COMMITTEE PAPER FOR DISCUSSION **ACNFP/128/03**

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

OLIGONOL®

Issue

The Committee last reviewed this application at the April 2016 meeting. Queries were raised in relation to the effectiveness of controls to exclude lychee nut from the Oligonol® starting material in the production process, to rule out the potential for allergenicity. The applicant has now provided further protein analysis of the product to support their suggestion that the lychee nut is not present in Oligonol®. The Committee is asked to consider whether it recommends authorisation of the product.

Background

1. This application from the Amino Up Chemical Company Ltd is for authorisation of Oligonol® (produced from lychee fruit and green tea extracts) as a novel food ingredient under 258/97. The novel ingredient is proposed to be added to a range of foods from non-alcoholic beverages to confectionary.
2. At its April 2016 meeting, the Committee continued to seek evidence to demonstrate either that the production process effectively excluded lychee nut from the lychee starting material or that lychee nut proteins were not present in the Oligonol® final product. The applicant was encouraged to either provide further evidence on this point or undertake an appropriate allergenicity risk assessment.
3. A letter to the applicant communicating these points is provided in **Annex A**. The applicant has now provided a response to the Committee's questions (**Annex B)**. The Secretariat has also provided a summary of the issues considered by the Committee on Oligonol® to date in **Annex C.** A draft opinion is provided in **Annex D** for consideration by the Committee if considered appropriate.

Production Process

4. The Committee had raised concerns that the lychee extract starting material could contain lychee nut and therefore were keen to rule out any potential allergenicity risk. The applicant had previously provided details of the production process for the lychee extract and the steps taken to exclude lychee nut from the starting material. They have received confirmation from the producer of the extract that the lychee extract does not contain lychee nut. The Committee

sought further information on how this was achieved or evidence that these controls are effective and that lychee nut protein is not present in Oligonol®.

5. To verify the effectiveness of the controls the applicant has undertaken a further protein analyses which they consider confirm the lychee nut is not present. The applicant has undertaken a LC-MS analysis of the flesh of lychee, lychee nut and Oligonol® and compared the profiles generated.
6. In their response the applicant details the extraction method used and the trypsin digestion conditions. Analysis has been undertaken for three batches of Oligonol®. The applicant suggests there are characteristic peaks seen in the nut that do not appear in the flesh or Oligonol® profiles. On this basis they suggest that the lychee nut proteins are not present in Oligonol®.

Committee Action Sought

7. The Committee is asked whether the response from the applicant is sufficient to address its concerns in regard to the issues discussed in April 2016.
8. If so, the Committee is asked, whether it is content to recommend approval of Oligonol® produced by Amino Up Chemical Company. A draft opinion is provided for consideration at **Annex D**.
9. If not, the Committee is asked to indicate what further data is required and the feedback that should be given to the applicant.

Secretariat
April 2017

Annexes attached

Annex A – Letter sent to applicant following April 2016 meeting

Annex B – Applicant's response

Annex C - Summary of concerns raised by the Committee with Oligonol®

Annex D – Draft opinion on Oligonol®

Annex C

Summary of concerns to date on Oligonol® and the information provided by the applicant in response.

Concern raised	Evidence presented	Outcome based on Committee discussion
Specifications The Committee requested further information on the level of catechins in the product and sought characterisation of the unaccounted for polyphenols in Oligonol®.	The applicant provided a further explanation of the catechin levels and how these were calculated. The applicant highlighted the technical challenges of further characterising the remaining polyphenols.	The Committee was content that the potential concern on the catechin content of the product had been considered. The explanation of the difficulties of further characterising the polyphenols was noted. It was considered possible to characterise these further but was not felt to be essential for the risk assessment.
Analytical data Concerns were raised with the presentation of the data. Three batches of the pesticide analyses were requested along with information on whether these were compliant with EU pesticide residue requirements.	The applicant provided translation of the relevant analytical certificates to allow assessment. The applicant provided further batches of Oligonol® and the two starting materials. The applicant commented that they have included pesticide residues as part of their control process for the product.	The Committee accepted the translated certificates and felt these were adequate for assessment. The Committee was reassured by the information provided on pesticide residues at the April 2016 meeting.
Production process The Committee requested further information on the columns used in the purification step and how residues from the column were minimised. In light of concerns on pesticide residues and the potential presence of lychee nut in the starting material, production process diagrams and updated protocol to ensure these controls would be present in commercial operation were requested.	The applicant provided further information on the columns used in the purification step. Information was also provided on a pre-rinse step recommended by the column manufacturer to minimise potential residues. Revised documents outlining the production process used in production were provided as requested. This was supported by a flow diagram of the process.	The Committee was reassured that the potential for residues from the columns used in the production process had been considered and steps taken to mitigate the risk through use of a suitable quality of column and a methanol prewash step. The Committee welcomed the further information to ensure the risks identified would be managed during production.
Toxicology Members asked a number of questions in relation to the toxicology studies. These		

included: • Requests for full reports of some of the studies undertaken on Oligonol including the literature review relating to green tea associated toxicity (liver effects). • Follow up on particular outcomes of some of the studies e.g. the 90 day animal study (Leuschner et al) and whether the changes in grip strength were a concern. • Requesting further information on the human study by Walshe et al • Members requested further reasoning for dismissing the observed effects of increased polyploidy in the chromosome aberration test. • Clarification of the data generated by the Oligonol like material and its role in supporting the application.	The applicant provided the full text of the further studies and literature review requested. Clarification was given on the queries on individual toxicological studies including the NOAEL selection. On the Leuschner study further information was provided on why the applicant considered the statistical analysis was appropriate and the findings not considered adverse. The applicant explained the Walshe study was intended as supporting information and had not been published. The applicant suggested the Chinese Hamster Lung cell line used for the test is known to have given false positives with similar substances. As the chromosome aberration assay did not detect aberrations at the highest concentrations and no genotoxic activity was seen in an in-vivo mouse micronucleus test, the applicant concluded that genotoxicity is not a concern. It was clarified that the Oligonol like material was very similar to Oligonol® and the studies on this material were intended to support the information on Oligonol® in the dossier.	The Committee accepted the detailed explanations on the individual toxicological studies and therefore that the NOAEL identified could be used in identifying the dose to be used in products entering the EU market. The Committee were content that the statistically significant findings in relation to slight movements and increased activity in the Leuschner study are not of biological relevance. The Committee noted the human study and considered this as part of the wider safety assessment of the product. The applicant's explanation on the genotoxicity assessment was accepted. The Committee noted the differences between Oligonol® and the Oligonol like product and took account of this when considering their assessment of the toxicological package as a whole.
Allergenicity Members requested further details relating to the production of lychee extract, including information relating to whether the extract is prepared from the entire lychee fruit, including the nut component	The applicant has provided a number of responses to explain how lychee nut is excluded during the production of the lychee extract. This has been verified by the supplier and clarified in production documents. To demonstrate that proteins from the lychee nut are not present in Oligonol® further protein analyses have been developed and are detailed in the main body of the paper.	The Committee was reassured by the process when the starting material had arrived at the production plant. The Committee noted the production material was extracted with ethanol and considered this would exclude most of the allergenic material which may have been present. Further information was

		requested to confirm that the lychee nut protein is not found in Oligonol® - Consideration ongoing