ANALYSIS OF ALTERNATIVES, SOCIO-ECONOMIC ANALYSIS AND SUBSITUTION PLAN

PUBLIC VERSION

Legal name of authorisation	Abbott Laboratories Limited
Submitted by:	Abbott Laboratories Limited
Date:	17 December 2024
Substance:	4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated
Use title:	Professional use as a surfactant in the final use of In-Vitro Diagnostic Devices (IVDs) for clinical testing using ARCHITECT, Alinity and ABBOTT PRISM automated analyser systems.
Use number:	1

CONTENTS

List of Tables

List of Figures

LIST OF ABBREVIATIONS

4-tert-OP	4-(1,1,3,3-tetramethylbutyl) phenol
4-tert-OPnEO	4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated
AfA	Application for Authorisation
AfU	Applied for Use
AoA	Analysis of Alternatives
CLSI	Clinical and Laboratory Standards Institute
CMV	Cytomegalovirus
COVID-19	Severe Acute Respiratory Syndrome Coronavirus 2
CSR	Chemical Safety Report
DU	Downstream User
EC	European Commission
ECHA	European Chemicals Agency
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EQS	Environmental Quality Standards
EU	European Union
FTE	Full Time Equivalent
GB	Great Britain
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HSE	Health and Safety Executive
HTLV	Human T-cell Leukemia-Lymphoma Virus
IBP	Integrated Business Planning
IVD	*In-Vitro* Diagnostic Device
IVDD	*In-Vitro* Diagnostic Device Directive
IVDR	*In-Vitro* Diagnostic Medical Device Regulation
Kg	kilogram
Koc	Organic carbon-water partition coefficient
Kow	Octanol-water partition coefficient

LVS	Low Volume Site
mg/kg dw	milligram/kilogram dry weight
mg/l or mg/L	milligram/litre
mg/m^3	milligram/metre cubed
MVS	Medium Volume Site
N/A	Not Applicable
NB	Notified Body
NPnEO	Nonyl Phenol Ethoxylate
NPV	Net Present Value
NUS	Non-Use Scenario
ONS	Office for National Statistics
PEC	Predicted Environmental Concentration
PM	Program Management
PMO	Program Management Office
R&D	Research and Development
REACH	The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SEA	Socio-Economic Analysis
SEAC	Socio-Economic Assessment Committee
STP	Sewage Treatment Plant
SVHC	Substances of Very High Concern
UK	United Kingdom of Great Britain and Northern Ireland
VHVS	Very High Volume Site
Y	Year

DECLARATION

We, the Authorisation Holder, are aware of the fact that further evidence might be requested by UK Authority to support the information provided in this document.

Also, we request that the information blanked out in the "public version" of the Analysis of Alternatives and Socio-economic Analysis is not disclosed. We hereby declare that, to the best of our knowledge as of today 17 December 2024, the information is not publicly available, and, in accordance with the due measures of protection that we have implemented, a member of the public should not be able to obtain access to this information without our consent or that of the third party whose commercial interests are at stake.

Signature: Date, Place:

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17 Dec 2024, Longford, Ireland

1. SUMMARY

1.1. Background

In 2021, Abbott Laboratories Limited (henceforth, the Authorisation Holder) applied for authorisation for the following use:

- USE 1. Professional use as a surfactant in the final use of In-Vitro Diagnostic Devices (IVDs) for clinical testing using ARCHITECT, Alinity and ABBOTT PRISM automated analyser systems.

The final Decision of the Secretary of State for Environment, Food and Rural Affairs, and Scottish and Welsh Ministers was granted on 3 July 2023 granting the Applicant an Authorisation for the use, with a review period of 5.5 years, until 30 December 2027.

Due to factors outside of the Authorisation Holder's control, which include regulatory requirement changes, increased percentage of assays requiring further optimisation, the substitution timeline to remove 4-tert-OPnEO has been impacted. As a result, substitution will not be complete by the end of the current authorised review period of 30 December 2027. Therefore, this review report is being submitted for Use 1 of the original GB Application of Authorisation (AfA), to modify the expected 4-tert-OPnEO substitution timeline and to extend the UK authorised review period. The factors affecting the substitution timing, are outlined in the accompanying Substitution Plan in Section 4.1.3 below.

This review report will only contain information that has been modified from the original AfA. The Authorisation Holder has demonstrated excellent progress in removing 4-tert-OPnEO from its products and is committed to removing 4-tert-OPnEO from the remaining products.

The products with the highest 4-tert-OPnEO usage, namely Pre-Trigger and Trigger system solutions, were prioritised for substitution and are already free of 4-tert-OPnEO. This equates to a reduction of [redacted] kg as compared to 2021 usage. In addition, 4-tert-OPnEO use in [redacted] of [redacted] GB products will have either completed substitution or been discontinued by the end of 2024, eliminating an additional [redacted] kg of 4-tert-OPnEO. A total reduction through 2024 of [redacted]% of the substance has been achieved compared to 2021 quantities.

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Due to the previously referenced constraints, the Authorisation Holder is unable to meet the current authorisation end-date of 30 December 2027 and hereby request an extension of the review period until 04 January 2033. This new date also aligns with the Authorisation Holder's EU Authorisation end date, to gain efficiencies in completing substitution. It should also be noted that several competitors in GB have a similar authorisation review period through the end of 2032. Based on the reformulation efforts and learnings to date, the Authorisation Holder is confident of meeting this proposed end date.

1.2. Comparison of costs and benefits

The economic impacts from a refused modification to the authorised review period, affect not only the revenue and profit losses of the Authorisation Holder from the GB market, but there would also be a wide variety of collateral interests impacted. The refusal would affect the Authorisation Holder's customers, who could face increased costs to find alternative suppliers of testing instruments and IVD kits. Employees in the UK could lose their jobs in the event of a refused authorisation and the social cost of the unemployment would be substantial. Most critically, patients could face delayed diagnoses of serious health conditions related to increased times in generating diagnostic test results.

A granted authorisation would allow the Authorisation Holder to continue offering highly precise IVD tests to their customers to carry out tests necessary for the diagnosis of serious health conditions and for the required screening of life-saving blood donations. The Authorisation Holder would continue providing their GB customers with IVD kits to run more

than [redacted] million clinical chemistry and immunoassay tests annually. At the same time, their customers would continue testing over [redacted]% of the GB blood and plasma donations. Given the critical role of the Authorisation Holder's instrument systems in laboratory testing, transitioning to a replacement competitive system due to a refused authorisation would be a lengthy process for our customers. This includes steps such as sourcing, tendering, installation, qualification, and validation, potentially leading to shortages in testing capacity for blood components in the UK/GB. CBI b g

In addition, many of the Authorisation Holder's assays are used for monitoring patient conditions and drug levels. Changing the testing methodology used to monitor these conditions and drug levels, particularly for immunosuppressant drugs administered in solid organ transplants, may introduce additional risk to the patient because of variances between competitor assay performance offerings such as sensitivity, specificity, and precision.

In the Non-Use Scenario, the Authorisation Holder's GB employees would need to be laid off, because the Authorisation Holder's operations would be redundant if no products were marketed in GB. The unemployment created from a refused authorisation would have a significant social cost to GB society in general.

Table 1.1 summarises the total monetised costs from a refused authorisation.

Table 1.1: Costs of non-use per unit of release from 2028-2032

	Over 5 years (2028-2032)
Total costs (£)	10 - 100 ([redacted]) million
Total releases (kg)	10 – 100 ([redacted])
Ratio (£/kg)	100,000 – 1,000,000 ([redacted])

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The cost of a refused authorisation per kg of prevented 4-tert-OPnEO emissions is between £100,000 and £1,000,000 ([redacted]) per kg for the GB impacts. The economic costs include the expected net profit losses of the Authorisation Holder as well as the social costs of unemployment for the Authorisation Holder's employees that would likely lose their jobs. The cost to replace the Authorisation Holder's instruments could also be a significant economic impact to customers.

The current substitution plan of the Authorisation Holder aims to remove the remaining 4-tert-OPnEO from reagent solutions. Substituting 4-tert-OPnEO would require only a small fraction of the cost of a refused authorisation. For comparison, the cost of the project for substitution in the reagents across the EU is £100-1,000 (£[redacted] million). However, at the end of the current authorised review period on 30 December 2027, [redacted] products would be remaining to complete substitution. The portion of the cost associated with development and launch of 4-tert-OPnEO free products is £[redacted] million. With GB sales being 1-25% ([redacted]%) of the Authorisation Holder's EU sales, the proportional cost of substitution used for this analysis would be £1-10 (£[redacted] million), equating to 5,000 – 50,000 ([redacted]) £/kg. Compared to the Authorisation Holder's substitution efforts, a refused authorisation is an ~10-fold less cost-effective option. CBI d CBI b

Overall, if the length of the review period is not extended to the proposed 4 January 2033 as examined in this SEA, there would be a disproportionate impact to the Authorisation Holder, their GB customers, and their employees. Most importantly, the lives of patients who are in need of blood transfusion and blood products (e.g. emergency or operations) and those who are being tested for serious diseases and conditions (e.g. thyroid or cancer) with the immunoassay and clinical chemistry IVD kits of the Authorisation Holder would be significantly impacted.

As many of Abbott's competitors are distributing products containing 4-tert-OPnEO under an authorisation expiring at the end of 2032, the impact to the environment may not improve as the emissions could be similar from the alternative competitor products. This SEA shows that the benefits of a modified authorisation outweigh the risks to the environment.

2. AIMS AND SCOPE

2.1. Aims and Scope

2.1.1. Aims of the AoA and SEA

Abbott Laboratories Limited (the Authorisation Holder) applied for authorisation for this use of 4-tert-OPnEO in November 2021:

- USE 1. Professional use as a surfactant in the final use of In-Vitro Diagnostic Devices (IVDs) for clinical testing using ARCHITECT, Alinity and ABBOTT PRISM automated analyser systems.

The final Decision of the Secretary of State for Environment, Food and Rural Affairs, and Scottish and Welsh Ministers was granted on 3 July 2023 granting the Applicant an Authorisation for the use, with a review period of 5.5 years, until 30 December 2027.

The aim of this combined AoA and SEA report is to justify the need to extend the length of the GB authorised review period as it has been identified that the timeline presented in the original Application for Authorisation is not feasible due to factors outside of the Authorisation Holder's control, including regulatory and technical issues during 4-tert-OPnEO reformulation. For those products which have not completed 4-tert-OPnEO substitution by the end of 2027 (i.e., the end of the current review period), products could still be sold in all countries excluding GB. The most efficient and economical manner to extend the substitution timeline for the UK would be align with that of the EU, which is 4 January 2033 which is also the GB authorisation end-date of a number of Abbott's direct competitors.

In addition, the amount of 4-tert-OPnEO used by the authorisation Holder's downstream users will be updated to reflect the updated substitution plan. The Authorisation Holder has already completed substitution in its Pre-Trigger and Trigger Solutions which equates to a [redacted] kg reduction of 4-tert-OPnEO used by downstream users as compared to 2021. The ABBOTT PRISM instruments and reagents were discontinued at the end of 2022, which accounts for [redacted] kg of the 4-tert-OPnEO usage. An additional [redacted] kg (used in [redacted] of the Authorisation Holder's products sold in GB) has been eliminated due to completing remediation on the reagents, which equates to an overall reduction of [redacted] kg ([redacted]%) of 4-tert-OPnEO by the Authorisation Holder's downstream users in GB. The Authorisation Holder is also making good progress on the remaining [redacted] kg associated annually with the reagents, as will be discussed in Section 4.1.3 (Substitution Plan). This document will provide an update of the Authorisation Holder's substitution activities and will demonstrate that the benefits of modifying the authorised review period to 4 January 2033 outweigh the risks to the environment from the continued use of 4-tert-OPnEO.

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2.1.2. Temporal and geographic scope of the SEA

The Authorisation Holder was granted a 5.5-year review period for professional use of its IVD kits by their GB customers. The impact of modifying the authorised review period to 10 years (4 January 2033) will be addressed for the period from 2028 until the end of the requested extended review period (in practice, end of 2032). As this use impacts the ability of GB customers to test blood and tissue samples for various conditions and diseases, only the impact on the GB market will be assessed, including impacts on the Authorisation Holder, suppliers, laboratories and blood banks, and the Authorisation Holder's employees. Northern Ireland and related information will not be included within this assessment due to the terms of The Windsor Framework (which replaced the Northern Ireland Protocol) [1].

2.2. Information on the Authorisation Holder's products

2.2.1. The Authorisation Holder

Abbott is a worldwide healthcare company and has a broad range of branded generic pharmaceuticals, medical devices, diagnostics, and nutrition products. The company's *in-vitro* diagnostics (IVD) business provides immunoassays, including blood screening products, and clinical chemistry tests to customers worldwide. Its medical tests and diagnostic instrument systems are used by hospitals, laboratories and blood banks for clinical diagnosis and monitoring diseases. The Diagnostics business manufactures a broad range of tests, including HIV, hepatitis, SARS-CoV-2, traumatic brain injury, thyroid function, fertility and pregnancy, cardiology, renal and metabolic markers, therapeutic drug monitoring, detection of drugs of abuse and clinical chemistry assays as well as other indicators of health.

Abbott employs approximately 114,000 employees worldwide [2] and in 2023 had a combined sales value of $40.1 billion [3]. Abbott Core Diagnostics includes Core Laboratory and Transfusion, all of which are impacted by 4-tert-OPnEO. This division of Abbott employs approximately [redacted] employees globally. Three reagent manufacturing plants in the EU and a distribution centre, supply products to customers worldwide, including the UK. CBI e

Abbott distributes more than 600 different IVD products worldwide to more than 160 countries [2], through the central distribution centre (Abbott Diagnostics GmbH) located in Wiesbaden, Germany. Abbott Laboratories Limited (henceforth the Authorisation Holder) is the legal entity applying for an extended review period of an additional 5 years on behalf of their professional downstream users in GB for the use of 4-tert-OPnEO in reagent solutions.

2.2.2. Current market situation

2.2.2.1. Authorisation Holder's sales

The Authorisation Holder's global sales of blood and plasma screening, core laboratory immunoassay and clinical chemistry IVD kits, instruments and services were £1,000– 10,000 (£[redacted]) million in 2023. Approximately £10-100 (£[redacted]) million consisted of UK sales. CBI b

The Authorisation Holder's sales include three categories: instrumentation, solutions (reagents, calibrator/controls, system solutions), and services. These are all part of the sales packages offered to customers. The Authorisation Holder supplies the instruments needed to run the assays, along with the reagent kits for the individual tests, according to each customer's needs. Finally, there are supporting services such as training, maintenance and consulting that are offered as part of the overall package.

Table 2.1 shows an estimation of the Authorisation Holder's revenue and profits from sales of IVD kits within GB during the authorised review period. The sales include the costs of the instrument platforms used for carrying out the testing with the IVD solutions kits. As instruments were specifically designed for use with the Authorisation Holder's IVD solutions kits, loss of market for the kits would lead to loss of market for the instruments as well. In a typical contract between the Authorisation Holder and a customer, the Authorisation Holder supplies both the testing instrument platform and the IVD solutions kits. Profits are calculated using a 1-10% ([redacted]%) net profit margin, based on projections through the Authorisation Holder's long-range plan. The Authorisation Holder expects that sales will increase at a rate of 1-10% ([redacted] and [redacted] afterwards) until the end of the requested review period. CBI b

Table 2.1: GB revenue and profits from sales of the Authorisation Holder's IVD kits for the AfU Scenario (in £ million)

	Revenue	Profits
2022	[redacted]	
2023		
2024		
2025		
2026		
2027		
2028		
2029		
2030		
2031		
2032		
Total		
Total 2028-2032		

Note: These values were calculated from the Authorisation Holder's 2023 sales, assuming a [redacted] (discounted to 2023 prices using a 4% discount factor) afterwards in consumption, driven by increased demand.

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From 2028 through the end of the requested review period, the total GB revenue is estimated at £100-1000 (£[redacted]) million and the profits at £10-100 (£[redacted] million. The prices have been discounted to 2023 prices using a 4% discount factor.

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2.2.2.2. Upstream supply chain

The Authorisation Holder's GB sales account for 1-10% ([redacted]%) of their Global Sales in 2023. In the event of a refused authorisation, it is not anticipated that upstream, raw material suppliers in GB would be impacted.

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2.2.2.3. Downstream customer: clinics, hospitals, health practitioners, blood banks, etc.

The Authorisation Holder's customers are healthcare professionals that analyse patient samples daily, often across multiple shifts. More specifically, the main customers for the Authorisation Holder's IVD kits are:

- Core laboratories, based in or outside of hospitals, providing full day services to both adult and paediatric patients. The test menu includes general chemistries, therapeutic drug testing, endocrine testing, and comprehensive emergency toxicology and psychotropic drug testing services.
- Blood, plasma and organ banks, which obtain and test blood for transfusion/transplant with the need to test each blood/organ donation for transmissible medical conditions before it is used in transfusion or transplant. The blood or organ is sent to hospitals through dedicated distribution channels.
- Other customers, such as physicians' offices, government agencies, alternate care testing sites and plasma protein therapeutic companies.

In addition to performing the testing on the patient samples, customer laboratories make a profit on the services provided. The Authorisation Holder has supplied GB laboratories with over [redacted] instrument systems for use in testing patient samples using the Authorisation Holder's IVD kits. The profits seen by customer laboratories cannot be calculated with certainty, so these profits will not be calculated, nor carried forward within the SEA.

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3. ANALYSIS OF ALTERNATIVES

3.1 SVHC use applied for

The SVHC use being applied for: Professional use as a surfactant in the final use of In-Vitro Diagnostic Devices for clinical testing using ARCHITECT, Alinity and ABBOTT PRISM automated analyser systems.

The information provided in the original Analysis of Alternatives has not changed. The potential alternatives identified are actively being evaluated for use in products containing 4-tert-OPnEO. Even though the alternative is considered generally available, it will not be considered suitable or available for an individual product, until all design verification testing has been successfully completed and regulatory submissions have been approved, respectively.

The applied for use included the ABBOTT PRISM instruments and reagents. However, that analyser was discontinued world-wide at the end of 2022 and is not pertinent to the discussion throughout the AoA and SEA for 2023 and beyond.

3.1.1 Annual volume of the SVHC used

The use quantities presented in the original AfA for downstream user volumes were based on a mass balance approach, assuming an average amount of 4-tert-OPnEO per assay. This approach was used to provide a representative picture of the usage and potential emissions at specific downstream user sites at the time of preparation of the original AfA.

For the purposes of reporting 4-tert-OPnEO reductions over the review period, the mass balance approach also assumed that each product contributes equally to the total 4-tert-OPnEO quantity. Additionally, provided the use of a product containing 4-tert-OPnEO ceases within a calendar year, it is assumed to count fully towards the 4-tert-OPnEO usage for that year. This approach would likely overestimate the 4-tert-OPnEO quantities, as products without 4-tert-OPnEO launch throughout the year, however, it is assumed that the substance was used through the entire year.

The mass balance approach was re-evaluated based on the progress made on substitutions as well as projections of substitution completion using new factors identified since the original AfA was submitted in 2021. Each product pending substitution was assessed for technical and regulatory risk, with a risk level of low, medium, and high applied and based on the risk, a risk factor applied time of 1, 2 or 3 years was assigned to each product, respectively. The factors impacting the ability of the Authorisation Holder to complete substitution are discussed in detail in Section 4.1.3 below. Table 3.1 provides estimates of the annual 4-tert-OPnEO quantities through the end of the requested review period. The tonnage band beginning in 2028 when the extended review period is to become effective would be 10-100 kg/y.

Table 3.1: Estimated annual quantities of 4-tert-OPnEO by downstream users and number of products contributing to the annual quantity, compared to the annual quantities of 4-tert-OPnEO from the original AfA

Year	Annual Quantity 4-tert-OPnEO from original AfA for GB Customers (kg)	Number of Products Contributing to 4-tert-OPnEO	Annual Quantity 4-tert-OPnEO for GB Customers (kg)
2022	[redacted]	[redacted]	[redacted]
2023	[redacted]	[redacted]	[redacted]
2024	[redacted]	[redacted]	[redacted]
2025	[redacted]	[redacted]	[redacted]
2026	[redacted]	[redacted]	[redacted]
2027	[redacted]	[redacted]	[redacted]
2028	[redacted]	[redacted]	[redacted]
2029	[redacted]	[redacted]	[redacted]
2030	[redacted]	[redacted]	[redacted]
2031	[redacted]	[redacted]	[redacted]
2032	[redacted]	[redacted]	[redacted]
2033	[redacted]	[redacted]	[redacted]

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The substitution projections shown in the table above show that the number of products and the annual quantity of 4-tert-OPnEO used by downstream users is steadily decreasing over the review period. The total amount of 4-tert-OPnEO used over the extended review period, between 2028 and 2032, is [redacted] kg.

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Cumulative Releases

The Authorisation Holder is committed to removing 4-tert-OPnEO from its products. To date, the highest use of 4-tert-OPnEO was prioritised to remove the substance from the Pre-Trigger and Trigger solutions. Pre-Trigger and Trigger solutions were discontinued in the UK/GB in 2021 and has resulted in removal of [redacted] kg of the total 4-tert-OPnEO used by the Authorisation Holder's downstream users.

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In addition, the ABBOTT PRISM instrument and reagents were discontinued in the UK/GB at the end of 2022. This equated to [redacted] kgs per annum of 4-tert-OPnEO which had been disposed to solid waste and incinerated. The solid waste from the ABBOTT PRISM instrument and reagents is discussed in section 9.1 of the CSR from the AfA submitted in 2021, however, there are no longer emissions from this instrument, so it is not considered further in the calculations.

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Figure 3.1 shows the usage of 4-tert-OPnEO by the Authorisation Holder's GB customers, also indicating the significant reduction in usage achieved so far.

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Figure 3.1: Reduction of total 4-tert-OPnEO at downstream user sites

Compilation

Figure 3.2 shows the expected 4-tert-OPnEO reduction over the extended review period. Certain factors affecting the substitution timing are outside of the control of the Authorisation Holder, i.e., regulatory requirement changes, increased percentage of products requiring further optimisation, etc.

The Authorisation Holder is confident that all substitution activities will be completed by the end of the requested extended authorised review period, 04 January 2033, based on our progress and reformulation knowledge learned during this substitution program.

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Figure 3.2: 4-tert-OPnEO reagent reductions over the authorised review period

The quantity of 4-tert-OPnEO from reagents (excluding Trigger and Pre-Trigger Solutions) will have been reduced by approximately [redacted]% by the end of 2027 as compared to the emissions in 2021, with 2027 being the end of the authorised review period. The factors

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impacting the ability of the Authorisation Holder to complete 100% substitution by the current authorised review period are discussed in detail in Section 4.1.3.

4. SOCIO-ECONOMIC ANALYSIS

4.1. Continued use scenario

4.1.1. Summary of substitution activities

Since the original AfA was submitted in 2021, the Authorisation Holder has updated the substitution plan and roll out of new products which are 4-tert-OPnEO free has been following that plan. By the end of 2024, [redacted] products (from the [redacted] that were in scope of the original AfA) will have either been substituted or discontinued, including ABBOTT PRISM instruments and reagents which were retired in 2022. The remaining products are at various phases in the Authorisation Holder's substitution process and are expected to complete the removal of 4-tert-OPnEO by the end of the extended authorised review period. Figure 4.1 shows the status of the products within the Authorisation Holder's substitution plan that have completed each phase. See the original AfA for an explanation of each stage of the substitution process.

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Figure 4.1: Number and percentage of reagents completing phases of substitution

Substantial progress has been made in completing the Technical Feasibility stage which includes both Preliminary Feasibility and Design Verification. [redacted]% of products have completed feasibility studies using a 4-tert-OPnEO replacement and [redacted]% of products have completed Design Verification testing, leaving only the regulatory approvals and customer conversion. With the design verification manufacturing and testing complete, the risk of needing further optimization is reduced significantly.

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4.1.2. Conclusion on suitability of available alternatives in general

The Authorisation Holder has concluded through the screening process that Alternative No. 1, [redacted] (1a & b), has properties that most closely match those of 4-tert-OPnEO and therefore, is the best choice for substitution. Even though the potential alternative is available in general, it is not considered suitable for specific assays until it meets the requirements of the design verification testing and obtains regulatory approval for each individual product from the required countries.

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4.1.3. Substitution plan

The Authorisation Holder submitted a substitution plan with the original AfA in November 2021, requesting a review period of 5.5 years. In late 2022 - early 2023, new circumstances outside the control of the Authorisation Holder were identified that extended the overall duration of substitution activities beyond the review period requested, despite the Authorisation Holder's efforts. These circumstances include regulatory requirement changes (e.g. EU IVDR, China, Korea, etc.), increased percentage of products requiring further optimisation, etc. These are detailed in Section 4.1.3.1. Changes in the substitution timing can have a significant effect on the reduction profile.

Figure 4.1 shows the percentage of products that have completed each phase of the substitution process. Significant progress has been made. The Authorisation Holder is

confident that all substitution activities will be complete by the end of the requested extended review period on 04 January 2033.

4.1.3.1. Factors affecting substitution

Technical Feasibility of most likely alternatives

Preliminary technical feasibility studies with the primary alternative surfactants completed prior to submission of the original AfA, indicated that [redacted]% of the products would require further optimisation to meet expected performance. However, in studies completed since then in the subsequent design verification phase, which involves more extensive studies, a total of [redacted]% of the products required additional modifications to achieve acceptable performance. This required additional rounds of investigations, reformulation and/or other system changes, followed by a repeat of manufacturing and extensive verification studies. Drivers for the higher-than-expected rate of performance issues identified through design verification studies included: CBI d

- Evaluation of larger patient sample populations (circa. [redacted]) is required during the design verification phase. The larger sample population may identify certain events that require remediation (e.g., false positive results) for rare sample types. CBI d
- Following completion of preliminary feasibility, products were evaluated for robustness to analyser variation (contrived worst-case boundary conditions). This identified a subset of products for which further optimisation was required, which can add significant timing to the process.
- The Clinical Laboratories and Standards Institute (CLSI) updated their standards for linearity testing, which are used by the Authorisation Holder in their verification process, causing some products to require repeat testing. During testing, the current marketed product containing 4-tert-OPnEO, and the reformulated product are tested against the updated, modernised regulatory requirements. [redacted] This causes delays which complicate the implementation of the detergent substitution. CBI d
- Regulatory standards have been updated in some countries, such as South Korea which changed the protocol for testing for stability and China now requires administrative and technical changes be submitted separately. In some cases, the administrative changes are to be submitted first, delaying the submissions for the technical changes.
- The EU replaced the *in vitro* Device Directive (IVDD) with the *in vitro* Device Regulation (IVDR), causing increased regulatory approval times beyond the ability of the Authorisation Holder to influence, due to a majority of products requiring Notified Body review of changes prior to market entry. As a single product is manufactured for markets globally, any regulatory changes impact entry into all countries where the product is sold. The EU is often the first region an IVD product is registered in and the change in EU regulation for IVDR is the most important reason for the increased deadlines to succeed in substitution compared to the original plan.
- In some cases, the currently marketed version of the product to be reformulated is being evaluated for other potential changes (i.e., in addition to changing the surfactant). Once these changes are finalised, the alternative surfactant will require re-evaluation in the final configuration.
- The worldwide COVID-19 pandemic caused a decrease in resources available to manufacture and perform testing. Resource availability was staggered in order to maintain safe social distances within the laboratory and offices, which decreased the amount of testing that could be completed, causing timelines for testing to be extended.
- Due to the COVID-19 pandemic, sourcing of human serum, plasma, urine and other specimens required to validate the 4-tert-OPnEO changes was disrupted, due to the

availability of these specimens with elective hospital procedures, general physician visits and prospective specimen collections being curtailed. Regulatory authorities require the use of 'native' specimens for the disease state in question which can be very difficult to source in the best of conditions.

Significantly for the programme, the higher-than-expected rate of complex reformulations has delayed the completion of the technical feasibility phase by 12 months compared to what was originally envisaged. These activities are now due to complete by the end of 2026. Despite these challenges, the Authorisation Holder has made significant progress, as shown in Figure 4.1 above. Technical feasibility has been demonstrated for [redacted]% of products. An additional [redacted]% of products will not require design verification testing due to discontinuation of products, with [redacted]% already discontinued. [redacted]% of the products remain to complete design verification studies. [redacted]% of the total products required further optimisation as the initial design verification studies were not successful. Table 4.1 shows the status of Design Verification activities for all products.

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Table 4.1. Status of Design Verification studies

Status of Design Verification Activities	Number of Products
Studies not required (e.g., product retirements)	[redacted]
Studies complete with acceptable results	
Studies in process/pending	
Products that required further optimisation Status: - Optimisation complete and design verification complete ([redacted]) - Optimisation complete, pending verification ([redacted]) - Optimisation ongoing ([redacted])	

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Constraints of laboratory and manufacturing facilities

The process of establishing technical feasibility for any given product involves a complex multi-step IVD manufacturing process. Due to physical capacity constraints within the laboratories and manufacturing facilities, it is not possible to run technical feasibility studies on the 100 – 200 ([redacted]) IVD products in parallel. Capacity within the laboratories was further constrained with the introduction of physical distancing requirements during the Covid-19 pandemic. Moreover, studies have shown that the primary alternative is not technically feasible in some product applications ([redacted]% of products to date), thus additional studies with secondary alternatives are required on a case-by-case basis, which will delay the rollout of these products with the new surfactant.

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Availability for Implementation

The identified alternatives are already in use by the Authorisation Holder in a number of marketed products. Therefore, the Authorisation Holder has already qualified a supplier for the surfactants, and it has been confirmed that the increased demand for use in its 100 - 200 ([redacted]) assays can be met within the substitution timeframe. Although the identified alternatives are considered generally available to the Authorisation Holder, availability for implementation as a substitute is dependent on regulatory approvals of the change. In addition, several products are required to utilise multiple lots (lot diversity) of the alternative surfactant during design verification testing. Although the volume of the substitute is available, the number of lots of the alternative may not be available. This can cause a delay in the event additional lots of the substitute are required to be manufactured to meet the regulatory requirements for Design Verification and Validation. As each product is marketed

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in all impacted countries, change approval applications must be prepared and submitted by the Authorisation Holder with approvals granted by the regulatory authorities worldwide in all impacted countries where the IVDs are marketed prior to market entry, including GB. It is therefore concluded that the identified alternatives are not yet available for substitution to the Authorisation Holder for each of their specific products.

Regulatory Factors

EU Regulations

The IVD classification system was modified to adhere to the requirements of the In Vitro Diagnostics Regulation (Regulation (EU) 2017/746, IVDR) resulting in approximately 80% of the Authorisation Holder's IVD products requiring Notified Body (NB) certification, where previously only approximately 20% required certification via a notified body. As a result, there will be increased time in obtaining regulatory approvals in the EU/EEA, which in turn impacts the timing to market the product in other countries, including GB.

Specifically in the European Union, the due dates completing substitution overlap directly with new requirements being introduced under IVDR, where the majority of existing marketed products must undergo recertification under the new regulation. This adds additional complexity and can affect commercialisation dates in all countries (not just in EU), due to the need to accommodate both REACH and IVDR requirements for individual products. Notwithstanding this, the challenges associated with the implementation of the IVDR regulatory framework in the EU have proven much more demanding than anticipated, leading the EU to make the decision to delay and stagger the roll out of IVDR from May 2025 to May 2027 [4]. Some of the reasons that gave rise to this decision include:

- A shortage of NB capacity, including delays in designating NBs under IVDR.
- An approximate ten-fold increase in the number of products to be certified by NB under IVDR compared with the In Vitro Diagnostics Directive (Directive 98/79/EC, IVDD) where they would have been self-declared.
- Insufficient commensurate resources as well as systems capacity issues giving rise to elongated times for completion of conformity assessments, product, and site certifications.

These issues are also evident to the Authorisation Holder, as they are observing a significant increase in review and approval timing of IVDR submissions compared with what was originally assumed (approx. 12 months or more versus three months originally). Under IVDR, there is no identified responsible party to assess capacity within the EU Regulatory framework and whatever assessments are performed in an *ad hoc*, non-coordinated fashion across each of the stakeholders.

International Regulatory Approvals

From an international perspective, delays in the acquisition of required EU regulatory approvals to facilitate international change submissions have delayed the implementation of the surfactant changes globally. The products in scope are sold worldwide. Generally, international regulatory submissions can be initiated concurrently with the EU submissions when a product only has the substitution changes. However, the international regulatory submissions are initiated after EU approvals when other changes are being made, such as IVDR changes. Reformulated products are launched once all the relevant international regulatory authorities approve the change.

Additionally, since the original UK AfA was submitted 12 November 2021, there have been international regulatory developments that affect the timing of substitution. China introduced legislative changes in October 2021 that no longer permit administrative changes to be combined with technical changes (such as a surfactant change) in a single submission.

Administrative changes that were planned to be submitted concurrent with the surfactant change for some of the Authorisation Holder's products now must be submitted separately, with administrative changes in question preceding the technical changes. Because these products are sold worldwide, approvals from all countries are needed prior to distributing these products and removing the version of the assay containing 4-tert-OPnEO from the market.

EU Notified Body delays and other international regulatory developments have extended the regulatory approval phase by 18 months for multiple products. In combination with limited laboratory space, this delay can put a significant strain on the available resources, potentially delaying the substitution process in some assays.

Commercialisation dates for reformulated products are dependent on the timing of international regulatory approvals. Regulatory expectations for the design of verification studies and product performance are continuously evolving to align with best practices and standards, such as those issued by the CLSI. This can extend the timeframe for removing 4-tert-OPnEO from a product, as additional time may be needed to complete the revised studies. In limited cases, more substantive design changes may be needed to meet modern study requirements, i.e., beyond a surfactant replacement.

4.1.3.2. List of actions and timetable with milestones

The substitution process involves a number of individual steps that mirror the Authorisation Holder's IVD design process, taking account of regulatory and technical performance requirements. The steps involved in the substitution project are listed below and detailed in the original Application for Authorisation and have not changed.

1. Identification of Alternatives
2. Technical Feasibility Studies
3. External Clinical Performance Evaluation
4. Regulatory Approval
5. Implementation
6. Customer Conversion

4.1.3.3. Monitoring of the implementation of the substitution plan

The Authorisation Holder has established a program-level organisation dedicated to identifying and implementing alternatives for 4-tert-OPnEO in the Authorisation Holder's entire range of IVD products. Individual project managers are in place at each manufacturing site with responsibility for tracking and reporting progress on a weekly basis. A program management office is in place to provide overall monitoring of the implementation of the substitution plan with monthly and quarterly reporting up to divisional and executive management. Overall, approximately [redacted] full time head count (FTE) annually are dedicated to completing the phases described below, mainly in research & development area, but also including operations manufacturing personnel, program and project management, supply chain, marketing, quality, regulatory and finance. Table 4.2 presents a summary of the monitoring plan associated with each stage of the substitution plan.

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Table 4.2: Monitoring plan summary

Phase	Phase / Milestone Description	Actions	Resource	Timeframe and current status	Monitoring Progress	Identified risks/factors impacting substitution	Mitigation / Escalation
1.	**Identification of Alternatives**	• Literature search • Consultation with suppliers • Internal Consultation • Screening based on physicochemical properties	Internal/Consultants/ Literature search	Complete 2014	N/A	N/A	N/A
2.	**Technical Feasibility** a) Preliminary Studies	• Small scale manufacture. • Comparative performance studies.	Technical Personnel	*In progress* *2015-2026* [redacted] [redacted]% complete	Ongoing review of study results Weekly team meeting to review	Preliminary studies indicate that primary alternative is not suitable / results do not meet specifications or are not equivalent to	Follow further optimisation process, Repeat feasibility studies with alternate substitute for 4-tert-OPnEO. Perform additional characterisation studies for high-risk products and

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Phase	Phase / Milestone Description	Actions	Resource	Timeframe and current status	Monitoring Progress	Identified risks/factors impacting substitution	Mitigation / Escalation
					substitution progress	on-market product.	for new CLSI standards.
	Technical Feasibility b) Design Verification Studies	• Full scale production lots • Drafting production documentation • Complete design verification product requirement testing • Report creation & review and approval of the design • Ensure IVD regulatory requirements for testing are meet. • Verification for each product change	Technical Personnel	*In progress* *2018-2027* [redacted]% complete	Monthly management reviews	Product requirements not met, or results are not equivalent to on-market product.	Follow failure investigation process, determine root cause, implement corrective and preventive actions, repeat studies or return to preliminary feasibility phase and evaluate additional alternatives.
3.	**External Studies**	• Possible clinical setting testing (for some products, the number of specimens requiring testing can exceed 5,000).	Clinical Affairs	*Scheduled* *2025 – 2028* *Not required to date*	Clinical monitoring status	Resources not available to conduct studies	Management review to assess need for strategy changes and/or increased resource.

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Phase	Phase / Milestone Description	Actions	Resource	Timeframe and current status	Monitoring Progress	Identified risks/factors impacting substitution	Mitigation / Escalation	
4.	**Regulatory Approvals**	• Documentation delivery (Extensive documentation is required to be compiled on each product) • Obtain EU regulatory approvals • Obtain international regulatory approvals (up to 18 months to review a package)	Medical Writing Regulatory	*In progress* *2020 – 2029* [redacted]% complete	N/A	Resources or design data needed to support regulatory submissions insufficient; approval cycle times too long (can be 2-3 years); alignment with IVDR product modifications/ submissions; changing regulatory requirements in various countries requiring additional testing.	Management review to assess need for strategy changes and/or increased resource allocation.	CBI d h
5.	**Implementation**	• Change Control (creation of new documents) • Change of Labelling of inserts/operational manuals/safety data sheets • Manufacturing documentation updates	Technical Operations Labelling Environmental Health & Safety	*In progress* *2020 – 2030* [redacted]% complete	Weekly team meeting to review implementation progress. Monthly management reviews.	Resources insufficient to complete necessary document updates.	Management review to assess need for strategy changes and/or increased resource allocation.	CBI d h

Phase	Phase / Milestone Description	Actions	Resource	Timeframe and current status	Monitoring Progress	Identified risks/factors impacting substitution	Mitigation / Escalation
6.	**Customer Conversion**	• Inform customers (communication plan) • Last-lot-to-stock consumption per ordering patterns typically 2 months) • Validation Procedures (Cross-over testing studies may be required)	Commercial	*In progress 2021 – 2032* [redacted]% complete	Perform periodic reviews of customer service tickets and complaints.	Customer acceptance and/or assay validation progress inconsistent with timeline.	Consider additional customer communication and/or training activities.

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The REACH substitution program is monitored at multiple levels from Program Governance through Executive Management. The Integrated Business Plan (IBP) reviews flow from lowest level up to the highest levels within the Abbott Diagnostics Division. The various meetings range from weekly to quarterly, with the level of management increasing as information is elevated to the next level. There are several program level reviews which occur and escalate with reviews occurring at Divisional management and moving to Executive Management. Figure 4.2 graphically shows the meetings related to the REACH substitution program with the escalating review process.

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Figure 4.2: REACH Meeting Cadence – Multi-level review process

4.1.3.4. Conclusions

Suitability

The Authorisation Holder concluded through the screening process that [redacted] have properties that most closely match those of 4-tert-OPnEO and therefore, is the best choice for substitution. CBI h

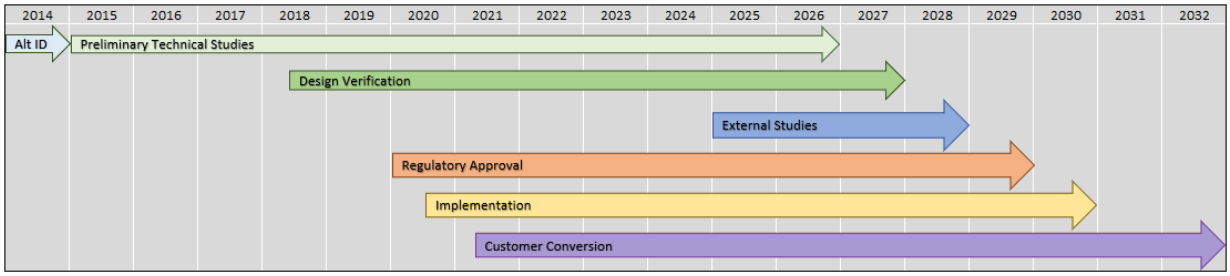

Figure 4.3: Summary timeline of the substitution plan

A final determination of technical feasibility has been established for [redacted]% of products ([redacted]% complete through design verification and an additional [redacted]% discontinued to date). Figure 4.3 shows the timing for completion of the various stages of the substitution plan. CBI d

Availability

Although the alternatives are considered generally available to the Authorisation Holder, availability for implementation as an alternative for specific assays is dependent on regulatory approvals of the change away from 4-tert-OPnEO. Change approval applications must be prepared and submitted by the Authorisation Holder and approvals granted by the regulatory authorities worldwide in all the impacted countries where the IVDs are marketed. It is therefore concluded that the identified alternative is not yet available for substitution for all the Authorisation Holder's assays until 2032 as shown in Table 4.2 and Figure 4.3. The substitution of 4-tert-OPnEO by the current primary alternative is considered economically feasible for the Authorisation Holder over the course of the authorised review period.

4.2. Risks associated with continued use

4.2.1. Impacts on humans

4-tert-OPnEO was not added to the Authorisation List for human health risks. Its impacts are limited to the environment, through its degradation to an environmental endocrine disruptor, 4-tert-OP. Health impacts to the general population related to the removal of the Authorisation Holder's assays from the market can be found in the original AfA.

4.2.2. Impacts on environmental compartments

Environmental releases

The users of the clinical chemistry and immunoassay IVD kits are hospitals, clinics, medical labs and blood banks. The tests using the reagents are carried out in the automated instrument systems provided by the Authorisation Holder. The bottles or cartridges containing the reagents with 4-tert-OPnEO are loaded and unloaded manually on the instrument, with all other operations carried out automatically by the instrument, including mixing of reagent with samples. Once processing is complete and the sample has been analysed, the contents of the reaction vessel/cuvette are discarded. A continuous discharge of small volumes of reagents occurs throughout the sample processing steps and mixes with

large volumes of wash solutions. ARCHITECT and Alinity systems discharge the solutions to liquid waste streams.

The ABBOTT PRISM instrument and reagents have been phased out since the original UK AfA, and no testing is carried out using this instrument anymore. Therefore, it is not relevant for the assessment of releases and is not examined further.

The Authorisation Holder evaluated the fate of waste generated at customer sites from testing with the reagent solutions. It was established that liquid discharge from the ARCHITECT and Alinity systems is directed to drain to be treated in the local STP. The release factor to the environment is assumed to be 100%, all of which is released to wastewater. Refer to section 9.0.1 of the CSR for the calculations performed.

The original quantity of 4-tert-OPnEO used by downstream users in the UK was calculated from the UK sales for 2023. For subsequent years, where substitution of 4-tert-OPnEO is planned, the quantities are reduced by the volume of 4-tert-OPnEO used in the substituted tests, adjusted by expected growth and proportional increase in sales.

In 2022, less than 100 kg ([redacted] kg) of 4-tert-OPnEO were consumed in immunoassay and clinical chemistry IVD kits by customers in GB. CBI a

Table 4.3 shows the quantities of 4-tert-OPnEO estimated to be released by the Authorisation Holder's customers in GB from reagents **after** the end of the current authorised review period assuming phase out as described in the Substitution Plan above.

Table 4.3: 4-tert-OPnEO releases by the Authorisation Holder's GB customers

Year	Reagent Releases (kg) after the end of the current review period for Use 1
2028	[redacted]
2029	
2030	
2031	
2032	
2033	
Total	

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From 2028 until the end of 2032, emissions of 4-tert-OPnEO from the use of the Authorisation Holder's IVD kits in GB customer laboratories are projected to be 10-100 ([redacted]) kg. CBI a

The Authorisation Holder's customers are very diverse and consist of small, local analytical laboratories, small and large diagnostic laboratories in clinics, hospitals and blood banks. The customer testing load ranges from a few tests each day up to several thousand individual immunoassay and clinical chemistry tests each day, in some of the largest customers. The Applicant has customers in all countries within GB.

Used containers / kits containing reagents and/or system solutions, from the ARCHITECT and Alinity instrument systems are disposed as solid waste. Based on information collected on some of the Authorisation Holder's customers, the fate of residual waste 4-tert-OPnEO in these containers and vessels varies, but, as a worst-case approach, it is assumed that they are discharged to wastewater. Accordingly, the releases shown in Table 4.3 are likely over-estimated.

Environmental concentrations

Even though all releases of 4-tert-OPnEO from reagents have been assumed to be released to the drain, it is estimated that the overall impact to the water bodies where the outflow will eventually be released is low.

Use of the Authorisation Holder's IVD kits takes place at multiple sites spread across GB. As part of the risk assessment in the CSR, a calculation of the predicted environmental concentrations (PEC) was carried out for ten downstream user sites covering a representative range of usage (covering from low- to highest usage sites) and release conditions (differently sized river, and coastal / tidal receiving bodies) across the Authorisation Holder's customers. The methodology is described in more detail in the CSR (Section 9.1). Compared to the CSR in the original submission, the modelling of the environmental emissions of 4-tert-OPnEO and 4-tert-OP was carried out following three different approaches, with regards to the rate of transformation of 4-tert-OPnEO to 4-tert-OP in the STP:

- "100% transformation" scenario: this scenario follows the same "worst-case" approach taken in the original AfA, where it is assumed that all quantities of 4-tert-OPnEO supplied to the downstream users (in reagents) are released to the wastewater stream as 4-tert-OPnEO, which is assumed to be completely converted to 4-tert-OP in the STP and released without further transformation to the environment. The scenario has been remodelled taking into consideration the updated annual tonnage for 2023.
- "0% transformation" scenario: this scenario was not modelled in the original AfA but discussed in the GB agency opinion to the AfA. This scenario reflects the opposite end of the approach taken in the "100% transformation" scenario. It is assumed that there is no conversion of 4-tert-OPnEO to 4-tert-OP in the STP, and that essentially all quantities of 4-tert-OPnEO supplied to the downstream users (in reagents) are released without further transformation to the environment, where they will be eventually fully transformed in 4-tert-OP, as a worst-case assumption.
- "2.5% transformation" scenario: this scenario was not modelled in the original AfA but indicated to be more realistic in the HSE Opinion to the AfA. It is assumed that 4-tert-OPnEO released to the wastewater stream after downstream user use, undergoes 2.5% transformation into 4-tert-OP in the STP and released without further transformation to the environment through the liquid outflow of the STP.

The outcome of the exercise is summarised in Table 4.4 and Table 4.5.

Table 4.4: Range of local Concentration and PEC for widespread downstream use

Protection Target	Substance	0% transformation scenario		2.5% transformation scenario		100% transformation scenario	
		Clocal	Local PEC	Clocal	Local PEC	Clocal	Local PEC
Fresh water mg/l	4-tert-OPnEO	2.98E-06	3.25E-06	2.90E-06	3.17E-06	0	0
	4-tert-OP	0	0	1.01E-08	1.03E-08	4.17E-07	4.26E-07
Sediment (freshwater) mg/kg dw	4-tert-OPnEO	2.98E-07	1.76E-05	-	1.72E-05	-	0
	4-tert-OP	0	0		1.04E-05		4.28E-04
Marine water mg/l	4-tert-OPnEO		3.24E-07	2.9E-07	3.16E-07	0	0
	4-tert-OP		0	1.01E-09	1.03E-09	4.17E-08	4.26E-08
Sediment (marine water) mg/kg dw	4-tert-OPnEO		1.76E-06	-	1.71E-06	-	0
	4-tert-OP		0		1.04E-06		4.27E-05
Sewage Treatment Plant mg/l	4-tert-OPnEO		2.98E-05	-	2.91E-05	-	0
	4-tert-OP		0		1.03E-07		4.23E-06
Air mg/m^3	4-tert-OPnEO	0	0	0	0	0	0
	4-tert-OP	0	0	6.52E-12	2.69E-11	2.69E-10	6.14E-10
Agricultural soil mg/kg dw	4-tert-OPnEO	3.04E-07	3.04E-07	2.97E-07	2.97E-07	0	0
	4-tert-OP	0	0	3.2E-06	3.2E-06	1.32E-04	1.32E-04

Table 4.5: Range of local Concentration and PEC for the ten representative downstream user sites evaluated

Protection target	AE	0% transformation scenario				2.5% transformation scenario				100% transformation scenario			
		CLocal		Local PEC		CLocal		Local PEC		CLocal		Local PEC	
		Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
Fresh water mg/L	4-tert-OPnEO	4.18E-7 (LVS)	2.12E-4 (VHVS)	1.13E-6 (LVS)	2.12E-4 (VHVS)	4.07E-7 (LVS)	2.06E-4 (VHVS)	1.1E-6 (LVS)	2.07E-4 (VHVS)	0	0	0	0
	4-tert-OP	0	0	0	0	1.42E-9 (LVS)	7.18E-7 (VHVS)	2.09E-9 (LVS)	7.18E-7 (VHVS)	5.84E-8 (LVS)	2.96E-5 (VHVS)	8.62E-8 (LVS)	2.96E-5 (VHVS)
Sediment (freshwater) mg/kg dw	4-tert-OPnEO	-	-	6.12E-6 (LVS)	1.15E-3 (VHVS)	-	-	5.96E-6 (LVS)	1.12E-3 (VHVS)	-	-	0	0
	4-tert-OP			0	0			2.1E-6 (LVS)	7.21E-4 (VHVS)			8.65E-5 (LVS)	0.03 (VHVS)
Marine water mg/L	4-tert-OPnEO	4.58E-8 (MVS)	6.5E-7 (VHVS)	1.15E-7 (MVS)	7.19E-7 (VHVS)	4.46E-8 (MVS)	6.34E-7 (VHVS)	1.12E-7 (MVS)	7.01E-7 (VHVS)	0	0	0	0
	4-tert-OP	0	0	0	0	1.55E-10 (MVS)	2.2E-9 (VHVS)	2151E-10 (MVS)	2.26E-9 (VHVS)	6.4E-9 (MVS)	9.09E-8 (VHVS)	8.87E-9 (MVS)	9.34E-8 (VHVS)
Sediment (marine water) mg/kg dw	4-tert-OPnEO	-	-	6.21E-7 (MVS)	3.9E-6 (VHVS)	-	-	6.06E-7 (MVS)	3.84E-6 (VHVS)	-	-	0	0
	4-tert-OP			0	0			2.16E-7 (MVS)	2.28E-6 (VHVS)			8.9E-6 (MVS)	9.37E-5 (VHVS)
Sewage Treatment Plant mg/L	4-tert-OPnEO	-	-	4.58E-6 (MVS)	4.58E-4 (VHVS)	-	-	4.46E-6 (MVS)	4.46E-4 (VHVS)	-	-	0	0
	4-tert-OP							1.58E-8 (MVS)	1.06E-5 (HVS)			6.5E-7 (MVS)	6.5E-5 (VHVS)
Air mg/m³	4-tert-OPnEO	0	0	0	0	0 (LVS)	0 (VHVS)	0 (LVS)	0 (VHVS)	0	0	0	0
	4-tert-OP	0	0	0	0	1.76E-11 (LVS)	2.74E-9 (VHVS)	1.76E-11(LVS)	2.75E-9 (VHVS)	7.25E-10 (LVS)	1.13E-7 (VHVS)	1.05E-9 (LVS)	1.13E-7 (VHVS)
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0 (LVS)	0 (VHVS)	0 (LVS)	0 (VHVS)	0	0	0	0
	4-tert-OP	0	0	0	0	1.78E-10 (LVS)	2.77E-8 (VHVS)	1.78E-10 (LVS)	2.81E-8 (VHVS)	7.33E-9 (LVS)	1.14E-6 (VHVS)	2.4E-8 (LVS)	1.16E-6 (VHVS)

The PEC_{local} for the widespread use are in line with those estimated in the previous review report. All the values are below the previously derived, as per reduced tonnage of use ([redacted] kg in 2023 instead of [redacted] kg used in 2021). CBI a

When taking into consideration the different modelled transformation scenarios, it is clear that the "100% transformation scenario", where it is assumed that 100% of 4-tert-OPnEO will be transformed to 4-tert-OP in the STP, results in an overestimation of environmental concentration to the freshwater and sediment compartments for 4-tert-OP and an underestimation of the PEC to soil for 4-tert-OPnEO. This was also argued by HSE in its opinion to the previous authorization report stating:

> *"risks to surface waters are likely to have been overestimated, as transformation of 4-tert-OPnEO to 4-tert-OP during or immediately after wastewater treatment is likely to be very limited"*, and more
>
> "*the applicant's modelling assumptions about the environmental fate and partitioning within the STP will have overestimated releases of 4-tert-OPn via sewage sludge spread to land, but have likely underestimated 4-tert-OPn concentrations in surface waters"*

Indeed, when taking into consideration the more realistic "2.5% scenario", the predicted PEC for fresh surface water for 4-tert-OPnEO (3.17E-6 mg/L) is higher than that predicted for 4-tert-OP (1.03E-8 mg/L). This is due to the higher percentage release of the STP to surface water (99.77%) for 4-tert-OPnEO compared with 4-tert-OP (42.9%) but still lower Kow and Koc and higher water solubility. These physicochemical properties play an important role in the distribution of the substance in the environment.

Regarding the evaluation of the local concentration of the substance from the ten representative sites, for the freshwater environment (water and sediment), air and agricultural soil are estimated at their highest for those sites where very high volume of 4-tert-OPnEO are used and the STP and receiving body do not provide the highest dilution, independent of the transformation scenario considered. Site 3 presents the highest values for freshwater environment, which are higher than the highest PECs estimated in the original AfA. This is due to the low water flow at the outfall points of the STP resulting in a lower dilution factor. For air and agricultural exposure, the quantity of use at Site 1 is the main factor affecting the highest PECs.

On the other hand, the PEC_{local} for the marine environment (water and sediment) are estimated at their highest and lowest for those sites where direct emission of 4-tert OPnEO to the marine environment is happening, independent from the scenario of transformation considered.

Overall, the results show a great variability of the local predicted concentration values depending on the STP site specific setting.

In conclusion, local PECs derived for the widespread are proved to be at least one order of magnitude lower than the EQS for 4-tert-OP (0.01 µg/L), in either scenario. It should be noted that the EQS are expressed as annual average, so the comparison with PEC_{local} is not appropriate, as the PEC_{local} refers to a single emission episode from the STP with a much different and lower time and spatial scale.

4.2.3. Compilation of human health and environmental impacts

No impact is expected on human health as 4-tert-OPnEO was not included on the Authorisation List for human health risks. Its impacts are limited to the environment, through its degradation to an environmental endocrine disruptor, 4-tert-OP. However, continued use of the substance allows hospitals, laboratories, and blood banks to continue testing patient specimens. Table 4.6 shows the releases remaining over the 5 years being requested to extend the current authorised review period (2028 -2032).

Table 4.6: Summary of remaining releases to the environment from 2028-2032

	Over 5 years (2028-2032)
Total releases in kg in 2028-2032 period	10-100 (CBI a)

4.3. Non-use scenario

This section will describe the Authorisation Holder's actions in the event the review period is not extended beyond the end of 2027. The most likely non-use scenario is identified with the impacts to stakeholders discussed and monetised where possible.

4.3.1. Summary of the consequences of non-use

The Authorisation Holder has been granted a 5.5-year review period in the UK until 30 December 2027. If a modification of the authorised 5.5-year review period is not granted, the Authorisation Holder would not have completed its substitution activities based on the factors impacting substitution discussed in section 4.1.3 of this SEA. This action could result in ceasing supply of IVD products that still contain 4-tert-OPnEO above 0.1% w/w concentration in GB, in turn resulting in downstream users no longer being able to use the Authorisation Holder's IVD kits containing 4-tert-OPnEO to test patient samples in GB.

4.3.2. Identification of plausible non-use scenarios

The Authorisation Holder evaluated the possible non-use scenarios in the event of a refused application. Those scenarios are listed below.

4.3.2.1. Scenario 1: Complete substitution prior to the end of 2027

This potential scenario addresses the Authorisation Holder's substitution of 4-tert-OPnEO out of the reagent solutions prior to the end of the current authorised review period, including leaving sufficient time for GB downstream users to consume their existing inventory of IVD kits containing 4-tert-OPnEO for core laboratory, transfusion and clinical chemistry applications. This option is not feasible as the Authorisation Holder would not have an alternative substance suitable for substitution for a large number of products, before the existing authorisation expires. The various factors that affect the ability of the Authorisation Holder to complete substitution by the end of the current review period are discussed in Section 4.1.3, and include:

- unanticipated higher rate of complex reformulations,
- the ability of Notified Bodies to review product changes,
- the changes to other country regulations, impacting the timing for submitting substitution changes.

Furthermore, the Authorisation Holder's downstream users may need time to complete cross-over studies using both the reagents containing 4-tert-OPnEO and those containing the substituted alternative to demonstrate equivalency of results obtained before and after the product change. As a result, a number of Abbott products will not have completed substitution activities prior to the authorised review period expiring at the end of 2027.

This is exacerbated by the particular requirements for substitution in a number of more complex products. These products need longer timeframe to complete their verification phase, as introducing an alternative will also require modifications to the instruments (i.e modifications to the probe dispenser). Performing these modifications earlier in the substitution process would delay substitution of all assays still using 4-tert-OPnEO, which would have to wait until the more complicated cases were finalised. As such, it was decided to schedule substitution for those assays towards the end of the substitution plan.

In addition, regulatory approvals are required from all the countries in which the product will be marketed, including the UK. Each product is marketed to be sold in all countries, therefore a delay in any country, causes a delay to all countries. In the EU, the IVDD is being replaced by the IVDR, with all products marketed in the EU to be registered under the new regulation, not just those products with modifications. As a result, there have been delays due to the Notified Bodies not being able to handle the workload. Therefore, any delays due to the IVDR approval will impact the substituted product from being marketed in the UK.

Based on the above, this scenario is very unlikely to materialise, so it is not considered a feasible option. Furthermore, it is not operationally practical to consider manufacturing GB-only IVDs hoping for a single country regulatory approval to speed market entry into the UK.

4.3.2.2. Scenario 2: Cease distribution of IVD kits containing 4-tert-OPnEO to GB

This scenario addresses the discontinuation of IVD products containing 4-tert-OPnEO to GB customers beginning in 2028, if the current authorised review period is not extended. Even though a much smaller number of products would remain to substitute the 4-tert-OPnEO ([redacted]% of immunoassay products in the end of 2027), the IVD kits are used in multiple panels, which would result in the entire panel being unusable. As a result, a full alternative supply of IVD kits not containing 4-tert-OPnEO would be required for GB downstream users, which could cause a delay in testing patient samples, leading to a disruption of patient results and a medical diagnosis. It should be noted that such kits without 4-tert-OPnEO may not be available, depending on the products, as the Authorisation Holder will need to follow their substitution timeline. In any case, distribution to non-GB customers would not be impacted.

CBI d

Currently, GB accounts for approximately 1-10% ([redacted]%) of the Authorisation Holder's worldwide immunoassay, blood screening and clinical chemistry sales. Commercial locations in GB would no longer be feasible to maintain, as customers would no longer require support from the Authorisation Holder.

CBI b

It is expected that, upon the loss of [redacted]% of the immunoassay products containing 4-tert-OPnEO manufactured by the Authorisation Holder, GB customers might move to an alternative instrument system (possibly offered by a competitor holding an extended Authorisation for 4-tert-OPnEO or NPnEO) that could support a full testing menu with all tests within a panel to be provided. Switching to an alternative supplier may not be possible immediately, as switching suppliers involves publishing a tender, evaluating offers, and making a decision, in addition to any lead time that will be required for delivery, setting up, qualifying and completing potential cross-over testing with the new instruments. Any new contract would require purchasing/leasing one or more new instruments from the Authorisation Holder's competitors. Considering the large number of the Authorisation Holder's instruments currently on the market in GB, it is unlikely that their competitors would be able to provide sufficient numbers of instruments to cover the demand in the short term. What's more, the sudden obsolescence of the Authorisation Holder's instruments would generate considerable costs for the UK taxpayer that are entirely avoidable. Additionally, many of the Authorisation Holder's direct competitors are also operating under 4-tert-OPnEO authorisations until the later date of end of 2032 and will have products available to the customer which will potentially have 4-tert-OPnEO in its formulations up until the end of 2032. There will be no overall environmental benefits if customers change to these competitive offerings during their extended authorisation period.

CBI d

4.3.2.3. Scenario 3: Pause distribution of IVD kits containing 4-tert-OPnEO to GB until completion of substitution program

This scenario addresses pausing the distribution of those IVD kits containing 4-tert-OPnEO in GB beginning in 2028 until substitution is complete for each product. As discussed in the Non-Use Scenario 2, [redacted]% of immunoassay tests would still contain 4-tert-OPnEO at the end of the current authorised review period (2027) based on the substitution plan described in Section 4.1.3. Similar to Non-Use Scenario 2, customers would still need to source an alternative supply of IVD kits not containing 4-tert-OPnEO. This could eventually cause delays in testing patient samples, potentially impacting diagnosis of serious medical conditions. To avoid disruption to their operations, GB customers would likely move to an alternative instrument system that could support a full testing menu upon the loss of the immunoassay products manufactured by the Authorisation Holder containing 4-tert-OPnEO. This scenario would result in the same outcome as Scenario 2, as it will be very difficult for the Authorisation Holder to regain the customers they will lose.

CBI d

On one hand, the contracts signed for the provision of the instruments and diagnostic kits last for several years (typically [redacted] years), and customers prefer to keep their existing suppliers unless extraordinary circumstances occur (e.g., one supplier withdrawing their service as a result of no authorisation). Furthermore, the Authorisation Holder will need to regain the trust of the customers, which would be lost due to their discontinuation of service. As in Scenario 2, the competitive offerings could still contain 4-tert-OPnEO as many of the Authorisation Holder's competitors are distributing products under an authorisation expiring the end of 2032.

CBI b

4.3.3. Conclusion on the most likely non-use scenario

Of the three scenarios, NUS 2 would be the most likely to occur. Many of the factors impacting the timing for substitution are out of the Authorisation Holder's control. The increased rate of complex reformulations was unexpected, as this was not evident when the preliminary studies were performed. The changes in regulatory requirements in several countries have led to significantly increased review times, including extended review times by the EU Notified Bodies. Approximately 80% of the Authorisation Holder's IVD products will be required to have Notified Body review per the IVDR, compared to just 20% under the IVDD. Consequently, the Authorisation Holder is at risk of not completing substitution of 4-tert-OPnEO prior to the current authorised review period of 5.5 years.

Without access to the full suite of the Authorisation Holder's IVD products, downstream users would be required to identify an alternative source for obtaining the missing test results. Based on space constraints in the testing laboratory, obtaining a competitor instrument to test the missing assays would not be possible. As a result, the only possible non-use scenario is scenario 2.

4.4. Societal costs associated with non-use

4.4.1. Economic impacts on authorisation holder

In the event the authorised review period is not extended to 4 January 2033, the Authorisation Holder would no longer be able to distribute products containing 4-tert-OPnEO within GB, so the sales and profits from GB would be lost. Markets outside of GB would not be affected.

The GB market for core laboratory immunoassays, clinical chemistry, and blood transfusion products accounts for approximately 1-10% ([redacted]%) of the Authorisation Holder's total sales in 2023 and would no longer be available to the Authorisation Holder. As customer contracts can last up to 7 years, an alternate source of IVDs would be required to continue customer testing activities. For the Authorisation Holder, it would be difficult to re-enter the GB market

CBI b

upon completion of substitution, as customers would have converted to an alternative instrument platform with the associated reagents and would likely have extended contracts with the new IVD supplier.

The economic impact was calculated following SEAC's approach to assessing changes in producer surplus [5], agreed at SEAC-52 on 15 September 2021. The approach explains that the producer surplus is a loss of profits arising from the premature retirement of productive tangible and intangible assets. 4-tert-OPnEO has a generally available substitute, therefore, default values of 2 years of profit losses are used, composed of an average of 3 years for tangible assets and 1.2 years for intangible assets, rounded to the nearest year.

The economic impact for the GB economy in this NUS would be the loss of the GB revenue and profits for the two years following expiry of the authorised review period as shown in Table 4.7.

Table 4.7: Lost GB revenue and profits from sales of the Authorisation Holder's IVD kits for the NUS Scenario (in £ million)

	Revenue	Profits	Revenue (2028 prices)	Profits (2028 prices)
2028	[redacted]			
2029				
2030				
2031				
2032				
Total			100-1,000 [redacted]	1-10 [redacted]
Note: These values were calculated from the Authorisation Holder's 2023 sales, assuming a [redacted] in consumption, driven by increased demand.				

CBI b

The estimated lost profits are estimated to be £1 – 10 (£[redacted]) million (discounted to 2028 prices using a 4% discount factor). There would be no impacts on the sales to customers/downstream users outside of GB.

CBI b

4.4.2. Economic impacts on the supply chain

4.4.2.1. Economic impacts on upstream users

In the non-use scenario, it is assumed that raw material suppliers would be minimally impacted, as GB is 1-10% ([redacted]%) of the Authorisation Holder's worldwide sales.

CBI b

4.4.2.2. Economic impacts on downstream users

If the Authorisation Holder could no longer supply customers with IVD kits and testing instrument platforms, the customers would be required to convert to a replacement system. Due to the number of organisations that rely on the Authorisation Holder's products, and how integrated those products are into the operations of the customers, it is unlikely that an alternative supplier could rapidly respond to the demand currently filled by the Authorisation Holder.

Alternative instrument systems would need to be available to cover the Authorisation Holder's instrument base for immunoassay, including blood screening, and clinical chemistry testing, along with the reagents associated with the instrument. Minimally, competitors may have sufficient instruments in warehouses that would be immediately available to cover the

demand to replace blood screening, other immunoassay and clinical chemistry testing, causing added costs to the downstream users to convert to instrument systems which have complete testing panels available. Sufficient resources to install the instruments would also need to be readily available in the short term.

The costs that customers would incur in switching to a competitor instrument system would be dependent on whether the instrument(s) is purchased or leased. If instruments are purchased, then the customer would incur both a cost to purchase new instruments, and a one-off cost of converting to new reagents, calibrators and controls. In the event the instrument is leased, only the one-off costs of the reagents associated with cross-over testing would be incurred by the customer. The manufacturer would be responsible for the depreciation costs associated with the instrument. The reagents would be used to perform cross-over testing between the old and the new instruments, before commercial use starts. The time to convert from one system to another could take 3 - 6 months, provided instrument availability. This is non-productive time, which would have been used for running tests on patient samples in the Applied for Use Scenario.

In any case, these costs would be brought forward by as much as 6 years, considering that the Authorisation Holder's contracts with their customers may be up to [redacted] years. Accurately calculating these costs is not possible without having to speculate on the competitors' capacity and pricing policies. In any case, an indicative calculation can be carried out, under the following assumptions: CBI b

- The Authorisation Holder's customers would need to purchase/lease new equipment and IVD kits at the same prices as they would under the contract with the Authorisation Holder. As a very conservative approach, the internal purchasing cost of an instrument system by the Authorisation Holder is used, which was approximately £0.1-1 million (£[redacted] million). CBI b
- The cost of new reagents, calibrators and controls to run cross-testing between the old and the new platform when converting to an alternative instrument system. The low value of £1,000-10,000 (approximately £ [redacted]) per product will be used with the assumption that each instrument needs to perform cross-over testing on 1-10 ([redacted]) products. CBI b
- It is possible that some of the Authorisation Holder's customers would have switched to a different supplier at the end of their contract regardless of the decision on authorisation. These will not be considered as additional costs. The Authorisation Holder estimates that this is on average [redacted]%. CBI b
- There will be additional costs to remove the existing instrument from customer sites. The instruments are bulky, and they will have to be disconnected from the utilities, possibly dismantled and transported to a suitable vendor for recycling. Similar costs would be incurred to connect the new instruments to the same utilities.

In this non-use scenario, all the instruments in GB would need to be replaced. If it is assumed that 90% of the customers would be required to convert to a new analyser, approximately 100-1,000 ([redacted]) new instruments would be needed. Currently, based on the Authorisation Holder's internal data, [redacted]% of instruments are leased and the remaining [redacted]% are purchased in the UK. CBI b

The cost of switching away from the Authorisation Holder's instruments may be £10-100 (£[redacted]) million immediately after the current authorisation would expire in 2027. However, switching to a competitor product may not decrease the 4-tert-OPnEO emissions, as many competitors have authorisation through the end of 2032. Table 4.8 shows how the cost of GB downstream users was determined. CBI b

Table 4.8: Costs for GB downstream users to convert to an alternative system (£)

	Rental	Purchased	Total
Number of instruments	[redacted]		
90% Instruments			
Instrument Cost (£)			
Reagent Cost (£)			
Total Cost (£)			

CBI b

4.4.3. Economic impacts on competitors

There are more than [redacted] of the Authorisation Holder's instruments generating more than 100 – 1,000 ([redacted]) million immunoassay, transfusion and clinical chemistry tests every year in GB. In the event that the authorised review period is not extended, the Authorisation Holder would be at risk of suppling IVD kits to GB customers beginning in 2028.

CBI b

In order for competitors to take over the testing from the Authorisation Holder, they would first need to replace the Authorisation Holder's instruments at customer sites, assuming that sufficient inventory to replace the Authorisation Holder's instruments in a short period is available. The Authorisation Holder is one of the largest providers of IVD tests in GB [6], so it is not considered likely that a sufficient number of instruments would be available immediately to replace the Authorisation Holder's base in the GB market.

Therefore, it is possible that the Authorisation Holder's customers could face a critical shortage of tests for transfusion, core laboratory and clinical chemistry diagnostic tests. The Authorisation Holder's largest competitors have also applied for authorisation related to the use of 4-tert-OPnEO and have review periods expiring from December 2027 to January 2033. Whether there would be an impact on the amount of 4-tert-OPnEO emitted to the environment would be directly related to whether the replacement test contains 4-tert-OPnEO and the amount of the substance in the test and the status of the chosen competitor's substitution plan in converting away from 4-tert-OPnEO.

4.4.4. Health impacts on the general population

The Authorisation Holder has a wide range of IVD kits that contain 4-tert-OPnEO and will still be undergoing testing and/or awaiting regulatory approval at the end of 2027 based on the substitution plan. It is difficult to determine the cost for an early diagnosis that leads to successful treatment of a disease with improved quality of life due to the vast types of diseases and illnesses covered by the Authorisation Holder's IVD kits. Even if only 1% of the over 0.1-1 billion tests identified an illness or condition requiring intervention to maintain or restore the health of an individual, that would be 1-10 million critical test results that would not be identified in a timely manner in a single year. The costs of maintaining quality of life could easily be in the hundreds of millions of pounds.

4.4.5. Social impacts

4.4.5.1. Direct Job losses

In 2023, the Abbott Diagnostics business employed more than 10,000 people globally. Of these, more than 150 ([redacted]) were based in GB. These numbers include both Authorisation Holder and contractor employees.

CBI e

Social costs of unemployment

Unemployment caused by a refusal of the authorised review period of 5.5 years for the use applied for may have impacts to the UK society. These impacts can be quantified using the

methodology described in Appendix I, which is based on the note by Dubourg (2016) that is published in ECHA's website [7]. This is the same methodology used in the original AfA. The numbers were updated using employee numbers from 2023. Additionally, it was assumed that the employees would be able to find a new position in half of the unemployment duration (see Appendix I).

Social Impact for the Non-Use Scenario

In the NUS, the Authorisation Holder would stop manufacturing IVD kits for GB customers, so the EU plants would only produce sufficient quantities to cover the demand for the rest of the world.

All GB sales would be lost because there would be no IVD sales in that market, so over 150 ([redacted]) commercial and other functional area jobs supporting the GB market would be lost. As sales outside of GB would continue normally, no jobs would be lost in non-GB facilities of the Authorisation Holder. Total number of direct job losses would be more than 150 ([redacted]) in GB. Table 4.9 summarises the social costs of unemployment for this non-use scenario. CBI e

Table 4.9: Summary of social costs for non-use scenario (£ million)

Lost output (£ million)	Scarring cost (£ million)	Value of leisure time (£ million)	Hiring costs (£ million)	Total unemployment cost (£ million)
1-10 [redacted]	1-10 [redacted]	1-10 [redacted]	1-10 [redacted]	2-20 [redacted]

CBI f

Overall, the total social cost of unemployment in the non-use scenario would be approximately £2-20 (£[redacted]) million. CBI f

4.4.5.2. Indirect and induced job losses

It has been estimated in a report published by the European Federation of Pharmaceutical Industries and Associations (EFPIA) that each job in the pharmaceutical sector can support a multiplier of 5.5 additional jobs in the EU, as a result of materials consumption and support of economies via the salary of the workers [8]. Therefore, in the non-use scenario, the indirect and induced job losses would be as high as 1,000-10,000 ([redacted]). CBI e

4.4.6. Wider economic impacts

Within GB, IVD testing influences as many as 70% of clinical decisions, with annual sales of £41 billion in 2017. [9] IVD testing accounts for 0.5% of total health expense in the UK and costs approximately €24.2 per citizen annually [10].

As discussed in Section 2.2.2, the Authorisation Holder is one of a few major suppliers of IVD products in GB. A refused extension of their authorisation for 4-tert-OPnEO could potentially result in them exiting the British market, with the most likely replacement products coming from one major competitor. This situation runs the risk of distorting the competition in the market, which may result in price increases and limited options for end users.

4.4.7. Compilation of socio-economic impacts

The costs associated with ceasing the use of 4-tert-OPnEO evaluated in this SEA consist of a semi-quantitative discussion of the impacts from a refused authorisation. The main impacts that could be quantified included the producer surplus, instrument/reagent replacement costs and the social impacts from the Authorisation Holder's operations due to lost sales in GB.

Other quantifiable or monetised impacts, which have higher uncertainty were examined separately and used to support the main argument are listed in Table 4.10 but will not be considered in the final calculations of costs of non-use per units of release.

Table 4.10: Societal costs associated with non-use

Description of major impacts	**Monetised / quantitatively assessed / qualitatively assessed impacts**	
1. Monetised impacts	**£**	
Producer surplus loss due to ceasing the use applied for (tangible and intangible assets)	£1 - 10 ([redacted]) million over 2 years	CBI b
Relocation or closure costs	Not relevant	
Loss of residual value of capital	£100-1,000 ([redacted]) thousand per instrument or £1-10([redacted]) million £1-10 ([redacted]) million for cross-over testing	CBI b
Social cost of unemployment	£2 – 20 ([redacted]) million	CBI f
Spill-over impact on surplus of alternative producers	Not relevant	
Sum of monetised impacts	£5 – 50 ([redacted]) million	CBI b f
2. Additional quantitatively assessed impacts	**[Over 5 years]**	
Lost jobs in the Authorisation Holder's GB operations	>150 ([redacted]) employees	CBI e
3. Additional qualitatively assessed impacts		
Lack of IVD testing due to unavailability of test kits; delayed test results with delayed diagnoses for patients	£100 million or more	

The impacts associated with ceasing use of 4-tert-OPnEO are listed in Table 4.107. The costs associated with the depreciation for instruments to be leased earlier than planned will not be used moving forward as these costs contain a high level of uncertainty.

A critical societal cost that could not be quantified is the inability to rapidly provide medical test results which are used to diagnose serious health conditions. The Authorisation Holder's instruments and reagents perform more than 0.1-1 billion tests per year in GB. Even if only 1% of these annual tests identified an illness or condition requiring intervention to maintain or restore the health of an individual, that's over 1-10 million critical test results that would not be performed in a timely manner in one year. The costs of maintaining quality of life could easily be in the hundreds of £ millions or more each year.

4.5. Combined impact assessment

The cost-benefit analysis in this SEA consists of a semi-quantitative discussion on the impacts from a refused authorisation for the applied for use. The main impacts that could be quantified, i.e., the prevented emissions of 4-tert-OPnEO, producer surplus, social impacts from the Authorisation Holder's operations are compared and used to carry out the cost effectiveness analysis comparing the benefits against the risks of continued use. It will be shown that the benefits of continued use of the substance outweigh the risks to the environment.

Table 4.11 compares the costs of non-use to the risks of continued use.

Table 4.11: Societal costs of non-use and risks of continued use

Societal costs of non-use		**Risks of continued use**		
Monetised impacts	£1 – 10 ([redacted]) million over 2 years	Monetised excess risks to directly and indirectly exposed workers	None; substance not listed for human health effects	CBI b
Additional quantitatively assessed impacts	£2 – 20 ([redacted]) million social costs of unemployment £1-10 ([redacted]) million for DU purchasing instruments £1-10 ([redacted]) million for cross-over testing	Monetised excess risks to the general population	None; substance not listed for human health effects	CBI b f
Qualitatively assessed impacts	Lack of IVD testing due to unavailability of test kits; delayed test results with delayed diagnoses for patients	Qualitatively assessed risks	Release of 10-100 ([redacted]) kg 4-tert-OPnEO over 2028-2032 to environment	CBI a
Summary of societal costs of non-use	£5 – 50 ([redacted]) million Lack of IVD testing due to unavailability of test kits; delayed test results with delayed diagnoses for patients	**Summary of risks of continued use**	Release of 10-100 ([redacted]) kg 4-tert-OPnEO over 2028-2032 to environment	CBI a b f

Table 4.12 shows the costs of non-use per the total releases in kilograms from 2028 through the end of the requested extended review period.

Table 4.12: Costs of non-use per unit of release from 2028-2032

	Over 5 years (2028-2032)	
Total costs (£)	10 - 100 ([redacted]) million	CBI a b f
Total releases (kg)	10-100 ([redacted])	
Ratio (£/kg)	100,000-1,000,000 ([redacted])	

The monetised economic impacts per kg of prevented 4-tert-OPnEO emissions in GB range from 100,000-1,000,000 ([redacted]) £/kg for the non-use scenario examined in the SEA. CBI a b f

The Authorisation Holder's R&D project to substitute 4-tert-OPnEO from reagents has an overall cost of £100-1,000 ([redacted]) million from products globally, including both the EU and the UK. The program was initiated to meet the requirement of the EU REACH Regulation, which at the time, included the UK. With the separation of the UK from the EU, the cost of substitution to be used for this analysis will be proportional based on the percentage of sales associated with GB in relation to the EU. The cost to substitute all reagents is £100-1,000 (£[redacted]) million with £[redacted] being attributed to [redacted] products remaining to be substituted after the current authorisation period expires. With GB sales being 1-25% ([redacted]) of the CBI d CBI d

Authorisation Holder's (EU + UK) sales, the cost of substitution attributed to GB would be £1-10 (£[redacted]) million to prevent 100-200 ([redacted]) kg of 4-tert-OPnEO during the extended review period (2028 – 2032) at a cost ratio of 5,000 – 50,000 ([redacted]) £/kg. This is much lower than that calculated for the GB emissions and economic impacts. Table 4.13 shows the cost per kg of 4-tert-OPnEO for the Authorisation Holder's substitution project. CBI a d

Table 4.13: Cost per kg of 4-tert-OPnEO for Authorisation Holder's substitution project

Total Project Cost for reagents (£ million)	Cost to Complete Remaining Products from 2028-2032 (£ million)	Products Remaining in 2028	UK portion of substitution (£ million)	kg to prevent from remaining products 2028-2032	£/kg of 4-tert-OPnEO
[redacted]	[redacted]	[redacted]	1 - 10 ([redacted])	100 - 200 ([redacted])	5,000–50,000 ([redacted])

CBI a b d

At the end of the authorised review period, the Authorisation Holder's R&D project would have the same effect as a refused authorisation, as there would be no use of 4-tert-OPnEO by the Authorisation Holder's customers. The Authorisation Holder's substitution projects are a substantially more (~10-fold) cost-effective option to reduce emissions of 4-tert-OPnEO to the environment.

4.6. Sensitivity analysis

IVD kit demand trends – changes in Authorisation Holder's sales

Throughout the socio-economic analysis, assumptions were required due to the length of the review period being requested (through 4 January 2033 or over 8 years), and the fact that the impacts would reach into the future.

The demand forecast for the Authorisation Holder's IVD kits was evaluated over the short term, with the assumption that the demand would remain relatively flat over the review period, however, the review period far exceeds the timing for an accurate forecast. A growth rate of 1-10% ([redacted]) was assumed, with the growth impacting both the financials, as well as the emissions. The period being evaluated is 2028 through 2032, from the current authorised review period through 4 January 2033. CBI b

Each year, the forecast can fluctuate between lower or higher rates, therefore the impacts for extreme cases of [redacted]% and [redacted]% growth throughout the review period were evaluated. As was seen in 2020, factors such as the emergence of a global pandemic can impact the growth rates (i.e., severe decrease in tests as elective procedures were cancelled and an increase as the procedures were reinstated and SARS-CoV-2 tests were authorised for emergency use). The releases being evaluated are those from 2028 through 2032. CBI b

Table 4.14 compares the GB cost per kg of prevented emissions for the modified sales growth over the timeframe of 2028-2032.

Table 4.14: Costs of non-use per unit of release with different sales growth

Impact upon condition implementation	**[redacted]% Sales growth**	**[redacted]% Sales growth**
GB lost profit (£ million)	[redacted]	
Cost of instruments/cross-over testing (£ million)		
GB social cost of unemployment (£ million)		
Total cost (£ million)		
Total releases (kg)		
Ratio (£/kg) = Total costs/ Total releases		

CBI b

CBI c

CBI a

Even at a low growth rate, the cost per kg of prevented 4-tert-OPnEO emissions is high when compared to the cost of the Authorisation Holder's ongoing substitution project (£5,000 – 50,000 per kg).

Net profit margin

A profit margin of 1-10% ([redacted]%) was assumed based on information from the Authorisation Holder's finance department and would provide a conservative estimate of the Authorisation Holder's business. Profit would be expected to fluctuate over the review period and could be higher or lower due to varying economic conditions, changes in the Authorisation Holder's strategies or improved manufacturing efficiencies and is expected to vary. CBI b

Table 4.15 compares the GB cost per kg of prevented emissions across a modified profit margin of [redacted] and [redacted]% over the timeframe of 2028-2032.

Table 4.15: Costs of non-use per unit of release with different profit margins

Impact upon condition implementation	[redacted]% Profit margin	[redacted]% Profit margin
GB lost profit (£ million)	[redacted]	[redacted]
Cost of instruments/cross-over testing (£ million)	[redacted]	[redacted]
GB social cost of unemployment (£ million)	[redacted]	[redacted]
Total cost (£ million)	[redacted]	[redacted]
Total releases (kg)	[redacted]	[redacted]
Ratio (£/kg) = Total costs/ Total releases	[redacted]	[redacted]

CBI c f

CBI a

The low profit margin scenario is much higher than the costs per kg expected to be achieved by the Authorisation Holder's substitution project (5,000 – 50,000 £/kg).

Social cost of unemployment – different unemployment duration

In calculating the social costs for the non-use scenario, certain assumptions were taken into consideration which, if modified, would impact the overall cost. Most of the assumptions tend to underestimate the overall cost. For example, no increase in salaries has been applied from 2024-2032, even though an annual increase is expected. No increase in the number of employees was applied, despite the expected growth in the Authorisation Holder's operations.

An uncertainty that could overestimate the social costs of unemployment assumed is the average duration of unemployment for each country, however, this could cause overestimation of the social costs. The methodology described by Dubourg in the ECHA document on unemployment costs was followed, using 2023 data from the UK Office for National Statistics. However, the average duration of unemployment, as calculated from ONS data, was halved to prevent overestimation of costs. The results are shown in Table 4.16.

Table 4.16: Comparison of GB social costs of unemployment in base case and with modified unemployment durations

Impact over review period	Non-use scenario
Base case (50% duration) (£ million)	[redacted]
50% duration with 3-month reduction (£ million)	[redacted]
Full duration (£ million)	[redacted]

CBI f

The impact of the unemployment period to the overall impacts and the £ per kg of prevented emissions is shown in Table 4.17.

Table 4.17: Costs of non-use per unit of release with modified unemployment

Impact upon condition implementation	50% duration + 3-month reduction	Full duration
GB lost profit (£ million)	[redacted]	
Cost of instruments/cross-over testing (£ million)		
GB social cost of unemployment (£ million)		
Total cost (£ million)		
Total releases (kg)		
Ratio (£/kg) = Total costs/ Total releases		

CBI b c f

CBI a

Summary of sensitivity analysis

The results of the SEA are considered robust. As the sensitivity analysis showed, even at a conservative scenario, the ratio of monetised costs per kg of prevented emissions of 4-tert-OPnEO is very high in GB, ranging from £100,000 – 1,000,000 per kg, and a refused authorisation is much less efficient than the Authorisation Holder's own R&D substitution plan £10,000-100,000 per kg 4-tert-OPnEO. Table 4.18 summarises the £/kg ratio for the various conditions reviewed throughout the sensitivity analysis.

Table 4.18: Summary of sensitivity analysis conditions on £/kg ratio

Condition	£/kg
Base Case	100,000 - 1,000,000
[redacted]% Sales Growth	[redacted]
[redacted]% Sales Growth	
[redacted]% Profit Margin	
[redacted]% Profit Margin	
50% duration + 3-month unemployment duration reduction	
Full unemployment duration	
Authorisation Holder's substitution project	5,000 – 50,000 [redacted]

CBI b f

CBI c

CBI d

It should be considered that, in all calculations of the cost per kg ratios, only costs related to profits of the Authorisation Holder and the social costs of unemployment were considered. The very high costs associated with switching customers to an alternative instrument have not been included in the calculations. If these were included, the overall economic costs would be significantly higher. Most importantly, the ratios do not consider the significant health cost for patients relying on test results from the Authorisation Holder's IVD kits. A refused authorisation may lead to delayed test results potentially leading to increased health risks for millions of patients in GB that need to have their samples tested with the Authorisation Holder's immunoassay and clinical chemistry kits.

The assumptions made in the SEA were based on a conservative approach. Even so, the overall benefits of a granted authorisation modification for the economy and the society far outweigh the impacts to the environment, as shown in the calculations made for the sensitivity analysis. Even in the worst possible scenario, the cost per kg ratio would still be high and much higher than the respective ratio of the Authorisation Holder's R&D project.

4.7. Information to support for the review period

The Authorisation Holder has been granted a review period of 5.5 years, ending 30 December 2027. As discussed in section 4.1.3.1, there are several factors outside the control of the Authorisation Holder that directly impacts the timing of the substitution plan. These factors include regulatory requirement changes, increased percentage of products requiring further optimisation, and others. As a result, an additional 5 years is being requested to extend the review period to 4 January 2033. This date was selected to align with the Authorisation Holder's EU expiry date, considering the newly emerged factors as it is not cost effective to manufacture a product for individual markets. The proposed end-date also aligns with the authorisation end-date for a number of direct competitors in GB. Overall, the Authorisation Holder is committed to reducing and eliminating the use of 4-tert-OPnEO in products.

5. CONCLUSION

The analysis completed in this document shows that a refusal to modify the review period to 4 January 2033, is not a cost-effective option for reducing emissions of 4-tert-OPnEO to the environment, particularly if compared to the Authorisation Holder's ongoing substitution project over the length of the authorised review period.

The Authorisation Holder has made significant progress in reducing 4-tert-OPnEO emissions overall. By the end of 2024, [redacted] kg (~ [redacted]%) of the total emissions have been eliminated by substituting the highest usage products containing 4-tert-OPnEO. This consists of [redacted] kg from substitution of the Pre-Trigger and Trigger solutions and [redacted] kg from the [redacted]% of reagent products that have either been retired or completed design verification, lowering the risk of additional complex reformulation. The remaining reagent products equate to only [redacted] kg of the total 4-tert-OPnEO emissions remaining with the downstream users in GB by the end of 2024 as compared to 2021. CBI d h CBI a

If the Authorisation Holder's IVD kits are removed from GB markets, as discussed in the non-use scenario, the potential for disruptions in the operations of clinics, hospitals and other medical facilities using the IVD kits is high. Capacity of these facilities to run tests to detect infections or other conditions (e.g., cancer, diabetes, traumatic brain injury, SARS-CoV-2) in patients, as well as analyses of important chemicals in patient samples may be at risk. This could increase risks to patients' health, in case a delayed or erroneous diagnosis is made.

The risks are significantly higher for blood screening services and blood banks, as the Authorisation Holder's transfusion products screen a significant share of the 1.5 million blood and plasma donations each year for transfusion-transmitted diseases such as HIV, HCV, HBV, HTLV, Syphilis, Chagas and CMV in GB. Interruption of supply of the Authorisation Holder's reagents, would impact the ability of GB to supply safe blood and plasma products, impacting blood and plasma needed for emergencies as well as regular blood recipients.

Over 150 positions would be at risk of being eliminated within GB if the current authorised review period is not modified, as evaluated within this SEA, causing impact to the regions where these employees reside.

The cost of authorisation, which includes lost profits for the Authorisation Holder and the social cost of unemployment, per kg of prevented 4-tert-OPnEO emissions was calculated. The ratio ranges between £100,000 and £1,000,000 per kg for the GB impacts, as shown in Table 4.12. This cost is significantly higher than the reduction in emissions expected to be achieved by the Authorisation Holder's R&D substitution project which is approximately £5,000 – 50,000 per kg 4-tert-OPnEO over the review period.

The Authorisation Holder has identified an alternative to replace 4-tert-OPnEO. However, prior to completing the substitution, extensive verification studies and regulatory approvals are required. The R&D project is an active program working to substitute 4-tert-OPnEO and other SVHCs from their products globally. A significant number of impacted products, 10 – 100 ([redacted]), are expected to be remaining at the end of the currently authorised review period. An extension of the current review period of 5.5 years by an additional 5 years to 4 January 2033 is required to complete substitution activities for IVD kits used in professional laboratories within GB, while concurrently meeting the regulatory requirements of the international community, including GB. Lastly, this date would harmonise substitution activities to that for the EU, as products impacted by substitution would require global regulatory approvals from all countries prior to distribution. CBI d

Therefore, based on the analysis completed in this SEA, **the benefits of modifying the 4-review period to 4 January 2033 significantly outweigh the risks to the environment over the extended review period.** It is therefore concluded that a refused Authorisation is not a cost-efficient option for reducing emissions of 4-tert-OPnEO, especially

compared to the Authorisation Holder's significant progress on substitutions to date and the ongoing substitution plan.

6. REFERENCES

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ANNEX – JUSTIFICATIONS FOR CONFIDENTIALITY CLAIMS

#	Blanked out item reference	Justification for blanking
a	*4-tert-OPnEO tonnage per use downstream users (total, annual and daily)*	**Demonstration of Commercial Interest:** Volumes of 4-tert-OPnEO imported and used are confidential information that are only to be used for the Authorisation Holder's planning and operations. Sharing them publicly may also breach anti-trust and competition laws in the UK. **Demonstration of Potential Harm:** If competitors got hold of this information, they could use it to determine the Authorisation Holder's output and market share or the weight of the particular products on their overall business. Competitors could use such sensitive information to gain a competitive advantage over the Authorisation Holder. Some of the redacted information could also be used to back-calculate sensitive information. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely
b	*Profit margin, profit, lost profits, revenue, sales, projected growth, number of instruments, market shares, product share within total sales, instrument conversion costs, contract details.*	**Demonstration of Commercial Interest:** Information on business commercial performance, such as manufacturing output, sales, revenue, and profit margins, as well as employment, are commercially sensitive information and are only known by the company. If they become publicly available, they will distort competition and may even be in breach of anti-trust laws in the UK. **Demonstration of Potential Harm:** If marketing (production, sales, revenue, and profits) information were to be released, it would provide the Authorisation Holder's competitors with proprietary knowledge of information on their market share and could give them an unfair competitive advantage. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely
c	*Economic impacts in sensitivity analysis*	**Demonstration of Commercial Interest:** Information on business commercial performance, such as manufacturing output, sales, revenue, and profit margins, as well as employment, are commercially sensitive information and are only known by the Authorisation Holder. If they become publicly available, they will distort competition and may even be in breach of anti-trust laws in the UK. **Demonstration of Potential Harm:** If this information were made publicly available, it could be used by competitors to calculate values covered by category b, which is commercially sensitive information. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely

#	Blanked out item reference	Justification for blanking
d	*Costs and progress of substitution, tracking and monitoring of substitution plan progress*	**Demonstration of Commercial Interest:** Substitution strategy, including costs, results and timelines is proprietary knowledge and indicative of the Authorisation Holder's commercial and development strategy. **Demonstration of Potential Harm:** Dissemination of this information could reveal R&D and marketing details to competitors of the Authorisation Holder and allow them to engage in aggressive commercial tactics using proprietary knowledge to gain an unfair competitive advantage. This would severely harm the commercial interests of the Authorisation Holder. **Limitation to Validity of Confidentiality** This claim is valid indefinitely
e	*Number of employees by division, site, functional area*	**Demonstration of Commercial Interest:** Details of Human resources data are not disclosed directly. Employment data, when made public, is rolled up to Abbott company level. **Demonstration of Potential Harm:** This strategic and commercially sensitive data should not be disclosed to competitors, suppliers, the public and/or customers. If information on employee salaries became public, it could be used by competitors to gain an understanding of the Authorisation Holder's operations and capabilities. **Limitation to Validity of Confidentiality** This claim is valid indefinitely
f	*Employee salaries and subsequent calculations*	**Demonstration of Commercial Interest:** This strategic and commercially sensitive data should not be disclosed to competitors, suppliers, the public and/or customers. It is also covered by The Data Protection Act 2018. **Demonstration of Potential Harm:** If information on employee salaries became public, it could be used by competitors to poach the Authorisation Holder's employees. In addition, as this data is also covered by The Data Protection Act 2018, releasing it would be violating the employees' personal rights. **Limitation to Validity of Confidentiality:** The validity of the claim is indefinite.
g	*Number of tests sold*	**Demonstration of Commercial Interest:** The number of tests performed by downstream users relate to sales and is therefore strategic and commercially sensitive data that should not be disclosed to competitors, suppliers, the public and/or customers. **Demonstration of Potential Harm:** If marketing (production, sales, revenue, and profits) information were to be released, it would provide the Authorisation Holder's competitors with proprietary knowledge of information on their market share and could give them an unfair competitive

#	Blanked out item reference	Justification for blanking
		advantage. **<u>Limitation to Validity of Confidentiality:</u>** The validity of the claim is indefinite
h	*Number of products that contain 4-tert-OPnEO and content of 4-tert-OPnEO and substitute substance per product for the Authorisation Holder's assays*	**<u>Demonstration of Commercial Interest:</u>** Information on the 4-tert-OPnEO in the Authorisation Holder's products is a trade secret. Specific details of product formulations are considered intellectual property of the Authorisation Holder and therefore not publicly disclosed. Quantities per product used in release estimations are also considered to be confidential business information as they could be translated to tests (sales) per location using non-confidential information on predicted environmental concentrations. **<u>Demonstration of Potential Harm:</u>** If this information became available to competitors, it could be used by them to gain a competitive advantage over the Authorisation Holder. It could give them insight into the Authorisation Holder's R&D processes and their products. **<u>Limitation to Validity of Confidentiality:</u>** The validity of the claim is indefinite

Appendix I – Methodology of calculation of unemployment costs

Overview

Calculation of the social costs associated with unemployment in case of a refused authorisation is based on the methodology developed by Dubourg [7]. According to its adaptation of the paper from Haveman and Weimer, there are seven major impacts arising from job loss [11]:

1. The value of wages / output that were lost while the person was unemployed
2. The cost of searching for a new job, along with hiring and firing employees
3. The 'scarring effect', i.e., the impact of being unemployed on future earnings and employment possibilities
4. The value of leisure time during the period of unemployment
5. The costs of health and other well-being effects of being unemployed on the unemployed person
6. The costs of health and other well-being effects of being unemployed on others
7. External costs of unemployment (e.g., health treatment costs paid by taxpayers)

The paper further describes calculation methods for elements 1-4 above, as available literature suggests the relationship between mental/physical health and unemployment is not well understood.

This appendix to the SEA contains the updated calculations for cost elements 1-4 above for a single impacted employee. These costs are then applied to the non-use scenario addressed within the SEA. As addressed within the SEA and AoA, the Authorisation Holder's manufacturing plants are in Ireland and Germany, while commercial offices are present in GB.

Methodology

The value of wages /output lost during unemployment

The methodology used to perform the calculations is the same as that performed in the original AfA, therefore, only the updated calculation tables will be provided in this appendix. Explanation of the costs can be found in Appendix I of the original AfA.

Labour costs

Table I-0.1 shows the average wage paid to the Authorisation Holder's employees and the total output, including employer's social contributions.

Table I-0.1: Average annual salaries for the Authorisation Holder's employees

Country	Average annual salary (£)	Employer social contributions rate*	Gross annual salary including employer contributions (£)
Great Britain	[redacted]	11.3%	[redacted]

Note: A 0.896 £/€ exchange rate was used to convert the average salaries from € to £.
* Calculated from data in reference (14)

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Unemployment duration

The second input required for the calculation of social output loss is the duration of unemployment for the employees that would lose their job in case of a refused authorisation.

The Authorisation Holder employs over [redacted] employees in GB, where commercial offices are located. CBI e

The average unemployment duration for GB employees was calculated using unemployment duration data collected from the Office for National Statistics (ONS) [12]. Table I-0.2 shows the employment duration and the number of employees directly employed by the Authorisation Holder, as well as contract employees. For this analysis, it will be assumed that the employees will obtain a position in half of the average unemployment duration.

Table I-0.2: Average unemployment duration for UK

Country	Number of Authorisation Holder's employees impacted by NUS	Average unemployment duration (months) per ONS	Average unemployment duration halved (months)	Average unemployment duration, halved (years)
Great Britain	[redacted]	7.85	3.93	0.33

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Calculation of lost output

The lost output in case of a refused authorisation is calculated as the product of the pre-tax gross salary, including employer's social contribution, and the average duration of unemployment for the Authorisation Holder's employees that would lose their jobs in GB. Table I-0.3 shows the output loss per employee in GB relevant to the Authorisation Holder.

Table I-0.3: Average loss of output per employee in GB

Country	Average unemployment duration (years)	Average real gross annual salary for Authorisation Holder's employees including employer contributions (£)	Average loss of output per employee (£)
Great Britain	0.33	[redacted]	

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Scarring costs

As wage scarring could persist for up to six years from the time the individual starts in a new position, the Net Present Value (NPV) is calculated, with 2026 as the base year, and using a default 4% discount factor. As the reduction would occur in January 2028, the first year after the current authorised review period would end; the first-year scarring cost covers 12 months. The NPV for a single employee was calculated for GB, and the results are shown in Table I-0.4.

Table I-0.4: Calculation of scarring costs for a single employee in GB (£)

Country	Scarring cost (/y)	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	NPV
Great Britain	[redacted]								
Note: A 4% discount factor is used. Y1 is 2028.									

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In the NUS, the total social cost from wage scarring was calculated as the product of the number of employees that would lose their job in GB and the NPV per employee calculated in Table I-5.

Reservation wages and value of leisure time

Table I-0.5 shows the steps to calculate the value of a single employee's leisure time in GB for the duration of their unemployment.

Table I-0.5: Value of leisure time per employee in GB

Country	Average employment duration (years)	Average employee tax and social contribution (%)	Average employee net wage (£/y)	Reservation wage (£/y)	Value of leisure time per employee (£)
Great Britain	0.33	22.8%	[redacted]		

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The total value of leisure time for the Authorisation Holder's workers that would lose their job in the NUS can be calculated by multiplying the value of leisure time per employee, with the number of employees that would lose their job. The sum will be deducted from the overall costs of unemployment.

Job search and hiring costs

The hiring costs for an individual employee in the impacted countries were calculated and shown in Table I-0.6.

Table I-0.6: Average hiring costs for individual employees in GB

Country	Average real gross annual salary for Application Holder's employees including employer contributions (£)	Average hiring costs per employee (£)
Great Britain	[redacted]	

CBI f

Total Unemployment costs

Table I-0.7 shows the components making up the unemployment cost per employee for GB. These numbers will be used to calculate impacts in the non-use scenario.

Table I-0.7: Total social costs of unemployment for individual employees in GB (£ thousands)

Country	Lost output (£)	Scarring cost (£)	Value of leisure time (£)	Hiring costs (£)	Total unemployment cost (£)
Great Britain	[redacted]				

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