

ASPARTAME

EVALUATION OF THE EUROPEAN RAMAZZINI FOUNDATION STUDY

**by the
Scientific Panel on Food Additives, Flavourings,
Processing Aids and Materials in Contact with Food
(AFC)**

THE ERF ASPARTAME CARCINOGENICITY STUDY IN RATS

- Lifetime study in male and female rats
- Large group sizes (100-150 animals/sex/dose)
- Animals exposed to approx. 5 - 5000 mg/kg bw/day
- Treated from 8 weeks of age until natural death
- Potential for increased sensitivity to pick up possible carcinogenic effects

ERF's INTERPRETATION OF THEIR FINDINGS

- ERF have concluded that aspartame is a “multipotential carcinogenic agent”

ERF's INTERPRETATION OF THEIR FINDINGS

ERF concluded there were increases in:

- Lymphomas and leukaemias especially in females
- Carcinomas and precursor changes of the kidney, ureter and bladder in females
- Malignant schwannomas of peripheral nerves
- Total number of malignant tumour-bearing animals

EVALUATION BY THE AFC PANEL

DATA REVIEWED BY THE PANEL & ITS WORKING GROUP (1)

- Looked in detail at the ERF publications, the study report and additional data provided to EFSA by the ERF
- Looked at the peer review of a limited number of histopathological findings from the ERF study carried out by the US National Toxicology Program (NTP)
- Evaluated any new data relevant to possible carcinogenicity of aspartame
- Including new NTP studies for detection of cancer in transgenic mice published in 2004

EVALUATION BY THE AFC PANEL

DATA REVIEWED BY THE PANEL & ITS WORKING GROUP (2)

- Re-evaluated all the available studies on genotoxic potential
- Carried out a detailed assessment of how aspartame is metabolised in the body, including its breakdown to methanol
- Considered previous evaluations by national and international bodies on the original four cancer tests in rats and mice conducted in the 1970s/early 1980s

EVALUATION BY THE AFC PANEL

CONCLUSION (1)

- **Lymphomas and leukaemias are unrelated to the aspartame treatment**

REASONING

- **High background rate of chronic respiratory disease (likely cause of tumours)**
- **Lack of clear positive dose-response (despite very wide dose range)**

EVALUATION BY THE AFC PANEL

CONCLUSION (2)

- **Findings (tumours and precursors changes) in the kidney, ureter and bladder are not relevant for humans**

REASONING

- **High-dose effect related to kidney calcification/irritation**
- **Considered to be rat-specific**

EVALUATION BY THE AFC PANEL

CONCLUSION (3)

- **Data on total malignant tumours do not provide evidence of carcinogenic potential**

REASONING

- **Adding together of all tumours is not justified**
- **In particular the inclusion of lymphomas/ leukemias and findings in the renal pelvis and ureter**

EVALUATION BY THE AFC PANEL

CONCLUSION (4)

- For malignant Schwannomas of peripheral nerves:
 - Number of tumours was low
 - Showed a positive statistical trend in males but the dose-response was very flat
 - There is uncertainty about the diagnoses
- An independent pathology review would allow a full evaluation of this finding

GENOTOXICITY

- Large number of studies on genotoxicity in different *in vitro* and *in vivo* test systems
- The Panel concluded that aspartame does not have genotoxic activity
- The “multipotential carcinogenic effect” suggested by ERF could not have an underlying genotoxic mechanism

PREVIOUS EVALUATIONS OF ASPARTAME

- Extensive database on aspartame, from human studies, animal studies, *in vitro* studies and intake studies
- The Panel took note of the various toxicological evaluations of aspartame carried out previously by national and international bodies
- All have concluded that aspartame does not have carcinogenic potential, based on previously conducted studies

OTHER RECENT STUDIES

- The US National Toxicology Program conducted studies for cancer in several strains of transgenic mouse
 - *The results did not show any carcinogenic potential (NTP, 2004)*

- The US National Cancer Institute has just presented a paper at the American Association for Cancer Research on an epidemiological study of aspartame consumption and cancer incidence in over 560,000 people
 - *It reported no association between aspartame consumption and an increased risk for blood and brain cancers*

INTAKES OF ASPARTAME

- Several studies on intakes of aspartame in Europe, conducted between 1992 and 2001, show similar results
 - *Intakes range up to 10 mg/kg bw/day, including in high consumers such as diabetics*
- The Panel noted this is well below the EU Acceptable Daily Intake of 40 mg/kg bw for aspartame

OVERALL CONCLUSIONS BY AFC PANEL

- **The Panel concluded, on the basis of all the evidence currently available, that there is no reason to revise the previously established ADI for aspartame of 40 mg/kg bw.**