COMMITTEE PAPER FOR DISCUSSION **ACNFP/129/01**

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

TONGKAT ALI ROOT EXTRACT: FURTHER RESPONSE FROM THE APPLICANT

Issue

At the September 2016 meeting the Committee reviewed the dossier submitted in support of the application for authorisation of Tongkat Ali Root Extract under the Novel Foods Regulation (EC) 258/97. The Committee requested further information from the applicant which was reviewed at the February 2017 meeting, but this was considered inadequate and a more specific request for data was made to the applicant. The additional data has now been received and the Committee is asked whether the available data now provides an adequate basis for a risk assessment, and if it recommends authorisation of this novel ingredient.

Background

1. At the February meeting and due to the lack of new data in the applicant's response, Members reiterated the necessity of providing the data stipulated and emphasised the need for further detailed information on the novel ingredient (NI). These were outlined in a letter to the applicant (**Annex A**) as follows:

    a) Composition

    b) Targeting of the NI

    c) Toxicology

    d) General comments (including sustainability and legibility of documents).

2. A summary of each comment/request from the Committee and the response from the applicant are given below. Biotropics Malaysia's response is attached to this paper in three different parts as **Annex B**, **Annex B Attachment 1** and **Annex B Attachment 2**.

Composition

3. Regarding the specification of the novel food, at the April meeting the Committee reiterated that there needs to be appropriate characterisation of the NI in terms of a detailed analysis to identify individual components using appropriate methods. This included the analysis of the protein, glycosaponin and carbohydrate (polysaccharide) components of Tongkat Ali. Analysis of the protein and

glycosaponin constituents was felt to be of particular importance for estimating the potential allergenicity and physiological activity of the NI.

Proteins

4. In their response the applicant has provided no new data on analysis of the protein component of the NI, but has reset the specification of Tongkat Ali standardised to a protein content as measured by the Kjeldahl method of between 7 and 15%. The applicant has also tested further batches of the NI using this method and provides the independent laboratory results in **Attachment 1 of Annex B** of this response.
5. The applicant has also had Tongkat Ali analysed for the standard allergens associated with food and covered under the mandatory labelling requirements of Regulation (EU) No 1169/2011. The results of these analyses can be found in **Attachment 2 of Annex B** a plant allergens screen by ELISA and DNA PCR Analysis for Tongkat Ali Standardized Root Extract (Batch No : P17/RE005). Analysis by ELISA indicates the absence of Gluten (Gliadin x 2) and Soya according to the applicant and the PCR screen was negative for the following known allergenic species:

   • Almond (Prunus dulcis)

   • Brazil Nut (Bertholletiaexcelsa)

   • Cashew Nut (Anacardiumoccidentale)

   • Hazelnut (Corylus avellana)

   • Macadamia Nut (Macadamia integrifolia)

   • Peanut (Arachis hypogea)

   • Pecan Nut (Caryaillinoinensis)

   • Pistachio Nut (Pistaciavera)

   • Walnut (Juglans regia)

   • Mustard (Brassica nigra)

   • Celery (Apium graveolens)

   • Lupin (Lupinus luteus)

6. The applicant has also proposed adding an additional labelling precaution derived from the same Regulation 1169/2011 (Article 21 point 1 (b)) as follows:
7. "*Tongkat Ali shall be emphasised through a typeset that clearly distinguishes it from the rest of the list of ingredients, for example by means of the font, style or background colour."*
8. Where no list of ingredients exists the applicant proposes that the word (phrase) 'contains' Tongkat Ali will be clearly marked on the label (or equivalent wording).

The Secretariat has noted the proposal and is also discussing this with our Food Allergy Policy Team as to whether this would be permitted under Regulation 1169/2011 EU.

9. The applicant claims that this will allow easy reporting and identification if a new allergenicity has been elicited and provide a basis for further patient investigations to see if it is the cause. Further information on established reporting procedures are summarised in **Annex B**.

Glycosaponins

10. The Committee had already expressed concerns that the application contained no substantial data on the glycosaponin component, which makes up 40-60% of the material in the NI. The Committee had requested that at least an HLPC analysis of the glycosaponins present in the NI be carried out, but the applicant argued that there are currently no suitable glycosaponin standards for the specific glycosaponin component in the Tongkat Ali extract to perform accurate HPLC analyses. This argument is used again, repeating that such information will be presented as soon it is available. The Secretariat will continue to liaise with the applicant on this point.

11. The applicant has however proposed that the one HPLC chromatogram available using the only known glycosaponin standards, be incorporated into the specification for the NI. The HPLC chromatogram is reproduced in Figure 1 of **Annex B** and replicates from different batches shown in Figures 2a-c.

Targeting of the novel food

12. The Committee were of the opinion that it is insufficient to refer to its traditional use in Malaysia over long periods as evidence of the safety of the NI for EU consumers. It was noted that its use in Malaysia was not the same as that proposed for the EU market, resulting in very different consumption levels for different population groups.

13. In response the Applicant has proposed removal of certain categories of foods from those that will contain the NI; notably cereal bars and confectionary. This leaves only tea and coffee based drinks, as well as sports and energy based drinks (See **Annex B**: Table IX.A-1 (revised)). The Applicant is willing to provide revised exposure estimates if the Committee is happy with this approach

Toxicology

14. Since the previous review of Tongkat Ali at the February meeting, the Committee has had the chance to review the raw data associated with the one year toxicology study carried out using Tongkat Ali.

15. Comments were collated from Committee members and combined by the Secretariat into an overall Committee view, which is attached as **Annex C** to this paper. Given the number of comments and questions from the Committee the Applicant has decided to take the time necessary to provide a comprehensive response that it will submit for consideration at the September meeting.

General comments

16. While assessment of the sustainability of a novel food is not a criterion for authorisation under the novel food regulation, concerns had been raised by the Committee on the consistency of composition of the source material for the novel ingredient. The Committee had noted that Tongkat Ali was currently obtained from the wild plant which may not be sustainable if production of the NI increases and new sources of material are required.

17. The Applicant has not provided any further reassurances regarding the sustainability of the supply of material necessary to manufacture TA to the required specification, but has provided details of the three cultivars it currently sources for the production of the NI and the HPLC trace of the eurycomanone fingerprint which it claims is characteristic of these cultivars (**Annex B** Fig. 3).

18. It was noted by the Committee that in some of the documents the confidentiality labelling (redaction) made it difficult to see or make sense of the information presented and the applicant was asked to address this.

19. The Applicant was unclear as to which specific documents the Committee was referring to. In relation to **Annex 1** of the response to the Committee of 4th January 2017, “Chemo profiling of Eurycoma longifolia extracts – DEREPLICATION and comparative analysis – Intermed Discovery GmbH dated 21/5/2008”, the Applicant has redacted the other tested samples as they do not relate to the NI (either they were prepared/extracted differently, or were unextracted etc.).

20. The Applicant states that didn’t want to confuse the Committee with unrelated information or prompt them to make comparisons with other preparations not related to the NI. The applicant can provide the full un-redacted report if the Committee wishes but advises it will not provide any new relevant data.

Committee action sought

21. The Committee is asked to consider whether the data now available are adequate to determine whether the NI complies with the criteria for acceptance under the

novel food regulation {subject to a satisfactory response concerning the one year toxicology study), namely:

- It does not present a danger to the consumer
- It does not mislead the consumer
- It is not nutritionally disadvantageous compared with foods which it might replace.

22. If so, the Committee is asked whether it is content to recommend approval for the NI to be used in the proposed food products.
23. If not, the Committee is invited to identify what further data or information should be provided.

Secretariat
June 2017

Annexes

Annex A: Letter to the Applicant Tongkat Ali 7Apr17 ACNFP Comments

Annex B: Tongkat Ali Root Extract EU Novel Food Response to ACNFP follow-up questions

Annex B: Attachment 1- Protein analysis of Tongkat Ali

Annex B: Attachment 2- Analysis of Tongkat Ali for the presence of known allergens

Annex C: Summary of the ACNFP comments on the one year toxicology study