EUROPEAN
COMMISSION

Brussels, 17.6.2024
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COMMISSION IMPLEMENTING DECISION

of 17.6.2024

granting an authorisation under Regulation (EC) No 1907/2006 of the European Parliament and of the Council to MeiraGTx Ireland Designated Activity Company 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/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 11 November 2022, MeiraGTx Ireland Designated Activity Company ('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 the use of 4-tert-OPnEO as a manufacturing aid in the production of gene therapies.

(3) The European Chemicals Agency sent the opinions[3] on the application adopted by its Committee for Risk Assessment (RAC) and its Committee for Socio-economic Analysis (SEAC) to the Commission pursuant to Article 64(5), second subparagraph, of Regulation (EC) No 1907/2006. On 14 November 2023, the Commission received the opinions.

(4) In its opinion, RAC concluded 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, Article 60(2) of Regulation (EC) No 1907/2006 does not apply to 4-tert-OPnEO and

[1] OJ L 396, 30.12.2006, p. 1, ELI: http://data.europa.eu/eli/reg/2006/1907/oj.

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

[3] https://www.echa.europa.eu/documents/10162/355a6b98-fc70-d786-6441-793eff5c57ed

an authorisation may therefore only be granted with respect to that substance under paragraph 4 of that Article.

(5) RAC noted that despite the absence of a dose-response relation, a risk to the environment cannot be excluded for 4-tert-OPnEO, 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 in limiting the risk to the environment posed by the use of 4-tert-OPnEO described in the application. In particular, RAC notes that all solid waste and wastewater are collected and disposed of for incineration so that the use for which authorisation is sought results in no releases of the substance to the environment. Hence the applicant has demonstrated that emissions have been prevented or reduced to a level as low as technically and practically possible. Having evaluated RAC's assessment, the Commission agrees with its conclusion.

(7) In its opinion, SEAC concluded that the societal costs of not granting an authorisation are higher than the monetised risk to the environment arising from the use of 4-tert-OPnEO. The Commission, having evaluated SEAC's assessment, concurs with that conclusion and considers that the applicant has demonstrated that the benefits of the use outweigh the risk to the environment arising from that use.

(8) For an alternative to be suitable it needs to 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, the applicant is required by Article 62(4), point (f), of Regulation (EC) No 1907/2006 to submit a substitution plan.

(9) 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.

(10) In its opinion, SEAC concluded that there were no suitable alternative substances or technologies available for the applicant and in the Union at the time of adoption of the opinion. The Commission, having evaluated SEAC's assessment and all relevant information available, notes that testing, verification and validation of the most promising alternative substance are still needed to ensure that the requirements established by the applicable regulatory framework for manufacturing the applicant's medicinal products are met, in particular in terms of its cell lysis efficiency. Therefore, the Commission considers that it cannot be deemed that the identified alternatives allow the functionality needed for the use for which an authorisation is sought. Thus, the Commission agrees with SEAC's conclusion that there are no suitable alternatives for the applicant and in the Union.

(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 described in the chemical safety report are applied and that the operational conditions described therein are fulfilled.

(12) The Commission has based its assessment on all relevant scientific evidence available, as assessed by RAC and SEAC, and, after having carried out a detailed examination, has concluded on the basis of a sufficient amount of material and reliable information.

(13) In its opinion, SEAC recommended that the review period referred to in Article 60(9), point (e), of Regulation (EC) No 1907/2006 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, RAC's conclusion that there are no releases of the substances to the environment, the socio-economic benefits of the future use of the substance, the lack of suitable alternatives within a shorter timeframe and the research and development efforts undertaken by the applicant, as well as the time required to substitute with an alternative.

(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 the 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.

(16) This Decision does not affect any obligation to comply with emission limit values or other requirements set in accordance with Directive 2008/50/EC[8] or Directive

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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, ELI: http://data.europa.eu/eli/dir/1998/24/oj).

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, ELI: http://data.europa.eu/eli/dir/1989/391/oj).

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, ELI: http://data.europa.eu/eli/dir/1992/85/oj).

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, ELI: http://data.europa.eu/eli/dir/1994/33/oj).

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, ELI: http://data.europa.eu/eli/dir/2008/50/oj).

2010/75/EU[9] of the European Parliament and of the Council, 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 any 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 to the following person for the following use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (EC No 799-991-7; CAS No 9036-19-5):

Authorisation number	Authorisation holder	Authorised use
REACH/24/20/0	MeiraGTx Ireland Designated Activity Company	Manufacturing aid in the production of gene therapies

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

Article 2

The review period shall expire on 11 November 2034.

The authorisation shall cease to be valid on 11 November 2034 if the authorisation holder has not submitted the review report in accordance with Article 61(1) of Regulation (EC) No 1907/2006 by 11 May 2033.

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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, ELI: http://data.europa.eu/eli/dir/2010/75/oj).

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, ELI: http://data.europa.eu/eli/dir/2000/60/oj).

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, ELI: http://data.europa.eu/eli/dir/2008/105/oj).

12 https://www.echa.europa.eu/documents/10162/31fe829b-b871-3826-6670-648741d5dec8 .

Article 3

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. The brief summary shall be drafted in an official language of that Member State.

Article 4

This Decision is addressed to:

MeiraGTx Ireland Designated Activity Company, Block K, Airport Avenue, Shannon Free Zone, V14 PT88, Shannon, Ireland.

Done at Brussels, 17.6.2024

For the Commission
Thierry BRETON
Member of the Commission

CERTIFIED COPY
For the Secretary-General

Martine DEPREZ
Director
Decision-making & Collegiality
EUROPEAN COMMISSION