EUROPEAN
COMMISSION

Brussels, 21.2.2023
C(2023) 1085 final

COMMISSION IMPLEMENTING DECISION

of 21.2.2023

partially granting an authorisation under Regulation (EC) No 1907/2006 of the European Parliament and of the Council to Takeda Manufacturing Austria AG and Baxalta Belgium Manufacturing SA for a use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated

(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/EC[1], 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 17 May 2019, Baxter AG[2] and Baxalta Belgium Manufacturing SA ('the applicants') submitted an application in accordance with Article 62 of Regulation (EC) No 1907/2006 for authorisation for a use of 4-tert-OPnEO[3]. The use for which authorisation was sought is as a detergent for virus inactivation via S/D (Solvent/Detergent) treatment in recombinant and plasma-derived medicinal products. The use takes place at four sites, identified by four different exposure scenarios (‘ES’)[4].

(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 Agency[5] 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 Baxter AG subsequently changed its corporate name to Takeda Manufacturing Austria AG.

3 Different names and abbreviations are used to refer to the substance, including ‘OPnEO’, in the chemical safety report.

4 The exposure scenarios referred to in this Decision are as described in the chemical safety report.

5 https://echa.europa.eu/documents/10162/37dcfad4-ab2c-191d-6337-4d5ade512073

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 Article 60(4) of that Regulation.

(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 not appropriate and effective in limiting the risk as regards ES1, where RAC noted that the wastewater originating from the first rinse of the cleaning-in-place of the virus inactivation installation is not collected for adequate treatment. Therefore, RAC proposed as a condition for authorisation that the applicant should further assess the feasibility of implementing additional risk management measures ensuring adequate treatment, and recommended a monitoring programme. RAC considered that the risk management measures and operational conditions described in the application are or are expected to be appropriate and effective in limiting the risk concerning ES2, ES3 and ES4. However, as regards ES2, in order to take into account the quantity of 4-tert-OPnEO used in the process on a yearly basis and to confirm the effectiveness of the risk management measures and operational conditions, RAC recommended a monitoring programme and a feasibility study. Having evaluated the RAC's assessment, the Commission agrees with its conclusion and recommendations.

(7) In its opinion, SEAC concluded that it has no substantial reservations on the quantitative and the qualitative elements of the applicants' assessment of the socio-economic benefits and the risk to the environment associated with the continued use of 4-tert-OPnEO. 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 4-tert-OPnEO, the estimated emissions across four sites of up to tens of kilograms of the substance per year, the estimated benefits due to avoided profit losses, relocation costs, and job losses at minimum in the order of billions of euro over the review period, the estimated costs of avoiding the remaining releases of the substance in the order of between millions of euro and tens of millions of euro per kilogram, the qualitatively assessed additional socio-economic benefits of the continued use of 4-tert-OPnEO due to the availability of recombinant and plasma-derived medicinal products, as well as any relevant distributional impacts, the Commission concludes that the applicants have demonstrated that the socio-economic benefits of the continued use of 4-tert-OPnEO outweigh the risk to human health or 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 for which authorisation is sought should be considered to be technically feasible.

(9) In its opinion, SEAC concluded that there were no suitable alternative substances or technologies available for the applicants by the sunset date. The Commission, having evaluated SEAC's assessment and all relevant information available, concludes that further research and development and testing are necessary to assess whether the

identified alternatives are compatible with the relevant manufacturing processes while achieving the necessary virus inactivation for the products currently developed by the applicants. The Commission therefore considers that the identified alternatives do not allow the functionality needed for the intended use.

(10) Nevertheless, the Commission acknowledges the possibility that the applicants may use 4-tert-OPnEO in new assays to be developed in the future, for which no analysis of alternatives had been provided, as highlighted by SEAC. In order to ensure that the authorisation covers only the use for which no suitable alternatives are available, the Commission considers it appropriate to further specify the authorised use by aligning it with the conclusions of the analysis of alternatives as presented in the application and as assessed by SEAC. Therefore, the use description should be limited as to read 'as a detergent for virus inactivation via solvent or detergent treatment in the recombinant and plasma-derived medicinal products listed in the Annex'.

(11) Therefore, the Commission considers that the applicants have discharged their burden of proof in demonstrating the absence of suitable alternatives both in the Union and for the applicants, only with regard to the use as limited by this Decision.

(12) 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, as limited by this Decision, provided that the risk management measures and operational conditions described in the chemical safety report, as well as the conditions set out in this Decision, are fully applied.

(13) The Commission has based its assessment on the relevant scientific evidence currently available, as assessed by RAC and SEAC, and, after having carried out a detailed examination, based its conclusions on the existence of 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 the generation of additional exposure and emission information.

(14) In its opinion, SEAC recommended that the review period referred to in Article 60(9), point (e), of Regulation (EC) No 1907/2006 should be set at 12 years. The Commission agrees with that recommendation, taking into account the relevant elements from RAC's and SEAC's assessments and, in particular, the socio-economic benefits, the estimated emissions, the lack of suitable alternatives within a shorter timeline, as well as the high performance requirements and regulatory approvals necessary for medicinal products.

(15) 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.

(16) 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/EC[6]. 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/EEC[7], 92/85/EEC[8], 94/33/EC[9] and 98/24/EC, as well as any national binding occupational limit values which may be stricter than the applicable limit values under Union law.

(17) This Decision does not affect any obligation to comply with emission limit values or other requirements set out in accordance with Directive 2008/50/EC of the European Parliament and of the Council[10] or Directive 2010/75/EU of the European Parliament and of the Council[11], 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 Council[12] or the environmental quality standards established in Directive 2008/105/EC of the European Parliament and of the Council[13]. Compliance with the provisions of this Decision does not necessarily imply compliance with any emission limit values or environmental quality standards under any other provisions of Union law, which may include further or more onerous requirements.

(18) 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 to the following persons for the following use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO):

Authorisation number	Authorisation holder	Authorised use

6 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).

7 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).

8 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).

9 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).

10 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).

11 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).

12 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).

13 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).

REACH/23/3/0	Takeda Manufacturing Austria AG	As a detergent for virus inactivation via solvent or detergent treatment in the recombinant and plasma-derived medicinal products listed in the Annex
REACH/23/3/1	Baxalta Belgium Manufacturing SA	

An authorisation is not granted for the use of 4-tert-OPnEO as a detergent for virus inactivation via solvent or detergent treatment in the recombinant and plasma-derived medicinal products other than those listed in the Annex.

The authorisation is granted subject to the risk management measures and operational conditions described in the chemical safety report[14] as well as to the conditions set out in Article 2.

Article 2

1. As regards ES1, the authorisation shall be subject to the conditions set out in paragraphs 2 to 5.

2. The authorisation holders shall finalise by 21 February 2024 and thereafter annually, a study to assess the feasibility of implementing additional risk management measures as to reduce the emissions of 4-tert-OPnEO to a level as low as technically and practically possible, including the collection of wastewater for adequate treatment. The authorisation holders shall act in accordance with the outcome of that study.

3. The authorisation holders shall carry out a monitoring programme of 4-tert-OPnEO and its principal degradation products in the wastewater prior to release to the municipal wastewater treatment plant. The monitoring programme shall:

   (a) provide an initial sampling frequency which is sufficient to demonstrate daily fluctuations;

   (b) once established, be carried out at least 4 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;

   (c) 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;

   (d) be recorded with details of the sampling point, the analytical method, the concentrations detected and the corresponding environmental release values.

4. The authorisation holders shall use the information gathered in accordance with paragraph 3 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.

[14] https://ec.europa.eu/docsroom/documents/44423

5. The authorisation holders shall document and keep the information obtained in accordance with paragraphs 2 and 3, including the contextual information associated with each set of measurements, as well as the outcome and conclusions of the review and of any action taken in accordance with paragraph 4. The authorisation holders shall submit that information, upon request, to the competent authority of the Member State where the authorised use takes place.

Article 3

1. The review period shall expire on 4 January 2033.

2. The authorisation shall cease to be valid on 4 January 2033 with respect to any authorisation holder who has not submitted the review report in accordance with Article 61(1) of Regulation (EC) No 1907/2006 by 4 July 2031.

Article 4

1. As regards ES2, the monitoring arrangements set out in paragraphs 2 to 5 shall apply.

2. The authorisation holders shall finalise by 21 February 2024 and thereafter when new information becomes available, a study to assess the feasibility of implementing additional risk management measures, as to reduce the emissions of 4-tert-OPnEO to a level as low as technically and practically possible, including the collection of wastewater for adequate treatment. The authorisation holders shall act in accordance with the outcome of that study.

3. The authorisation holders shall carry out a monitoring programme measuring the concentrations 4-tert-OPnEO and its principal degradation products in the wastewater prior and after the treatment in the on-site wastewater treatment plant. The monitoring programme shall:

   (a) provide an initial sampling frequency which is sufficient to demonstrate daily fluctuations;

   (b) once established, be carried out at least 4 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;

   (c) 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;

   (d) be recorded with details of the sampling point, the analytical method, the concentrations detected and the corresponding environmental release values.

4. The authorisation holders shall use the information gathered in accordance with paragraph 3 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.

5. The authorisation holders shall document and keep the information obtained in accordance with paragraphs 2 and 3, including the contextual information associated with each set of measurements, as well as the outcome and conclusions of the review

and of any action taken in accordance with paragraph 4. The authorisation holders shall submit that information, upon request, to the competent authority of the Member State where the authorised use takes place.

Article 5

Where an authorisation holder submits a review report as referred to in Article 61(1) of Regulation (EC) No 1907/2006, it shall include the information obtained in accordance with Articles 2(5) and 4(5).

Article 6

Upon request, the authorisation holders 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 7

This Decision is addressed to:

1. Takeda Manufacturing Austria AG, Industriestrasse 67, 1220, Vienna, Austria;
2. Baxalta Belgium Manufacturing SA, Boulevard René Branquart 80, 7860, Lessines, Belgium.

Done at Brussels, 21.2.2023

For the Commission
Thierry BRETON
Member of the Commission

CERTIFIED COPY
For the Secretary-General

Martine DEPREZ
Director
Decision-making & Collegiality
EUROPEAN COMMISSION