SUBSTANTIAL EQUIVALENCE OPINION

L-Alanyl-L-Glutamine

The Food Safety Authority of Ireland (FSAI) received an application in October 2016 from Kyowa Hakko Bio Co., Ltd. of Japan for an opinion on the substantial equivalence of its dipeptide, L-Alanyl-L-Glutamine to the same ingredient already on the EU market. The existing dipeptide is chemically synthesised while the novel counterpart is produced by fermentation with a genetically modified (GM) strain of *Escherichia coli* (AGW1) as a processing aid and has a purity of not less than 98%. This bacterial strain is deposited as NITE SD 00289 at the Biological Resource Centre (NBRC) of the Japanese National Institute of Technology and Evaluation (http://www.nite.go.jp).

The applicant declares that the existing ingredient is marketed in food supplements and Foods for Specific Groups (Regulation (EU) No 609/2013) excluding foods for infants and young children. The ingredient is considered to be novel and fall within the category of "*foods and food ingredients consisting of or isolated from micro-organisms, fungi or algae*" as set out in *Article 1.2(d)* of the novel food Regulation (EC) No. 258/97.

Composition

The novel ingredient is a white to off white crystalline powder with a purity specification of 98-102% compared to the existing counterpart at ≥90%. It is produced by fermentation involving a genetically modified (GM) strain of *E. coli* (AGW1), while the existing comparator is chemically synthesised. The novel ingredient is secreted into the fermentation medium and then adsorbed on to a resin column. Following elution from the resin, it is concentrated by evapouration and further processed by crystallisation to the final product. Manufacture of the novel ingredient results in a highly purified and well characterised ingredient that is compositionally comparable to the authorised counterpart. Due to the extensive isolation and purification process, DNA or protein from the GM *E. coli* is not detected in the final ingredient and therefore the fermenting bacteria can be classified as a processing aid and outside the scope of GM food labelling requirements. The applicant demonstrates that the novel ingredient is stable for at least 6 months under accelerated conditions (40 ± 2°C and 75 ± 5 % relative humidity) and at least 12 months in real-time (ambient) conditions.

Nutritional Value and Metabolism

The composition of the novel ingredient and its chemically synthesised counterpart are very similar and so the nutritional value and metabolism of the novel ingredient would not be expected to differ.

Intended Uses

The applicant intends placing the novel ingredient on the EU market in the same food categories and at the same maximum use levels as the authorised comparator. This includes food supplements, "Foods for Specific Groups" (excluding those intended for infants and young children) and foods specifically marketed to sports people. Food supplements will be marketed in accordance with Directive 2002/46/EC, Foods for Specific Groups will be marketed in accordance with Regulation (EU) No 609/2013 and sports drinks will be marketed in accordance with Regulation (EC) No 1925/2006.

Level of Undesirable Substances

Batch analyses demonstrate that heavy metals including lead, cadmium, mercury and arsenic comply with specifications and are within regulatory limits. Survival of the fermenting *E. coli* is not expected due to the processing and purification processes. In addition, analytical results have been provided by the applicant demonstrating the absence of *E. coli* in several batches.

Conclusions

The FSAI is satisfied from the information provided by the applicant that L-Alanyl-L-Glutamine produced by Kyowa Hakko Bio Co., Ltd. is substantially equivalent to synthetic L-Alanyl-L-Glutamine already on the EU market. The novel ingredient will be subject to the same conditions of general and specific legislation governing the marketing and use of the existing ingredient.