

**Item 4: FSA funded project T01054. Draft paper for publication. The effect of aspartame on self-reported aspartame sensitive individuals compared to controls – a double blind randomised placebo-controlled study. (RESERVED BUSINESS) – TOX/2013/39**

83. No interests were declared

84. This item was reserved business pending publication of the research.

85. The Chairman welcomed Professor Steve Atkin, Professor Richard Hammersley, Dr Alan Rigby and Dr T. Sathyapalan from Hull and York Medical School (HYMS), who had been commissioned by the FSA to undertake this research.

86. An initial discussion revolved around the appropriateness of the term “placebo” in the draft paper for publication. Members considered that use of the term placebo was misleading since it implied that a beneficial effect might be expected from the test chemical. The study had used a blinded, randomised cross-over design to control for “nocebo” effects. The comparison group of people who did not consider themselves sensitive to aspartame was included to check whether any effects of aspartame extended to individuals without known sensitivity. The contractor pointed out that “placebo” was a term commonly used by psychologists in experiments of this kind, but accepted that its use might be confusing. Members also suggested that the title would be clearer if it included “blinded cross-over study”, and that in the paper, the term “psychological effects” be replaced by “symptoms”.

87. Members highlighted the need to be clear about the reasons for including a sample of non-sensitive individuals – was this simply to explore whether any effects of exposure extended to the wider population, or was it also to allow case-control comparisons looking for factors that might influence the risk of becoming sensitive. No information had been provided about the source of the non-sensitive participants, but for case-control comparisons to be unbiased, the controls would need to be representative of the base population from which the cases were recruited, regarding their exposures to the risk factors under investigation. A Member noted a baseline difference in the triglyceride levels of the aspartame-sensitive group, which had not been discussed in the paper, but which might have implications for interpretation. This led to a discussion of possible reasons for the difference in lipid profile between the two groups of participants. It was also pointed out that, particularly since the findings of the study were negative and no a priori power calculation had been carried out, it would be preferable to present results as point estimates of effect with 95% confidence intervals. This would give an indication of how large an effect might have been missed simply by chance.

88. The handling of data gaps was discussed. The contractors explained that to minimise bias, patients had been left alone to fill in the questionnaire, without training or the help of clinical staff. However, this approach had resulted in missing data. The contractors described how the data gaps had been managed, and considered that despite caveats the data were fit-for-purpose. It was suggested that an alternative method of handling the missing data could be tested in a sensitivity analysis.

89. It was felt that the biochemistry data required a more comprehensive statistical evaluation. It was suggested that information on the quality assurance of the biochemical analyses be included in the paper. Members commented that the current format of the paper downplayed the metabolomics, and proposed that the contractors publish two papers, one focussing on symptoms, and the other on the biochemical and -omics outcomes.

90. Members recommended that further information be provided about the aspartame in the snack bars used for testing, including its stability and bioavailability.

91. The Chair thanked the contractors for their attendance and discussion, and stressed the importance of the study and the need for high quality papers to be submitted to journals. The Committee would not need to see further versions of the papers before publication.