SUBSTANTIAL EQUIVALENCE OPINION

L-Alanyl-L-Glutamine

The Food Safety Authority of Ireland (FSAI) received an application in January 2012 from Kyowa Hakko Europe GmbH 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 Kyowa counterpart is produced by bacterial fermentation which is purified from the growth media to a purity of greater than 98%. The applicant claims that the existing ingredient is marketed in food supplements and foods for particular nutritional uses (PARNUTS – specifically FSMPs), excluding foods for infants and young children. The Kyowa ingredient is intended to compete for market share in the same food categories as the existing ingredient which should not result in an increase in the current consumption levels. The applicant considers the ingredient 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

In a direct compositional comparison, the only difference of note is the specified purity of the novel ingredient (>98%) compared to the existing ingredient (>90%).

Manufacture of the novel ingredient

The novel ingredient is produced in a fermentation process while the existing comparator is chemically synthesised. The fermentation process utilises a genetically modified (GM) strain of *E. coli* (K-12) to which has been transferred genes from *Bacillus subtilis* that enable it to produce L-alanyl-L-glutamine from free alanine and glutamine. However, the authorisation and labelling of the novel ingredient according to GM food and feed Regulation EC No. 1829/2003 is not required as it is secreted

from the bacteria during the fermentation and subsequently isolated and purified from the growth media. 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 processing aids which are outside the scope of GM food and feed legislation.

Nutritional Value and Metabolism

L-alanyl-L-glutamine is the primary constituent in both the novel and existing ingredients. The overall composition of both ingredients is very similar and therefore the nutritional value and metabolism of the novel ingredient can also be assumed to be very similar. The applicant claims that real-time and accelerated stability studies demonstrate that the novel ingredient is stable for at least 12 months (under ambient conditions) and six months respectively. The stability of the novel ingredient was also examined under various pH conditions, simulating those in different beverage formulations.

Intended Uses

The applicant intends placing the novel ingredient on the EU market in the same food categories through which the existing ingredient is marketed, which includes food supplements and Foods for Particular Nutritional Purposes such as Foods for Special Medical Purposes (FSMPs - excluding foods for infants and young children) and those covered under Article 11 of Directive 2009/39/EC of the European Parliament and of the Council of 6 May 2009 on foodstuffs intended for particular nutritional uses (recast) (formerly Article 9 of the older version of this Directive).

Level of Undesirable Substances

The applicant provides analytical data on heavy metals covering lead and arsenic in several product batches. The survival of the fermenting *E. coli* is not expected due to the extensive processing and purification process. This is borne out by batch analysis where *E. coli* is not detected, while the overall microbiological profile is satisfactory.

Conclusions

The FSAI is satisfied from the information provided by the applicant that L-alanyl-L-glutamine produced by Kyowa is substantially equivalent to L-alanyl-L-glutamine

already on the EU market in food supplements and FSMPs. The Kyowa product will be subject to the same conditions of general and specific legislation governing the marketing and use of the existing ingredient.