Item 5: T01054 Determination of the symptoms of aspartame in subjects who have reported symptoms in the past compared to controls: a pilot double blind placebo crossover study. (RESERVED BUSINESS) – TOX/2013/10

33. Three members declared possible conflicts of interest. Professor Lake said that his employer was likely to be asked for consultancy advice on aspartame in the future. Professor Morris declared that he worked at the same institution as the principal investigator of the study to be discussed (Hull-York Medical School). Professor Coggon had provided epidemiological input to the draft EFSA opinion on aspartame that had been discussed at the previous COT meeting. It was agreed that none of these constituted a conflict of interests.

34. This item was held in reserved session as it involved pre-publication results. This was important to ensure that the results could be published in the peer-reviewed literature. Once the research had been published, the finalised contractors' report and minutes of the COT discussion would be made public.

35. The FSA had funded a double blind controlled study of possible effects of aspartame in self-reported aspartame-sensitive individuals and controls. To establish the feasibility of proposed methods and inform the final design, a comprehensive pilot study had been considered necessary, and draft reports of parts of this work were now presented to the Committee for discussion.

36. The pilot project had aimed to recruit 50 individuals with self-reported symptoms which they attributed to consumption of products containing aspartame, along with 50 control subjects. Each participant was studied twice. A granola bar containing aspartame was administered on one occasion, and a control bar containing sucrose but no aspartame on the other, the order of the two exposures being randomised. The dose of aspartame in the bars was 100 mg/bar – well below the Acceptable Daily Intake (ADI) of 40 mg/kg bodyweight (bw) established by EFSA. In a further experiment, 25 self-reported aspartame-sensitive individuals and 25 controls received the control bar on both occasions.

37. No adverse clinical effects were observed in either group of individuals, and analysis of biochemical parameters showed no differences, either at baseline or in response to aspartame. Analysis of data on symptoms was not available in time for the meeting.

38. In addition to the clinical observations and ascertainment of symptoms by questionnaire, a metabolomics study had been carried out on plasma and urine samples from the participants in the study. Professor Nigel Gooderham (Imperial College) gave a presentation on this aspect of the research. A difference in metabolic profile was observed between self-reported sensitive individuals and controls, which after un-blinding of the data was found to relate to body mass index (BMI). Self-reported sensitive individuals in the study population had higher BMI than the controls. Professor Gooderham suggested that the observed metabolomic differences could be due to differences in lipid metabolism. After allowance for BMI, no significant differences were found between the baseline samples of self-reported aspartame-sensitive and control individuals. Nor were there any significant differences between the groups after aspartame or sucrose was consumed.

39. Members were informed that the researchers had experienced great difficulty in recruiting self-reported aspartame-sensitive individuals to the study, and therefore it had taken much longer to complete than anticipated. The reason seemed to be that self-reported sensitive individuals thought that they might experience serious adverse effects if they participated in the study. Based on the recruitment difficulties in the pilot study and the lack of observed differences in the measured parameters on which to base power calculations, a full study was not considered to be warranted. Members were asked whether, taking into account the limitations of the pilot study, the findings provided reassurance that there were no differences in response to aspartame in either group of participants.

40. The draft report was considered to be interesting and useful. However, there were some reservations concerning the design of the study. It was mentioned that the diets of participants had not been standardised, and details of their diet before the study should have been included. More detailed statistical analysis was required, although it was recognised that the results presented were from interim analyses. It was noted that failure to detect aspartame metabolites, either by conventional or metabolomics methods, could be a consequence of the low aspartame dose in the bar and/or its formulation. Members suggested that it would have been useful also to have investigated levels of stress-related hormones.

41. The observed gender and BMI-related differences in the metabolomics data provided evidence of the sensitivity of the methods. However, the Committee advised that it could not be assumed that all participants with higher BMI were overweight. They might have greater muscle mass. It would be useful if distributions of BMIs among participants, including means and medians, were shown in the final report. Also, from experience in other studies, such as in asthmatic patients, it was suggested that individuals withdrawing from the study because of fear about serious adverse health effects might be the most sensitive. Therefore it would be helpful if the report described the past symptoms that were reported by sensitive individuals and the levels of exposure with which they had been associated.

42. Members agreed that symptoms reported by individuals who considered themselves aspartame-sensitive were diverse and non-specific. Although the study design could have been improved by, for example, incorporating standardised diets, measurements of food intake and more careful investigation of symptoms previously experienced by sensitive individuals, Members considered that a follow-up study was unlikely to be feasible, and subject to further results on symptoms following the experimental exposures, was probably not necessary.

43. The full study report would be presented to the Committee for discussion at a future meeting.