SUBSTANTIAL EQUIVALENCE OPINION

Citicoline

The Food Safety Authority of Ireland (FSAI) received an application in March of 2017 from Kyowa Hakko Bio Co., Ltd. of Japan for an opinion on the substantial equivalence of citicoline. The novel ingredient is compared with the same ingredient already authorised in 2014 to Kyowa Hakko Europe GmbH by Commission Implementing Decision 2014/423/EU.

The novel citicoline is produced by fermentation using a genetically modified strain of *E. coli* (BCT19/p40k) which has been deposited in the culture collection of the Biological Resource Centre (NBRC) of the Japanese National Institute of Technology and Evaluation (NITE SD 00294). The novel citicoline is recovered from the fermentation medium and purified using standard processes to yield a highly purified product. The novel ingredient is manufactured in accordance with Good Manufacturing Practice (GMP) using food-grade materials and quality controlled fermentation and purification processes. The applicant intends to market the novel citicoline for use in food supplements and in dietary foods for special medical purposes in accordance with *Article 1* of Commission Implementing Decision 2014/423/EU. The applicant contends that in view of the close compositional similarity of the novel and existing ingredients, the stability of the existing product established at 48 months as a minimum can also be taken as representative of the novel citicoline.

The applicant considers the ingredient to be novel and fall within the category of *"food and food ingredients consisting of or isolated from microorganisms, fungi, or algae"* as set out in *Article 1.2 (d)* of the novel food Regulation (EC) No. 258/97.

Composition

The novel citicoline is identical to the authorised comparator in terms of the parameters listed in the Annex to Commission Implementing Decision 2014/423/EU. It is a white crystalline powder composed of cytosine, ribose, pyrophosphate and choline with the results of batch analyses demonstrating production consistency. Data provided by the applicant on stability confirms that citicoline is stable for at least 48 months.

Parameter	Novel citicoline	*Decision 2014/423/EU*
Assay value (% dry matter)	≥98	≥98
Loss on drying (100˚C for 4 hr)	≤5.0	≤5.0
Ammonium (%)	≤0.05	≤0.05
Total heavy metals - as Pb (ppm)	≤10	≤10
Arsenic (ppm)	≤2.0	≤2.0
Free phosphoric acids (%)	≤0.1	≤0.1
5'-Cytidylic acid (%)	≤1.0	≤1.0

Nutritional value and metabolism

Considering that the specifications for the novel citicoline are identical to the existing comparator, no differences in nutritional value or metabolism would be expected.

Intended uses

The applicant intends to place the novel citicoline on the EU market in the same food categories and at the same use levels as the authorised comparator and which are set out in *Article 1* of Commission Implementing Decision 2014/423/EU. This includes food supplements at a maximum dose of 500mg/day and dietary foods for special medical purposes with a maximum dose of 250mg/serving and with a maximum daily consumption of 1,000mg from these types of foods. It will not be used in foods intended to be consumed by children.

Level of undesirable substances

Batch analysis results demonstrate that residues of methanol and ethanol, the only solvents used in the production of the novel ingredient are within the manufacturers' specifications and compliant with legal limits. Analytical results for heavy metals such as lead and arsenic were within specification, while results for possible microbial contaminants such as yeast and moulds were satisfactory and *E. coli* not detected.

Conclusion

The FSAI is satisfied from the information provided by Kyowa Hakko Bio Co. Ltd. that the novel citicoline is substantially equivalent to the authorised citicoline comparator. The designation of the novel ingredient in foods containing it will be "citicoline" in accordance with *Article 2* of Commission Implementing Decision 2014/423/EU.