Food Standards Agency
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Buidheann Inbhe-Bìdhe

PE1376/F
Fergus Cochrane
Clerk to the Public Petitions Committee
TG.01
The Scottish Parliament
Edinburgh
EH99 1SP

Reference: FAS/0034

14 February 2011

Dear Mr Cochrane

CONSIDERATION OF PETITION PE1376

I refer to your letter to the Food Standards Agency in Scotland dated 8 February seeking our response to the questions from the petitioner in his written submission PE1376/E. I am pleased to reply to your letter – as previously, our response covers the interests of the Agency as a whole and answers the questions put to Andrew Wadge and myself.

"*Why did the Advisory Forum delegates at the 36th AF meeting reject their own scientific experts recommendation that aspartame was safe"*

The minutes of the 36th Advisory Forum, which are available on the website of the European Food Safety Authority (EFSA), state:

"6.4 National expert report on aspartame
Jeffrey Moon presented the national expert report on aspartame. Since the scientific literature review had been addressed at the previous AF meeting, an analysis of repeatedly reported symptoms had been conducted. While the national experts noted that caution was needed in analysing and interpreting anecdotal data due to the collection of data in a non-scientific way, the resulting information could be useful in guiding the design of any future investigative study that may be undertaken to determine individual sensitivity to aspartame. He also provided a feedback on the comments received during the consultation on the national expert report and said that the comments would be published together with the national expert report. The AF took note of the national expert report and the consultation feedback and agreed to defer further consideration of the issue until results of the ongoing pilot study in the United Kingdom become available. "

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We do not draw the same conclusion as Mr McDonald from the outcome of this meeting. We note that in the opinion of EFSA and other independent expert bodies aspartame is safe at current levels of consumption. The work of the national experts and the AF have not led to EFSA issuing a different opinion or for the European Commission to propose to EU Member States there is a need for additional risk management measures on aspartame. Whilst there are anecdotal reports of adverse effects associated with aspartame consumption, these have not been reliably reproduced in controlled investigations. The Food Standards Agency has commissioned research to investigate these anecdotal reports and the A F has noted that it will look again at this issue when the results of that research are available.

" What scientific evidence do you have which confirms SFSA's contention that free methanol is safe to consume in regular daily doses irrespective of quantity"

The methanol released from aspartame is the same as that present naturally in food, released from pectin, produced endogenously or used industrially. It is the same chemical formula and structure and there is no chemical or biological precedent for assuming it will behave differently. The most important consideration is the dose consumed.

Within the body, a small proportion of the methanol is excreted unchanged in urine or breath, but most is broken down in a number of steps. Methanol becomes formaldehyde, then formate or formic acid (depending on pH) and finally carbon dioxide. The toxicity associated with methanol results from the accumulation of the breakdown product formate/formic acid when the reaction converting formate/formic acid to carbon dioxide is saturated for a sustained period. The toxicity occurs because formic acid binds to an enzyme within the mitochondria in cells and disrupts energy production and cell function. The specific visual damage is thought to occur because cells in retina and optic nerve have a rich blood supply and would be heavily exposed to formic acid and also have fewer mitochondria than other cells, and thus have lower reserves.

It has been estimated that 0.3 to 0. 6 g methanol/day is produced within the body from protein metabolism and that up to 1 g/day methanol may be consumed from food, particularly fruit and vegetables and their juices. The methanol released from aspartame (10% by weight) would provide a maximum of 0.24 g/day methanol if consumed at the Acceptable Daily Intake (ADI) of 40 mg/kg bw aspartame and therefore 4 mg/kg bw methanol– (240 mg/day in a 60 kg adult) of aspartame was consumed (though survey data suggest it may be much lower than this; for example, high level child consumers aged 1-4.5 years are exposed to 12 mg/kg bw aspartame from

diet soft drinks). The maximum permitted level of aspartame in soft drinks is 0.6 g/L, so that a maximum of 0.3 g methanol would be released from a 500 ml bottle and 0.2 g from a 330 ml can. Chronic consumption of diet soft drinks by 97.5%ile adult consumers would result in exposure to 0.45 mg aspartame/kg bw/day.

There are a number of studies available in which human volunteers were exposed to **pure methanol vapour** by inhalation at occupationally permitted levels (200 parts per million methanol over 8 hours, equivalent to 1.9 g methanol) or who have consumed small doses of methanol. These studies show that methanol concentrations increase in blood, and methanol and formate levels increase in urine, but blood formate concentration does not increase, that is, the methanol is being absorbed and converted to formate but that the formate is being readily converted to carbon dioxide or excreted and is not accumulating and therefore is not available to cause toxicity. Similar results are found in studies in which volunteers consumed high doses of aspartame (well above the ADI); a small increase in blood methanol and in urinary methanol and formate occurs, but there is no increase in blood formate, again, the formate is being readily converted to carbon dioxide and is not accumulating and therefore is not available to cause toxicity. In studies where the effects of aspartame doses close to the ADI were investigated, changes in blood methanol levels were not detected. No adverse effects were reported by the volunteers in the above studies.

The precise dose of methanol at which saturation of the conversion of formate/formic acid to carbon dioxide occurs and thus formate accumulates is unclear, and is dependent on the availability of a co-factor, folate. One research group has estimated the dose to be in the order of 210 mg/kg bodyweight or 12.6 g for a 60 kg adult, a dose which would be expected to cause toxicity on the basis of literature reports; this is 50 times higher than the methanol that would be released from aspartame at the level of the ADI

The lowest dose of methanol resulting in damage to vision is approximately 8 g (10 ml) and doses of 24 g (30 ml) methanol or more can be fatal.

The FSA has not suggested that free methanol is safe to consume regardless of quantity but has said that exposure to dietary levels of methanol would not be expected to result in adverse effects.

In summary, the concentrations of methanol present in food, including that released from aspartame would not be expected to result in the accumulation of formate and since the normal metabolic processes would not be overwhelmed, it would not be expected to cause toxicity.

“It is suggested by the petitioner that the current ADI for aspartame is 35 times higher than it should be because the toxicity of free methanol is not included – your comments please”

When the ADI for aspartame was established, it was known that the breakdown of aspartame resulted in the release of up to 10% methanol by weight; this was not thought to be relevant as comparable levels of methanol were present in foods, notably fruit juices; we believe that this is still the case. It should be noted that aspartame was tested in a range of studies in human volunteers and laboratory animals prior to approval, it would have been broken down by the body as described above, including the release of methanol, and any adverse effects detected and taken into account in the establishment of the ADI.

The ADI calculated by Mr McDonald is based on the 10% of the lowest level of methanol being reported to cause blindness then being divided by safety factors of 100 resulting in a value of 0.114 mg/kg body weight or 8 mg for a 70 kg adult, this is over the 30 times less than the amount of methanol (300 to 600 mg) produced by the body itself. Alternatively 8 mg methanol could be found in 100 ml of fresh orange juice (reported to contain 11-80 mg/L). Methanol becomes toxic when a specific reaction becomes saturated, ie a threshold is exceeded rather than through the gradual build up of toxic damage or metabolites, thus the application of safety factors in this way is not appropriate.

“The petitioner quotes the current Hull Pilot study as being “”a defining factor in the EFSA’s decision on the safety of aspartame”” could you explain please and what is the current progress of the study”

In July 2009 the Food Standards Agency funded a pilot double blind placebo crossover study which aims to determine the feasibility and statistical power required for an effective full scale study; the pilot aims to validate the proposed method, including whether the food product is fit for purpose, and will be used to confirm the robustness of the methodology for a future definitive clinical trial. So far over fifty percent of the required volunteers have been recruited to the study, which is ongoing. It is hoped the study team will report their findings during 2011.

The National Experts and the EFSA Advisory Forum are aware of the pilot study and have proposed that they await the results of the study. The results *will not* be seen as the “*defining factor in the EFSA’s decision on the safety of*

aspartame", they will simply add to the information already available in the draft National Experts report to be considered by the Advisory Forum.

I hope the above has addressed the issues raised here and should you require any clarification or any further information, please do not hesitate to contact me.

Yours sincerely

PROFESSOR CHARLES MILNE
Director, Scotland