REGULATIONS

COMMISSION IMPLEMENTING REGULATION (EU) 2020/16

of 10 January 2020

authorising the placing on the market of nicotinamide riboside chloride as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council and amending Commission 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 thereof,

Whereas:

(1) Regulation (EU) 2015/2283 provides that only novel foods authorised and included in the Union list 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]) establishing a Union list of authorised novel foods was adopted.

(3) Pursuant to Article 12 of Regulation (EU) 2015/2283, the Commission is to submit a draft implementing act authorising placing on the Union market of a novel food and on the updating of the Union list.

(4) On 10 May 2018, the company ChromaDex Inc. ('the Applicant') made a request to the Commission to place nicotinamide riboside chloride on the Union market as a novel food within the meaning of Article 10(1) of Regulation (EU) 2015/2283. The application requested for nicotinamide riboside chloride to be used as a source of niacin in food supplements intended for the general adult population at the maximum use levels of 300 mg/day. Furthermore, the application requested for nicotinamide riboside to be also added to the list of niacin forms specified in Annex II of Directive 2002/46/EC of the European Parliament and of the Council ([3]) as a source of niacin.

(5) The Applicant also made a request to the Commission for the protection of proprietary data for a number of studies submitted in support of the application namely, an in vitro study evaluating the metabolism of nicotinamide riboside in blood (Study No 160312) ([4]); an oral 7-day dose range finding toxicity study in juvenile dogs (StudyNo

([1]) OJ L 327, 11.12.2015, p. 1.

([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).

([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).

([4]) Keystone Bioanalytical Inc., The Metabolism of Nicotinamide Riboside in Human Blood (Study No 160312), 10 January 2018, unpublished.

17-921) ([5]); a hERG screening assay (Study No 20151223) ([6]); a 28-day repeat-dose oral toxicity study in juvenile dogs (Study No 17-940) ([7]); a 90-day repeated-dose oral toxicity study in Sprague–Dawley rats (Study No S14022) ([8]); a reproductive toxicity study (Study No G10959) ([9]); and a developmental toxicity study in rats (Study No G10957) ([10]).

(6) The Commission consulted the European Food Safety Authority ('Authority') on 8 October 2018, asking it to provide a scientific opinion on the safety of nicotinamide riboside as a novel food in accordance with Article 10(3) of Regulation (EU) 2015/2283, and on the assessment for the intended use as a food supplement.

(7) On 4 July 2019, the Authority adopted the scientific opinion on the 'Safety of nicotinamide riboside chloride as a novel food pursuant to Regulation (EU) 2015/2283 and bioavailability of nicotinamide from this source, in the context of Directive 2002/46/EC' ([11]). That scientific opinion is in line with the requirements of Article 11 of Regulation (EU) 2015/2283.

(8) In its opinion, the Authority concluded that nicotinamide riboside chloride is safe when used in food supplements at the maximum level of 300 mg/day for the general adult population, excluding pregnant and lactating women, and at the maximum level of 230 mg/day for pregnant and lactating women.

(9) The opinion of the Authority gives sufficient grounds to establish that nicotinamide riboside chloride under the assessed conditions of use complies with Article 12(1) of Regulation (EU) 2015/2283.

(10) The Authority considered that, in elaborating its opinion on nicotinamide riboside chloride as a novel food, data from the in vitro study evaluating the metabolism of nicotinamide riboside in blood (Study No 160312) served as a basis to assess the bioavailability of nicotinamide, while data from five toxicity studies (an oral 7-day dose range finding toxicity study in juvenile dogs (Study No 17-921); a 28-day repeat-dose oral toxicity study in juvenile dogs (Study No 17-940); a 90-day repeated-dose oral toxicity study in Sprague–Dawley rats (Study No S14022); a reproductive toxicity study (Study No G10959); and a developmental toxicity study in rats (Study No G10957)) served as a basis to assess the safety of nicotinamide riboside chloride. Therefore, it is considered that the conclusions on the safety of nicotinamide riboside chloride could not have been reached without the data from the unpublished reports of those studies.

(11) The Commission requested the applicant to further clarify the justification provided with regard to their proprietary claim over the in vitro study evaluating the metabolism of nicotinamide riboside in blood and the five toxicity studies, and to clarify their claim to an exclusive right of reference to these studies, as referred to in Article 26(2)(b) of Regulation (EU) 2015/2283.

(12) The Applicant declared that, at the time the application was submitted, it held ownership and proprietary exclusive right of reference to these studies, and that therefore third parties cannot lawfully access or use these studies or refer to that data.

(13) The Commission assessed all the information provided by the Applicant and considered that the Applicant has sufficiently substantiated the fulfilment of the requirements laid down in Article 26(2) of Regulation (EU) 2015/2283. Therefore, the in vitro study evaluating the metabolism of nicotinamide riboside in blood and the five toxicity studies contained in the Applicant's file should not be used by the Authority for the benefit of a subsequent applicant for a period of five years from the date of entry into force of this Regulation. Accordingly, the placing on the market within the Union of nicotinamide riboside chloride should be restricted to the Applicant for that period.

([5]) Experimur, Oral 7-Day Dose Range Finding Toxicity Study in Juvenile Dogs (Study No 17-921), 27 November 2017, unpublished.

([6]) IPS Therapeutique, Inc., Evaluation of the effects of Nicotinamide Riboside Chloride on the human potassium channel using human embryonic kidney (HEK) 293 cells transfected with a human ether-a-go-go-related gene (hERG), 25 March 2016, unpublished.

([7]) Experimur, Oral 28-Day Toxicity Study in Juvenile Dogs (Study No 17-940), 20 February 2018, unpublished.

([8]) Syngene International Limited, Comparative 90-Day Oral Toxicity Study in Sprague Dawley Rats (Study No S14022), 12 May 2015, unpublished.

([9]) Advinus Therapeutics Limited, Nicotinamide riboside chloride: one generation reproduction toxicity study through diet in Sprague-Dawley rats (Study No G10959), 21 November 2016, unpublished.

([10]) Advinus Therapeutics Limited, Nicotinamide riboside chloride: embryo-fetal developmental toxicity study in Sprague-Dawley rats by oral route (Study No G10957), 30 September 2016.

([11]) *EFSA Journal* 2019;17(8):5775.

(14) However, restricting the authorisation of nicotinamide riboside chloride and of the reference to the studies contained in the Applicant's file for the sole use of the Applicant does not prevent other 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 the authorisation under this Regulation.

(15) The Directive 2002/46/EC lays down requirements on food supplements. The use of nicotinamide riboside chloride should be authorised without prejudice to the requirements of that Directive.

(16) 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. Nicotinamide riboside chloride as specified in the Annex to this Regulation shall be included in the Union list of authorised novel foods established in Implementing Regulation (EU) 2017/2470.

2. For a period of five years from the date of entry into force of this Regulation only the initial Applicant:

— Company: ChromaDex Inc.;

— Address: 10900 Wilshire Boulevard Suite 600, Los Angeles, CA 90024 USA,

is authorised to place on the market within the Union the novel food referred to in paragraph 1, unless a subsequent applicant obtains authorisation for the novel food without reference to the data protected pursuant to Article 2 of this Regulation or with the agreement of ChromaDex Inc.

3. The entry in the Union list referred to in paragraph 1 shall include the conditions of use and labelling requirements laid down in the Annex.

4. The authorisation provided for in this Article shall be without prejudice to the provisions of Directive 2002/46/EC.

Article 2

The studies contained in the application file on the basis of which the novel food referred to in Article 1 has been assessed by the Authority, claimed by the Applicant as proprietary and without which the novel food could not have been authorised, shall not be used for the benefit of a subsequent applicant for a period of five years from the date of entry into force of this Regulation without the agreement of ChromaDex Inc.

Article 3

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

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, 10 January 2020.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

The Annex to Implementing Regulation (EU) 2017/2470 is amended as follows:

(1) the following entry is inserted in Table 1 (Authorised novel foods) in alphabetical order:

Authorised novel food	Conditions under which the novel food may be used		Additional specific labelling requirements	Other requirements	Data Protection
'Nicotinamide riboside chloride	*Specified food category*	*Maximum levels*	The designation of the novel food on the labelling of the foodstuffs containing it shall be "Nicotinamide riboside chloride"		Authorised on 20 February 2020. This inclusion is based on proprietary scientific evidence and scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283. Applicant: ChromaDex Inc., 10900 Wilshire Boulevard Suite 600, Los Angeles, CA 90024 USA. During the period of data protection, the novel food is authorised for placing on the market within the Union only by ChromaDex Inc. unless a subsequent applicant obtains authorisation for that 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 ChromaDex Inc. End date of the data protection: 20 February 2025.'
	Food Supplements as defined in Directive 2002/46/EC	300 mg/day for the general adult population, excluding pregnant and lactating women 230 mg/day for pregnant and lactating women			

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

Authorised Novel Food	Specification
'Nicotinamide riboside chloride	**Description/Definition:** The novel food is a synthetic form of nicotinamide riboside. The novel food contains ≥ 90 % nicotinamide riboside chloride, predominantly in its β form, the remaining components being residual solvents, reaction by-products and degradation products. Nicotinamide riboside chloride: CAS number: 23111-00-4 EC number: 807-820-5 IUPAC name: 1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]pyridin-1-ium-3-carboxamide;chloride Chemical formula: $C_{11}H_{15}N_2O_5Cl$ Molecular weight: 290,7 g/mol **Characteristics/Composition:** Colour: White to light brown Form: Powder Identification: Conforms by NMR (nuclear magnetic resonance) Nicotinamide riboside chloride: ≥ 90 % Water content: ≤ 2 % **Residual solvents:** Acetone: ≤ 5 000 mg/kg Methanol: ≤ 1 000 mg/kg Acetonitrile: ≤ 50 mg/kg Methyl tert-butyl ether: ≤ 500 mg/kg **Reaction by-products:** Methyl acetate: ≤ 1 000 mg/kg Acetamide: ≤ 27 mg/kg Acetic acid: ≤ 5 000 mg/kg **Heavy metals:** Arsenic: ≤ 1 mg/kg **Microbiological criteria:** Total Plate Count: ≤ 1 000 CFU/g Yeast and Mould: ≤ 100 CFU/g *Escherichia coli*: Absence in 10 g'