Fact Sheet on Low Calorie Sweeteners
October 2020

Low-calorie sweeteners (LCSs) are used in a variety of beverages and foods to provide sweet taste with few to no calories. The 2020 Dietary Guidelines Advisory Committee (DGAC) "recommends these food ingredients be considered as an option for managing body weight." This is because excess sugar intake may be a risk factor for gaining too much weight, and LCSs can be a means to help reduce sugar intake. The safety and utility of LCSs has been the subject of much scientific research.

- This fact sheet summarized the key safety resources on LCSs. More information can be found **here.**

LCSs are food ingredients that, in the U.S., fall into one of two categories: either food additives or ingredients that are Generally Recognized as Safe, or GRAS ingredients. FDA permits only ingredients for use in food when they have been demonstrated to have a reasonable certainty of no harm.[1] All permitted LCSs are therefore ingredients that have been found by qualified experts to be safe for use. The FDA and other regulatory agencies also provide guidance documents on the kinds of studies typically important for determining the safety of a food ingredient. This encompasses a wide range of studies, including, e.g., genotoxicity, pharmacokinetics or toxicokinetics (absorption, distribution, metabolism and excretion - ADME), short-term toxicity, subchronic toxicity, developmental and reproductive toxicity, chronic toxicity, and carcinogenicity studies. These studies are primarily in non-human species, which is partly so that extremely large doses can be used during testing. When large doses can be given daily for a long period of time, this can help researchers understand the potential toxicity of a substance. When studies in humans are available, these studies are also included in the reviews by the experts. Such studies often include reports that illustrate the similarities between humans and animals with respect to the ingredient's absorption, distribution, metabolism and excretion, and human tolerance studies, but can also extend to other types of clinical trials as well as epidemiological studies.

After rigorous review of all the research, a no-observed-adverse-effect level, or NOAEL, is determined. While the NOAEL is a dose for which no adverse effects were observed, FDA and other regulatory agencies set the acceptable daily intake, or ADI, at a far lower level. The NOAEL that is used to set the ADI is from the study with the longest duration and with the most sensitive endpoint. In general, the ADI is set at 100 times less than this NOAEL. This is to provide a wide margin for safety! The NOAEL is divided by 10 to represent the uncertainty associated with moving from an animal model to humans and divided again by 10 to account for interindividual variability in the human population.

Regulatory bodies rely on ADIs as a safety benchmark. It is important to understand that ADIs are not established based on a single animal study. The ADI, or daily intake of the food ingredient (usually in mg) divided by body weight (in kg), is the amount "that can be taken daily in the diet, even over a

[1] Guidance for Industry: Recommendations for Submission of Chemical and Technological Data for Direct Food Additive Petitions. US Food and Drug Administration. 2009. [Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-recommendations-submission-chemical-and-technological-data-direct-food-additive.]

lifetime, without appreciable risk."[2] In all, **ADIs represent a rigorous review of available scientific data and allow for a common goal** of ensuring "reasonable certainty of no harm" or "no appreciable risk" under the conditions of intended use.[3,4,5]

The ADI values for various sweeteners, as determined by the World Health Organization (WHO), the US FDA and Health Canada are summarized in the table that follows. LCSs that have been approved by the U.S. FDA include saccharin, aspartame, acesulfame potassium (Ace-K), sucralose, neotame, and advantame. Other LCSs permitted for use in food as generally recognized as safe substances (GRAS) include Steviol glycosides and Luo Han Guo (monkfruit) extracts.

Worldwide Acceptable Daily Intake (ADI) Values for Common High-Intensity Sweeteners: WHO, FDA and Health Canada

Sweetener	Sweetness Relative to Sugar[1]	JECFA[3]	FDA[1]	Health Canada[4]
		ADI (mg/kg body weight)		
Acesulfame K	200x	0-15	15	15
Advantame	20,000x	0-5	32.8	5
Alitame	2000x[2]	0-1	NA	NA
Aspartame	200x	0-40	50	40
Cyclamate	30x[2]	0-11	NA	11
Monk Fruit Extract	100-250x	NS	NS	3[a]
Neotame	7,000-13,000x	0-2	0.3	2
Saccharin	200-700x	0-5	15	5
Stevia	200-400x	0-4	4	4
Sucralose	600x	0-15	5	8.8

[a] **Monk fruit extract (Luo Han Guo) has a temporary ADI.**

Abbreviations: FDA: US Food and Drug Administration; JECFA: Joint FAO/WHO Expert Committee on Food Additives; NS: Not specified; NA: Not approved for use in food as of 2018.

[2] Toxicological evaluation of some food additives including food colours, thickening agents and others. Joint FAO/WHO Expert Committee on Food Additives. *FAO Nutr Meet Rep Ser*. 1975;(55A):1-89.[Available at: http://www.inchem.org/documents/jecfa/jecmono/v08je01.htm.]

[3] Food and Drug Administration. High-Intensity Sweeteners 2014 [Available from: https://www.fda.gov/food/food-additives-petitions/high-intensity-sweeteners.]

[4] World Health Organization. Principles for the safety assessment of food additives and contaminants in food. Environmental Health Criteria. Geneva, Switzerland: Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization in collaboration with the Food and Agriculture Organization of the United Nations; 1987. [Available at: http://www.inchem.org/documents/ehc/ehc/ehc70.htm].

[5] European Food Safety Authority. Guidance for submission for food additive evaluations. EFSA Journal. 2012;10(7):2760. [Available at: https://www.efsa.europa.eu/en/efsajournal/pub/2760].

More information on LCS is available from various governments and regulatory authorities:

European Food Safety Authority (EFSA)
https://www.efsa.europa.eu/en/topics/topic/sweeteners

Health Canada
https://www.canada.ca/en/health-canada/services/food-nutrition/food-safety/food-additives/sugar-substitutes.html

Joint FAO/WHO Expert Committee on Food Additives (JECFA)
http://www.inchem.org/documents/jecfa/jecmono/v08je01.htm

US FDA
https://www.fda.gov/food/food-additives-petitions/high-intensity-sweeteners
https://www.fda.gov/food/food-additives-petitions/additional-information-about-high-intensity-sweeteners-permitted-use-food-united-states