EUROPEAN
COMMISSION

Brussels, 24.2.2023
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COMMISSION IMPLEMENTING DECISION

of 24.2.2023

granting an authorisation under Regulation (EC) No 1907/2006 of the European Parliament and of the Council to Pfizer Ireland Pharmaceuticals for certain uses 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/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 10 June 2019, Pfizer Ireland Pharmaceuticals ('the applicant') 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 use of 4-tert-OPnEO as a surfactant in the manufacture of biopharmaceuticals - Viral Inactivation and associated processes ('use 1') and as a surfactant in the manufacture of biopharmaceuticals – Post-Production Cleaning ('use 2').

(3) On 6 April 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[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 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 a threshold for the purposes of Article 60(3), point (a), of that Regulation. As a result,

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

[2] Different names and abbreviations are used to refer to the substance, including 'Triton X-100' in the chemical safety report.

[3] https://echa.europa.eu/documents/10162/778610f1-499c-ae02-d2e3-94e9ae6f32f6 https://echa.europa.eu/documents/10162/b78367e3-d607-3f45-f542-d20a26fe152e

Article 60(2) of Regulation (EC) No 1907/2006 does not apply to that substance and an authorisation 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 on use 1, 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 posed by that use. RAC noted that 4-tert-OPnEO is used mainly in closed systems and all solid waste and wastewater contaminated with the substance are collected for incineration. However, taking into account that residual releases of 4-tert-OPnEO to wastewater might occur, and given the uncertainties in the methodology used by the applicant to estimate release to wastewater, RAC recommended to carry out a monitoring programme. Having evaluated RAC's assessment, the Commission agrees with its conclusions and recommendations.

(7) In its opinion on use 2, RAC concluded that the risk management measures and operational conditions described in the application are expected to be appropriate and effective to limit the risk to the environment posed by that use. RAC noted that all solid waste and wastewater contaminated with 4-tert-OPnEO will be collected for incineration resulting in zero releases to the environmental compartments. Having evaluated RAC's assessment, the Commission agrees with its conclusion.

(8) In its opinions, SEAC concluded that it has no substantial reservations on the quantitative and qualitative elements of the applicant's assessments of the socio-economic benefits and the risk to the environment associated with the uses of 4-tert-OPnEO. Taking into account SEAC's assessments, the lack of scientific knowledge at present to quantify or monetise the risk to the environment associated with the uses of 4-tert-OPnEO, the estimated emissions at the site of 152 grams of the substance per year for use 1 and no expected releases into the environment for use 2, the estimated combined benefits due to avoided profit losses and job losses at a minimum in the order of hundreds of millions of euro over the review period, the estimated cost of avoiding the remaining releases of the substance in the order of between millions and tens of millions of euro per kilogram for use 1, the qualitatively assessed additional socio-economic benefits of the future uses due to the avoided negative short-term impacts on hospitals and patients related to the unavailability of the drug products for the treatment of haemophilia and rheumatoid arthritis, as well as any relevant distributional impact, the Commission concludes that the applicant has demonstrated that the socio-economic benefits of the uses of the substance outweigh the risk to human health or 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 performance necessary for the use for which authorisation is sought should be considered to be technically feasible.

(10) In its opinions on uses 1 and 2, SEAC concluded that there were no suitable alternative substances or technologies available for the applicant by the sunset date. The Commission, having evaluated SEAC's assessment and all relevant information available, acknowledges that further testing is necessary to demonstrate whether the

identified alternatives provide the solubilisation of hydrophobic proteins and lipids for virus inactivation and the post-production cleaning process, required to obtain regulatory approvals. The Commission therefore considers that it cannot be deemed that the identified alternatives allow the functionality needed for the use applied for. Thus, the Commission agrees with SEAC's conclusion and considers that the applicant has discharged its burden of proof in demonstrating the absence of suitable alternatives both in the Union and 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 uses of 4-tert-OPnEO described in this Decision, provided that the risk management measures and operational conditions described in the chemical safety report are fully applied. However, for the sake of clarity, the description of use 1 for which authorisation is sought should be revised to read 'surfactant in the manufacture of biopharmaceuticals, as a processing aid in viral inactivation and associated purification processes', and the description of use 2 for which authorisation is sought should be revised to read 'surfactant in the manufacture of biopharmaceuticals for filter cleaning in viral inactivation processes'.

(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 the generation of additional emissions information.

(13) In its opinions, 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 for use 1 and 7 years for use 2. The Commission agrees with that recommendation, taking into account the relevant elements from RAC's and SEAC's assessments and, in particular, RAC's conclusion that the releases of 4-tert-OPnEO to the environment have been prevented or minimised as far as technically and practically possible, the significant socio-economic benefits of the uses of 4-tert-OPnEO, the lack of suitable alternatives by the sunset date, the ongoing research and development efforts as well as the regulatory approval process required for biopharmaceutical products.

(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/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, as well as 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 other requirements including emission limit values 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.

(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 uses of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO):

Authorisation number	Authorised use
REACH/23/7/0	Surfactant in the manufacture of biopharmaceuticals, as a processing aid in viral inactivation and associated purification processes

[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).

REACH/23/7/1	Surfactant in the manufacture of biopharmaceuticals for filter cleaning in viral inactivation processes

The authorisation is granted subject to the risk management measures and operational conditions described in the chemical safety report[12].

Article 2

1. As regards the authorisation bearing number REACH/23/7/0, the review period shall expire on 4 January 2033.

   The authorisation shall cease to be valid on 4 January 2033 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 2031.

2. As regards the authorisation bearing number REACH/23/7/1, the review period shall expire on 4 January 2028.

   The authorisation shall cease to be valid on 4 January 2028 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 2026.

Article 3

1. As regards the authorisation bearing number REACH/23/7/0, the monitoring arrangements set out in paragraphs 2 to 4 shall apply.

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

   (a) carried out at least annually and during the time of operation. The frequency of the measurements shall be such as to capture the variability in concentrations of 4-tert-OPnEO and its principal degradation products in the wastewater due to changes or operational fluctuations in the process;

   (b) based on an analytical method capable of adequately characterising 4-tert-OPnEO and its principal degradation products in the wastewater at an appropriately low limit of quantification;

   (c) recorded with 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 analysis and 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

[12] For use 1: https://ec.europa.eu/docsroom/documents/45353
For use 2: https://ec.europa.eu/docsroom/documents/45354

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 obtained in accordance with paragraph 2, including the contextual information associated with each set of measurements, as well as the outcome and conclusions of the review and any action taken in accordance with paragraph 3. The authorisation holder shall submit that information, upon request, to the competent authority of the Member State where the authorised uses take place.

5. Where the 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 paragraph 4.

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

Article 5

This Decision is addressed to Pfizer Ireland Pharmaceuticals, Ringaskiddy, Cork, Ireland.

Done at Brussels, 24.2.2023

For the Commission
Thierry BRETON
Member of the Commission