Author, Year, Study Design, Class, Rating	Number of Subjects	Age	Population	Dose of Aspartame	Side Effect Tested	Results
Butchko HH et al, 2001 Study Design: Narrative Review Class: R Rating: N	N/A	N/A	N/A	Varied among studies.	Review of research on safety since regulatory approval of aspartame. 1984-1992; detailed menu census surveys, from more than 2,000 households per year, were monitored for a 14-day survey.	The results of the intake studies, despite differences in methodology, demonstrated consistent intakes in various countries that were well below the ADI. The totality of scientific evidence clearly demonstrates that even in amounts many times what people typically consume, aspartame is safe.
Garriga MM, Berkebile C et al, 1991 Study Design: Randomized Controlled Trial Class: A Rating: N	Control N=11 (three males, eight females); suspected aspartame-sensitive group: N=20 (eight males, 12 females).	Age range 15 to 51 years; no age reported for 12 patients confirmed with sensitivity.	Cases: Individuals who reported sensitivity to aspartame; controls (atopic individuals).	Aspartame challenge: Food-grade aspartame administered each 30 minutes with increasing doses (zero, 10, 100, 500, 1,000 and 2,000mg).	Hypersensitivity reactions (urticaria, GI distress, rhinitis, wheezing).	No patient complaints during double-blind challenge; one patient developed hives during single-blind challenge; two subsequent double-blind challenges negative; one patient's complaint of throat tightness during single-blind challenge.

Geha R, Buckley CE et al, 1993 Study Design: Randomized Crossover Trial Class: A Rating:	21 (17 female, four male).	10 to 55 years (mean 34±12 years).	History of urticaria or angioedema within 12 hours of ingestion of an aspartame-containing product during the previous three years; history of chronic urticaria, which resolved without medication on cessation of aspartame consumption and recurred when consumption was resumed; positive histamine skin test result.	Capsule with 50mg aspartame at 8:00 A.M., followed by capsule with 300mg aspartame at 10:00 A.M., followed by capsule with 600mg aspartame at 12:00 P.M. This last dose was accompanied by 7.5mg aspartame + 15mg DKP (diketopiperazine). Both of these compounds are present in aspartame-containing products and were included to evaluate the possibility that allergic/hypersensitivity-type reactions could be caused by them, rather than by the parent compound.	Urticaria.	17 of the 21 who completed the study had no positive reactions during study; four subjects had urticaria during the study; two of four with urticaria had urticaria after placebo but not aspartame. No statistically significant difference in incidence of positive reactions (P=1.000) between aspartame and placebo challenges. Ten subjects had total of 17 other adverse events (throat tightness, light-headed, warm feeling, dyspnea, nausea, headache, small hives, pruritis, periorbital swelling, nasal congestion, slight tingling of tongue). No statistically significant differences (P=0.289) between aspartame and placebo challenges for adverse experiences.
Knopp 1976 Study Design: Randomized Controlled Trial	59 (55 completed study).	Mean age 19.3 years.	Healthy young people, primarily nursing students (Note: Age range was from 10 to 21; however, since mean age was 19.3	Three 300mg aspartame capsules administered three times per day for a total of 2.7g of aspartame per day for 13 weeks; 2.7g approximately four times the anticipated daily intake of	Toxicity of chronic aspartame ingestion in overweight children.	Aspartame is without detectable effect in this setting.

Class: A Rating:			years, this study was included in adult question).	ordinary use during weight loss.		
Lapierre KA, Greenblatt DJ et al, 1990 Study Design: Randomized Crossover Trial Class: A Rating:	14 subjects. Final N=10 (six males, four females), for dropout rate of 29%.	21 to 36 years, mean 26.3 years.	Healthy volunteers.	Aspartame (15mg per kg of body weight) or placebo capsules were taken with orange juice after an overnight fast; subjects refrained from drugs, alcohol and aspartame for 72 hours.	Hunger, sedation, changes in cognitive function, memory and reaction time.	No significant differences between aspartame and placebo were found in measures of sedation, hunger, headache, mood, reaction time, cognition or memory at any time during the study. Plasma phenylalanine levels were significantly higher after aspartame ($P<0.01$) than with placebo between one and six hours post-dosage, reaching a maximum difference of +3.36 mmol per dL at two hours. Plasma glucose concentrations were not significantly different between aspartame and placebo.
Leon AS, Hunninghake DB et al, 1989 Study Design: Randomized Crossover Trial	108 (57 females).	31.4±1.3 years for aspartame group; 29.5±1.4 for placebo group.	Students, faculty and staff at a midwestern university.	300mg aspartame or placebo three times per day with meals for 24 weeks (approximately 75mg per kg per day or 1.5 times the FDA's acceptable intake).	Blood methanol levels, serum folate levels, physical side effects.	There was no consistent pattern of occurrence of reported physical symptoms and no significant differences between control and study group in total number of symptoms, number of

Class: A Rating:						symptoms per subject, laboratory abnormalities or changes from baseline laboratory values and measures. Most blood methanol concentrations were less than detectable level of 0.31mmol per L. Two individuals who had the highest levels, one from the aspartame group and one from the control group, were both well below toxic levels. Serum folate levels during the study were unchanged in both groups.
Lim U, Subar AF et al, 2006 Study Design: Retrospective Cohort Study Class: B Rating:	3.5 million questionnaires mailed by authors.	50 to 71 years.	AARP (American Association of Retired Persons) members.	Consumption of aspartame (divided into cohorts based on aspartame content per 100g beverage, determined by self-administered baseline questionnaire including a food frequency questionnaire (FFQ) calibrated against two 24-hour recalls).	Hematopoietic and brain cancers.	Findings did not support the hypothesis that aspartame increases hematopoietic or brain cancer risk.
London RS, 1988 Study Design: Narrative Review	N/A	N/A	N/A	Varied among studies.	A review of some currently available information on the safety in pregnancy with recommendations formulated on their use in the periconceptional period	Primarily animal studies: saccharine and aspartame are generally safe to consume during pregnancy (unless mother is homozygous for PKU,

Class: R Rating: N					and pregnancy.	when aspartame is unsafe).
Pivonka EEA, Grunewald KK, 1990 Study Design: Non-Randomized Controlled Trial Class: C Rating: U	120 females.	18 to 30 years of age.	Young college women.	12 ounces of water, aspartame-sweetened beverage (180mg to 280mg aspartame) or sugar-sweetened beverage (50g sucrose).	Sleepiness, mood changes.	Sleepiness was induced in young women after ingestion of a sucrose-containing beverage in the afternoon hours. The aspartame-sweetened beverage did not affect any of the mood states tested in our study.
Rowan AJ et al, 1995 Study Design: Randomized controlled trial Class: A Rating: U	18 subjects: 16 adults and two children.	Two children, age 10 and 15 years; 16 adults, age 20 to 70 years (mean 35 years).	159 recruitment letters were sent to individuals who had become known to the FDA, CDC or the NutraSweet Company and who claimed to have experienced seizures after consuming aspartame or who had come to our attention as a result of canvassing of 8,760 adult and pediatric neurologists by letter.	50mg per kg dose. The total dose was divided into three equal doses administered at 8:00 A.M., 10:00 A.M. and 12:00 P.M.	Seizures.	No clinical seizures or adverse experiences were seen during the course of the study.

Ryan-Harshman et al 1987 Study Design: Class: A Rating: ☑	13 males.	20 to 35 years.	Healthy men.	Multiple doses of aspartame (zero, 0.84, 2.54 or 5.04g).	Mean energy consumed, percentage of carbohydrate, percentage of protein, percentage of fat, mood, arousal after consuming varying amounts of aspartame.	No significant differences among any endpoints tested.
Schiffman SS, Buckley CE et al, 1987 Study Design: Randomized Crossover Trial Class: A Rating: ☑	N=40 (70% female).	18.8 to 68.9 years (range), mean 33.5±1.90.	Individuals who had reported headache (to FDA or manufacturer) after aspartame use.	10mg per kg of 98% pure aspartame given three times during one of two challenge days.	Headache.	Incidence rate of headache after aspartame (35%) was not significantly different from that after placebo (45%), P<0.50.
Spiers PA et al, 1998 Study Design: Randomized Crossover Trial Class: A Rating: ☑	48 (24 males, 24 females).	18 to 35 years.	Healthy graduate or undergraduate college students.	High (45mg per kg of body weight) or low (15mg per kg of body weight) doses of aspartame.	Cognitive, neurophysiologic or behavioral functioning.	No effect on neuropsychologic, neurophysiologic or behavioral functioning in healthy young adults.
Stokes AF, Belger A et al, 1991	12 certified pilots, 4 female/8 male.	Adults.	Airline pilots.	Placebo capsules (dextrose), aspartame (50mg per kg body weight), or ethyl alcohol (positive control, estimated dose	Effect of aspartame on cognitive performance.	Cognitive impairment was detected in several tasks after consumption of the low dose of alcohol, but

Study Design: Randomized Controlled Trial Class: A Rating:				to raise blood alcohol 0.1%).		not with aspartame or placebo treatments.
Stokes et al 1994 Study Design: Randomized Controlled Trial Class: A Rating:	12 (gender not defined).	College students.	Young adults.	Aspartame capsules (50mg per kg body weight per day) for nine days, placebo capsules (dextrose) as a negative control, and an acute dose of ethyl alcohol to achieve 0.1% blood ethanol levels All participants received the placebo and ethanol treatments once and the aspartame treatment twice within a seven-day interval.	The effect of chronic aspartame exposure on cognitive performance and blood phenylalanine levels.	Although aspartame given at high doses (50mg per kg body weight per day) approximately doubled plasma phenylalanine levels, there is no evidence of impaired cognitive performance. Following ethanol treatments, participants scored lower on 14 tasks.
Weihrauch MR, Diehl V, 2004 Study Design: Narrative Review Class: R Rating:	N/A	N/A	N/A	Varied among studies.	Compared animal and human studies for cancer.	There is no evidence that the artificial sweetener aspartame bears a carcinogenic risk.