



2024/1037

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COMMISSION IMPLEMENTING REGULATION (EU) 2024/1037

of 9 April 2024

authorising the placing on the market of monosodium salt of L-5-methyltetrahydrofolic acid as a novel food and amending Implementing Regulation (EU) 2017/2470

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001 ⁽¹⁾, and in particular Article 12(1) thereof,

Whereas:

- (1) Regulation (EU) 2015/2283 provides that only novel foods authorised and included in the Union list of novel foods may be placed on the market within the Union.
- (2) Pursuant to Article 8 of Regulation (EU) 2015/2283, Commission Implementing Regulation (EU) 2017/2470 ⁽²⁾ has established a Union list of novel foods.
- (3) On 12 November 2020, the company Merck & Cie KmG ('the applicant') submitted an application for an authorisation to the Commission in accordance with Article 10(1) of Regulation (EU) 2015/2283 to place monosodium salt of L-5-methyltetrahydrofolic acid on the Union market as a novel food. The applicant requested for the novel food to be used in food supplements as defined in Directive 2002/46/EC of the European Parliament and of the Council ⁽³⁾, food intended for infants and young children (infant formula and follow-on formula; processed cereal-based food and baby food), food for special medical purposes and total diet replacement for weight control as defined in Regulation (EU) No 609/2013 of the European Parliament and of the Council ⁽⁴⁾, and fortified foods as defined in Regulation (EC) No 1925/2006 of the European Parliament and of the Council ⁽⁵⁾. Subsequently, on 13 February 2024, the applicant modified the initial request in the application on the use of monosodium salt of L-5-methyltetrahydrofolic acid in food supplements to exclude infants and children under three years of age.

⁽¹⁾ OJ L 327, 11.12.2015, p. 1, ELI: <http://data.europa.eu/eli/reg/2015/2283/oj>.

⁽²⁾ Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods (OJ L 351, 30.12.2017, p. 72, ELI: http://data.europa.eu/eli/reg_impl/2017/2470/oj).

⁽³⁾ Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements (OJ L 183, 12.7.2002, p. 51, ELI: <http://data.europa.eu/eli/dir/2002/46/oj>).

⁽⁴⁾ Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009 (OJ L 181, 29.6.2013, p. 35, ELI: <http://data.europa.eu/eli/reg/2013/609/2023-03-21>).

⁽⁵⁾ Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods (OJ L 404, 30.12.2006, p. 26, ELI: <http://data.europa.eu/eli/reg/2006/1925/2023-06-22>).

- (4) On 12 November 2020, the applicant also made a request to the Commission for the protection of the following proprietary data: analytical reports and methods of validation ⁽⁶⁾ regarding the novel food identification, characterisation ⁽⁷⁾, solubility ⁽⁸⁾, particle size and distribution ⁽⁹⁾, a dissolution study ⁽¹⁰⁾, stability studies ⁽¹¹⁾, a study on bioavailability ⁽¹²⁾, repeated-dose toxicity and genotoxicity studies ⁽¹³⁾ and an HACCP plan ⁽¹⁴⁾.
- (5) On 28 June 2021, the Commission requested the European Food Safety Authority ('the Authority') to carry out an assessment of monosodium salt of L-5-methyltetrahydrofolic acid as a novel food. Furthermore, the Commission considered that the novel food, monosodium salt of L-5-methyltetrahydrofolic acid, should be considered as a source of folate in the context of Directive 2002/46/EC, Regulation (EU) No 609/2013 and Regulation (EC) No 1925/2006. Therefore, the Commission requested the Authority to evaluate, following the outcome of the novel food assessment, the safety and bioavailability of the novel food when added for nutritional purposes as a source of folate to food supplements, food intended for infants and young children (infant formula and follow-on formula; processed cereal-based food and baby food), food for special medical purposes, total diet replacement for weight control, fortified foods and food for the general population.
- (6) On 26 October 2023, the Authority adopted its scientific opinion on the 'Safety of monosodium salt of L-5-methyltetrahydrofolic acid as a novel food pursuant to Regulation (EU) 2015/2283 and the bioavailability of folate from this source in the context of Directive 2002/46/EC, Regulation (EU) No 609/2013 and Regulation (EC) No 1925/2006' ⁽¹⁵⁾ in accordance with Article 11 of Regulation (EU) 2015/2283.
- (7) In its scientific opinion, the Authority concluded that the novel food, monosodium salt of L-5-methyltetrahydrofolic acid, is safe under the applicant's proposed conditions of use, as long as the combined intake of the novel food and other sources of folate under their authorised conditions of use is below the tolerable upper intake levels (UL) established for the different age groups of the general population. The Authority also considers that the novel food is a source from which folate is bioavailable. Therefore, that scientific opinion gives sufficient grounds to establish that monosodium salt of L-5-methyltetrahydrofolic acid, when used under the proposed conditions of use fulfils the conditions for its placing on the market in accordance with Article 12(1) of Regulation (EU) 2015/2283.

⁽⁶⁾ Arcofolin(R) Methods_V4; Method of analysis – updated report. Annex 4.1 In-house sodium assay validation; Certificates of analysis – HEM – Analytical data sheets on HEM; FIO_B-08-35-331 Quantitative SEM Assessment Quantitative assessment of Arcofolin® using SEM and BET analysis; HPLC Method MTHFDP_A-08-27-140; HPLC analysis for determining the content of 5-MeTHFS and its byproducts/degradation products in food supplements; 13_B-08-35-318 Evaluation on Esters_V02 Evaluation of Arcofolin® for ethanol mono- and di-esters, Document number B-08-35-318; B-08-35-322 Residual formaldehyde; Determination of formaldehyde.

⁽⁷⁾ 2_B-08-35-314 Id by CHNO Arcofolin® – Confirmation of identity by CHNO elemental analysis, Document number B-08-35-314; 2_I_FIO_B-08-35-313 – HPLC-UV-MS Arcofolin® – Confirmation of identity by HPLC-UV, Document number B-08-35-313; FIO_B-08-35-330 MS fragment pattern Mass spectrometry analysis of Arcofolin®; 2_I_FIO_E-08-35-314.A Ext Report CHNO External report CHNO, Document number E-08-35 314.A.

⁽⁸⁾ 3_B-08-35-311 Sol water pH 2 Solubility of Arcofolin® vs Metafolin® in water and at pH 2, Document number B-08-35-311; 15_M_FIO_B-08-35-316 Sol Arcofolin(R) Ethanol Solubility of Arcofolin® in ethanol, Document number B-08-35-311.

⁽⁹⁾ 2_I_FIO_B-08-35-315 – Optical rotation Arcofolin® – Determination of optical rotation, Document number B-08-35-315.

⁽¹⁰⁾ B-08-35-351 Dissolution studies of Arcofolin®; Dissolution studies of Arcofolin_V02 – Dissolution studies of Arcofolin® – updated report; Document No B-08-35-351

⁽¹¹⁾ Annex 4.4 Arcofolin stability study; 17_Stab_FIO_B-08-32-223 Stab Arcofolin BP Stability of Arcofolin® bulk powder, Document number B-08-32-223; Stability of Arcofolin(R) in powdered infant formula – B-08-32-362 Stability of Arcofolin(R) in powdered infant formula_V03_CONFIDENTIAL; Stability of Arcofolin(R) in spring water – B-08-32-382 Stability of Arcofolin(R) in spring water_V02_CONFIDENTIAL; Stability of Arcofolin® in sports nutrition – B-08-32-385 Stability of Arcofolin® in sports nutrition_V02_CONFIDENTIAL; 386 Stability of Arcofolin® in a B-Vitamin solution – B-08-32-386 Stability of Arcofolin® in a B-Vitamin solution_V02_CONFIDENTIAL; Stability of Arcofolin® in reconstituted infant formula prior to use B-08-32-397 Stability of Arcofolin® in reconstituted infant formula prior to use_V01_CONFIDENTIAL; Stability of Arcofolin® during breadmaking – B-08-32-399 Stability of Arcofolin® during breadmaking_V01_CONFIDENTIAL.

⁽¹²⁾ Menzel, D. 2019 Bioavailability study to compare (6S)-5-MethylTHF-Na (folate salt) with folic acid: a randomized, double-blind cross-over study in healthy subjects. 2019 Oct (unpublished).

⁽¹³⁾ Annex 4.7 OECD 408 with extended parameters from OECD 407 (study with Metafolin) – RCC Study Number 758316; Annex 4.5 OECD 471 – Bacterial reverse mutation test – Study Report 18-DA0269-0 (2018); Annex 4.6 OECD 473 – Chromosomal aberration study – Study Report 18-DA0271-0 (2019); Annex 4.12 OECD 487 – Micronucleus study in human lymphocytes (Study Number: 2117200).

⁽¹⁴⁾ B-13-11-143 HACCP Arcofolin (R)_V01_EN HACCP Arcofolin®, Document number B-13-11-143 Arcofolin(R) Methods_V3 15. Methods: Annex 2.1 and CoAs.

⁽¹⁵⁾ EFSA Journal, 2023;21:e8417.

- (8) In its scientific opinion, the Authority also noted that its conclusion on the safety of the novel food was based on the analytical reports and methods of validation regarding the novel food identification, characterisation, solubility, particle size and distribution, the dissolution study, the stability studies, the study on bioavailability, the repeated-dose toxicity and the genotoxicity studies and the HACCP plan, without which it could not have assessed the novel food and reached its conclusion.
- (9) The Commission requested the applicant to further clarify the justification provided with regard to its proprietary claim over those data and studies and to clarify their claim to an exclusive right of reference to them in accordance with Article 26(2)(b) of Regulation (EU) 2015/2283.
- (10) The applicant declared that it held proprietary and exclusive rights of reference to the analytical reports and methods validation regarding the novel food identification, characterisation, solubility, particle size and distribution, the dissolution study, the stability studies, the study on bioavailability, the repeated-dose toxicity and the genotoxicity studies and the HACCP plan, at the time it submitted the application, and that third parties cannot lawfully access, use or refer to those data.
- (11) The Commission assessed all the information provided by the applicant and considered that it has sufficiently substantiated the fulfilment of the requirements laid down in Article 26(2) of Regulation (EU) 2015/2283. Therefore, the analytical reports and methods validation regarding the novel food identification, characterisation, solubility, particle size and distribution, the dissolution study, the stability studies, the study on bioavailability, the repeated-dose toxicity and genotoxicity studies and the HACCP plan should be protected in accordance with Article 27(1) of Regulation (EU) 2015/2283. Accordingly, only the applicant should be authorised to place monosodium salt of L-5-methyltetrahydrofolic acid on the market within the Union during a period of five years from the entry into force of this Regulation.
- (12) However, restricting the authorisation of monosodium salt of L-5-methyltetrahydrofolic acid and the reference to the data contained in the applicant's file for their sole use does not prevent subsequent applicants from applying for an authorisation to place on the market the same novel food provided that their application is based on legally obtained information supporting such an authorisation.
- (13) It is appropriate that the inclusion of monosodium salt of L-5-methyltetrahydrofolic acid as a novel food in the Union list of novel foods contains the information referred to in Article 9(3) of Regulation (EU) 2015/2283.
- (14) Monosodium salt of L-5-methyltetrahydrofolic acid should be included in the Union list of novel foods set out in Implementing Regulation (EU) 2017/2470. The Annex to Implementing Regulation (EU) 2017/2470 should therefore be amended accordingly.
- (15) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

1. Monosodium salt of L-5-methyltetrahydrofolic acid is authorised to be placed on the market within the Union.

Monosodium salt of L-5-methyltetrahydrofolic acid shall be included in the Union list of novel foods set out in Implementing Regulation (EU) 2017/2470.

2. The Annex to Implementing Regulation (EU) 2017/2470 is amended in accordance with the Annex to this Regulation.

Article 2

Only the company Merck & Cie KmG ⁽¹⁶⁾ is authorised to place on the market within the Union the novel food referred to in Article 1, for a period of 5 years from 30 April 2024, unless a subsequent applicant obtains an authorisation for that novel food without reference to the scientific data protected pursuant to Article 3 or with the agreement of Merck & Cie KmG.

⁽¹⁶⁾ Im Laternenacker 5, 8200 Schaffhausen, Switzerland.

Article 3

The scientific data contained in the application file and fulfilling the conditions laid down in Article 26(2) of Regulation (EU) 2015/2283 shall not be used for the benefit of a subsequent applicant for a period of 5 years from the date of entry into force of this Regulation without the agreement of Merck & Cie KmG.

Article 4

This Regulation shall enter into force on the twentieth day following that of its publication in *the Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 9 April 2024.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

The Annex to Implementing Regulation (EU) 2017/2470 is amended as follows:
(1) in Table 1 (Authorised novel foods), the following entry is inserted:

Authorised novel food	Conditions under which the novel food may be used		Additional specific labelling requirements	Other requirements	Data protection
Monosodium salt of L-5-methyltetrahydrofolic acid	Specified food category	Maximum levels (expressed as folic acid)	- The designation of the novel food on the labelling of the foodstuffs containing it shall be “Monosodium salt of L-5-methyltetrahydrofolic acid (folic acid)”. - The labelling of food supplements containing monosodium salt of L-5-methyltetrahydrofolic acid shall bear a statement that the food supplements should not be consumed by infants and young children (children under 3 years of age)		Authorised on 30 April 2024. This inclusion is based on proprietary scientific evidence and scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283.
	Food supplements as defined in Directive 2002/46/EC, excluding food supplements for infants and young children	In accordance with Directive 2002/46/EC			Applicant: Merck & Cie KmG, Im Laternenacker 5, 8200 Schaffhausen, Switzerland. During the period of data protection, the novel food monosodium salt of L-5-methyltetrahydrofolic acid is authorised for placing on the market within the Union only by Merck & Cie KmG, unless a subsequent applicant obtains authorisation for the novel food without reference to the proprietary scientific evidence or scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283 or with the agreement of Merck & Cie KmG. End date of the date protection: 30 April 2029.’
	Infant formula and follow-on formula as defined in Regulation (EU) No 609/2013	In accordance with Regulation (EU) No 609/2013			
	Processed cereal-based foods and baby foods for infants and young children as defined in Regulation (EU) No 609/2013	In accordance with Regulation (EU) No 609/2013			
	Foods for special medical purposes as defined in Regulation (EU) No 609/2013	In accordance with Regulation (EU) No 609/2013			
	Total diet replacement for weight control as defined in Regulation (EU) No 609/2013	In accordance with Regulation (EU) No 609/2013			
	Food fortified in accordance with Regulation (EC) No 1925/2006	In accordance with Regulation (EC) No 1925/2006			

(2) in Table 2 (Specifications), the following entry is inserted:

Authorised Novel Food	Specification
'Monosodium salt of L-5-methyltetrahydrofolic acid	Description/Definition: The novel food is produced by chemical synthesis and consists of L-5-methyltetrahydrofolic acid. Molecular formula: C₂₀H₂₄N₇NaO₆ Chemical name: N-[4-[[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-(6S)-pteridiny]methyl]amino]benzoyl]-l-glutamic acid CAS number: 2246974-96-7 Molecular weight: 481,44 g/mol Characteristics/composition: Appearance: White to yellow or beige powder Assay & related compounds: Assay 5-MeTHFA-Na on dry basis: > 95 %; Sum of folate-related substances: ≤ 2,5 Sodium: 4 %-5 % w/w Water: ≤ 1,0 % Residual solvents: Ethanol: ≤ 0,5 %; Isopropanol: ≤ 0,5 % Diastereomeric purity: (6R)-Mefolate: ≤ 1,0 % area Elemental impurities: Boron: ≤ 10 mg/kg Platinum: ≤ 10 mg/kg (for foods intended for infants and young children and food supplements intended for pregnant women then ≤ 2 mg/kg) Arsenic: ≤ 1,5 mg/kg Cadmium: ≤ 0,5 mg/kg Lead: ≤ 1,0 mg/kg Mercury: ≤ 1,5 mg/kg (for foods intended for infants and young children and food supplements intended for pregnant women then ≤ 1 mg/kg) Microbiological criteria: Total aerobic microbial count: ≤ 100 CFU/g Total yeast and moulds count: ≤ 100 CFU/g <i>E. coli</i>: Not detected in 10 g Abbreviations: CFU: colony forming unit; IR: infra-red; MeTHFA: methyltetrahydrofolic acid.'