

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

MAGNOLIA BARK EXTRACT

**Issue**

Members are invited to consider the response provided by Wrigley's, to their comments raised at the November 2009 meeting, and whether this provides sufficient information for the Committee to conclude its evaluation of this novel food application.

**Background**

1. At the November meeting, Members requested further information on an application for the authorisation of Magnolia bark supercritical carbon dioxide extract (MBSE) as a novel food ingredient for use in chewing gum and mints (ACNFP 95/2). The application was placed on the ACNFP website for a 21 day public consultation and any comments received will be tabled at the meeting.
2. A letter detailing the ACNFP's comments from the September meeting was sent to the applicant on 4 December (**Annex A**) and sought additional information on two points:
  - (i) data were requested to confirm the absence of protein - although the applicant had conducted Bradford assays, it was not possible to see what exactly had been tested and how. The Committee also questioned whether the Bradford assay is capable of the reported detection limit of 1 ppm. As this is a non-specific test, the Committee advised that a more precise method to detect proteins such as mass spectrometry would be more valuable.
  - (ii) toxicology – the Committee remained concerned about the gender-specific statistically significant increases in blood total bilirubin levels (TBBL) observed during the 90 day rodent study. Although it was acknowledged that these increases in TBBL were apparently not accompanied by other signs of liver toxicity, Members requested a copy of the original study report in order to be satisfied about the relevance of this finding.

The Committee noted the historical control and reference ranges of TBBL in various strains of the Sprague Dawley (SD) rat but did not regard these data to be directly relevant as they relate to different strains of SD rat, obtained at different times and from different laboratories. Data from the same SD strain, obtained at the same time and from the same laboratory, would be more meaningful.

3. Wrigley's responded to these comments on 11 January (**Annex B**). The Secretariat wishes to highlight the following points:

**(i) protein analysis**

4. The applicant has subsequently provided a generic explanation of the Bradford assay and explained that the assay is capable of the reported detection limit of 1 ppm based on the standard curve for the microassay (the standard curve for the microassay was made using bovine serum albumin at concentrations of 0, 19, 20, 30, 40, 50 µg/ml) (**Annex B**). The applicant has subsequently provided an additional response and states that the original laboratory report included an incorrect detection limit and the laboratory has re-issued the certificate of analysis which should replace the earlier version. The applicant clarifies that the detection limit for this assay should in fact be 10 µg/ml. This additional information is attached as (**Annex C**).

**(ii) toxicology**

5. The applicant has provided a copy of the report of the original 90 day rodent study (Confidential) for the Committee's review (**Annex D**), which provides inter-individual animal data. The applicant states that the report does indicate a statistically significant difference in TBBL for females compared to controls at all three treatment doses. However, given the minor nature of the change, the lack of any dose response, lack of effect in males and no indication of liver toxicity based on the remainder of the clinical chemistry data, liver weight values and results of histopathological examinations, the applicant suggests that the TBBL observations do not appear to be biologically relevant.
6. The applicant also states that it was informed by the study authors that the historical control range for TBBL in SD female rats in their laboratory is 0.61-1.15 µmol/L. The range of TBBL observed in female rodents administered MBSE was between 0.88 and 0.93 µmol/L which is below the normal upper range for the SD rat within the laboratory.
7. The Secretariat has drafted an initial opinion (**Annex E**) that summarises discussions to date for the Committee's review.

### **Committee Action required**

8. The Committee is asked whether the applicant's responses provide sufficient information and adequately address the questions raised at the November meeting.
9. If not, the Committee is asked to indicate what additional information would be required.
10. The Committee is also asked to review the text of the draft initial opinion with a view to formulating a conclusion as to the acceptability of this novel ingredient.

**Secretariat**

**February 2010**

### **Annexes attached**

- Annex A** Letter of 3 December 2009 to the applicant with the Committee's comments
- Annex B** Response from the applicant of 11 January 2010.
- Annex C** Additional response from the applicant on the Bradford assay.
- Annex D** 90 day rodent study report
- Annex E** Draft MBSE Initial Opinion



**ACNFP/96/2 Annex A**

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Letter of 3 December 2009 to the applicant with the Committee's comments

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Response from the applicant of 11 January 2010.

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Additional response from the applicant on the Bradford assay.

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**ACNFP/96/2 Annex D**

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90 day rodent study report.

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Draft MBSE Initial Opinion

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