration, depression, and general dysphoria (feeling unwell or unhappy) were seen at the same time as subjects noted increased intakes of sweeteners (and carbohydrates in general). Interestingly, any alleviation of these feelings (as stated in self reports) is followed by a more prolonged period of the original negative feelings (160). Frequently, these negative feelings are not remembered because of the high motivation of the

subjects to remove them. The subjects' wish to alleviate the negative mood is very strong, yet the effect does not last long, resulting in self-defeating behaviors. On the other hand, epidemiologic analyses have noted a relationship between sugar consumption (based on food availability data) and major depression (165). Obviously, more research is needed. Given the weak and conflicting clinical evidence, the sweeteners mood theory has yet to be validated (160,166).

More recently, interest has turned to an "addictive" effect of sweeteners (167,168). Levine and colleagues (145) reviewed animal data that suggest sucrose consumption creates neurochemical changes in several brain areas, including those involved with pleasure-seeking behaviors (eg, reward). Changes in levels of opiods and dopamine with glucose administration suggest a complex relationship between these neurochemicals in response to glucose. To date, few human studies have been conducted; therefore, any application to humans at this time is not justified.

As part of the FDA approval process, toxicology testing can examine the impact of nonnutritive sweeteners on behavior. The approved nonnutritive sweeteners did not show significant effects on behavior, especially when consumed within the acceptable daily intakes.

Attention has been paid to the association between aspartame and a range of central nervous system and behavioral conditions including headaches, seizures, cognitive impairment, and mood disorders; a recent critical review of the scientific literature refutes all such associations (75). Upon initial approval, the Centers for Disease Control (169) and the FDA (170) reviewed behavioral complaints and concluded that there was not a specific cluster of effects associated with aspartame use and that it did not present a public health hazard. Headache is the most frequent consumer report, followed by dizziness, mood changes, and nausea/vomiting, based on a 1995 FDA review of over 7,000 consumer reports (171). Most properly designed clinical studies do not show a significant difference in headache frequency between aspartame and placebo (75,172). Nonetheless, individuals who contend that aspartame associates with headaches can use the food label to assist in avoiding this nonnutritive sweetener. Controlled clinical studies also have not supported associations between aspartame and risk of seizure (75), even in those who report aspartame-related seizures in response to an acute aspartame load (50 mg/kg bw/day). An aspartame load also did not appear to exacerbate cognitive and behavioral tasks on the short term in people with attention deficit disorder (173). The alleged association between hyperactivity and aspartame has also not been scientifically supported (161). The speculation that aspartame intake is associated with greater risk of brain tumors (174) has not been supported by scientists or regulatory and government agencies (75), including the FDA (175) and the SCF (89).

IMPLICATIONS FOR DIETETICS PROFESSIONALS

Nutritive and nonnutritive sweeteners add to the pleasure of eating. Consumers can enjoy a wide range of sweeteners in a wide variety of foods and beverages. Consumers can incorporate nutritive sweeteners into a healthful eating plan and meet current guidelines for healthful diets. The range of nutritive and nonnutritive sweeteners allows choice in the type and amount of sweeteners to include in the diet. The ingredients declaration on the food label provides information to consumers on types of sweeteners contained in food and beverages, although the amount of added sugars is not listed in the Nutrition Facts panel.

Nonnutritive sweeteners are safe for use within the approved regulations. They can increase the palatability of fruits, vegetables, and whole-grain breads/cereals and thus have the potential to increase the nutrient density of the diet while promoting lower energy intakes. The trend in sweetener blending will maximize sweetening potential and support intakes of nonnutritive sweeteners well within the acceptable levels. National surveillance of intakes of nonnutritive sweeteners, and the foods and beverages to which they are added, is important to assess whether they assist consumers in meeting recommended dietary goals.

Dietetics professionals play an important role in educating the public and their colleagues about the use, safety, and health implications of both nutritive and nonnutritive sweeteners. The issue of sweeteners can be contentious with some health-related and consumer groups, who encourage the reduction or elimination of sweetened foods and beverages from the diet (especially for children). The issue of sweeteners can engender emotional feelings, which may have greater personal meaning than statistical arguments (176). Dietetics professionals must use science-based evidence when making recommendations on use of nutritive and nonnutritive sweeteners. The research to date does not support a specific level of intake of nutritive sweeteners, only a maximal amount (25%) at which dietary quality is affected. This Position Statement, supported by research evidence, affirms inclusion of nutritive and nonnutritive sweeteners *within* the context of current dietary and physical activity recommendations for the public. Dietetics professionals should empower consumers to translate these recommendations into a plan that meets personal health and dietary goals as well as to individualize recommendations based on specific health conditions.

Dietetics professionals can lead the dialogue to help consumers and others in addressing the following issues of concern:

- recognize that sweeteners can add to the pleasure of eating and that these sweeteners can assist consumers in improving the quality of the diet if selected in appropriate quantities and in forms that are high in micronutrients;
- assist consumers in reading food and beverage labels to determine appropriate personal choices about consumption of nutritive and nonnutritive sweeteners; and
- facilitate the incorporation of sweeteners within the context of the *total* diet instead of simply examining the health benefits or risks of *individual* foods or beverages (56).

In terms of recommendation for fu-

ture research needs, dietetics professionals can provide support for studies to do the following:

- evaluate the influence of nutritive and nonnutritive sweeteners on dietary quality;
- examine the impact of nutritive and nonnutritive sweeteners on satiety, energy intake, and weight management; and
- monitor intakes of fructose in relationship to health including gastrointestinal tolerance and hyperlipidemia in individuals who may present risk of these conditions.

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