EUROPEAN
COMMISSION

Brussels, 16.3.2022
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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 Eli Lilly Kinsale Limited 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 24 May 2019, Eli Lilly Kinsale Limited ('the applicant') submitted an application in accordance with Article 62 of Regulation (EC) No 1907/2006 for authorisation for a use of 4-tert-OPnEO[2]. The use for which authorisation was sought is industrial use as a patient safety viral inactivation reagent in the manufacture of human medicines produced from biological systems.

(3) On 11 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 the 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 (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 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).

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1 OJ L 396, 30.12.2006, p. 1.

2 Different names and abbreviations are currently used to refer to the substance, including 'TX-100' in the chemical safety report.

3 https://echa.europa.eu/documents/10162/eb96af22-4ef6-50e7-25a0-599ed2581162

(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 opinon, 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 substance is handled in closed systems and all solid and liquid waste, as well as most of the wastewater contaminated with 4-tert-OPnEO, are collected for incineration so that releases to the environmental compartments have been minimized as far as technically and practically possible. However, since wastewater streams with minor amounts of 4-tert-OPnEO are treated in the on-site wastewater treatment plant which discharges some 4-tert-OPnEO directly into the marine environment, and taking into account the expected increase of 4-tert-OPnEO in those direct releases over the next decades, RAC recommended a condition to assess the feasibility of implementing an appropriate treatment of residual wastewater other than incineration in order to improve the on-site biological wastewater treatment with the aim of ensuring that releases of 4-tert-OPnEO to environmental compartments are further prevented or minimised as far as technically and practically possible. RAC also recommended to carry out monitoring programmes. Having evaluated the RAC 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 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 emissions at one site of up to five kilograms of the substance per year, the estimated benefits due to avoided profit losses and job losses at minimum in the order between billions of euros to tens of billions of euros over the entire review period, the estimated cost of avoiding the remaining releases of the substance between tens of millions and hundreds of millions of euros per kilogram, the qualitatively assessed additional socio-economic benefits of the use due to the availability of biomedicines, 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 alternative substances or technologies available by the sunset date. The Commission, having evaluated SEAC's assessment and all relevant information available, concludes that the identified alternatives do not allow achieving the necessary virus inactivation across the entire range of biomolecules manufactured on the biotechnology platform used by the applicant, required to obtain regulatory approvals. The Commission therefore considers that the identified alternatives do not allow the functionality needed for the use applied for. Therefore, 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.

(10) 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, as well as the condition set out in this Decision, are fully applied.

(11) 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.

(12) 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 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 of the continued use of the substance, the lack of suitable alternatives within a shorter timeline, as well as the regulatory approvals and quality requirements for medicinal products.

(13) 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.

(14) 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, or any national binding occupational limit values which may be stricter than the applicable limit values under Union law.

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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

(15) 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.

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

Authorisation number	Authorised use
REACH/22/6/0	Industrial use as a patient safety viral inactivation reagent in the manufacture of human medicines produced from biological systems

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.

Article 2

The authorisation shall be subject to the following condition: the authorisation holder shall undertake a feasibility study, by 16 March 2023, on the implementation of a treatment process which would improve the efficiency of the treatment of the residual wastewater at the on-site biological wastewater treatment plant and shall act according to the outcome of that study.

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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).

12 https://ec.europa.eu/docsroom/documents/41823

The relevant actions shall be documented and made available, 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 if the review report has not been submitted in accordance with Article 61(1) of Regulation (EC) No 1907/2006 by 4 July 2031.

Article 4

1. The monitoring arrangements referred to 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 after release from the on-site wastewater treatment plant. That monitoring programme shall:

   (a) be carried out at least four times per year and during the time of operation. The frequency of measurements shall be as 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 so 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 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. The authorisation holder shall document and keep the information obtained from the monitoring programme referred to in paragraph 2, as well as the outcome and conclusions of the review and of 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 use takes place.

Article 5

In the event that 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 referred to in Article 2 and Article 4(4) of this Decision.

Article 6

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 7

This Decision is addressed to Eli Lilly Kinsale Limited, Dunderrow, Kinsale, P17 NY71 Cork, Co. Cork Ireland.

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