

Artificial Sweeteners and Cancer

Key Points

- Artificial sweeteners are regulated by the U.S. Food and Drug Administration (see Question 1).
- There is no clear evidence that the artificial sweeteners available commercially in the United States are associated with cancer risk in humans (see Question 2).
- Studies have been conducted on the safety of several artificial sweeteners, including saccharin, aspartame, acesulfame potassium, sucralose, neotame, and cyclamate (see Question 3).

1. What are artificial sweeteners and how are they regulated in the United States?

Artificial sweeteners, also called sugar substitutes, are substances that are used instead of sucrose (table sugar) to sweeten foods and beverages. Because artificial sweeteners are many times sweeter than table sugar, smaller amounts are needed to create the same level of sweetness.

Artificial sweeteners are regulated by the U.S. Food and Drug Administration (FDA). The FDA, like the National Cancer Institute (NCI), is an agency of the Department of Health and Human Services. The FDA regulates food, drugs, medical devices, cosmetics, biologics, and radiation-emitting products. The Food Additives Amendment to the Food, Drug, and Cosmetic Act, which was passed by Congress in 1958, requires the FDA to approve food additives, including artificial sweeteners, before they can be made available for sale in the United States. However, this legislation does not apply to products that are "generally recognized as safe." Such products do not require FDA approval before being marketed.

2. Is there an association between artificial sweeteners and cancer?

Questions about artificial sweeteners and cancer arose when early studies showed that cyclamate in combination with saccharin caused bladder cancer in laboratory animals. However, results from subsequent carcinogenicity studies (studies that examine whether a substance can cause cancer) of these sweeteners have not provided clear evidence of an association with cancer in humans. Similarly, studies of other FDA-approved sweeteners have not demonstrated clear evidence of an association with cancer in humans.

3. What have studies shown about a possible association between specific artificial sweeteners and cancer?

Saccharin

Studies in laboratory rats during the early 1970s linked saccharin with the development of bladder cancer. For this reason, Congress mandated that further studies of saccharin be performed and required that all food containing saccharin bear the following warning label: *"Use of this product may be hazardous to your health. This product contains saccharin, which has been determined to cause cancer in laboratory animals."*

Subsequent studies in rats showed an increased incidence of urinary bladder cancer at high doses of saccharin, especially in male rats. However, mechanistic studies (studies that examine how a substance works in the body) have shown that these results apply only to rats. Human epidemiology studies (studies of patterns, causes, and control of diseases in groups of people) have shown no consistent evidence that saccharin is associated with bladder cancer incidence.



Because the bladder tumors seen in rats are due to a mechanism not relevant to humans and because there is no clear evidence that saccharin causes cancer in humans, saccharin was delisted in 2000 from the U.S. National Toxicology Program's *Report on Carcinogens*, where it had been listed since 1981 as a substance reasonably anticipated to be a human carcinogen (a substance known to cause cancer). More information about the delisting of saccharin is available at <http://ntp.niehs.nih.gov/ntp/roc/eleventh/append/appb.pdf> on the Internet. The delisting led to legislation, which was signed into law on December 21, 2000, repealing the warning label requirement for products containing saccharin.

Aspartame

Aspartame, distributed under several trade names (e.g., NutraSweet® and Equal®), was approved in 1981 by the FDA after numerous tests showed that it did not cause cancer or other adverse effects in laboratory animals. Questions regarding the safety of aspartame were renewed by a 1996 report suggesting that an increase in the number of people with brain tumors between 1975 and 1992 might be associated with the introduction and use of this sweetener in the United States. However, an analysis of then-current NCI statistics showed that the overall incidence of brain and central nervous system cancers began to rise in 1973, 8 years prior to the approval of aspartame, and continued to rise until 1985. Moreover, increases in overall brain cancer incidence occurred primarily in people age 70 and older, a group that was not exposed to the highest doses of aspartame since its introduction. These data do not establish a clear link between the consumption of aspartame and the development of brain tumors.

In 2005, a laboratory study found more lymphomas and leukemias in rats fed very high doses of aspartame (equivalent to drinking 8 to 2,083 cans of diet soda daily) (1). However, there were some inconsistencies in the findings. For example, the number of cancer cases did not rise with increasing amounts of aspartame as would be expected. An FDA statement on this study can be found at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108650.htm> on the Internet.

Subsequently, NCI examined human data from the NIH-AARP Diet and Health Study of over half a million retirees. Increasing consumption of aspartame-containing beverages was not associated with the development of lymphoma, leukemia, or brain cancer (2).

Acesulfame potassium, Sucralose, and Neotame

In addition to saccharin and aspartame, three other artificial sweeteners are currently permitted for use in food in the United States:

- Acesulfame potassium (also known as ACK, Sweet One®, and Sunett®) was approved by the FDA in 1988 for use in specific food and beverage categories, and was later approved as a general purpose sweetener (except in meat and poultry) in 2002.
- Sucralose (also known as Splenda®) was approved by the FDA as a tabletop sweetener in 1998, followed by approval as a general purpose sweetener in 1999.
- Neotame, which is similar to aspartame, was approved by the FDA as a general purpose sweetener (except in meat and poultry) in 2002.

Before approving these sweeteners, the FDA reviewed more than 100 safety studies that were conducted on each sweetener, including studies to assess cancer risk. The results of these studies showed no evidence that these sweeteners cause cancer or pose any other threat to human health.

Cyclamate

Because the findings in rats suggested that cyclamate might increase the risk of bladder cancer in humans, the FDA banned the use of cyclamate in 1969. After reexamination of cyclamate's carcinogenicity and the evaluation of additional data, scientists concluded that cyclamate was not a carcinogen or a co-carcinogen (a substance that enhances the effect of a cancer-causing substance). A food additive petition was filed with the FDA for the reapproval of cyclamate, but this petition is currently being held in abeyance (not actively being considered). The FDA's concerns about cyclamate are not cancer related.

4. Where can people find additional information about artificial sweeteners?

For more information about artificial sweeteners, contact the FDA at:

Address: 10903 New Hampshire Avenue
Silver Spring, MD 20993
Telephone: 1-888-INFO-FDA (1-888-463-6332)
Internet Web site: <http://www.fda.gov/>

Selected References

1. Soffritti M, Belpoggi F, Esposti DD, Lambertini L. Aspartame induces lymphomas and leukaemias in rats. *European Journal of Oncology* 2005; 10(2):107-116.
2. Lim U, Subar AF, Mouw T, et al. Consumption of aspartame-containing beverages and incidence of hematopoietic and brain malignancies. *Cancer Epidemiology, Biomarkers and Prevention* 2006; 15(9): 1654-1659.

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Related NCI materials and Web pages:

- *What You Need To Know About™ Bladder Cancer* (<http://www.cancer.gov/cancertopics/wyntk/bladder>)
- *What You Need To Know About™ Brain Tumors* (<http://www.cancer.gov/cancertopics/wyntk/brain>)

How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, cancer researchers, advocates, and the public.

- **Call** NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237)
- **Visit** us at <http://www.cancer.gov> or <http://www.cancer.gov/espanol>
- **Chat** using LiveHelp, NCI's instant messaging service, at <http://www.cancer.gov/livehelp>
- **E-mail** us at cancergovstaff@mail.nih.gov
- **Order** publications at <http://www.cancer.gov/publications> or by calling 1-800-4-CANCER
- **Get help** with quitting smoking at 1-877-44U-QUIT (1-877-448-7848)

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