This draft has not been adopted or endorsed by the European Commission. Any views expressed are the preliminary views of the Commission services and may not in any circumstances be regarded as stating an official position of the Commission.

COMMISSION REGULATION (EU) …/…

of XXX

amending Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council as regards the food additive titanium dioxide (E 171)

(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 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives[1], and in particular Article 10(3) thereof,

Having regard to Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings[2], and in particular Article 7(5) thereof,

Whereas:

(1) Annex II to Regulation (EC) No 1333/2008 lays down a Union list of food additives approved for use in foods and their conditions of use.

(2) Annex III to Regulation (EC) No 1333/2008 lays down a Union list of food additives approved for use in food additives, food enzymes, food flavourings, nutrients and their conditions of use.

(3) Titanium dioxide (E 171) is a substance authorised as a colour in certain foods, in accordance with Annex II to Regulation (EC) No 1333/2008.

(4) Pursuant to Article 3(1) of Regulation (EC) No 1331/2008, the Union list of food additives may be updated either on the initiative of the Commission or following an application.

(5) Article 32(1) of Regulation (EC) No 1333/2008 provides that all food additives that were already permitted in the Union before 20 January 2009 are subject to a new risk assessment by the European Food Safety Authority ('the Authority').

(6) On 14 September 2016, the Authority published a scientific opinion on the re-evaluation of the safety of titanium dioxide (E 171) as a food additive[3] concluding that the margins of safety calculated in the opinion would not be of concern. Nevertheless, the Authority recommended additional toxicological testing, an extended 90-day study or a multigeneration or extended-one generation reproduction toxicity study according to the current OECD guidelines, in order to be able to establish a health-based guidance value (acceptable daily intake - ADI) for titanium dioxide (E 171). The Authority also recommended amendments to the Union specifications for titanium dioxide (E 171) by introducing a characterisation of the particle size distribution and the percentage of

[1] OJ L 354, 31.12.2008, p. 16.
[2] OJ L 354, 31.12.2008, p. 1.
[3] EFSA Journal 2016;14(9):4545.

particles in the nanoscale present in titanium dioxide (E 171) used as a food additive, and revising the maximum limits for impurities of toxic elements.

(7) On 30 January 2017, the Commission launched a public call for scientific and technological data on titanium dioxide (E 171), targeting the data needs identified in the scientific opinion on the re-evaluation of this substance as a food additive.

(8) On 2 October 2017 and 29 June 2018, in view of the recommendations made by the Authority, business operators made a proposal for the amendment of the specifications for titanium dioxide (E 171) and submitted the necessary data. On 7 August 2018, the Commission requested the Authority to provide a scientific opinion on whether the data provided adequately support the proposed amendment of the specifications for titanium dioxide (E 171).

(9) On 12 July 2019, the Authority published a scientific opinion on the proposed amendments of the specifications for titanium dioxide (E 171) used as a food additive. The Authority concluded on additional parameters related to particle size distribution to be included in the specifications and recommended a revision of the definition of the food additive titanium dioxide (E 171) in the Union specifications. The Authority also concluded that, based on the proposed change in the specifications, revisiting the toxicological database on titanium dioxide (E 171) as a food additive should consequently be conducted in line with the data requirements specified in the 2018 'Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain'[4].

(10) On 6 March 2020, the Commission requested the Authority to assess the safety of the food additive titanium dioxide (E 171), taking into account the proposed amendments of the specifications, the data from an extended one generation reproductive study submitted by a consortium of interested business operators in reply to the public call for data launched in 2017 as well as all new relevant data available since the completion of the re-evaluation of titanium dioxide (E 171) in 2016, including the data considered to be in line with the data requirements specified in the 2018 Guidance on nanotechnology.

(11) On 6 May 2021, the Authority published a scientific opinion on the safety assessment of titanium dioxide (E 171) as a food additive[5]. In light of the opinion on the proposed amendments of the specifications and following the 2018 Guidance on nanotechnology, the opinion also takes into account, in addition to all new relevant data, the data on the potential genotoxicity of titanium dioxide nanoparticles published before 2016, that had not previously been identified as relevant for the 2016 re-evaluation. In its opinion the Authority indicated that, based on all the evidence available, a concern for genotoxicity could not be ruled out, and given the many uncertainties, it concluded that titanium dioxide (E 171) can no longer be considered safe when used as a food additive. The Authority neither identified nor recommended any new studies that could alleviate the genotoxicity concern and other remaining uncertainties.

(12) In light of the conclusion of the 2021 Authority's opinion about the safety of titanium dioxide (E 171) when used as a food additive, it is appropriate to remove the authorisation to use titanium dioxide (E 171) in foods. As titanium dioxide (E 171) would no longer be authorised for use in foods, it is also appropriate to remove the reference to it from the entry on the use of potassium aluminium silicate (E 555) as a carrier laid down in Part 1 of Annex III to Regulation (EC) No 1333/2008.

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4 EFSA Journal 2018;16(7):5327.

5 EFSA Journal 2021;19(5):6585.

(13) However, given that the Authority did not identify an immediate health concern linked to titanium dioxide (E 171) used as a food additive, it is appropriate that foods containing titanium dioxide (E 171) that have been lawfully placed on the market before this measure becomes applicable may continue to be marketed until their date of minimum durability or 'use by' date. In turn, taking into account the uncertainties about the safety of titanium dioxide (E 171), no new foods containing this food additive should be placed on the market after the date of entry into force of this Regulation.

(14) Directive 2009/35/EC of the European Parliament and of the Council[6] restricts the use of colours in human and veterinary medicinal products to those authorised in accordance with Regulation (EC) No 1333/2008 on food additives, for which specifications are laid down in Commission Regulation (EU) No 231/2012[7]. Uses of excipients other than colours in medicinal products are subject to the Union rules on medicinal products and are evaluated as part of the overall benefit risk profile of a medicinal product.

(15) In response to a request from the Commission, the European Medicines Agency (EMA) provided on 8 September 2021 a scientific analysis on the technical purpose of the use of titanium dioxide (E 171) in medicinal products, the feasibility of replacement and possible timeframes for alternatives. In its conclusions, EMA indicated that titanium dioxide is mainly used in medicinal products as a colour and opacifier, even if it has multiple functions. It also stressed that titanium dioxide is used frequently in a number of essential medicinal products in oral-solid and oral semi-solid dosage forms. EMA also stressed that, from a technical point of view, it should be possible to find alternatives to replace titanium dioxide (E 171)-containing coatings, both as colour and for other uses. However, it also underlined that its feasibility is not confirmed at this stage, as replacing titanium dioxide (E 171) would impact in a negative manner the quality, safety and efficacy of medicinal products. EMA highlighted the need to carefully assess alternatives, notably to ensure their compatibility with the various components of individual pharmaceutical products. The replacement of titanium dioxide (E 171) in authorised medicinal products would require an individual review and assessment, possibly requiring bioequivalence studies. Furthermore, EMA concluded that it is difficult at this stage to recommend a precise transition period timeframe for the replacement of titanium dioxide (E 171) used in medicinal products, as the time needed to reformulate each individual product could take several years, depending on the complexity of reformulation and studies required. Finally, considering the scale of the use of this excipient and the volume of products impacted, and taking into account global supply chains, EMA stressed that a requirement to replace titanium dioxide (E 171) would almost certainly cause significant medicines shortages on the Union market.

(16) On the basis of the EMA scientific analysis, and in order to avoid shortages of medicinal products that could have impacts on public health, titanium dioxide (E 171) should remain provisionally on the list of authorised additives to allow its use in medicinal products as a colour, pending the development of adequate alternatives to replace it while ensuring the quality, safety and efficacy of the medicinal products concerned.

(17) It is of critical importance that the pharmaceutical industry makes any possible efforts to accelerate the research and development of alternatives that would be used as a replacement for titanium dioxide (E 171) in medicinal products, and to submit the

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6 Directive 2009/35/EC of the European Parliament and of the Council of 23 April 2009 on the colouring matters which may be added to medicinal products (OJ L 109, 30.4.2009, p. 10).

7 Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council (OJ L 83, 22.3.2012, p. 1).

necessary variation to the terms of the marketing authorisations concerned. In the absence of such efforts, competent authorities may request the concerned stakeholders to submit objective and verifiable reason explaining the non-feasibility of the replacement.

(18) The Commission is committed to review the necessity to maintain titanium dioxide (E 171) or otherwise delete it from the Union list of food additives for exclusive use as a colour in medicinal products within three years after the date of entering into force of this Regulation. This review should be based on an updated assessment of the EMA to be performed before 1 April 2024. It should take into account the progress made during this period to develop alternatives to titanium dioxide (E 171) in medicinal products both for new products and for replacing it in authorised products, and possible impacts on quality, safety and efficacy, as well as on the availability of medicinal products. Where replacement of titanium dioxide (E 171) in medicinal products has not taken place or been initiated within this period, only objective verifiable reasons related to the lack of feasibility of its replacement should be taken into account.

(19) Annexes II and III to Regulation (EC) No 1333/2008 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,

HAS ADOPTED THIS REGULATION:

Article 1

Annexes II and III to Regulation (EC) No 1333/2008 are amended in accordance with the Annex to this Regulation.

Article 2

Foods containing titanium dioxide (E 171) which have been placed on the market before xxxx (date of entry into force of this Regulation) in accordance with the rules applicable before that date, may continue to be placed on the market. After that date, they may remain on the market until their date of minimum durability or 'use by' date.

Article 3

The Commission shall, following consultation on the European Medicines Agency, review the necessity to maintain titanium dioxide (E 171) or to delete it from the Union list of food additives for the exclusive use as colour in medicinal products in Part B of Annex II to Regulation (EC) No 1333/2008 within three years after the date of entering into force of 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,

For the Commission
The President
Ursula VON DER LEYEN