COMMISSION REGULATION (EU) 2022/860

of 1 June 2022

amending Annex III to Regulation (EC) No 1925/2006 of the European Parliament and of the Council as regards monacolins from red yeast rice

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

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

Having regard to 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 ([1]), and in particular Article 8(2)(a)(ii) and (b) thereof,

Whereas:

(1) Pursuant to Article 8(2) of Regulation (EC) No 1925/2006, on its own initiative or on the basis of information provided by Member States, the Commission may initiate a procedure to include a substance or an ingredient containing a substance other than a vitamin or a mineral in Annex III to that Regulation listing the substances whose use in foods is prohibited, restricted or under Union scrutiny, if that substance is associated with a potential risk to consumers as provided for in Article 8(1) of Regulation (EC) No 1925/2006.

(2) In 2010, the European Food Safety Authority ('the Authority') was asked to provide an opinion on scientific substantiation of a health claim related to monacolin K submitted pursuant to Article 13 of Regulation (EC) No 1924/2006 of the European Parliament and of the Council ([2]). On 30 June 2011 ([3]), the Authority issued a scientific opinion on the substantiation of a health claim related to monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations. The Authority concluded that a cause and effect relationship has been established between the consumption of monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations at the level of 10 mg daily dose.

(3) In 2012, the Authority was asked to provide an opinion on the scientific substantiation of a health claim submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 related to the combination of ingredients, among which monacolin K from red yeast rice. On 12 July 2013 ([4]), the Authority issued a scientific opinion establishing a cause and effect relationship between the consumption of a product containing 2 mg of monacolin K from red yeast rice in combination with other ingredients, and the reduction of blood LDL-cholesterol concentrations.

(4) In the abovementioned scientific opinions, in relation to restrictions of use, the Authority referred to the Summary of Product Characteristics (SmPC) for lovastatin-containing medicinal products available on the Union market, as the Authority considered that monacolin K in lactone form is identical to lovastatin. The SmPC provides information to healthcare professionals on the safe and effective use of these medicinal products. The SmPC for lovastatin-containing medicinal products describes the properties and officially approved conditions for their use and includes special warnings and precautions for use that refer to the risk of myopathy/rhabdomyolysis, which is increased by concomitant use of lovastatin with certain other medicinal products, and discourages use of lovastatin by pregnant and lactating women.

(5) During discussions of the working group on nutrition and health claims on the abovementioned scientific opinions, the Member States raised potential safety concerns associated with the consumption of foods containing monacolins from red yeast rice.

([1]) OJ L 404, 30.12.2006, p. 26.
([2]) Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods (OJ L 404, 30.12.2006, p. 9).
([3]) *EFSA Journal* 2011;9(7):2304.
([4]) *EFSA Journal* 2013;11(7):3327.

(6) Red yeast rice is made by fermentation of rice with yeasts, mainly *Monascus purpureus*, resulting in the production of monacolins, the most abundant of which is monacolin K. It is traditionally used in China as a food colouring and as a traditional remedy to promote digestion and blood circulation. In the EU, it is not authorised for use as a food colour as it is not included in the Union list of Regulation (EC) No 1333/2008 of the European Parliament and of the Council ([5]) on food additives. Food supplements containing red yeast rice preparations have been marketed and consumed to a significant degree before 15 May 1997 and therefore, are not subject to Regulation (EU) 2015/2283 of the European Parliament and of the Council ([6]) on novel foods. The use of red yeast rice preparations in other food categories is subject to an authorisation under Regulation (EU) 2015/2283 on novel foods. The application of the provisions of this Regulation is without prejudice to Regulations (EU) 2015/2283 and (EC) No 1333/2008.

(7) The Commission, on its own initiative, started the procedure under Article 8 of Regulation (EC) No 1925/2006 for monacolins in red yeast rice as it considered that on the basis of the available information that was provided by the Member States during a consultation on the safety of monacolins from red yeast rice, the necessary conditions and requirements laid down in Article 8 of that Regulation and Articles 3 and 4 of Commission Implementing Regulation (EU) No 307/2012 ([7]) were fulfilled. This available information included an opinion from the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) on the risk associated with the presence of 'red yeast rice' in food supplements ([8]). That opinion concluded that 'due to the composition of red yeast rice and in particular: the presence of monacolin K (also called lovastatin when marketed as a drug) that shares the adverse effects of statins; the presence at varying levels of the other monacolins, compounds whose safety has not been established, consumption of "red yeast rice" exposes some consumers to a health risk'. The available information also included a scientific advisory report adopted by the Belgian Superior Health Council on 13 February 2016 ([9]) that provided an evaluation of the supposed beneficial effects and possible toxicity of dietary supplements based on red yeast rice for the Belgian population. That report referred to the risk associated with the presence of monacolins, in particular monacolin K, in red yeast rice that includes adverse effects identical to those observed in patients taking statin drugs and referred to a higher risk of developing toxic effects for certain vulnerable groups such as pregnant women, people suffering from liver, kidney and muscle disorders, persons aged over 70 years and children and adolescents. Another relevant scientific assessment was carried out by the German research funding organisation DFG in 2013 ([10]) that concluded that 'red mould rice is not a safe food/food supplement'.

(8) Therefore, the Commission in 2017, in accordance with Article 8 of Regulation (EC) No 1925/2006, requested the Authority to deliver a scientific opinion on the evaluation of the safety of monacolins in red yeast rice.

(9) On 25 June 2018 ([11]), the Authority adopted a scientific opinion on the safety of monacolins in red yeast rice. The Authority considered that monacolin K in lactone form was identical to lovastatin, the active ingredient of several medicinal products authorised for the treatment of hypercholesterolemia in the EU. Monacolin K from red yeast rice is available in food supplements at varying recommended daily intakes for its effect on the maintenance of normal blood LDL-cholesterol levels. On the basis of the information available, the Authority concluded that intake of monacolins from red yeast rice via food supplements could lead to estimated exposure to monacolin K within the range of the therapeutic doses of lovastatin. The Authority noted that the profile of adverse effects to red yeast rice

([5]) Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives (OJ L 354, 31.12.2008, p. 16).

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

([7]) Commission Implementing Regulation (EU) No 307/2012 of 11 April 2012 establishing implementing rules for the application of Article 8 of Regulation (EC) No 1925/2006 of the European Parliament and of the Council on the addition of vitamins and minerals and of certain other substances to foods (OJ L 102, 12.4.2012, p. 2).

([8]) ANSES Opinion Request No 2012-SA-0228: Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the risks associated with the presence of 'red yeast rice' in food supplements, 14 February 2014.

([9]) Avis du Conseil Superieur de la Sante N° 9312 : Compléments alimentaires à base de «levure de riz rouge », 3.2.2016.

([10]) Stellungnahme der Gemeinsamen Experten kommission BVL/BfArM: Einstufung von Rotschimmelreisprodukten, 8.2.2016.

([11]) *EFSA Journal* 2019;16(8):5368.

was similar to that of lovastatin. It reported, through consultation of four sources ([12]) of case reports, that the most important targets for adverse events were musculoskeletal and connective tissue (including rhabdomyolysis), liver, nervous system, gastro-intestinal tract, skin and subcutaneous tissue, in descending order of occurrence. The Authority considered that the available information on the adverse effects reported in humans were judged to be sufficient to conclude that monacolins from red yeast rice when used as food supplements were of significant safety concern at the use level of 10 mg/day. The Authority further considered that individual cases of severe adverse reactions had been reported for monacolins from red yeast rice at intake levels as low as 3 mg/day taken for a period of between 2 weeks and 1 year, and that cases of rhabdomyolysis, hepatitis and skin disorders occurred and required hospitalisation.

(10) On the basis of the information available and several uncertainties highlighted in its opinion, the Authority was unable to provide advice on a daily intake of monacolins from red yeast rice that does not give rise to concerns about harmful effects to health, for the general population, and as appropriate, for vulnerable subgroups of the population as requested by the Commission. The Authority explained that there are uncertainties as to the composition and content of monacolins in food supplements containing red yeast rice and that monacolins in red yeast rice are used in multi-ingredient products, the components of which have not been fully evaluated individually or in combination. Furthermore, due to the lack of data, the safe use of monacolins in certain vulnerable groups of consumers cannot be evaluated and there is uncertainty as to the effects of concomitant consumption of red yeast rice-based food supplements with foods or drugs that inhibit the enzyme (CYP3A4) that is involved in the metabolism of monacolins.

(11) In accordance with Article 4(5) of Implementing Regulation (EU) No 307/2012 and following publication by the Authority of its opinion on monacolins from red yeast rice, the Commission received comments from interested parties on the scientific risk assessment carried out by the Authority. Interested parties also provided statements to support the safe use of monacolins from red yeast rice in combination with adequate consumer information on the safe use of the substance.

(12) Those comments that were of a scientific nature were clarified by the Authority during post-adoption teleconferences held with the interested parties. The Authority provided clarifications on the sources of evidence for its scientific opinion and explained why certain studies submitted by interested parties during a public call for data were not considered to be sufficiently reliable and scientifically robust to be included in its safety assessment. The Authority explained the scientific rationale for considering safety data for lovastatin as relevant for the safety assessment of monacolins and clarified how post-marketing data on adverse events provided by interested parties was used as supporting evidence in its assessment.

(13) The Commission asked the Authority for technical assistance on two scientific studies, a systematic review and meta-analysis of the safety of red yeast rice supplementation ([13]), and a review and expert opinion on the role of red yeast rice supplementation in plasma cholesterol control ([14]), that were submitted to the Commission by an interested party following adoption of the scientific opinion by the Authority. The Authority noted that irrespective of the results of any intervention study or meta-analysis on the safety of red yeast rice supplementation, reports of side effects associated with the consumption of red yeast rice in humans exist and monacolin K in lactone form is identical to lovastatin for which adverse effects are well documented, and therefore those submitted studies would have to be considered together with the whole body of evidence to draw an overall conclusion. The Authority explained that the existence of reports of adverse effects cannot be neglected or invalidated by results of trials that were relatively small in size and not designed to detect these effects, and that studies, such as the review and expert opinion study submitted, providing comparative risk-benefit ratio of products containing red yeast rice were not relevant to the evaluation of the safety of substances intentionally added to food.

([12]) World Health Organisation; French Agency for Food, Environmental and Occupational Health and Safety; Italian Surveillance System of Natural Health Products; Food and Drug Administration.

([13]) Fogacci F, Banach M, Mikhailidis DP et al. Safety of red yeast rice supplementation: A systematic review and meta-analysis of randomized controlled trials. Pharmacological Research 143 (2019) 1–16.

([14]) Banach M, Bruckert E, Descamps OS et al. The role of red yeast rice (RYR) supplementation in plasma cholesterol control: A review and expert opinion. Atheroscler Suppl. 2019 Aug 17.

(14) Considering that no daily intake of monacolins from red yeast rice that does not give rise to concerns for human health could be set, and considering the significant harmful effect on health associated with the use of monacolins from red yeast rice at levels of 10 mg/day, and individual cases of severe adverse health reactions at levels as low as 3 mg/day, the use of monacolins from red yeast rice at levels of 3 mg and more per portion of the product recommended for daily consumption should be prohibited. That substance should therefore be placed in Part B of Annex III to Regulation (EC) No 1925/2006 and its addition to foods or its use in the manufacture of foods should only be allowed under the conditions specified in that Annex.

(15) Food supplements are required by Article 6 of Directive 2002/46/EC of the European Parliament and of the Council ([15]) to be labelled with the portion of the product that is recommended for daily consumption together with a warning not to exceed the stated recommended daily dose. As different foods or food supplements containing monacolins from red yeast rice may be consumed simultaneously, there is the possibility of exceeding the limit laid down in Annex III to Regulation (EC) No 1925/2006, therefore, it is necessary to provide for appropriate labelling requirements for all foods containing monacolins from red yeast rice.

(16) In order to provide complete information about the content of monacolins on the labels of foods containing monacolins from red yeast rice, it is necessary to provide for appropriate labelling requirements for all foods containing monacolins from red yeast rice.

(17) As the Authority identified a risk of adverse effects due to interactions with medicinal products, it is necessary to warn persons using cholesterol-lowering medicines, to avoid concomitant use of foods containing monacolins from red yeast rice. The Authority noted that the profile of adverse effects to red yeast rice was similar to that of lovastatin, therefore, it is appropriate to warn persons to seek medical advice if they experience any health problems. Furthermore, as the Authority could not evaluate the safe use of monacolins in certain vulnerable groups of consumers because of the lack of data, and as therefore, there is still the possibility of harmful effects on health associated with the use of monacolins from red yeast rice, it is appropriate to advise against the use of foods containing monacolins from red yeast rice for pregnant or lactating women, persons aged over 70 years, children and adolescents. Considering the above, it is necessary to provide for appropriate labelling requirements for all foods containing monacolins from red yeast rice.

(18) The Authority could not identify a dietary intake of monacolins from red yeast rice that does not give rise to concerns about harmful effects to health, for the general population, and as appropriate, for vulnerable subgroups of the population. As there is still a possibility of harmful effects on health associated with the use of monacolins from red yeast rice, but scientific uncertainty in this regard persists, and considering that monacolins from red yeast rice may only be used in food supplements and that the extent of use of those food supplements could not be determined by the Authority, the use of monacolins from red yeast rice in food supplements should be placed under Union scrutiny and therefore, should be included in Part C of Annex III to Regulation (EC) No 1925/2006. Considering the uncertainties outlined by the Authority in its scientific opinion and considering the statements given by interested parties on the safety profile of monacolins from red yeast rice, those interested parties have under Article 8(4) of Regulation (EC) No 1925/2006 the possibility to submit data demonstrating the safety of monacolins from red yeast rice to the Authority in accordance with Article 5 of Implementing Regulation (EU) No 307/2012. In accordance with Article 8(5) of Regulation (EC) No 1925/2006 the Commission should take a decision within four years from the entry into force of this Regulation, whether to list monacolins from red yeast rice in Annex III, Part A or Part B, as appropriate, taking into account the opinion of the Authority on any submitted data.

(19) Regulation (EC) No 1925/2006 should therefore be amended accordingly.

(20) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

([15]) 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).

HAS ADOPTED THIS REGULATION:

Article 1

Annex III to Regulation (EC) No 1925/2006 is amended as follows:

1. The following entry is added in the table in Part B 'Restricted substances' in alphabetical order:

Restricted substance	Conditions of use	Additional requirements
'Monacolins from red yeast rice	Individual portion of the product for daily consumption shall provide less than 3 mg of monacolins from red yeast rice.	The label shall provide the number of individual portions of the product for maximum daily consumption and a warning not to consume a daily amount of 3 mg of monacolins from red yeast rice or more. The label shall indicate the content of monacolins per portion of the product. The label shall include the following warnings: "Should not be consumed by pregnant or lactating women, children below 18 years old and adults above 70 years old". "Seek advice from a doctor on consumption of this product if you experience any health problems"; "Should not be consumed if you are taking cholesterol-lowering medication"; "Should not be consumed if you are already consuming other products containing red yeast rice".'

2. The following entry is added in the table in Part C 'Substances under Community scrutiny' in alphabetical order:
'Monacolins from red yeast rice'

Article 2

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, 1 June 2022.

For the Commission
The President
Ursula VON DER LEYEN