Re-evaluation of Aspartame

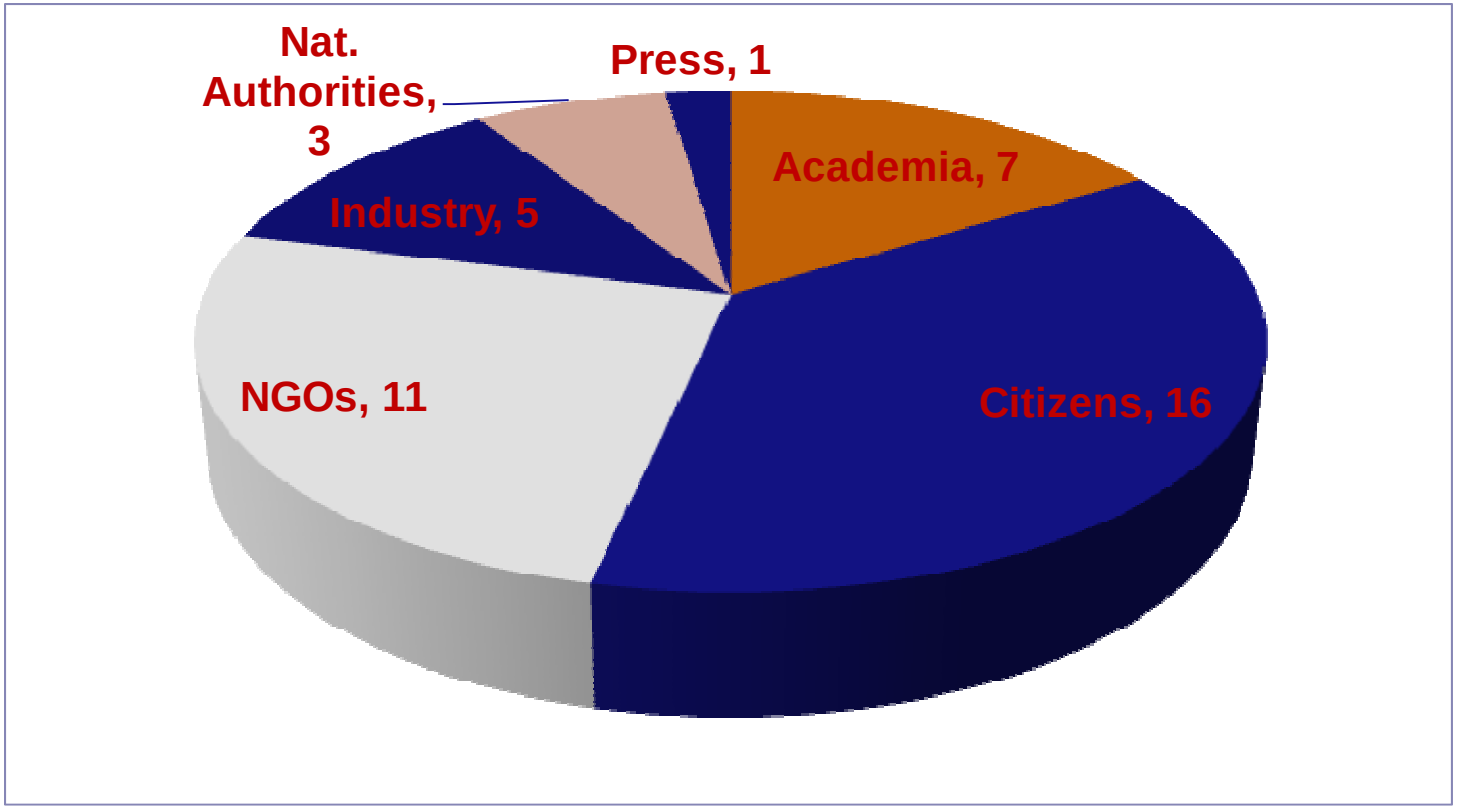
- Overview of the comments received during the public consultation -

Dr George Kass
FIP Unit

Brussels
9 April 2013

Some Statistics

- Total number of comments received: 217
- Total number of contributors: 43
- Total number of countries: 10 (3 non-EU)



Types of Comments Received

1. **Editorials**
   - Language and other clarification proposals

2. **Non-scientific comments**
   - No non-English version of the draft opinion
   - Conflicts of interests for the experts involved in the Panel and Working Group

3. **Scientific**
   - General approach
   - Specific
   - Conclusions

General Scientific Comments

efsa
European Food Safety Authority

Choice of studies

- Use of industry study reports that have not been peer-reviewed
- Use of academic but industry-funded studies
- Old studies from 1970's versus modern studies following GLP and OECD guidelines

'Any "safe" study by the manufacturer or those they fund should be suspect.'

Study validity criteria

- Dismissal of case reports and anecdotal evidence
- Dismissal of studies supplied by non-commercial organisations or concerned citizens following call for scientific data
- Unequal threshold of acceptance of positive findings versus negative findings

'the hurdle set for apparent positives was exceptionally high, whereas the hurdle that apparently negative studies needed to cross to be deemed reliable was far lower.'

Specific Scientific Comments

European Food Safety Authority

Toxicity of aspartame - cancer

- Searle's long term studies are old and used small numbers of animals and lacked statistical power.
- Searle's studies are flawed and have been manipulated.
- The studies by Soffritti and co-workers have been dismissed by EFSA, yet
  - they used a larger number of animals
  - they used in utero exposure and life-long exposure
  - they are contemporary
  - they are supported by the recent epidemiological study by Schernhammer et al. (2012) that suggests a link between artificial sweetener intake and leukaemia
- Searle's long term studies use protocols that are close enough to OECD guidelines to be used in the risk assessment.
- There is concern about the validity of the tumour incidence data as reported in the ERF studies.

Specific Scientific Comments

efsa
European Food Safety Authority

Toxicity of DKP - cancer

- *'The main concern for us regarding DKP which EFSA chooses to ignore here, is its possible potential to promote Brain tumours, a so far unpublished UK study remarked'*

- *'The data (…) clearly show that there is no risk from the decomposition of aspartame to DKP. The conclusions are supported by an extensive database on DKP data/literature, including 2 year high-dose dietary studies in rats and mice.'*

Specific Scientific Comments

efsa
European Food Safety Authority

Neurotoxicity of aspartame

- Phenylalanine causes neurotoxicity in humans.
- Aspartic acid is a neurotoxic agent.
- Anecdotal evidence that aspartame is addictive.
- Recent studies in experimental animals suggesting oxidative stress in the brain and neurotoxic effects of aspartame

Metabolic effects of aspartame

- Effects on insulin sensitivity and glucose homeostasis.

Specific Scientific Comments

efsa
European Food Safety Authority

Human studies

- Fagherazzi et al. Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes (…). Am J Clin Nutr. 2013 Jan 30.
- Comments on the epidemiological studies on premature delivery by Halldorsson et al. (2010) and Englund-Ögge et al. (2012).
- Comments on the epidemiological studies on urinary tract tumours by Andreatta et al. (2008) and leukaemia by Schernhammer et al. (2012).
- Two case reports on aspartame-induced fibromyalgia.
- Several anecdotal reports.

Specific Scientific Comments

efsa
European Food Safety Authority

Methanol

- Methanol is a metabolite of aspartame and is converted to formaldehyde, a highly toxic molecule.

  'Formaldehyde can only get into our bloodstream whilst disguised as the Trojan horse methanol – methanol carries formaldehyde to parts of our bodies it would not normally have access to'

- There is no ADI for methanol and therefore the current ADI of aspartame cannot be correct.

- Formaldehyde from aspartame binds to proteins and nucleic acids.

- Formaldehyde is a recognised human carcinogen.

- Methanol is considered to be a chemical with reproductive/developmental concerns.

- Methanol toxicity has been associated with multiple sclerosis and Alzheimer's disease.

Specific Scientific Comments

efsa
European Food Safety Authority

Exposure assessment

- The exposure assessment was too conservative because of the usage of Maximum Permitted Levels (MPLs) and maximum reported use levels in all food categories

- Uncertainties of the estimates
  - to better characterise the degree of uncertainties leading to an over-estimation
  - to mention that these uncertainties and conservativeness also apply to the metabolites and breakdown products whose exposure is also estimated (DKP, phenylalanine, methanol, aspartic acid).

- All usage data received by EFSA were not taken into consideration

Comments on Mode of Action approach

- The use of the PKU model that rests on the sole toxicity of Phe, even though appearing pertinent, could be incomplete as it does not take all potential mechanisms into account.
- *'The MoA analysis in relation to phenylalanine is welcomed because it provides a more comprehensive assessment of the possibility of aspartame ingestion giving rise to plasma concentrations of phenylalanine that would be of concern.'*
- *'This 'modes of action' section is strong primarily because of the human PKU patient data and the biological plausibility.'*
- *'The use of the IPCS Mode of action framework for a non-cancer end-point and its application was thorough and well described.'*
- *'I welcome the use of the Mode of Action approach to increase the transparency of the risk assessment approach, particularly on the toxicity of phenylalanine.'*

Comments on the overall conclusions and ADI for aspartame

- *'A new ADI of 20 µg/m^3 could be set, which is 2000 times lower than the current ADI.'*
- *'The ADI of aspartame must be lowered to at most 7.0mg/kg.'*
- '*An additional uncertainty factor (…) would be advisable.'*
- *'This represents an extremely comprehensive and thorough overview and analysis of the huge body of science on aspartame.'*
- *'The draft opinion was based on a very thorough and critical review of relevant evidence not only of the parent compound but also including metabolites and breakdown products.'*
- *'Re-evaluation of new data over the past 10 years has consistently confirmed the ADI of 40 mg/kg bw per day.'*

Thank you for your attention

and most importantly,

Thank you for your comments!