# SCIENTIFIC SUMMARY

## A Selection of Recent Publications Supporting the Use of Low and No Calorie Sweeteners

**The safety and efficacy of low and no calorie sweeteners (LNCS) have been researched for decades.** This summary provides a selection of recent and well-designed scientific studies, articles, and position statements. Please see **page 6** for a quick summary of the evaluation and regulatory review of LNCS in the U.S. and globally. This resource is provided by Heartland Food Products Group, the manufacturer of SPLENDA® Brand Sweeteners.

## ACADEMIC & SCIENTIFIC EXPERTS' REPORT CONSENSUS ON LOW CALORIE SWEETENERS

- A substantial body of evidence reviewed by regulatory food safety agencies around the world confirm the safety of LNCS.
- When used in place of sugars, LNCS can help reduce calorie intake and assist with weight/ diabetes management.
- In people with and without diabetes, LNCS have no adverse effect on blood glucose and insulin regulation (HbA1c, fasting and post-prandial glucose and insulin levels).
- There is a need to research and develop evidence-based strategies to communicate facts to consumers, health professionals, and policy makers.
- Experts agree that with the reduction of sugars being recommended globally to lower the risk and prevalence of obesity, LNCS is a strategy to consider.
- Efforts should be made to understand and, where possible, reconcile policy discrepancies between organizations and reduce regulatory hurdles that impede product development and reformulation designed to reduce sugars and calories.

**Ashwell, M., Gibson, S., Bellisle, F., Buttriss, J. (2020).** Expert consensus on low-calorie sweeteners: facts, research gaps and suggested actions. **Cambridge Univ. Press.**

## INTERNATIONAL HEALTH ORGANIZATIONS AND PROFESSIONAL ASSOCIATIONS

### Nutrition Therapy for Adults with Diabetes or Prediabetes: A Consensus Report.

Diabetes Care. 2019;42(5): 731-754.

**About LNCS (abridged with relevant statements):** *"…FDA has reviewed several types of sugar substitutes for safety and approved them for consumption by the general public, including people with diabetes...Replacing added sugars with sugar substitutes could decrease daily intake of carbohydrates and calories. These dietary changes could beneficially affect glycemic, weight, and cardiometabolic control... If sugar substitutes are used to replace caloric sweeteners, without caloric compensation, they may be useful in reducing caloric and carbohydrate intake…"*

### American Diabetes Association (ADA) – 2019 Standards of medical care of diabetes.

Diabetes Care. S1-S183. Section 5. Lifestyle Management. S46-S60.

**About LNCS (abridged from table 5.1)**: *"The use of nonnutritive sweeteners may have the potential to reduce overall calorie and carbohydrate intake if substituted for caloric (sugar) sweeteners and without compensation by intake of additional calories from other food sources."*

### Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes.

Dyson PA, et al. Diabetic Medicine. 2018;35(5):541-547.

**Summary:** *Diabetes UK is the British-based patient, healthcare professional and research association for diabetes. They reviewed and updated their nutrition guidelines in 2018 for the prevention and management of diabetes, and stated "Non-nutritive (artificial) sweeteners are safe and may be recommended."*

### European Food Safety Authority (EFSA) panel on food additives and nutrient sources added to food. Statement on the validity of the conclusions of a mouse carcinogenicity study on sucralose (E 955) performed by the Ramazzini Institute.

Aguilar F, et al. European Food Safety Authority Journal. 2017;15(5):4784.

**Summary:** *EFSA published a positive scientific opinion on the safety of sucralose regarding carcinogenicity. This statement is consistent with myriad global scientific consensus and regulatory authorities' conclusions that sucralose is safe and does not cause cancer.*

### Academy of Nutrition and Dietetics Position Paper: Use of nutritive and nonnutritive sweeteners.

J Acad Nutr Diet. 2012;112(5):739-758.

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

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**World Health Organization (WHO), International Agency for Research on Cancer (IARC), IARC monographs on the identification of carcinogenic hazards to humans, report of the advisory group to recommend priorities for the IARC Monographs during 2020-2024.**

316 pages, 2019.

**Summary:** *Sucralose was one of hundreds of substances reviewed in 2019. The monograph states: "Sucralose safety tests have indicated no acute, sub-chronic, or chronic toxicity [meaning harm] at levels well above expected human intakes." The report further states that safety tests on sucralose have indicated no harm when observing sucralose consumption at levels well above expected human intakes. This report downgraded sucralose to low-priority for follow up.*

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**American Academy of Pediatrics Policy Statement from council on school health, committee on nutrition. Snacks, sweetened beverages, added sugars, and schools.**

Pediatrics. 2015;135(3):575 - 583.

**About LNCS:** *"Additional improvements in nutrient density of sweet-tasting products could be obtained if nonnutritive sweeteners are used as a tool to replace added sugars and help lower caloric intake. Several nonnutritive sweeteners have been accepted by the US Food and Drug Administration as safe and have shown good safety over time. However, data are scarce on long-term benefits for weight management in children and adolescents or on the consequences of long-term consumption. Continued research is needed."*

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**Academy of Nutrition and Dietetics Position Paper: Interventions for the treatment of overweight and obesity in adults.**

J Acad Nutr Diet. 2016;116(1):129-147.

**Summary***: The value of reducing sugar-sweetened beverages (SSBs) to reduce weight is discussed covering data from two RCTs that demonstrate greater weight loss with the replacement of LNCS beverages for SSBs.*

## META-ANALYSES, SYSTEMATIC AND LITERATURE REVIEWS

**Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses of the evidence from human and animal studies.**

Rogers PJ, et al. International J Obesity. 2016;40:381–394.

**Objective:** Review a large and lengthy body of evidence including numerous types of animal and human studies on LNCS.

**Type:** Systematic review with meta-analyses

**Conclusions:** Consistent with other systematic reviews of LNCS, this study demonstrated decreased energy intake and body weight with consumption of LNCS used in place of added sugars.

**Substitution of SSBs with other beverage alternatives: a review of long-term health outcome.**

Zheng M, et al. J Acad Nutr Diet. 2015;115(5):767-779.

**Objective:** Cull studies from six literature databases to identify prospective cohort studies (PCS) and randomized controlled trials (RCT) in children and adults with four month or longer duration on substitution of SSB.

**Type:** Systematic review

**Design:** Six PCS and 4 RCT were included.

**Conclusions:** Replacing sugar sweetened beverages (SSBs) with a variety of LNCS-sweetened beverages demonstrate a favorable effect on long term body weight.

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**Association between intake of non-sugar sweeteners and health outcomes: Systematic review and meta-analyses of randomized and non-randomised controlled trials and observational studies.**

Toews I, et al. BMJ. 2019;364:1-13.

**Objective:** Assess association between intake of LNCS and potential health benefits in generally healthy or overweight / obese adults and children.

**Type:** Systematic review

**Design:** Included 56 studies, 17 RCTs. Studies allowed direct comparison of no intake or lower intake of LNCS with higher LNCS intake. Intervention duration > 7 days.

**Conclusions:** Several health benefits were found. Reduction in calorie consumption, no effect on feelings of hunger or appetite, not causing a rise in glucose levels, and not contributing to tooth decay.

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**Stevia leaf to stevia sweetener: Exploring its science, benefits, and future potential.**

Samuel P, et al. J Nutrition. 2018;148(7):1186S-1205S.

**Objective:** This global comprehensive report, based on a symposium held after the 2017 American Society for Nutrition meeting, aims to cover the science, safety, acceptable daily intake (ADI) and potential health benefits of high-purity steviol glycosides.

**Type:** Comprehensive report

**Conclusions:** Regarding science and safety, the report states: "all major global scientific and regulatory bodies have determined, through their rigorous evaluation processes, that high-purity steviol glycosides are safe for the general population." In healthy individuals and those with diabetes the use of steviol glycosides, in place of some carbohydrate and sugars, support reduction in postprandial glucose levels and reduced carbohydrate and sugar intake.

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**Low-calorie sweeteners and body weight and composition: A meta-analysis of randomized controlled trials and prospective cohort studies.**

Miller PE, et al. Am J Clin Nutr. 2014;100:765–77.

**Objective:** Provide meta-analysis of randomized control trials (RCT) and prospective cohort studies (PCS) on LCS and body weight, fat mass, BMI, and waist circumference.

**Type:** Meta-analysis

**Conclusions:** Results showed that in RCT, LNCS reduced body weight compared to placebo modestly, but significantly reduced BMI, fat mass, and waist circumference.



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## SAFETY AND CARCINOGENICITY

### Critical review of the current literature on the safety of sucralose.

Magnuson BA, et al. Food and Chem Toxicol. 2017;106: 324-355.

**Objective:** Provide an in-depth review of studies conducted over past forty years including the effects of sucralose on growth, development, reproduction, neurotoxicity, immunotoxicity, carcinogenicity and overall health status. The review of more recent studies focused on the effect of sucralose on the gut microflora and glycemic control.

**Type:** Literature review

**Conclusions:** Sucralose is safe for its intended use as a LNCS.

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### Sucralose non-carcinogenicity: a review of the scientific and regulatory rationale.

Berry C, et al., Nutrition and Cancer. 2016 Nov-Dec;68(8):1247-1261.

**Objective:** To comprehensively review the safety literature on sucralose through a database search using key terms. Studies include independently conducted and industry-funded research on sucralose chemistry, pharmacokinetics, metabolism, toxicity, genotoxicity, and long-term safety, including carcinogenicity.

**Type:** Literature review

**Conclusions:** Sucralose is non-carcinogenic. It is safe for all consumers. The review supports four key points: 1) there is no evidence of chemical concerns or toxicity; 2) no metabolites in sucralose were found to be carcinogenic; 3) no changes to genes were observed to indicate any cancer-causing effects; 4) at doses thousands of times the maximum expected daily human intake toxicity and long-term carcinogenicity studies showed no evidence of carcinogenic potential.

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### Biological fate of low calorie sweeteners.

Magnuson BA, et al, Nutrition Reviews. 2016; 74(11):670–689.

**Objective:** Provide comprehensive review on commonly used LNCS, including acesulfame potassium, aspartame, saccharin, stevia leaf extract (steviol glycoside) and sucralose detailing biological fates, including absorption, distribution, metabolism, and excretion pathways (ADME). The review also compares the chemical differences between the LNCS and details global regulatory status.

**Type:** Literature review

**Conclusions:** The only trait that LNCS have in common is that they provide sweetness. Beyond this they are a diverse group of compounds with important differences in their metabolic fate including: ADME. An extensive body of evidence exists on ADME in both animal models and humans because it is a prerequisite for approval by global regulatory agencies. It's critical to use the existing knowledge of ADME to address potential controversies surrounding their use. Safety concerns about their use can often be addressed with this knowledge.

### Lack of potential carcinogenicity for sucralose – Systematic evaluation and integration of mechanistic data into the totality of the evidence.

Chappell GA, et al. Food and Chem Toxicol. 2019. https://doi.org/10.1016/j.fct.2019.110898.

**Objective:** Conduct a systematic assessment on the potential carcinogenicity of sucralose.

**Type:** Systematic assessment of mechanistic data

**Design:** Researchers used a framework developed for the quantitative integration of data related to the proposed key characteristics of carcinogens (KCCs). Data from peer-reviewed literature and the ToxCast/Tox21 database were evaluated using an algorithm that weighs data for quality and relevance.

**Conclusions:** The overall lack of activity for sucralose as tested in various models and across mechanistic endpoints organized by KCCs, coupled with the lack of carcinogenicity in standard two-year cancer bioassays in rodents, reinforces regulatory conclusions that sucralose does not present carcinogenic hazard to humans. These findings support prior conclusions that sucralose is unlikely to be carcinogenic in humans.

## GUT HEALTH, GLYCEMIC CONTROL, HUNGER AND APPETITIE

### Assessing the in vivo data on low/no-calorie sweeteners and the gut microbiota.

Lobach AR, et al. Food and Chemical Toxicology. 2019;124:385-399.

**Objective:** Explore the literature for any published studies with gut microbiome measures in either animal or human subjects exposed to LNCS and studies that investigated the general nature of the gut microbiome.

**Type:** Systematic review

**Conclusions:** No credible evidence has revealed that LNCS adversely affect health through an effect on the gut microbiome. Authors found clear evidence that dietary changes unrelated to LNCS consumption are likely the major determinants of change in gut microbiota numbers and phyla.

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### Low calorie sweeteners: Evidence remains lacking for effects on human gut function.

Bryant C, McLaughlin J. Physiology & Behavior, 2016;164, Part B, 482–485.

**Objective:** To review the cellular, animal, and clinical studies on human gut function and put the results into context with the gut-brain axis and its regulation of food intake.

**Type:** Review

**Conclusions:** Human studies do not support a clinically meaningful effect of ingested LNCS on hormones involved in gut signaling. Sucralose, aspartame, and ace-K had no greater effect than water on secretion of GLP-1, insulin, PYY, or ghrelin, nor any impact on appetite.



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### Glycemic impact of non-nutritive sweeteners: A systematic review and meta-analysis of randomized controlled trials.

Nichol AD, et al. Eur J Clin Nutr. 2018;72:796-804.

**Objective:** Quantitatively synthesize existing research from Randomized Control Trials (RCT) on the impact of 4 LNCS (aspartame, saccharin, steviosides, and sucralose) on glycemia in normoglycemic individuals and a subset of people with diabetes.

**Type:** Systematic review and meta-analysis

**Design:** Search PubMed and Web of Science databases for 29 RCT. Used PRISMA guidelines. Two authors screened the titles and abstracts of candidate publications. The third author was consulted to resolve discrepancies. A total of 741 subjects were included in the analysis.

**Conclusions:** The LNCS studied did not increase blood glucose levels, rather levels gradually decreased. The impact of LNCS on glycemia varied to some extent by age, body weight, and whether people had diabetes or not.

### Short-term impact of sucralose consumption on the metabolic response and gut microbiome of healthy adults.

Thomson P, et al. Brit J Nutr.2019;122:856–862.DOI: https://doi.org/10.1017/S0007114519001570

**Objective:** Examine short-term effect of sucralose consumption on glucose homeostasis and gut microbiome of healthy male volunteers.

**Type:** Randomized, double-blind study

**Design:** 34 subjects randomized into 2 groups. One was administered sucralose capsules (780 mg/d) for 7 days. The control group was given placebo. Before and after the intervention, glycemic and insulin responses were assessed with a oral glucose load (75 g). Insulin resistance was determined using homeostasis model assessment of insulin resistance and Matsuda indexes. The gut microbiome was evaluated before and after the intervention by 16S rRNA sequencing.

**Conclusions:** Glycaemic control and insulin resistance were not affected during the 7 day period. At the phylum level, gut microbiome was not modified in any group. Independent of consuming sucralose or placebo, individuals with a higher insulin response after the intervention had lower bacteroidetes and higher firmicutes abundances. High doses of sucralose for 7 days does not alter glycaemic control, insulin resistance, or gut microbiome in healthy individuals. However, subjects with an increase vs. decrease in insulin response after sucralose and placebo were found to have different gut microbiome compositions.

### Impact of diet composition on blood glucose regulation.

Russell WR, et al. Critical Reviews in Food Science and Nutrition, 2016;56(4):541-590.

**Objective:** Explore human studies focused on various dietary components and their impact on blood glucose levels to prevent and manage type 2 diabetes. This included the impact of the major macronutrients, micronutrients, nonnutrient phytochemicals, and LNCS as well as research on various LNCS related to glucose regulation including impact on gut hormones and glucose, C-peptide and insulin levels.

**Type:** Review

**Conclusions:** The use of LNCS in subjects with or without diabetes does not affect glucose levels, however, dietary components have significant and clinically relevant effects on blood glucose modulation.

### Associations of diet soda and non-caloric artificial sweetener use with markers of glucose and insulin homeostasis and incident diabetes: the Strong Heart Family Study.

Jensen PN, et al. Eur J Clin Nutr. 2019; doi:10.1038/s41430-019-0461-6.

**Objective:** Assess associations of diet soda and LNCS consumption with: 1) early markers of insulin and glucose homeostasis (cross-sectionally) and 2) incidence of a diabetes diagnosis (over ave. of 8 years follow-up) in American Indian population with high rates of obesity and type 2 diabetes.

**Type:** Retrospective analysis using the Strong Heart and Family Study (SHFS) database, a family-based longitudinal study of genetics and risk factors for CVD in 12 American Indian communities (AZ, OK, ND, SD).

**Design:** 1,359 SHFS participants without CVD or diabetes who participated in the 2007–2009 study exam. LNCS beverages and LNCS consumption were assessed and FPG and insulin levels were measured during the study exam. Participants were followed for diagnosis of diabetes through 2017 with a phone interview and medical record review.

**Conclusions:** 40% of participants reported regularly consuming diet soda. 41% used LNCS to sweeten beverages. 98 cases of diabetes were found. Data indicate no statistically significant associations of diet soda or LNCS consumption with fasting insulin, fasting glucose, or incident diabetes. Authors note that results may not be generalizable to other populations.

### Do low-calorie sweetened beverages help to control food cravings? Two experimental studies.

Maloney NG, et al. Phys & Behav. 2019:208:112500. https://doi.org/10.1016/j.physbeh.2019.03.019

**Objective:** Investigate the effect of priming hedonic eating motivations on ad libitum energy intake in frequent and non-consumers of LNCS beverages.

**Type:** Prospective experimental, human

**Design:** In study 1 (N =120) frequent and non-consumers of beverages sweetened with LNCS were exposed to either chocolate or neutral cues (craving vs. control condition) and then completed several tests. Ad libitum energy intake from sweet and savory snacks and beverages (including LNCS) was then assessed. Study 2 followed a similar protocol, but included only frequent consumers (N=172) and manipulated the availability of LNCS beverages in the ad libitum eating context (available vs. unavailable). Measures of guilt and perceived behavioral control were also included.

**Conclusions:** LNCS beverages did not consistently protect consumers from craving-induced increases in energy intake. However, frequent consumers of LNCS beverages consumed fewer calories overall when they were available. These participants also perceived more control over their food intake and felt less guilty.

### The role of low-calorie sweeteners in diabetes.

Johnson CA, et al. Eur Endocrinol. 2013; 9(2): 96–98.

**Objective:** Review literature on the role of LNCS in the prevention and management of type 2 diabetes with focus on the prevention of weight gain and assistance in weight loss.

**Type:** Literature review

**Conclusions:** With brief exploration of the literature on LNCS regarding the common concerns of increased appetite, weight gain, and insulin and hormonal response, this review refutes these concerns. The review concludes that the use of LNCS can be a replacement for sucrose and other sources of carbohydrate and can assist people at risk of or with type 2 diabetes achieve their health goals with greater flexibility.



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## WEIGHT MANAGEMENT

### Low calorie sweetener (LCS) use and energy balance.

Peters, JC, Beck J. Physiology & Behavior, 2016;164, Part B, 524-528.

**Objective:** Review over 30 years of research and reviews on LNCS, energy balance, and weight management.

**Type:** Literature review

**Conclusions:** While older, observational longitudinal cohort studies suggested that LNCS may promote weight gain, more recent studies nearly uniformly show either weight loss or prevention of weight gain.

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### The role of low-calorie sweeteners in the prevention and management of overweight and obesity: Evidence v. conjecture.

Rogers PJ: Proceedings of the Nutrition Society. 2017;77(3):230-238.

**Objective:** Examine 3 common claims about the effects of LNCS on energy intake and preference for sweetness: 1) the sweet taste confusion hypothesis; 2) the sweetness without calories and sweet tooth hypothesis; and 3) the conscious overcompensation hypothesis.

**Type:** Literature review

**Conclusions:** The author substantiates the lack of evidence for the 3 claims and concludes that intervention studies generally show consumption of LNCS in place of (some) sugar reduces energy intake and body weight.

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### A randomized controlled trial contrasting the effects of 4 low-calorie sweeteners and sucrose on body weight in adults with overweight or obesity.

Higgins KA, Mattes RD: Am J Clin Nutr. 2019; 109:1288–1301.

**Objective:** Compare effects of consumption of 4 LNCS and sucrose on body weight, ingestive behaviors, and glucose tolerance over 12 week intervention in overweight or obese adults.

**Type:** Randomized controlled trial

**Design:** In a parallel-arm design, 154 participants consumed either 1.25–1.75 L of beverage sweetened with sucrose, aspartame, saccharin, sucralose, or reb A daily for 12 weeks. Sucrose containing beverage contained 400–560 kcal/d. The LNCS beverages contained <5kcal/d. Anthropometric indexes, energy intake, energy expenditure, appetite, and glucose tolerance were measured at baseline. Body weight measured every 2 weeks with energy intake, expenditure, and appetite assessed every 4 weeks compliance was determined.

**Conclusions:** Of the 123 subjects completing the study, those in sucrose and saccharin groups had significant increases in body weight compared with aspartame, reb A, and sucralose. Weight change in the sucralose group was greater than saccharin, aspartame, and reb A groups. LNCS should be categorized as distinct entities because of their differing effects on body weight.

### The effects of water and non-nutritive sweetened beverages on weight loss and weight maintenance: A randomized clinical trial.

Peters JC, et al. Obesity. 2016;24(2):297-304.

**Objective:** Evaluate the effects of water vs. beverages sweetened with LNCS on body weight in subjects enrolled in a year-long behavioral weight loss treatment program at 12 weeks and 1 year.

**Type:** Randomized equivalence design trial (2 study sites)

**Design:** 303 people with overweight or obesity were randomized. The study group was instructed to drink 24 fl oz/day diet beverages (DB) and the control group 24 fl oz/day of water and no diet beverages. All participants participated in the same weight loss program.

**Conclusions:** DB group lost significantly more weight at 12 weeks, averaging 13 pounds, or 44 percent more than the control group which averaged 9 pounds. 64% of study group lost >5% of body weight, compared with 43% of control group. DB group experienced significantly less hunger. At one year, after completing the 9 month maintenance phase, the DB group showed statistically significant greater weight loss than subjects in the water treatment group.

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### Low/no calorie sweetened beverage consumption in national weight control registry (NWCR).

Catenacci VA, et al. Obesity. 2014;22(10):2244-2251.

**Objective:** Evaluate prevalence of and strategies behind LNCS beverage consumption in successful weight loss maintainers.

**Type:** Cross-sectional

**Design:** Administer an online survey to 434 members of the NWCR who have lost >13.6 pounds and maintained weight loss for >1 year to determine consumption of beverages sweetened with LNCS.

**Conclusions:** Greater than half the participants surveyed reported regularly consuming LNCS beverages, 10% regularly consumed sugar sweetened beverages. 78% of LNCS beverage consumers reported these helped them control calorie intake and noted that their choice of beverage was “very important” for weight loss (42%) and weight maintenance (40%).

## HEALTHY DIETARY PATTERNS WITH LCS INTAKE AND LCS CONSUMPTION LEVELS

### Low-/No-calorie sweeteners: A review of global intakes.

Martyn D, et al. Nutrients. 2018;10(3):357.

**Objective:** Examine published data since 2008 to determine the global intake of the seven most commonly used LNCS, including: aspartame, acesulfame-K, saccharin, sucralose, cyclamate, thaumatin, and steviol glycosides.

**Type:** Literature review

**Conclusions:** The review raised no concern regarding excess intake of these 7 LNCS among the general population and other sub populations like children and people with diabetes. The data did not demonstrate any significant increase or decrease of LNCS over the 10 year period but do suggest a possible increase in the number of people consuming products containing LNCS.



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**Estimation of exposures to non-nutritive sweeteners from consumption of tabletop sweetener products: a review.**
Tennant DR. Food Additives & Contaminants. Part A, 36:3, 359-365, DOI: 10.1080/19440049.2019.1566784.
**Objective:** Reliable estimation of intake of LNCS is complex, in part because there's considerable variation in the forms of Table Top Sweeteners (TTS) products. This paper examines the suitability of existing food consumption databases for estimation of LNCS intake from TTS and proposes an alternate method for estimates.
**Type:** Review and analysis
**Design:** Review current intake estimation models for TTS.
**Conclusions:** Data suggest that using upper percentile consumption figures for powdered forms is a critical factor in intake estimations and may be a more realistic method by which overall exposure estimates could be obtained. When estimates are based on maximum concentration levels in powdered TTS products, and 95th percentile consumption figures for TTS products, intakes are below ADI values for all age groups.

**Low-calorie beverage consumption, diet quality and cardiometabolic risk factor in British adults.**
Patel L, et al. Nutrients. 2018;10:1261.
**Objective:** Verify the association between LNCS beverage consumption, diet quality and cardiometabolic risk factors in British adults.
**Type:** Cross-sectional study
**Design:** Data from over 5,000 individuals 16 years of age and older obtained from two waves of the National Diet and Nutrition Survey Rolling Programme (2008–2012 and 2013–2014) was analyzed.
**Conclusions:** LNCS beverage consumption, compared with sugar sweetened beverages (SSB) was associated with lower energy consumption and lower free (added) sugar intake. Consumption of other nutrients was not significantly different. Nor was plasma glucose, total cholesterol, LDL, HDL, or triglycerides. Replacing LNCS beverages, for SSBs can positively impact diet quality and energy consumption.

## Safety Evaluation and Regulatory Review of Low-Calorie Sweeteners in U.S. and Globally

The U.S. Food and Drug Administration (FDA) regulates low-calorie sweeteners either through the Food Additive Approval Process or the Generally Recognized As Safe (GRAS) process[1]. Both processes follow established rigorous protocols and meet the FDA standard of safety[1]. Whether the LNCS is evaluated as a Food Additive or GRAS ingredient, it is allowed for use by the entire population, including children, pregnant and lactating women, and people with diabetes.

To start the **Food Additive Approval Process**, a manufacturer or entity submits a food additive petition for review to FDA. The petition must provide a complete safety assessment of the ingredient based on the principles of food toxicology[5]. The ingredient is not allowed to be used in foods until FDA completes their review and grants approval[5]. Sucralose, the sweetening ingredient in SPLENDA® Zero Calorie Sweetener, is an example of a LNCS that received FDA approval as a Food Additive.

Foods that are generally recognized, among qualified experts, to be safe under the conditions of their intended use are considered **Generally Recognized as Safe (GRAS)** and are exempt from the premarket review and approval by FDA's Food Additive Review Process[7]. The manufacturer notifies the FDA of their intent to use the ingredient in foods by obtaining a review from experts on the ingredient and submitting the review as a "GRAS Notification" to the FDA[7]. The FDA responds with either a No Objection letter (approval) or notification that the ingredient does not provide a basis for use as a GRAS ingredient[7]. Steviol glycosides Reb A and Reb D, the sweetening ingredients in SPLENDA® Stevia, are an example of LNCS that received FDA approval as GRAS[6].

Across the globe, the sweetening ingredients used in SPLENDA® and SPLENDA® Stevia products have been authorized or adopted for use by many regulatory bodies, including Health Canada[2,3]. The safety evaluation and regulatory processes to allow the use of LNCS around the globe depends on the country or area of the world. Some have their country or area-based regulatory body. As examples, Canada has their regulatory body, Health Canada, and countries in Europe look to the European Food Safety Authority (EFSA). Many countries use guidance from the Joint Expert Committees for Food Additives (JECFA) administered jointly by the Food and Agriculture Organization of the United Nations and the World Health Organization[4].

References: [1]Roberts, A. (2016). The safety and regulatory process for low-calorie sweeteners in the United States. Physiology & Behavior. 164, Part B, 439-444. [2]International Food Information Council Foundation. What is Sucralose? [3]Samuel P, Ayoob KT, Magnuson BA, Wolwe-Rieck U, Jeppesen PB, Rogers PJ, Rowland I, Mathews R. (2018). Stevia Leaf to Stevia Sweetener: Exploring its Science, Benefits and Future Potential. J Nutrition. 148(7):1186S-1205S. [4]World Health Organization. Joint FAO/WHO Expert Committee on Food Additives (JECFA). [5]FDA. (2007). Guidance for Industry and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients (Redbook). [6]Perrier JD, Mihalov JJ, Carlson SJ. (2018). FDA Regulatory Approach to Steviol Glycosides. Food and Chemical Toxicology. 122:132-142. [7]FDA. (2019). Generally Recognized as Safe (GRAS).

The literature cited here is consistent with the extensive evidence of LNCS, which concludes safety and benefits of using LNCS including to help lose or maintain weight, help manage diabetes, or to reduce added sugars, calories, or carbohydrates.

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