Department for Environment Food & Rural Affairs

Authorisation Decision

by Robbie Moore, Parliamentary Under Secretary of State

On behalf of the Secretary of State for Environment, Food and Rural Affairs

Decision date: 3 July 2024

Application Ref: AFA020-01

UK REACH authorisation No.:

Authorisation number	Authorisation holder	Authorised use
UKREACH/24/07/0	Abbott Laboratories Limited	Professional use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO) as a surfactant, in wash buffer components used in conjunction with fluorescence in situ hybridisation (FISH) test kits and/or their laboratory developed test (LDT) equivalents, in clinical diagnostic use for medical analysis of human tissue and blood samples to identify characteristic genetic abnormalities related to specific disease conditions.

Preliminary matters

- 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated ('4-tert-OPnEO') is listed in Annex XIV to assimilated regulation (EC) No 1907/2006 concerning the registration, evaluation, authorisation and restriction of chemicals ('UK REACH').[1]

[1] References to regulation (EC) No 1907/2006, referred to in this decision as UK REACH, are to the assimilated law available online at https://www.legislation.gov.uk/eur/2006/1907/contents.

As such, 4-tert-OPnEO is subject to the authorisation requirement referred to in Article 56(1) of UK REACH.

- 4-tert-OPnEO was included in Annex XIV because it meets the criteria set out in Article 57(f) of UK REACH. There is scientific evidence of probable serious effects to the environment from its endocrine-disrupting properties when it degrades to 4-tert-OP.
- This application is made by: Abbott Laboratories Limited of Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE ('the Applicant').
- Article 127GA of UK REACH applied to this application. The latest application date for 4-tert-OPnEO for this use was therefore extended to 30 June 2022.[2] The sunset date for this use was 30 June 2022.
- On 29 June 2022, the Applicant submitted an application ('the Application') to the Health and Safety Executive ('the Agency') for the professional use of 4-tert-OPnEO as a surfactant, in wash buffer components used in conjunction with FISH test kits and/or their LDT equivalents (the 'test kits'), in clinical diagnostic use by downstream users for medical analysis of human tissue and blood samples to identify characteristic genetic abnormalities related to specific disease conditions.
- On 16 October 2023, the Agency sent its opinion (the 'Opinion') to the Secretary of State for Environment, Food and Rural Affairs, and Scottish and Welsh Ministers.

Decision

1. This decision is addressed to the Applicant.
2. An authorisation is granted to the Applicant in accordance with Article 60(4) of UK REACH for the following use of 4-tert-OPnEO:
    a. Professional use of 4-tert-OPnEO as a surfactant, in wash buffer components used in conjunction with fluorescence in situ hybridisation (FISH) test kits and/or their laboratory developed test (LDT) equivalents, in clinical diagnostic use for medical analysis of human tissue and blood samples to identify characteristic genetic abnormalities related to specific disease conditions.
3. This Authorisation is time limited. This authorisation will cease to be valid and the time limited review period will end on 31 January 2030 unless the authorisation holder submits a review report in accordance with Article 61(1) by 31 July 2028.

[2] This provided time for applicants to submit their application under UK REACH following the transition from EU REACH, where certain criteria were met.

4. The authorisation is subject to the following conditions (as well as the requirement in Article 60(10) of UK REACH to ensure exposure is reduced to as low a level as is technically and practically possible):

   a. The authorisation holder and its downstream users must adhere to the risk management measures ('RMMs') and operational conditions ('OCs') described in the chemical safety report referred to in Article 62(4)(d) of UK REACH;[3] subject to the conditions at subparagraphs b and c below.

   b. By 3 October 2024, the authorisation holder must amend the GB data safety sheet:
      i. to include instructions to downstream users on the use of batch processing to limit the volume of 4-tert-OPnEO.
      ii. to include guidance to downstream users to incinerate the remainder of the waste containing 4-tert-OPnEO;

   c. By 3 November 2024, the authorisation holder must supply the amended GB safety data sheet to downstream users.

5. In the event that a review report is submitted in accordance with Article 61(1), I recommend that this includes:

   a. The results of a new representative survey of the authorisation holder's downstream users including details of their disposal procedures for waste containing 4-tert-OPnEO with regard to national and local regulations. I recommend that the survey is conducted within three years of submission of any review report. These recommendations are not conditions of this authorisation or conditions for any future review report.

6. The authorisation is not subject to any monitoring arrangements.

Background

7. This decision is made under Article 60(4) of UK REACH having obtained the consent of Scottish and Welsh Ministers.

8. In making this decision I have taken into account:

   a. The Application submitted to the Agency;

[3] This is a reference to the chemical safety report submitted by Abbott Laboratories on 22 June 2022 as part of its Application. The risk management measures and operational conditions are described in sections 9 (exposure assessment) and 10 (risk characterisation related to combined exposure).

b. The provisions of Article 60 of UK REACH, including the elements referred to in Article 60(4) and the requirements of Article 60(5);

c. The Agency Opinion.

Reasons

9. In the Application, the Applicant did not derive predicted no-effect concentrations ('PNECs'). Therefore, the Agency concluded that for the purposes of the assessment of this Application it was not possible to determine PNECs for the endocrine disrupting properties of 4-tert-OPnEO for the environment.

10. In accordance with Article 60(3)(a) of UK REACH, this means that Article 60(2) of UK REACH does not apply to this Application. Article 60(2) does not apply to substances for which it is not possible to determine a threshold in accordance with Section 6.4 of Annex I. Therefore, an authorisation may only be granted on the basis of Article 60(4) of UK REACH.

11. An authorisation may only be granted under Article 60(4) of UK REACH if it is shown that the socio-economic benefits outweigh the risk to human health or the environment arising from the use of 4-tert-OPnEO and if there are no suitable alternative substances or technologies.

Risk to the environment

12. 4-tert-OPnEO presents a risk to aquatic life when it degrades to 4-tert-OP in water. When degraded, it can adversely affect the endocrine systems of aquatic organisms. I note that this risk cannot be excluded even at low levels.

13. In the Application, the Applicant explained that its downstream users are widely dispersed, and their rate of use of the test kits varies. This means there is uncertainty regarding the release rates on a local and regional scale. The Applicant explained that the test kits are used by professionals in laboratories and clinics that would normally be expected to handle hazardous waste and that disposal routes are already in place. However, in the absence of a downstream user survey, the level of compliance for collection and disposal of waste containing 4-tert-OPnEO by downstream users is not known. Therefore, the Applicant provided modelled data of worst-case scenario releases, based on the downstream user with the highest use.

14. The Applicant's worst-case scenario assumed that 100% of used test kit solutions containing 4-tert-OPnEO are disposed of to the public foul sewer by 10 to 100 downstream users. The Applicant estimated that, based on the worst-case scenario, 6 kg to 60 kg of 4-tert-OPnEO (1.8 kg to 18 kg of 4-tert-OP) emissions would be released to the environment via water, across all downstream users until the end of January 2030.

15. In its Opinion, the Agency concluded that it is satisfied that the Applicant's estimated releases represent a reasonable worst-case scenario for environmental exposure from the use of the test kits. The Agency concluded that the Applicant's modelling approach is likely to lead to a significant overestimate of actual environmental concentrations of 4-tert-OP and is therefore highly conservative. The Agency concluded that the overall modelling approach is appropriate.

16. In its Opinion, the Agency assessed environmental risk by reference to a well-characterised endocrine disruptor with the same mode of action; ethinylestradiol (EE2), which is known to be more potent than the degradation product 4-tert-OP. Based on this comparison, the Agency concluded that the worst-case emissions in the use applied for are unlikely to cause discernible impacts on aquatic species through endocrine disruption.

17. In the Application, the Applicant was not able to demonstrate that all downstream users comply with appropriate waste disposal. However, the Applicant has demonstrated to the Agency how it intends to instruct downstream users to carry out adequate disposal of the waste containing 4-tert-OPnEO. The Applicant also intends to provide downstream users with instructions to process tests in batches to reduce the volume of 4-tert-OPnEO utilised. The Applicant has noted that as the volume of liquid waste containing 4-tert-OPnEO generated will be relatively small, with the updated instructions this would result in a significantly reduced risk factor. In its Opinion, the Agency agreed that the Applicant's intended actions should be included as conditions for the authorisation. The Agency therefore concluded that the Applicant has demonstrated that exposure to the environment has been minimised to an appropriate and effective level.

18. I note that the downstream users of the applied for use are trained professional clinical technicians using the test kits in controlled environments in small quantities, and that they are expected to dispose of their waste 4-tert-OPnEO containing solutions in line with their institution's guidelines and procedures, which may include measures such as incineration. Nevertheless, I agree with the Agency's recommended conditions, and I consider that specifying that this waste must be incinerated will provide certainty to the Applicant and its downstream users about the treatment method that should be applied.

19. As outlined in paragraph 13, no downstream user survey was completed for this application, and so the level of compliance for collection and disposal of waste containing 4-tert-OPnEO by downstream users is not known. Therefore, in the event the Applicant should submit a review report, I recommend that the Applicant conducts a new representative survey of its downstream users. This would confirm, at the time of any review, the continued effectiveness of the Applicant's OCs and RMMs and demonstrate how downstream users are disposing of liquid waste containing 4-tert-OPnEO in accordance with national

and local regulations. In turn, this would support any future assessment by the Agency at the time of any review.

Socio-economic analysis

20. In its Opinion, the Agency concluded that the Applicant's socio-economic analysis is considered proportionate, and that the evidence in the Application is sufficient for the Agency to reach a definitive conclusion.

21. In its Opinion, the Agency assessed both the socio-economic benefits arising from the applied for use and the socio-economic implications of a refusal to authorise. The Agency concluded that the Applicant has demonstrated that the socio-economic benefits of granting authorisation are estimated to be £0.05 million to £2.7 million. This figure accounts for the avoided profit losses to the Applicant.

22. In addition to the monetised benefits, the Agency concluded that quantitatively assessed impacts would also have a positive net benefit to society, due to the monetised avoided producer surplus losses, as well as qualitatively assessed impacts such as avoided healthcare impacts and avoided consumer profit losses due to use of inferior comparable tests. The Agency accepted that should authorisation not be granted, the subsequent impact on the reduced availability of tests would likely have significant negative outcomes on cancer patients. Therefore, the Agency concluded that it is confident that the true social benefit of authorisation being granted far exceeds the final monetised value.

23. The Agency has concluded that although the precise magnitude of benefits of the applied for use is uncertain because many major benefits (such as patient welfare) are not monetised, the Applicant has demonstrated that such socio-economic benefits would likely be significant over the appraisal period of authorisation.

24. Having evaluated the Agency's assessment, I agree with its conclusions on the quantitative and qualitative benefits.

Conclusion on whether the benefits outweigh the risks

24. I consider that the Applicant has shown that the socio-economic benefits of granting the authorisation outweigh the risk to the environment because of:

    a. The likely quantitative benefits, in respect of avoided profit losses for the Applicant and the avoided reduction in available diagnostic tests;

    b. The likely significant qualitative benefits in respect of avoided reduction in healthcare provision and avoided consumer profit loss; and

    c. The likelihood of low emissions in Great Britain and no discernible environmental impacts in relation to endocrine disruption.

Alternatives

25. The Agency concluded in its Opinion that there were no available alternative substances or technologies with the same function and a similar level of performance that were technically and economically feasible for the Applicant by the sunset date.

26. The Applicant has focused on testing alternative surfactants that could fulfil the function of 4-tert-OPnEO. The Applicant stated that the basic principles of its test kits are similar and that the functions performed by the wash buffers are the same. The Applicant concluded that one surfactant should act as the alternative for all of the test kits. The Applicant tested 20 alternative surfactants and shortlisted the top ranked potential alternatives for feasibility testing and hazard screening. The results of the initial feasibility studies indicated that all the top ranked alternatives provided acceptable results as a substitute for 4-tert-OPnEO in the wash buffer. The Applicant also concluded that any of the alternative surfactants chosen would lead to an overall reduction in risk in comparison to 4-tert-OPnEO. Therefore, the Applicant chose the alternative with the best hazard profile and requested until the end of January 2030 to secure regulatory approval of the chosen alternative.

27. The Agency agreed with the Applicant's assessment that none of the potential alternatives were implementable prior to the sunset date due to the complexity of the substitution products, regulations on in-vitro diagnostic devices (IVD) production and possible extensive validation phases.

28. Having evaluated the Agency's assessment, I agree with the conclusion that there were no available alternatives before the sunset date and consider that the Applicant has discharged their burden of proof in demonstrating the absence of suitable alternatives. In reaching this conclusion, I have considered the Agency's assessment of the technical and economic feasibility of alternative substances already on the market. The Agency did not evaluate the risk of alternatives due to the alternatives not being technically feasible for the Applicant by the sunset date.

Review period

30. In its Opinion, the Agency recommended the review period referred to in Article 60(9)(e) of UK REACH should be until 31 January 2030 (as requested by the Applicant).

31. The Applicant provided a substitution plan which began in 2014. The Applicant is seeking regulatory approval for all products using the alternative by the end of 2025, with a full phase out of 4-tert-OPnEO by the end of January 2030, to coincide with its EU REACH substitution plan. By the end of the requested review

period, the alternative surfactant is expected to be implemented and all existing test kits containing 4-tert-OPnEO will be used up. In its Opinion, the Agency accepted that the estimated time to completely substitute 4-tert-OPnEO from all of the Applicant's products, including shelf life and regulatory approvals, will take up until January 2030.

32. I agree with the Agency's conclusions on these points and its recommendation for a review period until 31 January 2030.

Conclusion

33. For the reasons set out above I conclude that the socio-economic benefits outweigh the risk to the environment for the use of 4-tert-OPnEO referred to in paragraph 2 and that there are no suitable alternative substances or technologies.

34. The Scottish Ministers and the Welsh Ministers have given their consent to this decision in accordance with the requirements of UK REACH.

Robbie Moore

On behalf of the Secretary of State for Environment, Food and Rural Affairs