EUROPEAN
COMMISSION

Brussels, 16.3.2022
C(2022) 1506 final

COMMISSION IMPLEMENTING DECISION

of 16.3.2022

granting an authorisation under Regulation (EC) No 1907/2006 of the European Parliament and of the Council to Octapharma AB and others, for certain uses of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

COMMISSION IMPLEMENTING DECISION

of 16.3.2022

granting an authorisation under Regulation (EC) No 1907/2006 of the European Parliament and of the Council to Octapharma AB and others, for certain uses of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

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 subject to the authorisation requirement in Article 56(1), point (a), of that Regulation.

(2) On 17 May 2019, Octapharma AB, Octapharma Pharmazeutika Produktionsgesellschaft m.b.H, Octapharma S.A.S., and Octapharma Produktionsgesellschaft Deutschland mbH ('the applicants') submitted an application in accordance with Article 62 of Regulation (EC) No 1907/2006 for authorisation for certain uses of 4-tert-OPnEO[2]. The uses for which authorisation was sought are as detergent for a virus inactivation step (solvent/detergent treatment) during the manufacture of plasma-derived and recombinant medicinal products ('use 1') and as component of a chromatography column regeneration solution during the manufacture of a recombinant-derived Factor VIII ('use 2').

(3) On 17 June 2020, 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[3] and sent to it pursuant to Article 64(5), second subparagraph, of Regulation (EC) No 1907/2006.

(4) RAC concluded in its opinions that it is not possible to determine a predicted no-effect concentration (PNEC) 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

[1] OJ L 396, 30.12.2006, p. 1.

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

[3] https://echa.europa.eu/documents/10162/c0c657df-4e1e-f0c0-81f6-a9da65685f38
https://echa.europa.eu/documents/10162/261a9273-6238-f4d4-cfbe-21cb82dc45e5

1907/2006 and that therefore 4-tert-OPnEO is a substance for which it is not possible to determine 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).

(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 on use 1, RAC concluded that the risk management measures and operational conditions described in the application, together with the additional risk management measures and operational conditions further detailed by the applicants at RAC's request, are expected to be appropriate and effective in limiting the risk, once those additional risk management measures and operational conditions are implemented and adhered to. Therefore, RAC recommended, as a condition for authorisation, that those additional risk management measures and operational conditions are duly implemented, to ensure that releases to environmental compartments are prevented or minimised as far as technically and practically possible. Moreover, in order to confirm the effectiveness of the risk management measures and operational conditions, RAC also recommended monitoring arrangements. Having evaluated RAC's assessment, the Commission agrees with its conclusion and recommendations.

(7) In its opinion on use 2, RAC concluded that the risk management measures and operational conditions described in the application, and further detailed by the applicant at RAC's request, are appropriate and effective in limiting the risk. RAC also made recommendations for the review report. Having evaluated RAC's assessment, the Commission agrees with that conclusion and those recommendations.

(8) In its opinions on both uses, 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 and future uses 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 combined estimated emissions from all sites of up to 165 kg of the substance per year, the combined estimated benefits due to avoided profit losses and avoided job losses at minimum in the order of hundreds of millions of euros, over the entire review period, the estimated cost of avoiding the remaining releases of the substance in the order of hundreds of thousands of euros per kilogram, the qualitatively assessed additional socio-economic benefits of the continued and future uses of the substance that are due to the availability of plasma-derived and recombinant medicinal products, the Commission concludes that the applicants have demonstrated that the socio-economic benefits of the continued and future uses of the substance outweigh the risk to human health and the environment arising from those uses.

(9) 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.

(10) In its opinions, SEAC concluded that there were no available alternative substances or technologies by the sunset date. The Commission, having evaluated SEAC's assessment and all relevant information available, acknowledges that the identified alternatives are not compatible with the relevant manufacturing process while achieving the necessary virus inactivation. Taking into account patient safety and the requirements to obtain regulatory approvals for the entire range of medicinal products, the Commission considers that the identified alternatives do not allow the functionality needed for the uses applied for. Therefore, the Commission agrees with SEAC's conclusion and 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.

(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 uses of 4-tert-OPnEO described in the application, provided that the risk management measures and operational conditions described in the chemical safety report, and further detailed by the applicants at RAC's request, as well as the condition set out in this Decision are fully applied.

(12) 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 request that additional exposure and emission information be submitted.

(13) SEAC recommended in its opinion on use 1 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 SEAC's assessment, and, in particular, the socio-economic benefits, the lack of suitable alternatives within a shorter timeline, the long investment cycle and substantial investment required to develop pharmaceuticals, as well as the regulatory approvals and quality requirements for medicinal products.

(14) SEAC recommended in its opinion on use 2 that the review period referred to in Article 60(9), point (e), of Regulation (EC) No 1907/2006 should be set at 4 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 ongoing substitution efforts and the expected timeline to assess and transition to an alternative.

(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 uses take place. Therefore, in order to facilitate supervision and enforcement of compliance with the authorisation, it is appropriate to require the authorisation holders 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 holders 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 holders 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[4]. 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[5], 92/85/EEC[6], 94/33/EC[7], and 98/24/EC, or 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 in accordance with Directive 2008/50/EC of the European Parliament and of the Council[8] or Directive 2010/75/EU of the European Parliament and of the Council[9], 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[10] or the environmental quality standards established in Directive 2008/105/EC of the European Parliament and of the Council[11]. 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.

(18) The measures provided for in this Decision are in accordance with the opinion of the Committee established under 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 uses of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO):

Authorisation	Authorisation holder	Authorised use

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).

number		
REACH/22/5/0	Octapharma AB	As detergent for a virus inactivation step (solvent/detergent treatment) during the manufacture of plasma-derived and recombinant medicinal products
REACH/22/5/1	Octapharma Pharmazeutika Produktionsgesellschaft m.b.H	
REACH/22/5/2	Octapharma S.A.S.	
REACH/22/5/3	Octapharma Produktionsgesellschaft Deutschland mbH	
REACH/22/5/4	Octapharma AB	As component of a chromatography column regeneration solution during the manufacture of a recombinant-derived Factor VIII

The authorisation is granted subject to the risk management measures and operational conditions described in the chemical safety report[12], and to the condition set out in Article 2 of this Decision.

Article 2

The authorisation bearing numbers REACH/22/5/1 and REACH/22/5/2 shall be subject to the following condition: the authorisation holders shall ensure that the additional risk management measures and operational conditions described in the application and listed in the Annex are applied.

Article 3

1. As regards the authorisation bearing numbers REACH/22/5/0 to REACH/22/5/3, the review period shall expire on 4 January 2033.

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

[12] https://ec.europa.eu/docsroom/documents/41824
https://ec.europa.eu/docsroom/documents/44774

2. As regards the authorisation bearing number REACH/22/5/4, the review period shall expire on 4 January 2025.

The authorisation shall cease to be valid on 4 January 2025 if the review report for that use has not been submitted in accordance with Article 61(1) of Regulation (EC) No 1907/2006 by 4 July 2023.

Article 4

1. The monitoring arrangements set out in paragraphs 2 to 5 shall apply.

2. 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 local sewage treatment plant. That monitoring programme shall:

   (a) be carried out at least four times per year throughout the whole time while the plant is in 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 holders shall use the information gathered in the measurements referred to in paragraph 2 and related contextual information to regularly 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. As regards the authorisation bearing numbers REACH/22/5/0 and REACH/22/5/4, the authorisation holder shall assess, by 16 March 2023, the feasibility of implementing additional risk management measures and operational conditions with the aim of further reducing emission of 4-tert-OPnEO containing effluent to water, with focus on rinsing procedures. The authorisation holder shall act in accordance with the outcome of that study.

5. The authorisation holders shall document and keep the information obtained in accordance with paragraph 2, the outcome and conclusions of the review and of any action taken in accordance with paragraph 3, as well as the outcome and conclusions of the feasibility study and of any actions taken pursuant to paragraph 4. The authorisation holders shall submit that information, upon request, to the competent authority of the Member State where the authorised uses take place.

Article 5

In the event that the authorisation holders submit a review report, it shall include:

(a) the information referred to in Article 4(5);

(b) As regards the authorisation bearing numbers REACH/22/5/0 and REACH/22/5/4, any new risk management measures and operational conditions introduced pursuant to Article 4(4).

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 uses take place in an official language of that Member State.

Article 7

This Decision is addressed to:

1. Octapharma AB, Lars Forssells gata 23, SE-11275 Stockholm, Sweden
2. Octapharma Produktionsgesellschaft Deutschland mbH, Wolfgang-Marguerre-Allee 1, 31832 Springe, Germany
3. Octapharma S.A.S. 72 rue du Maréchal Foch, 67381 Lingolsheim, France
4. Octapharma Pharmazeutika Produktionsgesellschaft m.b.H, Oberlaaer Straße 235, A-1100 Vienna, Austria

Done at Brussels, 16.3.2022

For the Commission
Thierry BRETON
Member of the Commission

CERTIFIED COPY
For the Secretary-General

Martine DEPREZ
Director
Decision-making & Collegiality
EUROPEAN COMMISSION