

REPORT 3 OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH (A-08)
The Health Effects of High Fructose Syrup
(Resolution 407, A-07)
(Reference Committee D)

EXECUTIVE SUMMARY

Objective: To review the chemical properties and health effects of high fructose corn syrup (HFCS) in comparison to other added caloric sweeteners and to evaluate the potential impact of restricting use of fructose-containing sweeteners, including the use of warning labels on foods containing high fructose syrups.

Methods: Literature searches for articles published through December 2007 were conducted in the PubMed database and the Cochrane Database of Systematic Reviews using the search terms “high fructose corn syrup” and “high fructose syrup.” Web sites managed by federal and world health agencies, and applicable professional and advocacy organizations, were also reviewed for relevant information. Additional articles were identified by reviewing the reference lists of pertinent publications.

Results: HFCS has been increasingly added to foods since its development in the late 1960s. The most commonly used types of HFCS (HFCS-42 and HFCS-55) are similar in composition to sucrose, consisting of roughly equal amounts of fructose and glucose. The primary difference is that these monosaccharides exist free in solution in HFCS, but in disaccharide form in sucrose. The disaccharide sucrose is easily cleaved in the small intestine, so free fructose and glucose are absorbed from both sucrose and HFCS. The advantage to food manufacturers is that the free monosaccharides in HFCS provide better flavor enhancement, stability, freshness, texture, color, pourability, and consistency in foods in comparison to sucrose. Concern about HFCS developed after ecological studies, using per capita estimates of HFCS consumption, found direct correlations between HFCS and obesity. In addition, human and animal studies have found direct associations between fructose and adverse health outcomes. However, the adverse health effects of HFCS, beyond those of other caloric sweeteners, most of which contain fructose, are not well established. Consumption of added caloric sweeteners in general has increased over the last 30 years, as has total calories. Likewise, rates of obesity have risen even in countries where little HFCS is consumed. Only a few small, short-term experimental studies have compared the effects of HFCS to sucrose, and most involved some form of industry support. Epidemiological studies on HFCS and health outcomes are unavailable, beyond ecological studies, because nutrient databases do not contain information on the HFCS content of foods and have only limited data on added sugars in general.

Conclusions: Because the composition of HFCS and sucrose are so similar, particularly on absorption by the body, it appears unlikely that HFCS contributes more to obesity or other conditions than sucrose. Nevertheless, few studies have evaluated the potentially differential effect of various sweeteners, particularly as they relate to health conditions such as obesity, which develop over relatively long periods of time. Improved nutrient databases are needed to analyze food consumption in epidemiological studies, as are more strongly designed experimental studies. At the present time, there is insufficient evidence to restrict use of HFCS or other fructose-containing sweeteners in the food supply or to require the use of warning labels on products containing HFCS.

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 3- A-08

Subject: The Health Effects of High Fructose Syrup
(Resolution 407, A-07)

Presented by: Mary Anne McCaffree, MD, Chair

Referred to: Reference Committee D
(Robert T. M. Phillips, MD, PhD, Chair)

1 Resolution 407 (A-07), introduced by the International Medical Graduates Section at the 2007
2 American Medical Association (AMA) Annual Meeting and referred to the Board of Trustees, asks:

3
4 That our AMA urge the US Food and Drug Administration (FDA) and the US Department of
5 Agriculture (USDA) to require the food industry to use non-fructose sweeteners and limit the
6 use of high fructose syrups in their products; and

7
8 That our AMA urge the FDA and USDA to require the food industry to clearly label products
9 containing high fructose syrups with an indication that “this product contains high fructose
10 syrup; excessive intake of high fructose syrup may lead to obesity.”

11
12 This report reviews the chemical properties and health effects of high fructose corn syrup (HFCS) in
13 comparison to other added caloric sweeteners and evaluates the potential impact of restricting the use
14 of fructose-containing sweeteners, including the use of warning labels on foods that contain high
15 fructose syrups.

16
17 Current AMA Policy on Food and Nutrition Labeling and Poor Nutritional Value of Added Sugars

18
19 AMA Policy H-150.971 (AMA Policy Database) on food labeling and advertising states that
20 “warning statements on food labels are not appropriate for ingredients that have been established as
21 safe for the general population.” This policy further states that the FDA has not defined descriptors
22 for foods that are relatively higher in sugar than other foods because there are no established scientific
23 data indicating the level at which sugars would become harmful in an individual food.

24
25 Other AMA policies encourage restaurants and schools to limit their use of added sugars. Policy
26 H-150.945 urges restaurants to improve the nutritional quality of menu items by using less added
27 sugars and sweeteners. Policies H-150.960 and D-150.987 support the replacement of sugar-added
28 products in schools with healthier alternatives. (See Appendix for complete policy statements.)

29
30 Methods

31

Action of the AMA House of Delegates 2008 Annual Meeting: Council on Science and Public Health Report 3 Recommendations Adopted, and Remainder of Report Filed.

1 Literature searches for articles published through December 2007 were conducted in the PubMed
2 database and the Cochrane Database of Systematic Reviews using the search terms “high fructose
3 corn syrup” and “high fructose syrup.” Web sites managed by federal and world health agencies, and
4 applicable professional and advocacy organizations, were also reviewed for relevant information,
5 including the World Health Association, the USDA, and the Corn Refiners Association. Additional
6 articles were identified by reviewing the reference lists of pertinent publications.

7 8 Background

9
10 High fructose syrups (HFS) are sweeteners produced from starches such as corn, rice, tapioca, wheat,
11 potato, and cassava.^{1,2} Corn is the primary starch used to produce HFS in the United States, which
12 manufactures more HFS than any other country;² thus, HFCS is the most prevalent HFS.

13
14 HFCS is pervasive in the US food supply, found in many breakfast cereals, beverages, breads, sauces,
15 spreads, salad dressings, canned fruits, snack foods, desserts, meat and fish products, condiments,
16 dairy products, frozen dinners, soups, and other products.³ Rising rates of obesity since the early
17 1980s, shortly after HFCS was widely introduced into the US food supply, have fueled concerns
18 about its potential adverse health effects. The adverse metabolic effects of fructose have likewise
19 raised concerns about excessive amounts of fructose in the American diet.

20 21 Generally Recognized as Safe Status of HFCS

22
23 The FDA has affirmed (1983) and reaffirmed (1996)^{4,5} the generally recognized as safe (GRAS)
24 status of HFCS. There is no limitation on its use beyond good manufacturing process.⁵

25 26 Sweeteners in the Food Supply

27
28 Caloric sweeteners include sugar (sucrose), HFCS, honey, molasses, crystalline fructose, and fruit
29 juice concentrates. As described below, most caloric sweeteners contain fructose and all provide 4
30 kcal per gram. The most commonly used sweeteners are refined sugars and HFCS, which account for
31 45% and 42%, respectively, of added caloric sweeteners in the US food supply.⁶ Corn-derived
32 glucose (dextrose) and glucose syrups comprise an additional 12% of the added sweetener market,
33 with honey and edible syrups (maple syrup, molasses, etc.) comprising the remaining 1%.⁶ The per
34 capita availability of crystalline fructose and fruit juice as sweeteners is not tracked by the USDA’s
35 Economic Research Service.

36
37 Low-calorie and non-nutritive sweeteners are increasingly used in food products,⁷ although the per
38 capita use of these sweeteners is not available from the Economic Research Service. Sugar alcohols,
39 also known as polyols, are not fully absorbed from the gastrointestinal tract, and provide an average
40 of 2 kcal per gram (range: 0.2–3.0 kcal/g).^{8,9} These low-calorie sweeteners include sorbitol, mannitol,
41 xylitol, erythritol, isomalt, lactitol, maltitol, and hydrogenated starch hydrolysates.^{8,9} Tagatose and
42 trehalose are sugars that are similar to the sugar alcohols in function and provide 2 kcal and 4 kcal per
43 gram, respectively.⁸ Non-nutritive sweeteners include sucralose, neotame, aspartame, acesulfame
44 potassium, and saccharin. The non-nutritive sweeteners do not contain any calories, except for
45 aspartame, which has 4 kcal per gram. Due to their intense sweetness, very small quantities of these
46 non-nutritive sweeteners are needed, making the amount of energy actually consumed even from
47 aspartame negligible.⁸

1 Since 1966, the amount of added caloric sweeteners in the US food supply increased 27%, from 113
2 pounds per person per year to 143 pounds per person per year in 2005.⁶ Increased consumption of
3 soft drinks and fruit drinks contributed to more than half of this increase in added sugar intake.¹⁰ The
4 availability of HFCS in the food supply grew more than 100-fold since its introduction in 1967.¹⁰
5 Meanwhile, availability of sucrose (from refined cane and beet sugars) decreased 33%. HFCS, at a
6 cost of 14 cents per pound, is half the price of sugar (sucrose), which cost 30 cents per pound in 2005.
7 However, use of HFCS appears to have leveled off, after peaking in 1999 at 64 pounds per person,
8 with 59 pounds per person in 2005. This appears to be due to the increased use of non-caloric
9 sweeteners, as reflected by the increased availability of diet soft drinks and bottled water, and
10 declines in consumption of regular soft drinks.⁷ Increased corn prices in response to ethanol
11 production are expected to have little impact on the price of HFCS, raising the price of soft drinks by
12 an expected 1%.¹¹

13 14 Chemical Properties of HFCS Compared with Sugar

15
16 The term “high fructose corn syrup” implies that the syrup is primarily comprised of fructose.
17 However, the types of HFCS used in most food products are only high in fructose as compared with
18 regular corn syrup, which does not contain any fructose. Regular corn syrup is mainly used as a non-
19 sweet thickener and consists of pure glucose and glucose polymers. HFCS was developed in 1967
20 through the partial enzymatic isomerization of glucose to fructose, resulting in HFCS-42,¹⁰ which
21 contains 42% fructose, 53% glucose, and 5% higher saccharides (Table).¹² In the 1970s, HFCS-90
22 was developed (90% fructose) and combined with HFCS-42 to create HFCS-55 (55% fructose).¹²

23
24 The monosaccharide content of HFCS-42 and HFCS-55 is similar to sucrose (table sugar), which is a
25 disaccharide composed of 50% fructose and 50% glucose.¹² In contrast to sucrose, the
26 monosaccharides fructose and glucose exist free in solution in HFCS. In addition, HFCS-42 and
27 HFCS-55 have significantly higher moisture contents than sucrose (29% and 23% versus 5%,
28 respectively).

29
30 Other caloric sweeteners (with the exception of pure glucose) contain similar or even higher amounts
31 of fructose. Honey has a molecular composition similar to sucrose and HFCS,¹³ as does molasses,
32 which is the least refined form of sugar (Table).⁸ Fruit juices also contain similar amounts of
33 fructose, although the exact composition varies by type. For example, orange and grape juices have
34 equal amounts of fructose and glucose, while apple juice has about twice as much fructose as glucose
35 (Table).^{3,14} Crystalline fructose, which can be made from HFCS as well as from sucrose, contains
36 98% to 100% fructose.^{1,4} Crystalline fructose is the sweetest monosaccharide, with a sweetness of
37 173 relative to crystalline sucrose, which as the standard has a reference value of 100 (glucose has a
38 relative sweetness score of 74).¹²

39
40 The different types of HFCS have distinct uses in food production. HFCS-55 was formulated to have
41 the same level of sweetness as sucrose and is used primarily in carbonated soft drinks, other
42 sweetened beverages, ice cream, and frozen desserts.¹² HFCS-42 has less fructose than sucrose and is
43 therefore slightly less sweet. HFCS-42 is used in baked goods, canned fruits, condiments, dairy
44 products, and other products.^{3,12} HFCS-90 is used to produce HFCS-55, as well as in “light” foods,
45 where only a small amount is needed due to its more intense sweetness.

46
47 HFCS has several advantages over sucrose in food manufacturing:

- 1 • Enhances other flavors because its sweetness is detected quickly and early by the taste buds,
2 but does not linger, resulting in a clearer and crisper perception of other flavors.
- 3 • Maintains freshness and prolongs shelf life through improved moisture control and less
4 microbial spoilage, resulting in firmer canned fruits and less freezer burn in frozen fruits.
- 5 • Maintains the soft texture of baked goods by retaining moisture and resisting crystallization.
- 6 • Provides better browning and flavor in baked goods, and better color retention in products
7 such as ketchup and strawberry preserves.
- 8 • Maintains its structural stability over a range of temperatures and acidity levels.
- 9 • Maintains the pourability of frozen products due to its lower freezing point.
- 10 • Increases fermentability, which makes it more economical in producing breads.^{3,4}

11
12 Many of the above noted advantages of HFCS are due to the colligative properties of the free fructose
13 and glucose molecules, which depend on the concentration of the solute, not on their identity.¹ For
14 example, the smaller monosaccharides generate higher osmotic pressures and lower freezing points
15 than the disaccharide sucrose. Likewise, free fructose and glucose in HFCS are “reducing sugars,”
16 while sucrose is non-reducing; this provides better browning of baked goods and better retention of
17 red colors.¹ The properties of free fructose are particularly significant in enhancing the versatility of
18 HFCS, such as its greater ability to adsorb and retain moisture compared with sucrose.¹

19
20 In products sweetened with sucrose, the covalent bond between the fructose and glucose molecules
21 breaks down in low acid environments, such as those found in soft drinks, as well as at high
22 temperatures, such as during storage in hot climates.^{1,15} A recent study reported that the sucrose
23 content of a cola beverage decreased from 36% of total sugars to only 10% of sugars three months
24 after manufacture, and the free fructose content increased from 32% to 44% of total sugars.¹⁵ This
25 creates variability in the taste profile of the product. In contrast, HFCS maintains its structural
26 stability over a range of temperatures and acidic conditions.¹

27 28 Fructose and Glucose in the Body

29
30 Since the hydrolysis of sucrose under low pH or high temperatures results in free fructose and
31 glucose, as found in HFCS, beverages containing either sweetener should be absorbed similarly by
32 the body. Even if sucrose is not hydrolyzed before consumption, the covalent bond between the
33 fructose and glucose molecules in sucrose is easily cleaved by the enzyme sucrase in the brush-border
34 cells of the small intestine.^{10,12,16} Thus, the body is absorbing free fructose and glucose molecules
35 regardless of whether they originated as part of HFCS or sucrose. The only difference is the greater
36 osmotic pressure generated by the smaller monosaccharides compared with the disaccharide sucrose,
37 which affects the amount of fluid secreted in the stomach.^{16,17}

38
39 Many of the concerns about HFCS are, in fact, concerns about the role of fructose in appetite and
40 metabolism. Fructose is more quickly emptied from the stomach compared with other sugars, and is
41 absorbed in the intestines more slowly and less completely than glucose.^{18,19} Unlike glucose, fructose
42 intake does not stimulate insulin secretion, which is likely due to the lack of fructose transporters
43 (Glut-5) in the β cells of the pancreas.^{10,20} Insulin is believed to directly and indirectly (though effects
44 on leptin secretion) inhibit food intake.¹⁰ The brain and central nervous system also lack Glut-5
45 transporters, further inhibiting the ability of fructose to provide satiety signals.^{10,20} In addition,
46 fructose can more easily be incorporated into phospholipids and triacylglycerols than glucose, as
47 fructose metabolism bypasses the key rate limiting step in the liver that slows glucose metabolism.²⁰

1 Thus, consumption of excess amounts of fructose, but not the same amount of glucose, have been
2 found to significantly increase rates of lipogenesis.²⁰ In addition, fructose consumption does not
3 increase leptin or decrease ghrelin levels, in contrast to the hormonal response after glucose
4 ingestion.²¹ (Leptin generally inhibits food intake and increases energy expenditure,²⁰ while ghrelin
5 appears to increase hunger and appetite.²¹)
6

7 The chemical-reducing properties of free fructose allow it to form stable complexes with iron that
8 promote both iron and zinc absorption.²² Fructose and sucrose both reduce the bioavailability of
9 copper in animals at high intakes, but not in humans at intakes of 20% of total energy,²² which is
10 higher than most people consume.^{10,23} Because HFCS contains free fructose, it is possible that HFCS
11 could affect the balance of certain minerals in the body. HFCS and sucrose did not affect the balance
12 of iron, magnesium, calcium, and zinc over 2 weeks in one study that examined this issue,²⁴ although
13 another study found HFCS-sweetened beverages to adversely affect magnesium, calcium, and
14 phosphorous homeostasis over 6 weeks.²⁵
15

16 Fructose and Adverse Health Outcomes

17

18 Human and animal studies have found direct associations between high intakes of fructose and
19 adverse health outcomes, including obesity and the metabolic syndrome. In most animal models,
20 diets high in fructose increase total energy intake, insulin resistance, weight gain, dyslipidemia, and
21 hypertension.^{20,26} In humans, fructose has been associated with increased total energy intake, body
22 weight, hepatic and adipose tissue insulin resistance, and dyslipidemia.^{20,26} Individuals with diabetes
23 and hyperinsulinemia may be particularly sensitive to these adverse effects of excessive fructose
24 intake.²⁷ However, fructose in both sucrose and HFCS appears equally detrimental, although the
25 adverse effects appear limited to high intakes and not to the small amount of naturally occurring
26 fructose in fruits and vegetables (approximately 15 g/d; for comparison, a 12 oz serving of a soft
27 drink may contain 25 g of fructose,²⁶ and average fructose intakes are about 97 g/d).²⁰
28

29 More immediate adverse consequences of excessive fructose intake include diarrhea, flatulence,
30 borborygmus, abdominal distention, and abdominal pain.^{18,19} More than half of healthy individuals
31 report symptoms of gastrointestinal distress after consuming 25 g or more of crystalline (pure)
32 fructose.¹⁸ However, when fructose is consumed with glucose, as it is usually found in citrus juices,
33 sucrose, and HFCS, absorption of fructose is improved and malabsorption and its associated
34 symptoms are less likely to occur.^{18,19} In addition, frequent consumers of fructose may have greater
35 tolerance or threshold for these potential side effects.¹⁸
36

37 Calorically Sweetened Beverages and Adverse Health Outcomes

38

39 Calorically sweetened beverages are a significant source of HFCS in the American diet.¹⁰ They have
40 been associated with overconsumption of calories and with weight gain in animals and humans,¹⁰ as
41 well as with other adverse health outcomes. The body does not appear to compensate for extra
42 calories from beverages as well as those from soups or solid foods.^{10,28} A recent review and meta-
43 analysis found that soft drinks, whether sweetened with HFCS or sucrose, were strongly and
44 consistently associated with higher total calorie consumption in cross-sectional, longitudinal, and
45 long-term experimental studies, with the strongest associations seen in the experimental studies.²⁸
46 Several studies have found higher energy intakes than could be explained by consumption of the soft
47 drinks alone, suggesting that soft drinks may reduce feelings of satiety, increase hunger, or acclimate
48 individuals to prefer sweeter and generally more calorie-dense foods.²⁸ In addition, soft drink

1 consumption has been positively associated with body mass index (BMI), particularly in experimental
2 studies.²⁸ A much smaller body of literature reports soft drink consumption to be inversely associated
3 with consumption of milk, calcium, fruit, and dietary fiber, and with overall dietary quality, and
4 directly associated with dental caries, kidney stones, diabetes, and systolic and diastolic blood
5 pressure.²⁸ In general, industry-funded studies reported significantly smaller effect sizes, particularly
6 those examining the relationship between soft drinks and energy intake.²⁸

7 8 HFCS and Obesity 9

10 At present, insufficient evidence exists that HFCS consumption has contributed to obesity more than
11 sucrose, increased consumption of total calories (from any source), or decreased physical activity.¹²
12 Recent studies have not found statistically significant differences between HFCS and sucrose on total
13 energy intake, macronutrient intake, taste, hunger, thirst, overall satiety, or concentrations of insulin,
14 glucose, glucagon-like peptide 1 (GLP-1), uric acid, leptin, and/or ghrelin.^{15,16,29,30} Both beverages
15 sweetened with HFCS and those sweetened with sucrose contribute to the overconsumption of
16 calories at meals served 50 to 120 minutes later compared with a diet beverage or no beverage.^{15,16} In
17 addition, men and women may respond to the sweeteners differently, as one study found that men
18 experienced significantly less hunger after consuming HFCS than sucrose, while women experienced
19 less hunger after consuming sucrose-sweetened beverages.¹⁶ However, another study found increased
20 hunger in women the day after consuming 30% of calories from sucrose as compared with HFCS.²⁹

21
22 Unfortunately, these small experimental studies examined only the short-term effects of sucrose and
23 HFCS and may have been underpowered. At least two of the studies (which provided details on their
24 statistical power) were only powered to detect 120 to 150 kcal differences in response,^{15,30} even
25 though smaller differences in energy intake may contribute long-term to obesity or other health
26 outcomes. In one study, the authors expressed concern about their lack of statistical power to detect a
27 difference between sucrose and HFCS and repeated the experiment comparing sucrose to solutions of
28 free glucose and free fructose, but not to HFCS.³⁰ However, this second experiment was only
29 powered to detect a 120 kcal difference in response between 20% glucose:80% fructose and 80%
30 glucose:20% fructose solutions, not to detect differences between the more similarly composed
31 sucrose and HFCS beverages.³⁰ In fact, intake was 192 kcal greater at the test meal after consumption
32 of the 50:50 solution of free glucose/free fructose compared with the sucrose solution, but this
33 difference was not statistically significant.³⁰ Moreover, all four of these recent studies received
34 financial support from the sweetener industry or involved investigators who have consulted with the
35 sweetener industry.

36
37 It has been hypothesized that the extra 5% fructose in HFCS-55 compared to sucrose has acclimated
38 individuals to a sweeter diet,¹⁰ although the sweetness intensity of HFCS-55 is similar to that of
39 sucrose.^{3,12} Food use data show that between 1909 and 1997, there was an 86% increase in per capita
40 use of added caloric sweeteners in the United States,²³ with added caloric sweeteners now comprising
41 about 16% of total calories,¹⁰ and HFCS comprising 7% to 10% of total calories.^{10,23} Among the 20%
42 of Americans consuming the most HFCS (conservatively estimated at 11% of total calories), half of
43 their carbohydrate intake comes from caloric sweeteners.¹⁰ The affordability and versatility of HFCS
44 compared to sucrose may have contributed to the sweetening of the American diet. However, the
45 replacement of some sucrose with HFCS has not altered the ratio of fructose to glucose in the food
46 supply. In 1966, before the use of HFCS, the ratio of fructose to glucose was 0.78, compared with
47 0.79 in 2002.¹²

1 Epidemiologic studies have yet to directly measure total HFCS intake in individuals, because food
2 databases do not contain data on the HFCS content of foods. The increase in HFCS in the food
3 supply has been highly correlated with the increased prevalence of obesity and type 2 diabetes, but
4 because there are no individual-level data on HFCS consumption,²³ only ecological associations are
5 available for consideration. It is possible that other aspects of diet and physical activity that occurred
6 simultaneously with increases in HFCS consumption may play a larger role in the rising rates of
7 obesity and diabetes seen in recent years. For example, calorie intake increased by 523 kcal/d
8 between 1970 and 2003.³¹ Additionally, obesity rates are rising even in those countries where trade
9 barriers have limited the use of HFCS.³²

10 Guidelines on Caloric Sweeteners

11 Dietary guidelines generally recommend limiting intake of added caloric sweeteners of any type. In
12 order to meet required nutrient needs and limit weight gain, sample diets in the Dietary Guidelines for
13 Americans recommend limiting discretionary calories, including those from added sugar, to no more
14 than 32 g (8 tsp or 128 kcal) per day on a 2,000 calorie diet, which is less than that found in most
15 calorically sweetened soft drinks.³³ While the sample diets are just suggestions, current average
16 intakes, estimated at 318 kcal/d, far exceed these limits.¹⁰ Additionally, an Expert Consultation for
17 the World Health Organization and the Food and Agriculture Organization of the United Nations
18 recommended limiting intake of “free sugars” to < 10% of total calories to improve overall diet
19 quality and prevent overweight and dental caries. In this recommendation, “free sugars” includes all
20 monosaccharides and disaccharides added to foods by manufacturers, food preparers, and consumers,
21 as well as sugars naturally found in honey, syrups, and fruit juices.³⁴

22 Potential Impact of Limiting Fructose-containing Sweeteners

23 Regarding the first resolve of Resolution 407 (A-07), a ban on the use of fructose-containing
24 sweeteners would include not just pure fructose and high fructose syrups, but also naturally occurring
25 sweeteners such as honey, cane and beet sugars, and fruit juices. Regulation to limit the use of HFS,
26 including HFCS, will likely result in the replacement of HFS with sucrose and other caloric
27 sweeteners in food products, not in a reduction in the use of added sugars by food manufacturers.
28 This replacement would not change the calorie content of sweetened foods and beverages, and would
29 likely not change the ratio of fructose to glucose in the food supply.

30 Regarding the second resolve of Resolution 407, HFCS is generally recognized as safe (GRAS) by
31 the FDA; thus, in accordance with AMA policy (H-150.971), warning labels on products containing
32 HFCS would be unwarranted. At the present time, there is insufficient evidence that HFCS is more
33 likely to contribute to adverse health outcomes than sucrose or any other caloric sweetener. The
34 GRAS status of HFCS is unlikely to be revoked unless such evidence is found.

35 Areas Requiring Further Research or Attention

36 More information is needed to clarify the impact of HFCS and other sweeteners on health. While a
37 few studies have examined the metabolism of HFCS compared to sucrose, more research is needed on
38 the long-term effects of high consumption of these sweeteners to confirm their similarities. In
39 addition, research is needed on the possible effects of different sweeteners in various subpopulations,
40 including overweight and obese individuals, or those at risk of obesity due to family history or other
41 conditions.¹² It is important that the research be free of potential bias, as most previous studies were

1 conducted by researchers who had received funds from the sweetener industry. While this does not
2 necessarily bias the results, the bias found in the soft drink studies discussed above suggests the need
3 for more independent research.

4 Information on HFCS should be added to the USDA food composition and nutrient databases to
5 allow for epidemiological research on intakes of HFCS in individuals and its relationship with health
6 outcomes.¹² While the USDA has constructed a database containing the added sugar content of
7 selected foods,³⁵ it does not distinguish between types of added sweeteners. There is currently no
8 analytical method for differentiating between naturally occurring sugars of any type and added
9 sugars^{12,35}; thus, the values in the database were calculated by the USDA from the ingredients listed
10 on product labels.³⁵ Improved databases on the amount of added sweeteners in all foods are still
11 needed.

12 13 Summary and Conclusion

14
15 HFCS is a common food ingredient in the United States. The most commonly used types of HFCS
16 (HFCS-42 and HFCS-55) are similar in composition to sucrose, consisting of roughly equal amounts
17 of fructose and glucose. The primary difference between HFCS and sucrose is that these
18 monosaccharides exist free in solution in HFCS, but in disaccharide form in sucrose. The free
19 monosaccharides in HFCS provide better flavor enhancement, stability, freshness, texture, color,
20 pourability, and consistency to foods in comparison with sucrose. As use of HFCS increased over the
21 last 30 years, so did rates of obesity and diabetes. Human and animal studies have found direct
22 associations between fructose and adverse health outcomes, including obesity. However, the adverse
23 health effects of HFCS, beyond those of other caloric sweeteners, most of which contain fructose, are
24 not well established. Consumption of added caloric sweeteners in general increased over the same
25 period, as did total calories. Likewise, rates of obesity have risen even in countries where little HFCS
26 is consumed.

27
28 The literature on HFCS consists mostly of ecological or small, short-term experimental studies, many
29 of which have been industry-supported. Because the composition of HFCS and sucrose are so
30 similar, particularly on absorption by the body, it appears unlikely that HFCS contributes more to
31 obesity or other conditions than sucrose. Nevertheless, it is difficult to thoroughly examine the
32 potentially differential effect of various sweeteners, particularly as they relate to health conditions
33 such as obesity, which develop over relatively long periods of time. Improved nutrient databases are
34 needed to analyze food consumption in epidemiological studies, as are more strongly designed
35 experimental studies. At the present time, there is insufficient evidence to restrict use of HFCS or
36 other fructose-containing sweeteners in the food supply or to require the use of warning labels on
37 products containing HFCS.

38 39 RECOMMENDATIONS

40
41 The Council on Science and Public Health recommends that the following statements be adopted in
42 lieu of Resolution 407 (A-07) and the remainder of this report be filed:

- 43
44 1. That our American Medical Association (AMA) recognize that at the present time,
45 insufficient evidence exists to specifically restrict use of high fructose corn syrup (HFCS)
46 or other fructose-containing sweeteners in the food supply or to require the use of
47 warning labels on products containing HFCS. (Directive to Take Action)

- 1 2. That our AMA encourage independent research (including epidemiological studies) on
2 the health effects of HFCS and other sweeteners, and evaluation of the mechanism of
3 action and relationship between fructose dose and response. (Directive to Take Action)
4
- 5 3. That our AMA, in concert with the Dietary Guidelines for Americans, recommend that
6 consumers limit the amount of added caloric sweeteners in their diet. (Directive to Take
7 Action)

Fiscal Note: \$500

References

1. Hanover LM, White JS. Manufacturing, composition, and applications of fructose. *Am J Clin Nutr.* 1993;58:724S-732S.
2. Vuilleumier S. Worldwide production of high-fructose syrup and crystalline fructose. *Am J Clin Nutr.* 1993;58:733S-736S.
3. Corn Refiners Association. Questions and answers about high fructose corn syrup. Available at: <http://www.corn.org/HFCSBrochure.pdf> . Accessed 02/29/08.
4. Fructose Information Center. Facts about fructose. Available at: <http://www.fructose.org/facts.asp>. Accessed 02/29/08.
5. Food and Drug Administration. High fructose corn syrup. Code of Federal Regulations. Washington, DC; US Government Printing Office. *Federal Register.* 1996; 61(165): 43447-43450 (21CFR184.1866).
6. U.S. Department of Agriculture, Economic Research Service. US per capita caloric sweeteners estimated deliveries for domestic food and beverage use by calendar year: 1966-2006. Table 50. Available at: <http://www.ers.usda.gov/Briefing/Sugar/Data.htm>. Accessed 02/29/08.
7. U.S. Department of Agriculture, Economic Research Service. High-fructose corn syrup usage may be leveling off. *Amber Waves.* 2008; 6(1):4.
8. Position of the American Dietetic Association: use of nutritive and nonnutritive sweeteners. *J Am Diet Assoc.* 2004;104:255-275.
9. Kroger M, Meister K, Kava R. Low-calorie sweeteners and other sugar substitutes: a review of the safety issues. *Compr Rev Food Science Food Safety.* 2006;5:35-47.
10. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *Am J Clin Nutr.* 2004;79:537-543.
11. Leibtag, Ephraim. Corn prices near record high, but what about food costs? *Amber Waves.* 2008; 6(1):10-15.
12. Forshee RA, Storey ML, Allison DB, et al. A critical examination of the evidence relating high fructose corn syrup and weight gain. *Crit Rev Food Sci Nutr.* 2007;47:561-582.
13. Hein GL, Storey ML, White JS, Lineback DR. Highs and lows of high fructose corn syrup: a report from the Center for Food and Nutrition Policy and its Ceres Workshop. *Nutr Today.* 2005;40:253-256.
14. U.S. Department of Agriculture, Agricultural Research Service. 2007. USDA National Nutrient Database for Standard Reference, Release 20. Available at: <http://www.ars.usda.gov/nutrientdata>. Accessed 02/29/08.
15. Monsivais P, Perrigue MM, Drewnowski A. Sugars and satiety: does the type of sweetener make a difference? *Am J Clin Nutr.* 2007;86:116-123.

16. Soenen S, Westerterp-Plantenga MS. No differences in satiety or energy intake after high-fructose corn syrup, sucrose, or milk preloads. *Am J Clin Nutr.* 2007;86:1586-1594.
17. Bray GA, Nielsen SJ, Popkin BM. Reply to MF Jacobson. *Am J Clin Nutr.* 2004;80:1081-1082.
18. Beyer PL, Caviar EM, McCallum RW. Fructose intake at current levels in the United States may cause gastrointestinal distress in normal adults. *J Am Diet Assoc.* 2005;105:1559-1566.
19. Riby JE, Fujisawa T, Kretchmer N. Fructose absorption. *Am J Clin Nutr.* 1993;58:748S-753S.
20. Elliott SS, Keim NL, Stern JS, Teff K, Havel PJ. Fructose, weight gain, and the insulin resistance syndrome. *Am J Clin Nutr.* 2002;76:911-922.
21. Wylie-Rosett J, Segal-Isaacson CJ, Segal-Isaacson A. Carbohydrates and increases in obesity: does the type of carbohydrate make a difference? *Obes Res.* 2004;12(Suppl 2):124S-129S.
22. O'Dell BL. Fructose and mineral metabolism. *Am J Clin Nutr.* 1993;58:771S-778S.
23. Gross LS, Li L, Ford ES, Liu S. Increased consumption of refined carbohydrates and the epidemic of type 2 diabetes in the United States: an ecologic assessment. *Am J Clin Nutr.* 2004;79:774-779.
24. Ivaturi R, Kies C. Mineral balances in humans as affected by fructose, high fructose corn syrup and sucrose. *Plant Foods Hum Nutr.* 1992;42:143-151.
25. Milne DB, Nielsen FH. The interaction between dietary fructose and magnesium adversely affects macromineral homeostasis in men. *J Am Coll Nutr.* 2000;19:31-37.
26. Rutledge AC, Adeli K. Fructose and the metabolic syndrome: pathophysiology and molecular mechanisms. *Nutr Rev.* 2007;65:S13-S23.
27. Glinsmann WH, Bowman BA. The public health significance of dietary fructose. *Am J Clin Nutr.* 1993;58:820S-823S.
28. Vartanian LR, Schwartz MB, Brownell KD. Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis. *Am J Public Health.* 2007;97:667-675.
29. Melanson KJ, Zukley L, Lowndes J, Nguyen V, Angelopoulos TJ, Rippe JM. Effects of high-fructose corn syrup and sucrose consumption on circulating glucose, insulin, leptin, and ghrelin and on appetite in normal-weight women. *Nutrition.* 2007;23:103-112.
30. Akhavan T, Anderson GH. Effects of glucose-to-fructose ratios in solutions on subjective satiety, food intake, and satiety hormones in young men. *Am J Clin Nutr.* 2007;86:1354-1363.
31. U.S. Department of Agriculture, Economic Research Service. U.S. food consumption up 16 percent since 1970. *Amber Waves.* 2005; 3(5):5.

32. Anderson GH. Much ado about high-fructose corn syrup in beverages: the meat of the matter. *Am J Clin Nutr.* 2007;86:1577-1578.
33. U.S. Department of Health and Human Services and U.S. Department of Agriculture. Dietary Guidelines for Americans, 2005. 6th ed. Washington, DC: U.S. Government Printing Office; 2005.
34. Diet, nutrition and the prevention of chronic diseases. *World Health Organ Tech Rep Ser.* 2003;916:i-149.
35. U. S. Department of Agriculture, Agricultural Research Service, Beltsville Human Nutrition Research Center, Nutrient Data Laboratory. USDA Database for the added sugars content of selected foods, release 1. Available at: http://www.nal.usda.gov/fnic/foodcomp/Data/add_sug/addsug01.pdf. Accessed 02/29/08.

TABLE. Estimated molecular composition of common caloric sweeteners (%)^{3,4,12-14}

	Fructose	Glucose	Higher saccharides
HFCS-42	42	53	5
HFCS-55	55	42	3
HFCS-90	90	9	1
Sucrose	50	50	0
Honey	49	43	8
Molasses	50	48	3
Apple juice	59	31	10
Orange juice	51	49	0
Crystalline fructose	100	0	0

APPENDIX.

Current AMA Policy on Food Labeling and Poor Nutritional Value of Added Sugars

H-150.971 Food Labeling and Advertising

Our AMA believes that there is a need for clear, concise and uniform labeling on food products and supports the following aspects of food labeling: (1) Required nutrition labeling for all food products that includes a declaration of carbohydrates, protein, total fat, total saturated and polyunsaturated fatty acids, cholesterol, sodium and potassium content, and number of calories per serving. (2) Use of and/or ingredient labeling to declare the source of fats and oils. Knowledge of the degree of saturation is more important than knowing the source of oils in food products. It is not uncommon for manufacturers to use blends of different oils or to hydrogenate oils to achieve specific functional effects in foods. For example, vegetable oils that are primarily unsaturated may be modified by hydrogenation to more saturated forms that bring about desired taste, texture, or baking characteristics. This recommendation is therefore contingent upon nutrition labeling with saturated fat content. (3) The FDA's proposed rule on food labeling that requires quantitative information be provided on both fatty acid and cholesterol content if either one is declared on the label, as an interim step. (4) Warning statements on food labels are not appropriate for ingredients that have been established as safe for the general population. Moreover, the FDA has not defined descriptors for foods that are relatively higher in calories, sodium, fat, cholesterol, or sugar than other foods because there are no established scientific data indicating the level at which any of these substances or calories would become harmful in an individual food. (5) Our AMA commends the FTC for its past and current efforts and encourages the Commission to monitor misleading food advertising claims more closely, particularly those related to low sodium or cholesterol, and health claims. (6) Our AMA supports the timely approval of the Food and Drug Administration's proposed amendment of its regulations on nutrition labeling to require that the amount of trans fatty acids present in a food be included in the amount and percent daily value, and that definitions for "trans fat free" and "reduced trans fat" be set. (BOT Rep. C, A-90; Reaffirmed: Sunset Report, I-00; Appended: Res. 501, A-02; Reaffirmation A-04; Reaffirmed: in lieu of Res. 407, A-04)

Policy H-150.945 Nutrition Labeling and Nutritionally Improved Menu Offerings in Fast-Food and Other Chain Restaurants

Our AMA: (1) supports federal, state, and local policies to require fast-food and other chain restaurants with 10 or more units (smaller, neighborhood restaurants could be exempt) to provide consumers with nutrition information on menus and menu boards; (2) recommends that nutrition information in fast-food and other chain restaurants include calorie, fat, saturated fat and trans fat, and sodium labeling on printed menus, and, at a minimum, calories on menu boards, since they have limited space, and that all nutrition information be conspicuous and easily legible; (3) urges federal, state, and local health agencies, health organizations, and physicians and other health professionals to educate people how to use the nutrition information provided in restaurants to make healthier food choices for themselves and their families; and (4) urges restaurants to improve the nutritional quality of their menu offerings--for example, by reducing caloric content; offering smaller portions; offering more fruits, vegetables, and whole-grain items; using less sodium; using cooking fats lower in saturated and trans fats; and using less added sugars/sweeteners. (Res. 419, A-07)

Policy H-150.960 Improving Nutritional Value of Snack Foods Available in Primary and Secondary Schools

The AMA supports the position that primary and secondary schools should replace foods in vending machines and snack bars, which are of low nutritional value and are high in fat, salt and/or sugar, with healthier food choices which contribute to the nutritional needs of the students. (Res. 405, A-94; Reaffirmation A-04; Reaffirmed: in lieu of Res. 407, A-04; Reaffirmed: CSA Rep. 6, A-04)

D-150.987 Addition of Alternatives to Soft Drinks in Schools

Our AMA will seek to promote the consumption and availability of nutritious beverages as a healthy alternative to high-calorie, low nutritional-content beverages (such as carbonated sodas and sugar-added juices) in schools. (Res. 413, A-05)