



Brussels, 30.9.2022
C(2022) 6886 final

COMMISSION IMPLEMENTING DECISION

of 30.9.2022

granting an authorisation under Regulation (EC) No 1907/2006 of the European Parliament and of the Council to Vetter Pharma-Fertigung GmbH & Co. KG for a use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO)

(Only the English text is authentic)

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THE EUROPEAN COMMISSION,

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

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC¹, and in particular Article 64(8) thereof,

Whereas:

- (1) 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated ('4-tert-OPnEO') is listed in Annex XIV to Regulation (EC) No 1907/2006 and uses of that substance are subject to the authorisation requirement in Article 56(1), point (a), of that Regulation.
- (2) On 21 June 2019, Vetter Pharma-Fertigung GmbH & Co. KG ('the applicant') submitted an application in accordance with Article 62 of Regulation (EC) No 1907/2006 for authorisation for a use of 4-tert-OPnEO². The use for which authorisation was sought is as an emulsifier in the siliconisation of glass containers (syringes and cartridges) used as primary packaging material for 44 medicinal products of several pharmaceutical companies listed in the confidential Appendix 1 to the analysis of the alternatives. These products cover several therapeutic areas, and approximately 40 % of them are listed on the World Health Organisation (WHO) Model List of Essential Medicines (EML).
- (3) On 4 January 2021, the Commission received the opinions on the application adopted by the Committee for Risk Assessment (RAC) and by the Committee for Socio-economic Analysis (SEAC) of the European Chemicals Agency³ and sent to it pursuant to Article 64(5), second subparagraph, of Regulation (EC) No 1907/2006.
- (4) RAC concluded in its opinion that it is not possible to determine a predicted no-effect concentration for the endocrine disrupting properties for the environment of 4-tert-OPnEO in accordance with Section 6.4 of Annex I to Regulation (EC) No 1907/2006 and that therefore 4-tert-OPnEO is a substance for which it is not possible to determine

¹ OJ L 396, 30.12.2006, p. 1.

² Different names and abbreviations are used to refer to the substance, including 'Octylphenoethoxylates' and 'OPnEO' in the chemical safety report.

³ <https://echa.europa.eu/documents/10162/c4bc957a-91f4-cc70-0586-a06a09f6488f>

a threshold for the purposes of Article 60(3), point (a), of that Regulation. As a result, Article 60(2) of Regulation (EC) No 1907/2006 does not apply to that substance and authorisations may therefore only be granted with respect to that substance under paragraph 4 of that Article.

- (5) RAC noted that the risk to the environment cannot be excluded for non-threshold substances, even at low exposure levels. Consequently, RAC takes the emissions of the substance as a proxy for the risk.
- (6) In its opinion, RAC concluded that the risk management measures and operational conditions described in the application are appropriate and effective to limit the risk to the environment. In particular, RAC noted that the applicant has demonstrated that releases to environmental compartments have been prevented or minimised as far as technically and practically possible based on the risk management measures and operational conditions in the exposure scenarios. Nevertheless, RAC noted that the applicant has not provided monitoring data of 4-tert-OPnEO and its degradation products in the wastewater. Therefore, it recommended to carry out a monitoring program to corroborate the estimated releases in wastewater prior to release to the municipal sewage treatment plant. Moreover, RAC noted that a residual amount of 4-tert-OPnEO in the order of tens of grams per year is released into wastewater during the cleaning and sanitising of the compounding equipment and siliconisation equipment. Nevertheless, RAC also acknowledged the technical constraints for collecting such wastewater and of the expected substitution of 4-tert-OPnEO within five years. Having evaluated RAC's assessment, the Commission agrees with its conclusion and recommendation.
- (7) In its opinion, SEAC concluded that it has no substantial reservations on the quantitative and the qualitative elements of the applicant's assessment of the socio-economic benefits and the risk to the environment associated with the continued use of the substance. Taking into account SEAC's assessment, the lack of scientific knowledge at present to quantify or monetise the risk to the environment associated with the use of the substance, the estimated remaining emissions of a hundred grams over five years in the worst case scenario, the estimated quantified benefits due to avoided job losses and losses of earnings before interest, taxes, depreciation, and amortisation at minimum in the order between millions of euros and hundreds of millions of euros in the most likely scenario over the entire review period, the estimated cost of avoiding the remaining releases of the substance in the order between hundreds of millions and billions of euros per kilo, the latter in the worst-case scenario, and the qualitatively assessed additional socio-economic benefits of the continued use due to the availability of medicinal products for patients, the Commission concludes that the applicant has demonstrated that the socio-economic benefits of the continued use of the substance outweigh the risk to human health and the environment arising from that use.
- (8) A suitable alternative should be safer, available, and technically and economically feasible. Where suitable alternatives are available in the Union, but not technically or economically feasible for the applicant or its downstream users, an authorisation may be granted if the applicant for authorisation submits a substitution plan. An alternative that provides the functionality and level of technical performance necessary for the use applied for should be considered to be technically feasible.
- (9) In its opinion, SEAC concluded that there were no suitable alternatives available for the applicant by the sunset date. The Commission, having evaluated SEAC's

assessment and all relevant information available, acknowledges that the identified alternative could potentially provide the functionality needed for the use applied for and that it is already available and implemented in the Union, but that the applicant still needs to conduct stability testing in order to obtain the required regulatory approvals for the marketing of specific medicinal products. The Commission therefore considers that it cannot be confirmed yet that the identified alternative allows the functionality needed for the use applied for. Thus, the Commission agrees with SEAC's conclusion that there are no suitable alternatives for the applicant for the use applied for, but concludes that suitable alternatives are available in the Union.

- (10) In its opinion, SEAC concluded that the substitution plan submitted by the applicant is credible and consistent with the analysis of alternatives and the socio-economic analysis. The Commission, having evaluated SEAC's assessment, concurs with that conclusion. Therefore, the Commission considers that the applicant has discharged its burden of proof in demonstrating the absence of suitable alternative substances or technologies for the applicant.
- (11) Therefore, having regard to the conditions laid down in Article 60(4) of Regulation (EC) No 1907/2006, it is appropriate to authorise the use of 4-tert-OPnEO described in the application, provided that the risk management measures and operational conditions described in the chemical safety report are fully applied. However, for the sake of legal clarity, the description of the use authorised by this Decision should be 'as emulsifier in the siliconisation of glass containers (syringes and cartridges) used as primary packaging material for medicinal products of several pharmaceutical companies listed in the confidential Appendix 1 to the analysis of alternatives included in the application'.
- (12) The Commission has based its assessment on all relevant scientific evidence currently available, as assessed by RAC and SEAC, and, after having carried out a detailed examination, based its conclusions on a sufficient amount of material and reliable information allowing it to conclude. Nevertheless, additional scientific evidence would allow the Commission to perform its assessment on a more robust or broad evidentiary base in the future. Hence, it is appropriate to require additional emission information be generated.
- (13) SEAC recommended in its opinion that the review period referred to in Article 60(9), point (e), of Regulation (EC) No 1907/2006 should be set at five years. The Commission agrees with that recommendation, taking into account the relevant elements from RAC's and SEAC's assessments and, in particular, the time necessary to substitute the substance for all medicinal products and obtain the necessary marketing authorisations.
- (14) The language used to describe the risk management measures and operational conditions in the application for authorisation may be different from the official language of the Member State where the use takes place. Therefore, in order to facilitate supervision and enforcement of compliance with the authorisation, it is appropriate to require the authorisation holder to submit, upon request, a brief summary of those risk management measures and operational conditions to the competent authority of that Member State in an official language of that Member State.
- (15) This Decision does not affect the obligation of the authorisation holder to ensure that a use of a substance does not adversely affect human health or the environment, having regard to the principle set out in Article 1(3) of Regulation (EC) No 1907/2006.

Furthermore, this Decision does not affect the obligation of the authorisation holder under Article 60(10) of that Regulation to ensure that the exposure is reduced to as low a level as is technically and practically possible or the obligation of the employer to eliminate or reduce to a minimum risks to the health and safety of workers at work involving hazardous chemical agents in accordance with Article 5(2) of Council Directive 98/24/EC⁴. This Decision does not affect the application of Union law in the area of health and safety at work, in particular Council Directives 89/391/EEC⁵, 92/85/EEC⁶, 94/33/EC⁷ and 98/24/EC, or any national binding occupational limit values which may be stricter than the applicable limit values under Union law.

- (16) This Decision does not affect any obligation to comply with any emission limit values or other requirements set in accordance with Directive 2008/50/EC of the European Parliament and of the Council⁸ or Directive 2010/75/EU of the European Parliament and of the Council⁹, nor any obligation to comply with emission limit values set to achieve compliance with the environmental quality standards established by Member States in accordance with Directive 2000/60/EC of the European Parliament and of the Council¹⁰ or the environmental quality standards established in Directive 2008/105/EC of the European Parliament and of the Council¹¹. Compliance with the provisions of this Decision does not necessarily imply compliance with emission limit values or environmental quality standards under any other provisions of Union law, which may include further or more onerous requirements.
- (17) The measures provided for in this Decision are in accordance with the opinion of the Committee established by Article 133 of Regulation (EC) No 1907/2006,

HAS ADOPTED THIS DECISION:

Article 1

An authorisation is hereby granted in accordance with Article 60(4) of Regulation (EC) No 1907/2006 for the following use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO):

⁴ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ L 131, 5.5.1998, p. 11).

⁵ Council Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work (OJ L 183, 29.6.1989, p. 1).

⁶ Council Directive 92/85/EEC of 19 October 1992 on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding (tenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ L 348, 28.11.1992, p. 1).

⁷ Council Directive 94/33/EC of 22 June 1994 on the protection of young people at work (OJ L 216, 20.8.1994, p. 12).

⁸ Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe (OJ L 152, 11.6.2008, p. 1).

⁹ Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control) (OJ L 334, 17.12.2010, p. 17).

¹⁰ Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (OJ L 327, 22.12.2000, p. 1).

¹¹ Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council (OJ L 348, 24.12.2008, p. 84).

Authorisation number	Authorised use
REACH/22/29/0	As emulsifier in the siliconisation of glass containers (syringes and cartridges) used as primary packaging material for medicinal products of several pharmaceutical companies listed in the confidential Appendix 1 to the analysis of alternatives included in the application

The authorisation is granted subject to the risk management measures and operational conditions described in the chemical safety report¹².

Article 2

1. The review period shall expire on 4 January 2026.
2. The authorisation shall cease to be valid on 4 January 2026 if the review report has not been submitted in accordance with Article 61(1) of Regulation (EC) No 1907/2006 by 4 July 2024.

Article 3

1. The monitoring arrangements set out in paragraphs 2 to 4 shall apply.
2. The authorisation holder shall carry out a monitoring programme measuring the concentrations of 4-tert-OPnEO and its principal degradation products in the wastewater prior to release to the local sewage treatment plant. The monitoring programme shall:
 - (a) be carried out at least four times per year and during the time of operation. The frequency of the measurements shall be such as to capture the variability in concentrations of the substance and its principal degradation products in the wastewater due to changes or operational fluctuations in the process;
 - (b) be based on an analytical method capable of adequately characterising the substance and its principal degradation products in wastewater with appropriately low limit of quantification;
 - (c) be recorded as to include details of the sampling point, the analytical method, the concentrations detected and the corresponding environmental release values.
3. The authorisation holder shall use the information gathered in the measurements referred to in paragraph 2 and related contextual information to review, at least annually, the appropriateness and effectiveness of the risk management measures and operational conditions and, if needed, to introduce measures to further reduce emissions of 4-tert-OPnEO to a level as low as technically and practically possible.
4. The authorisation holder shall document and keep the information gathered in accordance with paragraphs 2 and 3 and submit it, upon request, to the competent authority of the Member State where the authorised use takes place.
5. If the authorisation holder submits a review report as referred to in Article 61(1) of Regulation (EC) No 1907/2006, it shall include information in accordance with paragraph 4.

¹² <https://ec.europa.eu/docsroom/documents/44406>

Article 4

Upon request, the authorisation holder shall submit a brief summary of the applicable risk management measures and operational conditions described in the chemical safety report to the competent authority of the Member State where the authorised use takes place in an official language of that Member State.

Article 5

This Decision is addressed to Vetter Pharma-Fertigung GmbH & Co. KG, Schützenstrasse 87, 88212 Ravensburg, Germany.

Done at Brussels, 30.9.2022

For the Commission

Thierry BRETON

Member of the Commission

