

Aspartame

Aspartame is an artificial sweetener that is found in more than 6,000 products used by more than 200 million people worldwide. Typical consumption is 2-3 mg/kg per day, but can be much higher.

Aspartame passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

- Ecological studies
 - Time-related studies of brain tumor incidence and consumption of aspartame: Roberts (1991), Olney *et al.* (1996)
- Cohort study
 - Prospective cohort study of aspartame consumption and hematopoietic and brain malignancies: Lim *et al.* (2006)
- Case-control studies
 - Integrated analysis of several Italian case-control studies of various cancers and aspartame consumption: Gallus *et al.* (2007)

Animal carcinogenicity data

- Long-term diet studies in rats
 - Two-year studies in male and female Charles River rats: Hazelton Laboratories (1973)
 - Studies in male and female Sprague-Dawley rats (eight weeks old at start of treatment, fed for life): Soffritti *et al.* (2005), Belpoggi *et al.* (2006), Soffritti *et al.* (2006)
 - Transplacental plus entire lifetime exposure studies in male and female Sprague-Dawley rats: Soffritti *et al.* (2007)

Other relevant data

- Genotoxicity
 - Review: Magnuson *et al.* (2007)
- Metabolism
 - Aspartame metabolism to known carcinogens, including methanol and formaldehyde: Soffritti *et al.* (2006); Magnuson *et al.* (2007)

Reviews

- Magnuson *et al.* (2007)
- Soffritti *et al.* (2008)

References¹

Belpoggi F, Soffritti M, Padovani M, Esposti DD, Lauriola M, Minardi F (2006). Results of long-term carcinogenicity bioassay on Sprague-Dawley rats exposed to aspartame administered in feed. *Ann NY Acad Sci* **1076**:559-577.

Gallus S, Scotti L, Negri E, Talamini R, Franceschi S, Montella M, Giacosa A, Dal Maso L, La Vecchia C (2007). Artificial sweeteners and cancer risk in a network of case-control studies. *Ann Oncol* **18**:40-44.

Hazelton Laboratories, Inc. (1973). Two-year toxicity study in the rat, FINAL REPORT, submitted to Searle Laboratories.

Lim U, Subar AF, Mouw T, Hartge P, Morton LM, Stolzenberg-Solomon R, Campbell D, Hollenbeck AR, Schatzkin A (2006). Consumption of aspartame-containing beverages and incidence of hematopoietic and brain malignancies. *Cancer Epidemiol Biomarkers Prev* **15**(9):1654-1659.

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Soffritti M, Belpoggi F, Esposti DD, Lambertini L (2005). Aspartame induces lymphomas and leukaemias in rats. *Eur J Oncol* **10**(2):107-116.

Soffritti M, Belpoggi F, Esposti DD, Lambertini L, Tibaldi E, Rigano A (2006). First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats. *Environ Health Perspect* **114**(3):379-385.

Soffritti M, Belpoggi F, Tibaldi E, Esposti DD, Lauriola M (2007). Life-span exposure to low doses of aspartame beginning during prenatal life increases cancer effects in rats. *Environ Health Prespect* **115**(9):1293-1297.

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¹ Copies of these listed references, as either the abstract, the relevant sections of the publication, or the complete publication, have been provided to members of the Carcinogen Identification Committee. These references have been provided in the order in which they are discussed in this document.

Magnuson BA, Burdock GA, Doull J, Kroes RM, Marsh GM, Pariza MW, Spencer PS, Waddell WJ, Walker R, Williams GM (2007). *Crit Review Toxicol* **37**:629-727.

Olney JW, Farber NB, Spitznagel E, Robins LN (1996). Increasing brain tumor rates: is there a link to aspartame? *J Neuropath Experimental Neurol* **56**(1):1115-1123.