CHEMICAL SAFETY REPORT

Legal name of Authorisation Holder(s):	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

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TABLES

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
AEG	Assessment Entity Group
AfA	Application for Authorisation
AoA	Analysis of Alternatives
CC	Clinical Chemistry
CHESAR	Chemical Safety Assessment and Reporting tool
CSR	Chemical Safety Report
DEHP	Di(2-ethylhexyl) phthalate
DU	Downstream User
ECHA	European Chemicals Agency
ECS	Environmental Contributing Scenario
EE2	17α-ethinylestradiol, a synthetic estrogen
EEA	European Economic Area / European Environment Agency
EQS	Environmental Quality Standards
ERC	Environmental Release Category
ES	Exposure Scenarios
EU	European Union
GB	Great Britain
GJ	Gigajoule
HIV	Human immunodeficiency virus
HSE	Health and Safety Executive
IA	Immunoassays
IVD	In Vitro Diagnostic Device
IVDR	In Vitro Diagnostic Medical Device Regulation
kg	Kilogram
kg/mol	Kilogram/mole
kJ/kg	Kilojoule/kilogram
Koc	Organic carbon-water partition coefficient
Kow	Octanol-water partition coefficient
KPa	Kilopascal
L or l	Litre

LAD	Latest Application Date
LVS	Low Volume Site
mg/kg	Milligram/kilogram
mg/kg dw	Milligram/kilogram dry weight
mg/kg ww	Milligram/kilogram wet weight
mg/l	Milligram/litre
mg/m^3	Milligram per metre cubed
m^3	Metre cubed
MVS	Medium Volume Site
MW	Molecular Weight
N/A	Not Applicable
NPnEO	Nonylphenol ethoxylate
Pa	Pascal
PEC	Predicted Exposure Concentration
PNEC	Predicted No-Effect Concentration
REACH	Registration, Evaluation, Authorisation and Restrictions of Chemicals
RMM	Risk Management Measures
RV	Reaction Vessel
SDS	Safety Data Sheet
SEA	Socio-Economic Analysis
SP	Substitution Plan
spERC	Specific Environmental Release Category
(S)R&D	Scientific Research and Development
STP	Sewage Treatment Plant
SVHC	Substances of Very High Concern
UK	United Kingdom
VHVS	Very High-Volume Site
vPvB	Very Persistent and very Bioaccumulative
WCS	Worker Contributing Scenario
WWTP	Waste Water Treatment Plant
y	Year

DECLARATION

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

Also, we, Abbott Laboratories, Limited, request that the information blanked out in the "public version" of the Chemical Safety Report 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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Part A

1. SUMMARY OF RISK MANAGEMENT MEASURES

Professional use as a surfactant in the final use of In-Vitro Diagnostic Devices (IVDs) for clinical testing using ARCHITECT and Alinity automated analyser systems (detailed info can be found in section 9.1 of the CSR)

ECS and WCS	Task (ERC/spERC or PROC)	Widespread use Annual amount (tonnes /year)	Technical RMMs	Organisational RMMs	PPE (characteristics)	Effectiveness of wastewater and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Transformation scenario	Local release rate	
ECS 1	Professional use of IVD reagents ERC 8a	0.01-0.1 ([redacted]) From all customer sites combined CBI a	Analysers are completely closed systems such as fume cupboard, to avoid air emissions. Reagent cartridges and bottles have spill proof caps.	Instruments and reagents are handled only by trained professional clinical technicians Technical training and guidance material; instrument operations manuals, safety data sheets (SDS)	N/A	Biological STP: Standard [Effectiveness Water: 57.08% for 4-tert-OP; 0.23 % for 4-tert-OPnEO] Air: N/A	**Release factor before RMM:** Water: 10-100 ([redacted]) % Air: 10-100 ([redacted]) % Soil: 0% **Release factor after RMM** Water: 10-100 ([redacted]) % Air: 0% Soil: 0%	100% transformation 4-tert-OPnEO into 4-tert-OP	**Water**: [redacted] kg/day 4-tert-OPnEO; [redacted] kg/day 4-tert-OP **Air:** 0 kg/day 4-tert-OPnEO and 4-tert-OP **Soil:** 0 kg/day 4-tert-OPnEO and 4-tert-OP	CBI a c
								0% transformation 4-tert-OPnEO into 4-tert-OP	**Water**: [redacted] kg/day 4-tert-OPnEO; [redacted] kg/day 4-tert-OP **Air:** 0 kg/day 4-tert-OPnEO and 4-tert-OP **Soil:** 0 kg/day 4-tert-OPnEO and 4-tert-OP	CBI c

								2.5% transformation 4-tert-OPnEO into 4-tert-OP	**Water**: [redacted] kg/day 4-tert-OPnEO; [redacted] kg/day 4-tert-OP **Air:** 0 kg/day 4-tert-OPnEO and 4-tert-OP **Soil:** 0 kg/day 4-tert-OPnEO and 4-tert-OP
WCS	The activity includes the end use of the IVD reagents. The only manual step involves loading and unloading of containers of reagents onto the enclosed automated analyser systems PROC 0		Analysers are completely closed systems. Reagent cartridges and bottles have spill proof caps. There is limited, controlled manual intervention. Sample analysis takes place inside the closed instrument	Instruments and reagents are handled only by trained professional clinical technicians Technical training and guidance material; instrument operations manuals, safety data sheets (SDS).	N/A	N/A	N/A	N/A	N/A

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Abbreviations: WCS=Worker contributing scenario, ECS=Environmental Contributing Scenario, * ERC=Environmental Release Category (or spERC if available), PROC= Process category, PPE=Personal Protective Equipment

2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

Herewith the Authorisation Holder declares that the risk management measures (RMMs) referred to in Section 9 are implemented.

3. DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED TO DOWNSTREAM USERS

Herewith the Authorisation Holder declares that the RMMs for the identified use are communicated to downstream users by means of Product Information Letters, the Instrument Operations Manuals and Safety Data Sheets.

Part B

1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

The information in this section is unchanged from the previous CSR.

2. MANUFACTURE AND USES

This chapter only includes the information that has changed from the previous version of the CSR submitted in November 2021, namely the usage of 4-tert-OPnEO for Use 1 in scope of the Review Report. Please also note that the description of ES1 in Table 2.2.1 is the same as in the previous version of the CSR.

Table 2.1.1 Quantities (in tonnes/year)

Year	Tonnages (tonnes per year)
2023	Use: 0.01 – 0.1 ([redacted]) tonnes/year

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The quantities in Table 2.1.1 were determined by the GB sales of IVD kits in scope of this Application for Authorisation that contain 4-tert-OPnEO.

2.1 Manufacture

No information available on manufacture. This is out of scope of the Application for Authorisation and this Review Report, as the manufacturing occurs outside of the UK.

2.2 Identified Uses

Table 2.2.1: Uses

Identifier	Uses	Other information
ES1	**Environmental release category (ERC):** ERC 8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) **Sector of use:** SU20 Health services **Products Category:** PC21 Laboratory Chemicals **Technical function of the substance:** Surfactant **ES 2 - Worker Contributing scenario** is assigned the PROC code based on the task of manually loading and unloading of open/closed reagents containers onto the enclosed automated analysers systems. (PROC 0) • PROC 0: Other - Use in IVD Instruments with controlled exposures Exposure Scenario 1 involves the use of reagents containing 4-tert-OPnEO in the final use of the IVDs. The only manual step is the loading and unloading of open/closed containers with the reagents onto enclosed automated analyser systems.	**Number of sites:** Downstream use – multiple sites **Substance supplied to that use:** As a mixture

3. CLASSIFICATION AND LABELLING

4. ENVIRONMENTAL FATE PROPERTIES

5. HUMAN HEALTH HAZARD ASSESSMENT

6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICOCHEMICAL PROPERTIES

7. ENVIRONMENTAL HAZARD ASSESSMENT

8. PBT AND vPvB ASSESSMENT

NOTE: The information in sections 3-8 is unchanged from the previous CSR.

9. EXPOSURE ASSESSMENT (and related risk characterisation)

Abbott Laboratories Limited is a global healthcare company with 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 world-wide. It's in vitro diagnostic tests and instrument systems are used by hospitals, laboratories and blood banks for clinical diagnosis and monitoring diseases. The Authorisation Holder manufactures a broad range of tests, including SARS-CoV-2, HIV, hepatitis, thyroid function, fertility and pregnancy, cardiology, renal and metabolic markers, therapeutic drug monitoring, drugs of abuse monitoring, clinical chemistry assays and other indicators of health.

The Authorisation Holder operates three manufacturing sites and a distribution centre located within the EU, where the GB sites act as downstream users (DU) of reagents containing 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (4-tert-OPnEO).

The Authorisation Holder manufactures and markets each product as a single product worldwide, requiring all country approvals prior to placing the product on market. As will be seen in this review report, the substitution timing has been affected by several factors, including some significant factors outside the Authorisation Holder's control. As a result, this review report is being submitted to modify the 4-tert-OPnEO emissions profile and to extend the review period to 4 January 2033.

In GB, Abbott Laboratories, LTD (hereinafter known as 'the Authorisation Holder) applied for the Authorisation (Use 1) for the use of products containing 4-tert-OPnEO by their customers.

9.0. Introduction

9.0.1. Background

In 2021, the Authorisation Holder applied for authorisation in the UK 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.

On 3 July 2023, the final Secretary of State Decision granted a 5.5-year review period (until 30 December 2027) with the condition that the Authorisation Holder and Downstream Users adhere to the Risk Management Measures and Operational Conditions described in the Chemical Safety Report. [1]

Due to factors outside of the Authorisation Holder's control, which include regulatory requirement changes, increased percentage of assays requiring further optimisation, etc., the substitution timeline to remove 4-tert-OPnEO has been impacted. As a result, this review report is being submitted for Use 1 of the original GB AfA, to modify the 4-tert-OPnEO substitution timeline over the review period and to extend the UK authorised review period. The factors affecting the substitution timing, are outlined in the accompanying Substitution Plan and are summarised in Section 9.0.2.

9.0.2. Use Quantities and Reduction Profile over the Review Period

A mass balance approach[1] for calculating the 4-tert-OPnEO usage has been applied throughout the CSR. This is consistent with the approach used in the original application.

[1] Under the "mass balance approach", an average 4-tert-OPnEO content per assay was calculated from the total quantities of 4-tert-OPnEO used divided by number of assays containing 4-tert-OPnEO in a given year.

Table 9.0.1 shows the quantities of 4-tert-OPnEO used in 2023 in ABBOTT ARCHITECT and Alinity reagents. The quantities shown in Table 9.0.1 were calculated from 2023 sales data for GB.

The approach in this document has been updated from the original GB AfA in the following ways:

- The original GB quantities in the 2021 AfA were derived from the EEA sales, and more specifically from the share of tests carried out in the UK, which was further adjusted to only account for the GB quantities.
- The original AfA also covered tests for the now discontinued ABBOTT PRISM instrument. As this system is not in use since 2022, it is not in scope for the review report and no quantities for PRISM have been included in the assessment.

Table 9.0.1. 4-tert-OPnEO quantities used in ARCHITECT/Alinity products sold in GB in 2023

Platform	Number of Products containing 4-tert-OPnEO	Total 4-tert-OPnEO used in GB products in 2023 (kg)
ARCHITECT/Alinity	100-200 ([redacted])	10 – 100 ([redacted])

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Table 9.0.2 shows the overall reduction achieved by the Authorisation Holder since the initiation of the substitution programme. As the majority of the 4-tert-OPnEO tonnage in use was in the system solutions (Pre-Trigger and Trigger), these solutions were prioritized first for substitution. 4-tert-OPnEO had already been substituted in the system solutions when the original GB AfA was submitted, so there was no need to apply for an authorisation for that use.

Table 9.0.2. Kg reduction in 4-tert-OPnEO in GB products as of end 2024 compared to 2021.

Product Type	kg Reduction as of end 2024
Pre-Trigger and Trigger	[redacted]
ABBOTT PRISM Reagents	
Immunoassay and Clinical Chemistry Reagents	
Total	

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The reduction in 4-tert-OPnEO usage over the proposed review period per the revised substitution plan is shown in Table 9.0.3. It should be noted that the reduction profile is considered a worst-case approach. An additional contingency buffer of 1-3 years has been added to individual reformulation timeline, based on technical and regulatory complexity as explained in the combined AoA/SEA/SP Section 3.1.1. The assumption is that a product will be included for 4-tert-OPnEO calculations for the full calendar year even though conversion to the new 4-tert-OPnEO free product takes place within the calendar year. This conservative approach will overestimate the amount of 4-tert-OPnEO being reported.

Table 9.0.3: Product substitution status and reduction in 4-tert-OPnEO use quantities over the proposed review period

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

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[redacted]

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Figure 9.0.1. Reduction of 4-tert-OPnEO quantities over the authorised review period

Owing to the factors described in Section 4.1.3.1 of the Substitution Plan, the Authorisation Holder respectfully requests an extension of the review period to 4 Jan 2033. This is supported by the following reasoning:

- The factors described in Section 4.1.3 of the Substitution Plan are outside of the control of the Authorisation Holder (i.e., regulatory requirement changes, increased percentage of assays requiring further optimisation, etc).
- Other substances included in Annex XIV of the REACH regulation have had date extensions related to IVDR, for example DEHP. Transitional periods for DEHP were extended by two years per Commission Regulation (EU) 2023/2482 of 13 November 2023 [2]. The entry includes the rationale that '*Delays caused by the limited capacity of notified bodies should not penalise companies in the process of substituting DEHP in medical devices.'* This same argument pertains to companies substituting 4-tert-

OPnEO who are similarly impacted by notified body capacity constraints. While this is mainly relevant to the EU, it impacts product verification and regulatory timelines worldwide, as the EU is usually the first region in which new products are registered.

- At time of submission, [redacted] of products have demonstrated technical feasibility through successful completion of all design verification studies, with an additional [redacted]% of products being discontinued. Having completed the Preliminary Feasibility and Design Verification testing phase reduces the risk of further optimization as product requirements have been met. CBI e
- The Authorisation Holder is confident that all substitution activities will be complete by the end of the requested, extended review period, 04 Jan 2033.

9.0.3. Overview of uses and Exposure Scenarios

The Authorisation Holder is submitting a review report, including this CSR for Use 1:

- 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

This use occurs at over 100-200 ([redacted]) hospital, clinical laboratory and blood banking sites distributed across GB. These uses take place on dedicated instruments for clinical testing of human samples. Use 1 includes professional use of the immunoassay and clinical chemistry reagents formulated by the Authorisation Holder along with the professional use of immunoassay and clinical chemistry reagents formulated by the Authorisation Holder's Third-Party Manufacturing network. CBI f

4-tert-OPnEO is used in the final formulation of reagent, calibrator and control IVD kits, which are referred to collectively as 'Reagents' throughout the CSR. All reagents are developed to be used exclusively with Abbott instrument platforms; ARCHITECT and Alinity. The ABBOTT PRISM instrument platform, originally covered by the use applied for, was retired worldwide at the end of 2022, therefore no emissions from this platform will be assessed in this CSR.

Tonnage information:

Assessed tonnage: [redacted] (10-100) kg used in 2023 by the Authorisation Holder's customers in reagents for ARCHITECT and Alinity systems. CBI a

Table 9.0.4 lists the exposure scenario (ES) assessed in this CSR.

Table 9.0.4. Overview of exposure scenario and contributing scenario

Identifiers*)	Market Sector	Exposure scenario and the related contributing scenario	Tonnage (tonnes per year)
ES2-PW	-	Professional use as a surfactant in the final use of In-Vitro Diagnostic Devices (IVDs) for clinical testing using ARCHITECT and Alinity automated analyser systems**)	0.01-0.1 [redacted] CBI a
*) Professional end use: PW-# **) Please note that, while the name of the use applied for does not change, the description of the exposure scenario does not assess the ABBOTT PRISM products, which have been discontinued.			

9.0.4. Introduction to the assessment

9.0.4.1. Environment

Scope and type of assessment:

The substance was added onto Annex XIV of EU REACH (Authorisation list) [3] because it breaks down to a substance (4-tert-Octylphenol, CAS No: 140-66-9) that has endocrine disrupting properties for the environment. Annex XIV of EU REACH was retained in UK REACH (The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019; SI 2019 No. 758) [4] with the same Latest Application Date (LAD) and Sunset Date (SD). In this instance the Applicant was able to benefit from transitional provisions introduced in UK REACH (The REACH etc. (Amendment etc.) (EU Exit) (No. 3) Regulations 2019; SI 2019 No. 1144), allowing for adjustment of the LAD and SD to 22 July 2022, and 22 December 2023, respectively [5].

A threshold (PNEC) for such a substance is currently not available, therefore a non-threshold approach is being taken in this assessment as indicated in Table 9.0.6 below. Evaluation of any potential health hazards to humans is not required within the framework of this review report. Additionally, the EU REACH Annex XV dossier for 4-tert-OPnEO and for 4-tert-OP [6] details that there is no relevant information available regarding the potential endocrine effects for terrestrial organisms, in particular soil dwelling organisms or birds, and the authors concluded that they do not represent substances with strong endocrine disruption potency properties for the mammalian system.

Within the Water Framework Directive (Standards and Classification) Directions (England and Wales) 2015 [7], Environmental Quality Standards (EQS) have been developed for 4-tert-OP establishing a 0.1 µg/L of 4-tert-OP for inland surface waters and 0.01 µg/L of 4-tert-OP for other surface waters, as an annual average. These values were developed prior to the inclusion of 4-tert-OPnEO onto the Authorisation list and therefore they do not consider the endocrine disrupting properties of 4-tert-OP, so these values do not represent a definitive safe threshold value for the hazards associated with the substance. However, they can be used as benchmarks for regional environmental concentrations of 4-tert-OPnEO from the applied widespread use of the Authorization Holder.

In its assessment of the Authorisation Holder's original application, the HSE compared the surface water PECs for 4-tert-OPnEO to EQS proposed for EE2 [8], an endocrine disruptor with the same estrogenic mode of action:

- The chronic (annual average) EQS for freshwater was 0.0032 ng/L; and·
- The chronic (annual average) EQS for saltwater was 0.0016 ng/L.

It should be noted, however, that EE2 is considered much more potent than 4-tert-OP (HSE considers it to be 100 to 1,000 times more potent), so a more appropriate benchmark value for 4-tert-OP could be 0.0032 µg/l for freshwater and 0.0016 µg/l for marine water.

The focus of the environmental exposure are GB customer (DU) sites using the IVD kits in scope.

In the original AfA, the Authorisation holder submitted the environmental exposure assessment assuming, as a worst-case approach, that all quantities of 4-tert-OPnEO released to the environment were ultimately 100% converted to 4-tert-OP within the STP. This was done in accordance with the "Risk-related considerations in applications for authorisation for endocrine disrupting substances for the environment, specifically OPnEO and NPnEO" which was agreed at the 43rd meeting of ECHA's Risk Assessment Committee (RAC).According to it: Applicants as "a worst-case, can assume that all 4-tert-OPnEO released to the environment will eventually be present as 4-tert-OP" [9]. In the case of the

original AfA CSR, the Authorisation Holder assumed that all 4-tert-OPnEO breaks down to 4-tert-OP during residence in the STP.

In its Opinion, the UK competent authority (HSE) indicated that [8]:

> "*the actual release of 4-tert-OP to surface waters is likely to be a lot less (the SVHC support dossier[2] provides an estimated ~2.5% conversion from 4-tert-OPnEO to 4-tert-OP in STP). Given that typically 2.5% of 4-tert-OPnEO would be expected to be converted to 4-tert-OP during sewage treatment, total partitioning of both substances to sewage sludge would only account for around 1% of input mass. This is also supported by a UK environmental risk evaluation report of 4-tert-OP[3], where the amount of 4-tert-OP released in the effluent from a STP was estimated as 2.5% of the 4-tert-OPnEO entering the STP"*.

Hence, in this updated review report, the Authorisation Holder has modelled the environmental emissions of 4-tert-OPnEO with 3 different approaches:

- "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 [8] 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.

Due to the high volumes of liquid waste generated in the ARCHITECT and Alinity high throughput, fully automated analyser systems, the liquid waste is typically plumbed directly to drain at the customers' premises. The following assumptions were used for the exposure assessments:

- ARCHITECT and Alinity instrument liquid waste was assumed to be disposed directly to drain.
- Residual solution from excess and expired material/partially empty ARCHITECT and Alinity containers was assumed to be disposed directly to drain. It is understood that the empty containers are handled as hazardous waste and are sent for incineration.

The environmental releases of 4-tert-OPnEO from ten representative customer sites have been considered and the PEC_{locals} of 4-tert-OP and/or 4-tert-OPnEO were calculated, based on the specific product usage, amount of 4-tert-OPnEO per product, STP capacity, receiving

[2] https://echa.europa.eu/candidate-list-table/-/dislist/details/0b0236e1807db570

[3] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/290844/scho0405biyz-e-e.pdf

body of water flow rate and other relevant available information. To select the ten sites, the customers were grouped in four usage categories based on their usage of 4-tert-OPnEO as shown in Table 9.0.5. The selection then included four sites falling in the "very high" usage category, three sites from the "high" and "medium" usage categories and one site from the "low" usage category.

Table 9.0.5 Overview of Emission Categories

Emissions Category	Daily emissions range (kg)
Very High	> 0.00400
High	> 0.00100 to ≤ 0.00400
Medium	> 0.00010 to ≤ 0.00100
Low	≤ 0.00010

The total environmental releases of 4-tert-OPnEO from all the downstream users have been considered to calculate the $PEC_{regionals}$ of 4-tert-OP (background concentration).

Only the environmental release generated from liquid waste (ARCHITECT and Alinity) has been considered in the calculation of PEC_{local} for the ten DU sites, as it is assumed that no solid waste containing 4-tert-OPnEO is disposed of in the environment.

The aim of the CSR is to quantitatively assess the effort to reduce the emission of 4-tert-OP and assess the corresponding reduction in the PECs of 4-tert-OP and/or 4-tert-OPnEO. Considering the endocrine disrupting properties of 4-tert-OP, the risk is only qualitatively described in function of the available EQS that, as anticipated, only represent a benchmark but do not represent a safe threshold for the protection of environmental matrices from the endocrine disrupting effect.

Table 9.0.6 summarises the approach taken for each environmental target.

Table 9.0.6. Type of risk characterisation required for the environment

Protection target	**Type of risk characterisation**	**Hazard conclusion (see section 7)**
Freshwater	Qualitative	PEC_{local} / $PEC_{regional}$ value estimation Chesar 3.9
Sediment (freshwater)	Qualitative	PEC_{local} / $PEC_{regional}$ value estimation Chesar 3.9
Marine water	Qualitative	PEC_{local} / $PEC_{regional}$ value estimation Chesar 3.9
Sediment (marine water)	Qualitative	PEC_{local} / $PEC_{regional}$ value estimation Chesar 3.9
Sewage treatment plant	Qualitative	PEC_{local} value estimation Chesar 3.9
Air	Qualitative	No hazard identified
Agricultural soil	Qualitative	PEC_{local} / $PEC_{regional}$ value estimation Chesar 3.9

Comments on assessment approach

No measurements for 4-tert-OPnEO or relevant degradation products downstream of the STPs were conducted. It is not possible to perform measurements at downstream user sites due to the large number of customers and distribution across GB. There are also considerations in relation to sampling locations and frequency, as 4-tert-OPnEO can be present from other sources. The Authorisation Holder has specific data on sales of IVD kits containing 4-tert-OPnEO across GB, and these volumes were used to estimate the quantities used by each downstream user.

A mass balance approach that accounts for all quantities of 4-tert-OPnEO has been utilised throughout the CSR. As a worst-case scenario, 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.

The approach to assessing the environmental impacts will be qualitative since there is scientific debate about whether thresholds can be defined for endocrine disruption. The focus of the assessment is to demonstrate that releases of 4-tert-OPnEO have been reduced as far as is technically and practically possible.

The estimated regional environmental concentrations of 4-tert-OPnEO from the applied for widespread use are compared with the benchmark EQS value given in The Water Framework Directive (Standards and Classification) Directions (England and Wales) 2015 [7] for 4-tert-OP for inland surface waters (0.1 µg/l) and other surface waters (0.01 µg/l), as an annual average.

As discussed previously, the approach taken by HSE in its assessment of the Authorisation Holder's original application, surface water PECs for 4-tert-OPnEO were compared to the EQS of EE2 water taking in consideration its higher potency compared to 4-tert-OP resulting in a EQS for 4-tert-OPnEO of 0.0032 µg/l for freshwater and 0.0016 µg/l for marine [8].

To calculate the 4-tert-OP emissions and concentrations, a conversion factor of 0.33 is applied to the percentage of 4-tert-OPnEO quantities that are transformed to 4-tert-OP and released to the environment. This was derived from the relative molecular weights of 4-tert-OP (MW = 206.3) and 4-tert-OPnEO with an average of 9.5 ethoxylate units (MW = 625).

The defined assessment entity groups are reported in the following table.

Table 9.0.7. Assessment entity groups (AEG)

Transformation scenario	Composition of AEG	Justification
0% transformation	• 100% 4-tert-OPnEO • 0% 4-tert-OP	Worst-case scenario where 4-tert-OPnEO does not undergo any degradation in the STP
100% transformation	• 0% 4-tert-OPnEO • 33% 4-tert-OP	Worst-case scenario where 4-tert-OPnEO undergoes degradation in the STP and completely transforms in 4-tert-OP. The 0.33 conversion factor is applied to the 100% transformation to account for difference in MW. 100% 4-tert-OP *0.33= 33%
2.5% transformation	• 97.5% 4-tert-OPnEO • 0.8% 4-tert-OP	Realistic scenario where 4-tert-OPnEO undergo degradation in the STP but only 2.5% transforms in 4-tert-OP. The 0.33 conversion factor is applied to the 2.5% transformation to account for difference in MW. 2.5% 4-tert-OP *0.33= 0.8%

The following substance properties are used in the environmental fate estimation calculated by EUSES 2.1.2 integrated within the CHESAR tool. They correspond to the values reported in section 4 of the previous CSR.

Table 9.0.8. Key physicochemical property data used in the assessment for 4-tert-octylphenol

Substance property	4-tert-OPnEO	4-tert-OP
Molecular weight used for the assessment	646.9	206.3
Vapour pressure	$0.24 \cdot 10^{-11}$ Pa at 20 °C	0.001 kPa at 20 °C
Partition coefficient (Log Kow)	2.39 at 20 °C	4.8 at 22 °C
Water solubility	189 mg/l at 20 °C (critical micellar concentration)	19 mg/l at 22 °C
Melting point	Not available	84.5°C
Boiling point	Not available	289°C, at 101 kPa
Biodegradation in water: screening tests	inherently biodegradable	inherently biodegradable
Bioaccumulation: BCF (aquatic species)	Not available	740 dimensionless
Adsorption/Desorption: Koc at 20 °C	18.20	10,000

In a standard (modelled) biological STP, the emissions from the two substances are distributed as shown in Table 9.0.9.

Table 9.0.9. Fate (release percentage) in the modelled biological sewage treatment plant

	4-tert-OPnEO	4-tert-OP
Release to water	99.77%	42.91 %
Release to air	1.03E-11%	4.909 %
Release to sludge	0.227%	52.17%
Release degraded	0%	0%

The above fractions are calculated by the SimpleTreat 3.0 model integrated in EUSES (and CHESAR) based on their physicochemical properties.

The model predicts that 4-tert-OPnEO would partition almost exclusively in the liquid outflow of the STP, mainly due to the very low adsorption / desorption coefficient (Koc); while in the case of 4-tert-OP the substance would be released almost 50/50 between water and sludge. In practice, the situation is expected to be somewhere between these two extremes, with only partial degradation to 4-tert-OP occurring in the STP. The degradation products, according to information in the Annex XV dossier [6], would most likely be 4-tert-OP1/2EO, 4-tert-OPnEO and 4-tert-OP, that once entering the environment distribute variably to water, air and sediment. All these degradation products are expected to degrade to 4-tert-OP over time.

9.0.4.2. Man via environment

Scope and type of assessment:

The scope of this assessment focuses on the environmental exposure only. Human health exposure is not evaluated in this application as the substance has been placed onto Annex XIV of EU Regulation 1907/2006 (REACH) on the basis of its endocrine disrupting properties in environmental species. In accordance with ECHA Guidance Document R.16 on Environmental Exposure Assessment: "An assessment of indirect exposure of humans via the environment is generally only conducted if: a) the tonnage is >1,000 t/y or b) the tonnage >100 t/y and the substance is classified b1) as STOT RE 1; or b2) as a carcinogen or mutagen (any category); or b3) as toxic to reproduction (categories 1A or 1B)" [10]. The

substance 4-tert-OPnEO is used by the Authorisation Holder below the specified tonnage limits and is not classified for any of the mentioned hazard categories. As human health hazards are not relevant to this application for authorisation, an assessment of secondary exposure of man via environment is not considered necessary.

9.0.4.3. Workers

Scope and type of assessment:

The scope of this assessment focuses on the environmental exposure only. Risk characterisation required for workers is not evaluated in this application as the substance has been placed onto Annex XIV of REACH on the basis of its endocrine disrupting properties in environmental species and thus only its effects and impacts on the environment are of relevance. Worker exposure is not relevant for this application as determined in the Annex XV dossier [6].

Comments on assessment approach related to toxicological hazard:

Not relevant – worker hazards are not subject to assessment in this CSR.

Comments on assessment approach related to physicochemical hazard:

Not relevant – physicochemical hazards are not subject to assessment in this CSR.

General information on risk management related to toxicological hazard:

Not relevant – The substance is not assessed for toxicological hazards. Any Risk management measures (RMM) used by the downstream users of the Authorisation Holder's IVD kits relate to other components and reagents.

General information on risk management related to physicochemical hazard:

Not relevant – The substance is not assessed for any physicochemical hazards. If any RMM are by downstream users used to control such hazards, they are intended to control risks arising from other reagents.

9.0.4.4. Consumers

Scope and type of assessment:

Exposure assessment is not applicable as there are no consumer-related uses for the substance.

9.1. Exposure scenario

Market sector: IVD manufacturing – health services

Sector of use: SU20 Health Services

Article categories: N/A

Environment contributing scenario(s):

ERC 8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)

Worker/Consumer contributing scenario(s): PROC 0: Other – Use in IVD Instruments with controlled exposures

Subsequent service life exposure scenario(s): N/A – there is no service life as the substance is not part of an article.

Exposure scenario(s) of the uses leading to the inclusion of the substance into the article(s): N/A

* The exposure scenario involves the professional use of reagents containing 4-tert-OPnEO in the final use of the IVDs. The only manual step is the loading and unloading of open/closed containers with the reagents onto enclosed automated analyser systems (PROC 0).

Description of the activities and technical processes covered in the exposure scenario

4-tert-OPnEO is present in some of the reagents used by the Authorisation Holder's customers. They are used in core laboratory immunoassay, clinical chemistry and blood transfusion products. Reagents are used with the Authorisation Holder's high throughput automated instrument systems (ARCHITECT *i*, Alinity i, ARCHITECT *c*, Alinity c and Alinity s). Depending on the instrument, the Authorisation Holder supplies the reagents in either individual bottles or as cartridges fixed on a rigid frame, so they are loaded together on the instrument.

The bottles and cartridges are loaded and unloaded manually. This is the only routine manual task involving the reagent solutions containing 4-tert-OPnEO. All other operations are carried out automatically by the instrument. Each instrument performs the following general steps (in order):

- Use pipettors to aspirate the required quantities for each test from the bottles and to dispense in the reaction vessels (for immunoassays) and in the cuvettes (for clinical chemistry) on the processing centre.
- Mix reagents with samples and allow the solution to incubate at controlled temperature.
- After processing is over and the sample has been analysed, the contents of the reaction vessel / cuvette are discarded. After processing is complete in the CC instruments, cuvettes are washed by the instrument to remove leftover material. After testing is complete for IA instruments, the content of the reaction vessel is aspirated and discharged to liquid waste, with the empty reaction vessel discarded into solid waste.

There is no manual intervention in the processing of the samples and all work is carried out in an enclosed area. Figure 9.1.1 outlines the steps required to produce a test result using the ARCHITECT *i* system.

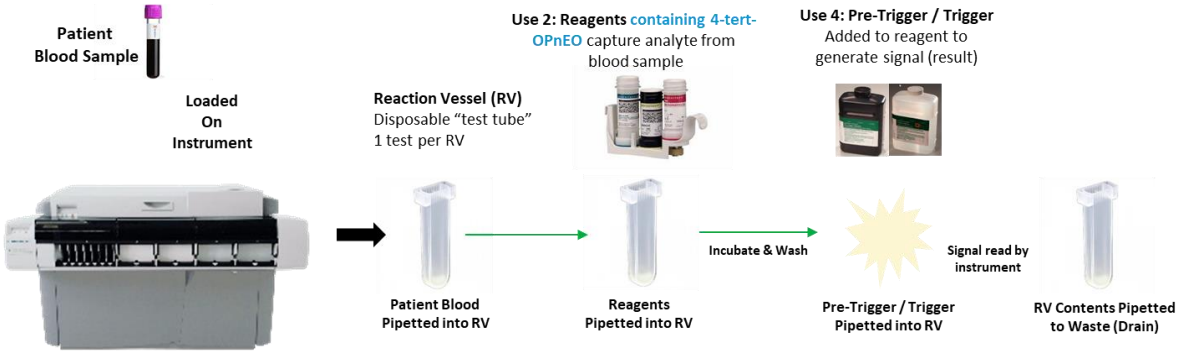

Figure 9.1.1. Steps required to produce a test result using the Authorisation Holder's ARCHITECT *i* system.

Solid waste
Solid waste from the ARCHITECT and Alinity test system is represented by the bottles and cartridges containing the substance. Any residual substance in the bottle is rinsed and poured down the drain.

It is possible that small quantities of ARCHITECT and Alinity reagent solutions remain in the bottles and cartridges when these are replaced. The empty containers are disposed of as solid waste. The main options of handling solid waste are landfilling and incineration. If the plastic bottles are incinerated, all quantities of 4-tert-OPnEO present in them will be destroyed. In case of landfilling, there is potential for release. However, the substance is not volatile, so no emissions to air are expected. Only possible emission route is from leaching into landfills. The leachate may be led to a biogas generating facility at the landfill site or it may reach nearby water bodies. In either case, only chance of releases will be to water.

As a conservative approach, it is assumed that all quantities of 4-tert-OPnEO included in reagents are used for testing and are discharged to the local municipal sewage systems. The release factor to the environment wastewater is assumed to be 100%.

Explanation on the approach taken for the ES:

Annual and daily releases of 4-tert-OPnEO
Downstream use of the Authorisation Holder's IVD kits takes place at multiple sites in GB by trained professional personnel. These sites are spread all over GB and vary in the level of IVD kit usage.

To assess the specific emissions in the environment of the ten representative sites, the exposure assessment has been performed as if the site were an industrial site (ERC 4), allowing the modification of the specific STP characteristics, which could not be otherwise been modified in the CHESAR tool at a professionals (widespread) use phase.

The annual usage of 4-tert-OPnEO for each site was derived by the annual sales for 2023. While some of these quantities will be used in the following year, it is assumed they are balanced of quantities carried over from the previous one. The daily release quantity was derived from the annual quantity, following an assessment of weekday versus weekend testing patterns in AbbottLink (an instrument data analytics system). While typical downstream user sites run testing 7 days per week, the number of tests run on weekdays is greater than the number of tests run on weekend days. Therefore, simply dividing the annual test volume by 365 days would underestimate the daily releases. Instead, a denominator value of 286 (based on Abbottlink data) was applied to the annual quantity to ensure that the daily release quantities were reflective of typical weekday test volume.

For the assessment of the release from the selected high-to-low volumes sites, the daily release quantity was derived from the annual quantity at the site divided by the amount of emitting days, either 296 or 275 (Abbottlink) depending on whether it was IA or CC testing. The site-specific information on the receiving STP, such as discharge rate and flow of receiving water body, were taken from the HydroWASTE database [11]. The receiving body of water was determined for each of the selected local areas, based on the location of the selected STP and the identification of the discharge point.

For the released quantities as widespread use, the daily release quantity was derived from the total annual quantity in 2023 divided by the number of emitting days, either 296 or 275 depending on the type of test. Further, as according to R.16 ECHA guidance [10], the release was estimated as per a standard town and taking into account:

- the fraction of the "tonnage for the use" used in the region (regional tonnage): 0.1;
- the fraction of the regional tonnage used in the standard town (proportional to the ratio of number of inhabitants in a standard town (10 000) compared to the number of inhabitants in a region (20 000 000)): 0.0005;

The resulting tonnage was multiplied by an assessment factor of 4 to take into account geographical or temporal peaks in the use of a substance.

It should be noted that the aim of this exposure assessment exercise is to highlight the low environmental concentrations arising from the use of the Authorisation Holder's IVD kits at customer sites. The Authorisation Holder is aware that the main assessment criterion for this non-threshold substance is the minimisation of releases to the environment and this is also the focus of their efforts, as discussed in Chapter 9.1.1.3 of this CSR, as well as in the accompanying SEA/SP report.

Receiving body of water
Receiving body of water dilution rates can impact the final concentration of 4-tert-OPnEO and/or 4-tert-OP in the environment. The population size and the water flow of the receiving body of water together account for the overall dilution achieved in the wastewater. The model used by CHESAR assumes a default dilution factor of 10 and it is suggested that the maximum dilution factor used with the model is 1000. These two values can be used to define the worst- and best-case environmental concentrations with the quantities of 4-tert-OPnEO used.

In this CSR, the receiving body of water was specifically determined for each of the 10 downstream users assessed, based on the location of the selected STP and the identification of the discharge point. STP site specific information have been extracted from the HydroWASTE database [11]. One third of the value provided for flow rate of the receiving bodies at the outfall point was used, as per the suggestion of ECHA's R16 Guidance Document (Appendix A.16-3.3.3) [10].

Sewage treatment plant analysis
Treatment of wastewater in sewage treatment plants is also known to affect environmental concentrations of 4-tert-OPnEO.

The default STP in ECHA's guidance on environmental exposure assessment [10] is for a town with population of 10,000. Many of the Authorisation Holder's customers, particularly high-volume, are located in larger cities, served by large STPs (for example, person equivalent (p.eq.) of over 500,000). This in turn could lead to a higher dilution factor which would significantly change the emission estimates in these high-volume locations.

For the assessment of the release from the selected high-to-low volumes sites, details of the relevant STP, such as discharge rate, receiving bodies, flow rate at the outflow point of the STP where, extracted from the HydroWASTE database [11], resulting in a more realistic dilution of the liquid waste stream containing 4-tert-OPnEO exiting the STP and entering the environment.

Detailed information related to the ten DU sites, regarding the quantity of 4-tert-OPnEO used and the parameters related to the releases (Population equivalent, STP discharge and receiving body) are available in Annex II – Table 1.

The values were used in the calculations of the site-specific assessment carried out in CHESAR 3.9, using the built-in EUSES 2.1.2 model. The exercise was carried out to determine the contribution of 4-tert-OPnEO in the Authorisation Holder's reagents to local environmental concentrations.

9.1.1. Environmental contributing scenario 1

9.1.1.1. Conditions of use

Product (article) characteristics
▪ Physical form of substance: Liquid ▪ Substance in preparation: Yes
Amount used, frequency and duration of use (or from service life)
• Daily local widespread use amount: <= [redacted] tonnes/day *The daily local widespread use amount (tonnes/day) is calculated as:* [redacted] *kg/day (tonnage for the use of the substance per day taking already in account days of emission (296 or 275)) * 4 (default factor taking into account geographical or temporal peaks in the use of a substance)* 0.1 (default fraction of the "tonnage for the use" used in the region)* 0.0005 (default fraction of the regional tonnage used in the standard town)*
• Percentage of GB tonnage used at regional scale: = 10 %
• Percentage of Regional tonnage used at local scale: = 100 % [10]
Conditions and measures related to biological sewage treatment plant
• Biological STP: Standard [Effectiveness Water: 57.08%] *See Appendix II for site specific STP data for the assessment of the ten sites*
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: No (no waste) *No solid waste is assumed.* *Liquid waste is not generated as any leftover of the substance in the containers is removed rinsing and pouring it in the drain and so accounted for in the yearly/daily amount of the substance.*
Other conditions affecting environmental exposure
• RMM limiting release to air [Effectiveness Air: 100%] *All operations involving 4-tert-OPnEO are in an enclosed instrument, such as fume cupboard, so, until release to the drain, the substance is never in the open. Therefore, no releases to air are assumed.*

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9.1.1.2. Releases

Table 9.1.1. Local releases to the environment of widespread use

Release	Release estimation method and factor		Substance	100% transformation scenario	2.5% transformation scenario	0% transformation scenario
				Local release rate (kg/day)		
Water	ERC	**Release factor before onsite RMM:** [redacted]	4-tert-OPnEO	[redacted]		
		Release factor after onsite RMM: [redacted]	4-tert-OP			
Air	ERC	**Release factor before onsite RMM:** [redacted]	4-tert-OPnEO			
		Release factor after onsite RMM: 0%	4-tert-OP			
Non-agricultural soil	ERC	**Release factor after onsite RMM:** 0% **Explanation:** All DU use operations are conducted in closed instruments which are directly connected to drain with no direct release to soil.	4-tert-OPnEO			
			4-tert-OP			

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The estimated local release rates for the "100% transformation" scenario for the widespread use is in-line with the original AfA where, for [redacted] (10-100) tonnes per year of 4-tert-OPnEO, it was estimated at 2.2 x 10-5 kg 4-tert-OP/day. CBI a

The exact quantity of 4-tert-OPnEO and/or 4-tert-OP released from the ten DU sites to the environment are reported in detail in Table 2, Table 3 and Table 4 in Appendix II. The estimated release values are in line with those presented in the original AfA.

Table 9.1.2 summarises the result from the ten representative sites, showing the highest releases among the selected sites, in the three transformation scenarios.

Table 9.1.2. Summary of highest local releases to the environment among representative sites

Release	Release estimation method and factor		Substance	100% transformation scenario	2.5% transformation scenario	0% transformation scenario
				Local release rate (kg/day)		
Water	ERC	Release factor before onsite RMM: [redacted]	4-tert-OPnEO	[redacted]		
		Release factor after onsite RMM: [redacted]	4-tert-OP			
Air	ERC	Release factor before onsite RMM: [redacted]	4-tert-OPnEO			
		Release factor after onsite RMM: 0%	4-tert-OP			
Non-agricultural soil	ERC	Release factor after onsite RMM: 0% **Explanation:** All DU use operations are conducted in closed instruments which are directly connected to drain with no direct release to soil.	4-tert-OPnEO			
			4-tert-OP			

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Releases to waste

Liquid waste

Solutions containing 4-tert-OPnEO are used to perform clinical chemistry and immunoassay (core laboratory and transfusion) tests in GB.

The users of the clinical chemistry and immunoassay IVD kits are hospitals, clinics, medical labs and blood banks. There are 100-200 ([redacted]) downstream users in GB. It was not possible to determine how each individual laboratory deals with liquid waste containing 4-tert-OPnEO, however as a worst case it was assumed that instrument liquid waste and residual solution from excess and expired material/partially empty containers is disposed directly to drain. CBI d

System operations manuals provide recommendations for waste handling, stating that each facility is responsible for labelling all waste containers and characterizing its waste stream to ensure waste is disposed of in accordance with the appropriate local, state, and national regulations.

It is possible that small quantities of reagent solutions remain in the bottles and cartridges when these are replaced. The empty containers are disposed of as solid waste. The main options of handling solid waste are landfilling and incineration. If the plastic bottles or cartridges are incinerated, all quantities of 4-tert-OPnEO present in them will be destroyed. In case of landfilling, there is potential for release. However, the substance is not volatile, so no emissions to air are expected. Only possible emission route is from leaching in landfills. The leachate may be led to a biogas generating facility at the landfill site or it may reach nearby water bodies. In either case, it is probable that all releases will be to water.

As a conservative approach, it is assumed that all quantities of 4-tert-OPnEO included in reagents are used for testing and are discharged to the local municipal sewage systems. The release factor to the environment wastewater is assumed to be 100%.

The quantity of 4-tert-OPnEO generated from the ten representative downstream user sites as liquid waste is accounted for in the estimated releases to the different environmental compartments as reported in Table 2 in Appendix II.

Solid Waste
No release from solid waste is assumed as its quantification was not feasible (see "Description of the activities and technical processes covered in the exposure scenario" for further details. As a conservative approach, it is assumed that all quantities of 4-tert-OPnEO included in reagents are used for testing and are discharged to the local municipal sewage systems. The release factor to the environment wastewater is assumed to be 100%.

Release factor to waste from the process:
Table 9.1.2. summarises the amount of 4-tert-OPnEO used and the quantities of 4-tert-OP released from the use of the Authorisation Holder's assays by GB downstream users. This includes the releases of liquid waste to STPs and solid waste to landfill.

Table 9.1.2: Summary of 4-tert-OPnEO used and released from the use of the Authorisation Holder's reagents in GB

Instrument System	Total annual use of 4-tert-OPnEO (kg/y)	Scenario	Total annual release of 4-tert-OPnEO (kg/y)	Total Release of 4-tert-OP (kg/y)
ARCHITECT and Alinity	[redacted] [10-100]	100% transformation	0	[redacted] Released from STP to water (43.0%): [redacted] air (4.9%): [redacted] sludge (52.2%): [redacted]
		0% transformation	[redacted] Released from STP to water (99.8%): [redacted] air (1.03E-11%): [redacted] sludge (0.227%): [redacted]	0
		2.5% transformation	[redacted] Released from STP to water (99.8%): [redacted] air (1.03E-11%): [redacted] sludge (0.227%): [redacted]	[redacted] Released from STP to water (43.0%): [redacted] air (4.9%): [redacted] sludge (52.2%): [redacted]

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9.1.1.3. Exposure and risks for the environment

The following tables provide Local (Clocal) emissions and Predicted Environmental Concentrations (PEC) of the widespread use of the substance (Table 9.1.3) and a summary of the minimum and maximum CLocal and PEC of the ten representative downstream user site locations and, for comparison, the estimated values from the original AfA. Detailed information on the emissions for each individual location are reported in Appendix II.

Table 9.1.3. Range of local Concentration and PEC for widespread downstream use

Protection target	AE	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-6	3.25E-6	2.9E-6	3.17E-6	0	0
	4-tert-OP	0	0	1.01E-8	1.03E-8	4.17E-7	4.26E-7
Sediment (freshwater) mg/kg dw	4-tert-OPnEO	2.98E-7	1.76E-5	-	1.72E-5	-	0
	4-tert-OP	0	0		1.04E-5		4.28E-4
Marine water mg/l	4-tert-OPnEO		3.24E-7	2.9E-7	3.16E-7	0	0
	4-tert-OP		0	1.01E-9	1.03E-9	4.17E-8	4.26E-8
Sediment (marine water) mg/kg dw	4-tert-OPnEO		1.76E-6	-	1.71E-6	-	0
	4-tert-OP		0		1.04E-6		4.27E-5
Sewage Treatment Plant mg/l	4-tert-OPnEO		2.98E-5	-	2.91E-5	-	0
	4-tert-OP		0		1.03E-7		4.23E-6
Air mg/m³	4-tert-OPnEO	0	0	0	0	0	0
	4-tert-OP	0	0	6.52E-12	1.49E-11	2.69E-10	6.14E-10
Agricultural soil mg/kg dw	4-tert-OPnEO	3.04E-7	3.04E-7	2.97E-7	2.97E-7	0	0
	4-tert-OP	0	0	3.2E-6	3.2E-6	1.32E-4	1.32E-4

Table 9.1.4. Range of local Concentration and PEC for the 10 selected downstream users

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)

Remarks on predicted environmental exposure:

The PEC_{local} for the widespread use are in line with those estimated in the original AfA. All the values are below the previously derived, as per reduced tonnage of use (kg/y instead than kg/y). CBI a

When taking into consideration the different modelled transformation scenarios, 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 [8] to the previous authorisation 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.

No data are available on the evaluation of the degradation pathways in surface water of octylphenol ethoxylates. However, data on nonylphenol ethoxylates (NPnEO) can be used to predict its behaviour in the environment. Data suggest that under aerobic conditions in fresh water, long chain nonylphenol ethoxylates will be degraded to intermediate metabolites long- and short-chain ethoxylates and carboxylates and eventually into 4-tert-OP. However, in saltwater this transformation might happen more slowly depending on the season [6]. Overall results indicate that alkylphenols ethoxylates may also degrade, but slower, to its corresponding alkylphenols in sediment [12]. Nevertheless, in a worst-case approach, the assessment of the endocrine effects of 4-tert-OPnEO is based on the relatively stable degradation product 4-tert-OP that has a much higher endocrine potency compared to 4-tert-OPnEO and its intermediate degradation products.

Regarding the evaluation of the local concentration of the substance from the representative ten 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 one order of magnitude 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.

Furthermore, the lowest PEC_{local} values have been observed for the site where the 4-tert-OPnEO usage is the lowest (site 10).

Furthermore, it should be noted that in the modelled 100% transformation scenario, where it is assumed that that 100% of 4-tert-OPnEO will be transformed in the STP to 4-tert-OP, environment concentration to the sediment compartment are overestimated.

Site 3 with high volumes of use at site and lower flow rate of the receiving body result in a local PEC of 0.03 mg/kg for freshwater sediment, which is an order of magnitude higher than the highest PEClocal (2.47E-3 mg/kg) for the same compartment estimated at site in the original AfA. This is the outcome of the overestimation on the transformation rate of 4-tert-OPnEO to 4-tert-OP, as the latter present a lower release percentage from the STP to the surface water, which in turn will end up mostly in the sediment compartment due to its higher adsorption potential (KoC 10,000).

In comparison, when modelling the exposure in the more realistic 2.5% transformation scenario a local PEC of 7.21E-4 mg/kg for freshwater sediment is derived for 4-tert-OP, which is instead an order of magnitude lower than the highest PEClocal (2.47E-3 mg/kg) derived in the previous report for the same compartment.

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 use are at least one order of magnitude lower than the EQS for 4-tert-OP (0.01 µg/L), in any of the scenarios. 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.

Conclusion on risk characterisation

Risk Management and Controls

Overall, the hierarchy of control principles have been followed with the Authorisation Holder's implementation of their ongoing substitution plan noted in the conclusions on risk management. The hierarchy of control is a widely accepted system where control methods at the top of hierarchy are potentially more effective and protective than those at the bottom. Following this hierarchy normally leads to the implementation of inherently safer systems, where the risk of illness or injury or release has been substantially reduced. The EU Chemical Agents Directive, Article 6, (Directive 98/24/EC) [13] defines occupational 'hierarchy of control' in order of priority from the top down as: 1) Elimination or substitution, 2) Engineering controls, 3) Collective protection measures and 4) Individual protection measures. Though generally considered a safety and health concept, the same principles can be considered for environmental control strategies with substitution at the top of a hierarchy for environmental risk management.

In the case of downstream users of 4-tert-OPnEO in the Authorisation Holder's IVD kits, greater emphasis is placed on elimination / substitution of 4-tert-OPnEO from these products. Engineering controls and general collective protection measures were also considered, as discussed in the following sections.

Substitution plan

The Authorisation Holder is applying all available resources to prioritise and expedite substitution of 4-tert OPnEO and other SVHCs in all products, where technically feasible. As discussed in the introduction (Table 9.0.2), substitution is complete for the Pre-Trigger and Trigger products that accounted for [redacted] kg of the total 4-tert-OPnEO used in GB products ([redacted] kg) in 2021. A further [redacted] kg reduction was achieved for the reagents in scope as of the end of 2024. Overall, this results in a [redacted] kg or [redacted]% reduction in 4-tert-OPnEO used in GB products relative to 2021 as the year just prior to the sunset date. This has significantly reduced the overall emissions of 4-tert-OPnEO in GB.

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Minimisation of releases and feasibility

Based on commercially available technology, collection and incineration of waste is the only treatment method available to eliminate releases of 4-tert-OPnEO from the instrument effluent. However, prevention of release to the environment through collection and incineration is not possible at hospital, blood screening and clinical laboratories due to space and infrastructure limitations.

It is important to note, when considering the feasibility of controlling releases of 4-tert-OPnEO from IVD kit reagent usage at downstream user sites, that concentrations in liquid waste are very low (maximum of 0.0001 – 0.001 ([redacted]) %, directly at the outflow of the analyser in 2022). Therefore, the volume of wastewater will be extremely high relative to the quantity of 4-tert-OPnEO. As a result, local regulations governing disposal generally allow the instrument effluent to be disposed of as non-hazardous wastewater. A standard core laboratory immunoassay analyser will generate approximately 5.5 L of liquid waste per hour, while a clinical chemistry analyser will produce between 15 – 54 L per hour depending on the system and throughput. Given this high volume of liquid waste generated, the analysers in place at downstream user sites are generally plumbed directly to the wastewater drain. CBI b

A typical customer will have several such devices that are plumbed directly to drain. Extensive infrastructural upgrades would be required to re-route drainage systems and divert the analyser waste from other facility wastewater. This could involve internal excavation work and navigation through wards, cleanrooms, and other controlled areas. Even if separate drainage systems could be established, in reasonable time and at reasonable cost (which in general we believe is not possible), then it would require large scale collection tanks to be installed externally, with secondary containment and enough room for a tanker lorry to manoeuvre to make regular wastewater collections. External space considerations would then come into play which again shows the practical infeasibility of waste collection. Hospitals are often limited in external as well as internal space.

Downstream users in scope of Use 1 performed **10 – 100 ([redacted]) million individual tests** in GB in 2023 using the Authorisation Holder's immunoassay and clinical chemistry systems. Workflow disruption during facility modifications would lead to a delay in generating and reporting test results, which in turn would lead to delayed diagnosis and adverse patient outcomes. CBI d

Technical Feasibility of Alternatives to Collection and Incineration: The logistical aspects of collection and incineration demonstrate the infeasibility of these measures. Accordingly, the Authorisation Holder has evaluated the technical feasibility of various treatment technologies that might be deployed at customer sites as an alternative to collection and incineration.

There are no widely available commercial treatment technologies with proven efficacy in reducing/preventing 4-tert-OPnEO release from the analyser liquid waste stream. Published studies for the removal of alkylphenol polyethoxylates from wastewater conclude that conventional treatments used in wastewater treatment plants such as biodegradation, sand filtration, carbon adsorption and/or chemical oxidation in place are not effective in their elimination. The same challenges pertain to the analyser effluent, since it is difficult to remove trace contaminants from complex mixtures in a way that is chemically effective, technologically simple, economically viable, and environmentally friendly [14].

The Authorisation Holder previously evaluated several technologies and determined they are not practical/feasible. This included advanced oxidation processes, activated carbon filtration and nanofiltration. Considerations included commercial availability, size/footprint of the system and timeframe for implementation, as well as the efficacy of 4-tert-OPnEO removal.

An additional literature review has been carried out in this CSR. According to the review, potential alternatives based on electrochemical oxidation process involving OH radicals [15], competitive adsorption mechanism of beta-cyclodextrin crosslinked citric acid (BCD-CA) [16] and microbial electrolysis cells (MECs) [17], have been identified. Nevertheless, none of

these alternatives can be considered a viable alternative to incineration and a suitable ready solution for the Authorisation Holder's downstream users. These technologies are not available commercially, so the entire quantity of wastewater would have to be collected and incinerated to prevent 4-tert-OPnEO releases from Use 1.

Economic feasibility: As shown in Table 9.1.5, in 2023, 10,000-20,000 ([redacted]) tonnes of wastewater would have to be collected and incinerated annually across GB to prevent all 4-tert-OPnEO releases this use. The cost effectiveness of such an approach would decrease significantly over time. Analyser liquid waste volume will remain constant, as it is not possible to separate the waste streams containing 4-tert-OPnEO from those that do not. On the other hand, the 4-tert-OPnEO concentration will reduce over time as individual products are substituted. The net result is that the incineration cost to prevent 1 kg 4-tert-OPnEO release will rise throughout the review period, exceeding £1 million per kg in 2032. These figures exclude facility modification costs (e.g., for installing the holding tanks) which are expected to far exceed the annual incineration costs.

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Table 9.1.5: Annual cost to incinerate liquid waste to prevent 1 kg 4-tert-OPnEO release from downstream users in GB

Year	kg 4-tert-OPnEO per year	Liquid waste volume (L)	Volume of waste to prevent 1 kg 4-tert-OPnEO release (L)	Incineration cost to prevent 1 kg 4-tert-OPnEO release (£)	Incineration cost discounted to 2023 prices (£)
2023	[redacted]				
2024					
2025					
2026					
2027					
2028					
2029					
2030					
2031					
2032					

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Notes
A 1-10% ([redacted]) annual increase in liquid waste volume, driven by increased demand is assumed.
Cost values are discounted to 2023 year-end price, using a 4% discount factor.

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Environmental Considerations:

The CO_2 emissions from incineration of downstream user waste containing 4-tert-OPnEO are significant and would partially offset the potential environmental benefit of prevented releases of 4-tert-OPnEO. It is not possible to compare those impacts since the risk to the environment from releases of 4-tert-OPnEO has not been monetised. The liquid waste is a very dilute solution, consisting almost entirely of water. The quantities of waste that would be incinerated annually are conservatively estimated to be 10,000-20,000 ([redacted]) tonnes in 2023 and are expected to gradually increase in the following years. It is possible to calculate the CO_2 emissions from the incineration given the following reasoning:

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- The water in the liquid waste must be vaporized before the 4-tert-OPnEO can be burned in the incinerator which takes energy.
- First, there is the energy needed to heat the water from 15 to 100°C. Since the energy required to raise the temperature of one gram of water 1°C (the calorie) is 4.1855 joules, the energy required to heat [redacted] m^3(tonnes) of water by 85 degrees

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is [redacted] X 85 X 4.1855 = [redacted] GJ. CBI g

- Secondly, there is energy required for the vaporization, known, as the heat of vaporization, which is a physical property of a substance. It is defined as the heat required to change one mole of liquid at its boiling point under standard atmospheric pressure, expressed as kg/mol or kJ/kg. When a material in liquid state is given energy, it changes its phase from liquid to vapor; the energy absorbed in this process is called heat of vaporization. The heat of vaporization of water is about 2,260 kJ/kg. The energy required to vaporize the wastewater can be calculated as [redacted] X 2,260 = [redacted] GJ. CBI g
- The total energy to incinerate the wastewater is therefore [redacted] GJ.
- Assuming that the required energy would be generated using Natural Gas, the most efficient of the fossil fuels, the carbon dioxide released by burning enough natural gas to produce [redacted] GJ can be calculated from the specific carbon dioxide emission factor for natural gas which is 56.1 kg CO_2/GJ. CBI g
- The carbon dioxide released from the incineration of the [redacted] m^3 (tonnes) of wastewater would therefore be 1,000 – 10,000 [redacted] tonnes ([redacted] X 56.1)/1000).

These calculations apply to this Authorisation Holder only. Adding other IVD manufacturers with high throughput analysers would significantly increase the overall burden at a time when the UK is working to reduce greenhouse gas emissions.

10. EXPOSURE ASSESSMENT (and related risk characterisation)

10.1. Introduction

10.1.1. Workers

No risk characterisation has been conducted for workers as it is not considered relevant for this substance.

10.1.2. Consumers

No risk characterisation has been conducted for consumers as it is not considered relevant for this substance as there is not consumer use.

10.2. Environment

10.2.1. All uses (regional scale)

10.2.1.1. Total releases

The total releases to the environment from all the exposure scenarios covered are presented in Table 10.2.1 below. This is the sum of the releases to the environment from all exposure scenarios addressed.

Table 10.2.1. Total releases to the environment per year from widespread use

Release route	Assessment entity	Total releases per year		
		100% transformation scenario (kg/y)	0% transformation scenario (kg/y)	2.5 % transformation scenario (kg/y)
Water	4-tert-OPnEO	[redacted]		
	4-tert-OP			
Air	4-tert-OPnEO			
	4-tert-OP			
Soil	4-tert-OPnEO			
	4-tert-OP			

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Table 10.2.2 shows the total releases from the ten representative sites evaluated in this CSR.

Table 10.2.2. Total releases per year from the ten selected sites

Release route	Assessment entity	Total releases per year		
		100% transformation scenario (kg/y)	0% transformation scenario(kg/y)	2.5 % transformation scenario (kg/y)
Water	4-tert-OPnEO	[redacted]		
	4-tert-OP			
Air	4-tert-OPnEO			
	4-tert-OP			
Soil	4-tert-OPnEO			
	4-tert-OP			

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10.2.2. Regional exposure

No measured regional concentrations of 4-tert-OPnEO are available in GB, as the Authorisation Holder is not the only user of 4-tert-OPnEO. Therefore, any measurements would not provide meaningful information for the contribution of the authorised use to the total concentrations.

An overview of the PECregional concentrations of 4-tert-OPnEO and 4-tert-OP are reported in Table 10.2.3. This shows the PEC calculated at regional scale considering the widespread use and environmental release from the 100-200 [redacted] downstream users in GB.

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Table 10.2.3. Predicted regional exposure concentrations (Regional PEC) for widespread use

Protection target	Assessment entity	Regional PEC		
		100% transformation scenario	0% transformation scenario	2.5% transformation scenario
Fresh water	4-tert-OPnEO	0 mg/l	2.69E-7 mg/l	2.62E-7 mg/l
	4-tert-OP	9.39E-9 mg/l	0 mg/l	2.28E-10 mg/l
Sediment (freshwater)	4-tert-OPnEO	0 mg/kg dw	1.33E-6 mg/kg dw	1.3E-6 mg/kg dw
	4-tert-OP	1.76E-5 mg/kg dw	0 mg/kg dw	4.26E-7 mg/kg dw
Marine water	4-tert-OPnEO	0 mg/l	2.64E-8 mg/l	2.57E-8 mg/l
	4-tert-OP	8.99E-10 mg/l	0 mg/l	2.18E-11 mg/l
Sediment (marine water)	4-tert-OPnEO	0 mg/kg dw	1.31E-7 mg/kg dw	1.28E-7 mg/kg dw
	4-tert-OP	1.52E-6 mg/kg dw	0 mg/kg dw	3.69E-8 mg/kg dw
Air	4-tert-OPnEO	0 mg/m³	0 mg/m³	0 mg/m³
	4-tert-OP	3.45E-10 mg/m³	0 mg/m³	8.37E-12 mg/m³
Agricultural soil	4-tert-OPnEO	0 mg/kg dw	0 mg/kg dw	0 mg/kg dw
	4-tert-OP	1.76E-8 mg/kg dw	0 mg/kg dw	4.28E-10 mg/kg dw

The $PEC_{regional}$ represents the background concentration of 4-tert-OP and/or 4-tert-OPnEO, depending on the transformation scenario, related to the widespread release from all downstream users. For completeness, PECregional concentrations of 4-tert-OPnEO and 4-tert-OP are provided for the ten selected sites in Appendix III Table 5.

As expected, the results reported in Table 10.2.3, show that the $PEC_{regional}$ concentrations follow a similar behaviour as PEC_{local}, with the lowest concentration in air, followed by water and sediment. This is due to the chemical physical properties of the 4-tert-OP, which tends to adsorb organic matter (Koc: 10,000) in the 100% and 2.5% transformation scenario. A similar pattern is also observed in the $PEC_{regional}$ concentrations of 4-tert-OPnEO, however in this case, due to the higher percentage released from the STP to surface water and the lower adsorption behaviour, the predicted concentration is generally two orders of magnitude higher than 4-tert-OP in water but one order of magnitude lower in sediment.

By comparing the 4-tert-OP and 4-tert-OPnEO EQS with $PEC_{regional}$, it is noted that all the $PEC_{regional}$ concentrations for freshwater results are five orders of magnitude lower than the EQS for other (non-inland) surface water (0.01 µg/l), either as 4-tert-OP or 4-tert-OPnEO.

This is also confirmed in the estimated $PEC_{regional}$ of 4-tert-OP and/or 4-tert-OPnEO for the ten representative sites (see Appendix III, table 6).

This is also true when the $PEC_{regional}$ are compared with the EQS value of EE2, as suggested in the HSE's opinion [8] to the original AfA, taking into account its higher potency than 4-tert-OP. All the estimated PECs, no matter the transformation scenario, are below the benchmark of 0.0032 µg/l for freshwater and 0.0016 µg/l for marine water, for either 4-tert-OP or 4-tert-OPnEO.

When comparing the estimated $PEC_{regional}$ for the 100% transformation scenario to 4-tert-OP with the estimated values in the original AfA, the reduction in the use of 4-tert-OPnEO from substitution completed by the Authorisation Holder to date has resulted in a further decrease of the $PEC_{regional}$ concentrations of 4-tert-OP, which are approximately one order of magnitude lower for the concentration to water (freshwater and marine). PECs of the sediment and soil environmental compartments are instead only slightly decreased but within the same order of magnitude, showing that in these instances, usage quantities and adsorption behaviour of the substance are the major drivers for the PEC concentrations of 4-tert-OP.

This is considered the most important result, as it supports the effectiveness of tonnage reduction as the main risk management measure that the Authorisation Holder has adopted to reduce the environmental release of 4-tert-OPnEO and environmental exposure to 4-tert-OP.

Overall, the outcome of this assessment shows that the assessed contribution of the downstream use of the Authorisation Holder's reagents is very low and comparable, if not orders of magnitude lower than the EQS for 4-tert-OP or EE2 (allowing for the difference in potency between the two substances).

Discussion

The Authorisation Holder is actively and aggressively working towards substituting 4-tert-OPnEO from the products marketed in GB, as per the substitution plan. As discussed in Section 9.1.1.3 and summarised below, collection of the wastewater containing 4-tert-OPnEO from each DU site is not a feasible option, especially considering the decreasing volumes of 4-tert-OPnEO in the IVD kits sold in GB.

In summary:

- In October 2017, the European Chemicals Agency (ECHA) published guidance [18] stating that the Scientific Research and Development (SR&D) exemption could be applied to analytical activities using in vitro diagnostic (IVD) medical devices, providing that these activities used volumes below one tonne/year per site and were

carried out under controlled conditions. Had collection been possible, the downstream use addressed in this CSR would have met the exemption criteria. The authorisation request was submitted on behalf of the downstream users specifically because collection of liquid waste is not feasible.

- Based on the hierarchy of control principles, substitution of 4-tert-OPnEO is considered the primary risk management measure. The Authorisation Holder prioritised substitution of Pre-Trigger and Trigger solutions which accounted for [redacted] kg of the total 4-tert-OPnEO used in GB products. All GB downstream users converted to the reformulated product in 2022. In addition, the results of the substitution plan to date has resulted in an additional [redacted] kg decrease in the quantities of 4-tert-OPnEO used by downstream users in GB. Overall, the Authorisation Holder has achieved a [redacted]% reduction in 4-tert-OPnEO used by downstream users in GB. CBI e CBI a e
- Wastewater volumes are very high. 10,000 – 20,000 ([redacted]) m^3 would have to be collected and incinerated annually in GB. CBI g
- If all the liquid waste were to be collected and incinerated, the carbon dioxide released from the incineration of the wastewater would be 1,000 – 10,000 ([redacted]) tonnes. CBI g
- Hospital and clinical laboratories do not have existing infrastructure or space to establish new infrastructure capable of handling this volume of wastewater. An authorisation was submitted on behalf of the downstream users because collection of waste is not possible.
- Even if they had the space, the disruption during facility modifications would be unacceptable. These laboratories operate 24/7 and provide critical diagnostic test results to support the provision of healthcare services across GB.
- In the timeframe it would take to complete facility modifications (re-routing of drainage networks and installation of large-scale external holding tanks), the Authorisation Holder will have completed most of the product reformulations to remove 4-tert-OPnEO.
- Estimated predicted concentration for the environment for the 2023 usage of the substance proven to be below the derived EQS for the substance and for the EE2 benchmark values.

The Authorisation Holder respectively submits that all reasonable efforts are being undertaken in order to minimise emissions of 4-tert-OPnEO from the use applied for to the degree that is technically and practically possible. Therefore, the authorisation review period should be extended to 4 January 2033.

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ANNEX 1- Justification for confidentiality claims

#	Redacted reference	Justification for redaction
a.	*Total tonnage 4-tert-OPnEO used for the assessment and by individual downstream users (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. This also applies to emission volumes, which can be used to back-calculate to volumes of 4-tert-OPnEO used. **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.	*Number of products that contain 4-tert-OPnEO and amount of 4-tert-OPnEO per product for the Authorisation Holder's assays*	**Demonstration of Commercial Interest:** Information on the 4-tert-OPnEO in the Authorisation Holder's products is a trade secret. Specific details of product formulations are considered the 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. **Demonstration of Potential Harm:** 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. **Limitation to Validity of Confidentiality:** The validity of the claim is indefinite
c.	*Initial and final release factors*	**Demonstration of Commercial Interest:** The initial and final release factors could be used to determine quantities of 4-tert-OpnEO used which relates to production capacity and customer testing volume. This is therefore strategic and commercially sensitive data that should not be disclosed to competitors, suppliers, the public and/or customers. The validity of the claim is indefinite. **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
d.	*Number of tests performed by downstream users*	**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 advantage. **Limitation to Validity of Confidentiality:** The validity of the claim is indefinite
e.	*Product substitution status*	**Demonstration of Commercial Interest:** Substitution strategy, including 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
f.	*Sales, market and other financial information relating to the operations of the Authorisation Holder.*	**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 supposed to be 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
g.	*Quantities of waste treated, incineration costs*	**Demonstration of Commercial Interest:** Incineration costs and other operating costs relate to profitability and are therefore strategic and commercially sensitive data that should not be disclosed to competitors, suppliers, the public and/or customers.

		Demonstration of Potential Harm: If such information were to be released, it would provide the Authorisation Holder's competitors with proprietary knowledge of information on their operations and financial performance, which could give them an unfair competitive advantage and could also be in breach of competition laws in the UK. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely.

Appendix I: Uncertainty analysis

A summary review of the uncertainties of the analysis are included at the end of this section as Appendix Table 1.

Sensitivity analysis discussion
The main uncertainty in the CSR would be the fate of 4-tert-OPnEO in the STP and the distribution of the 4-tert-OP. Various scenarios were evaluated, assuming all 4-tert-OPnEO degrades to 4-tert-OP and that none of the 4-tert-OPnEO degrades to 4-tert-OP within the STP. Furthermore, it is assumed that the distribution of 4-tert-OP at the waste streams exiting the STP (effluent, air, sludge) will be based on the 4-tert-OP or 4-tert-OPnEO properties, depending on the scenario being discussed. The approach taken in the original AfA (assumption that 4-tert-OPnEO fully degrades to 4-tert-OP in the STP) tends to overestimate the emissions through sludge. As shown in Table 9.0.5, there is a marked difference if the 4-tert-OPnEO properties are used to determine the distribution, with the majority expected to be in the liquid phase. This could affect the PECs for water and sediment, so it was decided to examine additional degradation scenarios within this review report.

The water PECs would be higher if the 4-tert-OPnEO properties are used. However, the PECs remain low in all cases. It should also be noted that, as discussed in Table 1 below, the background concentration is most likely overestimated, due to the use of standard STPs for the widespread use exposure assessment, which has a lower dilution factor compared to the actual STPs in the examined customer site locations.

Uncertainty conclusion
The Authorisation Holder has attempted to take a worst-case approach whenever possible with the aim of presenting an overall conservative result. It is considered that there is still uncertainty in the analysis, but it does not affect the conclusion that the Authorisation Holder has reduced emissions to the degree that is technically and practically possible. It should be noted that there is little uncertainty with regards to the emitted quantities and most of the uncertainties affect the predicted environmental concentrations provided.

Appendix Table 1: Uncertainty Analysis Review

Uncertainty	Impact for the CSR	Assumption
Fate of 4-tert-OPnEO in the Wastewater Treatment Plants. The substance is treated in a multitude of WWTPs across the EU, with different characteristics and processing methods.	Releases of 4-tert-OPnEO and 4-tert-OP from the WWTPs would differ from location to location. It is also possible that in some WWTPs, degradation of 4-tert-OP would also be observed, reducing the total emissions.	Three different scenarios were used to calculate the local and regional PECs, examining the potential range of 4-tert-OPnEO and 4-tert-OP releases and concentrations.
Quantity of 4-tert-OPnEO in reagents is not the same across the different assays but varies.	The analysis of releases of 4-tert-OPnEO from the downstream users' sites would not be accurate and could over- or underestimate specific local concentrations.	The total usage of 4-tert-OPnEO was aggregated and split evenly across all products to determine an average quantity of 4-tert-OPnEO per product. Due to the very large number of tests carried out in GB, this assumption is expected to have little impact to the final results.
It is possible that residual quantities in used bottles may be collected and treated as chemical waste in some sites, instead of emptied down the drain.	It would affect the total emissions as wastewater and the final environmental concentrations after the STP.	It is assumed that 100% of the residual quantities in used bottles at a customer site is discharged into wastewater. This could overestimate overall emissions and environmental concentrations.
Regional concentrations were calculated by Chesar from wide dispersive use using standard STP, which, as determined by the downstream user analysis by the Authorisation Holder, was not representative of the STPs in locations of the Authorisation Holder's customers.	The calculation seems to overestimate the background concentration levels, giving a higher PEC.	It was decided to retain the Chesar calculations as a conservative approach. The results from the 10 representative downstream users also show low environmental concentrations. Nevertheless, the regional concentrations are considered a more representative metric for comparison with the EQS for 4-tert-OP, as they are more relevant to the release from all downstream users and do not reflect a single emission episode from the STP, like the PEC_{local}.
It is possible that releases from a DU other than the selected DU of 4-tert-OPnEO could result in higher Clocal and PEClocal concentrations than those reported in Table 9.1.3.	The maximum C_{local} and PEC_{local} in Table 9.1.3 could be underestimated.	In CSR Version 2 all emission categories of 4-tert-OPnEO (very high, high, medium and low) were evaluated to establish a representative range of C_{local} and PEC_{local} environmental concentrations. Overall, the impacts of this uncertainty to the calculations in the CSR are not considered significant.

Appendix II: Site Specific Data: 10 selected downstream users of 4-tert-OPnEO

Appendix Table 2: Sites specific quantities and STP input data for modelling emission

Site	Usage Class	Total Sum Reagents		Treated wastewater discharged (m^3/day)	Receiving body of water	River discharge (m^3/day)
		4-tert-OPnEO (kg/year)	4-tert-OPnEO (kg/day)			
1	very high	[redacted]	[redacted]	[redacted]	River	[redacted]
2	very high	[redacted]	[redacted]	[redacted]	River	[redacted]
3	very high	[redacted]	[redacted]	[redacted]	River	[redacted]
4	very high	[redacted]	[redacted]	[redacted]	Coastal / Ocean	[redacted]
5	high	[redacted]	[redacted]	[redacted]	River	[redacted]
6	high	[redacted]	[redacted]	[redacted]	River	[redacted]
7	high	[redacted]	[redacted]	[redacted]	River	[redacted]
8	medium	[redacted]	[redacted]	[redacted]	Coastal / Ocean	[redacted]
9	medium	[redacted]	[redacted]	[redacted]	River	[redacted]
10	low	[redacted]	[redacted]	[redacted]	River	[redacted]

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Appendix Table 3: C_{local} and PEC_{local} of 4-tert-OPnEO and 4-tert-OP for ten selected DU sites for the 0% transformation scenario

	Site number	#1		#2		#3		#4		#5	
Protection target	**AE**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**
Fresh water mg/l	4-tert-OPnEO	8.24E-6	8.95E-6	2.32E-5	2.4E-5	2.12E-4	2.12E-4	NA	NA	3.02E-5	3.09E-5
	4-tert-OP	0	0	0	0	0	0	NA	NA	0	0
Sediment (freshwater) mg/kg dw	4-tert-OPnEO		4.85E-5		1.3E-4		1.15E-3		NA		1.67E-4
	4-tert-OP		0		0		0		NA		0
Marine water mg/l	4-tert-OPnEO	NA	NA	NA	NA	NA	NA	6.5E-7	7.19E-7	NA	NA
	4-tert-OP	NA	NA	NA	NA	NA	NA	0	0	NA	NA
Sediment (marine water)	4-tert-OPnEO		NA		NA		NA		3.9E-6		NA
	4-tert-OP		NA		NA		NA		0		NA
Sewage Treatment Plant mg/kg dw	4-tert-OPnEO		4.27E-5		3.63E-5		4.58E-4		6.5E-5		1.73E-4
	4-tert-OP		0		0		0		0		0
Air mg/m³	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	0	0	0	0	0	0	0	0	0	0
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	0	0	0	0	0	0	0	0	0	0
Predator's prey (freshwater) mg/kg ww	4-tert-OPnEO		8.41E-5		2.11E-4		1.78E-4		NA		2.66E-4
	4-tert-OP		0		0		0		NA		0
Predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		NA		3.1E-6		NA
	4-tert-OP		NA		NA		NA		NA		NA
Top predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		NA		1.8E-6		NA
	4-tert-OP		NA		NA		NA		NA		NA
Predator's prey (terrestrial) mg/kg ww	4-tert-OPnEO		6.96E-9		6.96E-9		6.96E-9		6.96E-9		6.96E-9
	4-tert-OP		0		0		0		0		0

	Site number	#6		#7		#8		#9		#10	
Protection target	**AE**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**
Fresh water mg/l	4-tert-OPnEO	8.87E-6	9.58E-6	3.36E-6	4.08E-6	NA	NA	1.33E-6	2.04E-6	4.18E-7	1.13E-6
	4-tert-OP	0	0	0	0	NA	NA	0	0	0	0
Sediment (freshwater) mg/kg dw	4-tert-OPnEO		5.19E-5		2.21E-5		NA		1.11E-5		6.12E-6
	4-tert-OP		0		0		NA		0		0
Marine water mg/l	4-tert-OPnEO	NA	NA	NA	NA	4.58E-8	1.15E-7	NA	NA	NA	NA
	4-tert-OP	NA	NA	NA	NA	0	0	NA	NA	NA	NA
Sediment (marine water)	4-tert-OPnEO		NA		NA		6.21E-7		NA		NA
	4-tert-OP		NA		NA		0		NA		NA
Sewage Treatment Plant mg/kg dw	4-tert-OPnEO		1.46E-4		3.09E-4		4.58E-6		6.34E-5		4.92E-6
	4-tert-OP		0		0		0		0		0
Air mg/m³	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	0	0	0	0	0	0	0	0	0	0
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	0	0	0	0	0	0	0	0	0	0
Predator's prey (freshwater) mg/kg ww	4-tert-OPnEO		8.93E-5		3.24E-5		NA		2.64E-5		1.86E-5
	4-tert-OP		0		0		NA		0		0
Predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		1.85E-6		NA		NA
	4-tert-OP		NA		NA		0		NA		NA
Top predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		1.55E-6		NA		NA
	4-tert-OP		NA		NA		0		NA		NA
Predator's prey (terrestrial) mg/kg ww	4-tert-OPnEO		6.96E-9		6.96E-9		6.96E-9		6.96E-9		6.96E-9
	4-tert-OP		0		0		0		0		0

Appendix Table 4: C_{local} and PEC_{local} of 4-tert-OPnEO and 4-tert-OP for ten selected DU sites for the 100% transformation scenario

	Site number	#1		#2		#3		#4		#5	
Protection target	**AE**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**
Fresh water mg/l	4-tert-OPnEO	0	0	0	0	0	0	NA	NA	0	0
	4-tert-OP	1.15E-6	1.18E-6	3.25E-6	3.28E-6	2.96E-5	2.096E-5	NA	NA	4.22E-6	4.24E-6
Sediment (freshwater) mg/kg dw	4-tert-OPnEO		0		0		0		NA		0
	4-tert-OP		1.18E-3		3.29E-3		0.03		NA		4.26E-3
Marine water mg/l	4-tert-OPnEO	NA	NA	NA	NA	NA	NA	0	0	NA	NA
	4-tert-OP	NA	NA	NA	NA	NA	NA	9.09E-8	9.34E-8	NA	NA
Sediment (marine water)	4-tert-OPnEO		NA		NA		NA		0		NA
	4-tert-OP		NA		NA		NA		9.37E-5		NA
Sewage Treatment Plant mg/kg dw	4-tert-OPnEO		0		0		0		0		0
	4-tert-OP		6.06E-6		5.15E-6		6.5E-5		9.23E-6		2.45E-5
Air mg/m³	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	1.13E-7	1.13E-7	4.91E-8	4.94E-8	4.97E-8	5E-8	1.38E-8	1.41E-8	4.12E-8	4.15E-8
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	1.14E-6	1.16E-6	4.96E-7	5.13E-7	5.02E-7	5.19E-7	1.4E-7	1.56E-7	4.167E-7	4.33E-7
Predator's prey (freshwater) mg/kg ww	4-tert-OPnEO		0		0		0		NA		0
	4-tert-OP		3.53E-4		9.64E-4		8.54E-3		NA		1.23E-3
Predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		NA		0		NA
	4-tert-OP		NA		NA		NA		9.56E-5		NA
Top predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		NA		0		NA
	4-tert-OP		NA		NA		NA		3.39E-6		NA
Predator's prey (terrestrial) mg/kg ww	4-tert-OPnEO		0		0		0		0		0
	4-tert-OP		8.78E-6		7.64E-6		7.65E-6		7.01E-6		7.5E-6

	Site number	#6		#7		#8		#9		#10	
Protection target	**AE**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**
Fresh water mg/L	4-tert-OPnEO	**0**	0	0	0	NA	NA	0	0	0	0
	4-tert-OP	1.24E-6	1.24E-6	4.71E-7	4.74E-7	NA	NA	1.86E-7	2.14E-7	5.84E-8	8.62E-8
Sediment (freshwater) mg/kg dw	4-tert-OPnEO		0		0		NA		0		0
	4-tert-OP		1.27E-3		5E-4		NA		2.15E-4		8.65E-5
Marine water mg/L	4-tert-OPnEO	NA	NA	NA	NA	0	0	NA	NA	NA	NA
	4-tert-OP	NA	NA	NA	NA	6.4E-9	8.87E-9	NA	NA	NA	NA
Sediment (marine water)	4-tert-OPnEO		NA		NA		0		NA		NA
	4-tert-OP		NA		NA		8.9E-6		NA		NA
Sewage Treatment Plant mg/kg dw	4-tert-OPnEO		0		0		0		0		0
	4-tert-OP		2.07E-5		4.38E-5		6.5E-7		9E-6		6.98E-7
Air mg/m³	4-tert-OPnEO	**0**	0	0	0	0	0	0	0	0	0
	4-tert-OP	2.34E-8	2.38E-8	1.26E-8	1.29E-8	1.27E-9	1.6E-9	8.18E-9	8.51E-9	7.25E-10	1.05E-9
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	2.37E-7	2.54E-7	1.27E-7	1.44E-7	1.28E-8	2.96E-8	8.26E-8	9.94E-8	7.33E-9	2.4E-8
Predator's prey (freshwater) mg/kg ww	4-tert-OPnEO		0		0		NA		0		0
	4-tert-OP		3.78E-4		1.03E-4		NA		7.45E-5		3.69E-5
Predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		0		NA		NA
	4-tert-OP		NA		NA		3.61E-6		NA		NA
Top predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		0		NA		NA
	4-tert-OP		NA		NA		2.18E-6		NA		NA
Predator's prey (terrestrial) mg/kg ww	4-tert-OPnEO		0		0		0		0		0
	4-tert-OP		7.19E-6		6.99E-6		6.79E-6		6.91E-6		6.78E-6

Appendix Table 5: C_{local} and PEC_{local} of 4-tert-OPnEO and 4-tert-OP for the ten selected DU sites for the 2.5% transformation scenario

	Site number	**#1**		**#2**		**#3**		**#4**		**#5**	
Protection target	**AE**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**
Fresh water mg/l	4-tert-OPnEO	8.03E-6	8.73E-6	2.27E-5	2.34E-5	2.06E-4	2.07E-4	NA	NA	2.94E-5	3.01E-5
	4-tert-OP	2.79E-8	2.86E-8	7.88E-8	7.95E-8	7.18E-7	7.18E-7	NA	NA	1.02E-7	1.03E-7
Sediment (freshwater) mg/kg dw	4-tert-OPnEO		4. 73E-5		1.27E-4		1.12E-3		NA		1.63E-4
	4-tert-OP		2.87E-5		7.98E-5		7.21E-4		NA		1.03E-4
Marine water mg/l	4-tert-OPnEO	NA	NA	NA	NA	NA	NA	6.34E-7	7.01E-7	NA	NA
	4-tert-OP	NA	NA	NA	NA	NA	NA	2.2E-9	2.26E-9	NA	NA
Sediment (marine water)	4-tert-OPnEO		NA		NA		NA		3.8E-6		NA
	4-tert-OP		NA		NA		NA		2.27E-6		NA
Sewage Treatment Plant mg/kg dw	4-tert-OPnEO		4.16E-5		3.54E-5		4.46E-4		6.34E-5		1.69E-4
	4-tert-OP		1.47E-7		1.25E-7		1.58E-6		2.24E-7		5.95E-7
Air mg/m^3	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	2.74E-9	2.75E-9	1.19E-9	1.2E-9	1.21E-9	1.21E-9	3.35E-10	3.43E-10	9.99E-10	1.01E-9
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	2.77E-8	2.81E-8	1.2E-8	1.24E-8	1.22E-8	1.26E-8	3.38E-9	3.79E-9	1.01E-8	1.05E-8
Predator's prey (freshwater) mg/kg ww	4-tert-OPnEO		8.2E-5		2.06E-4		1.74E-3		NA		2.59E-4
	4-tert-OP		8.55E-6		2.34E-5		2.07E-4		NA		2.98E-5
Predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		NA		3.02E-6		NA
	4-tert-OP		NA		NA		NA		2.34E-7		NA
Top predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		NA		1.76E-6		NA
	4-tert-OP		NA		NA		NA		8.21E-8		NA
Predator's prey (terrestrial) mg/kg ww	4-tert-OPnEO		6.78E-9		6.78E-9		6.78E-9		6.78E-9		6.78E-9
	4-tert-OP		2.13E-7		1.85E-7		1.86E-7		1.7E-7		1.82E-7

	Site number	#6		#7		#8		#9		#10	
Protection target	**AE**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**	**CLocal**	**Local PEC**
Fresh water mg/l	4-tert-OPnEO	8.65E-6	9.34E-6	3.28E-6	3.97E-6	NA	NA	1.3E-6	1.99E-6	4.07E-7	1.17E-6
	4-tert-OP	3.01E-8	3.08E-8	1.14E-8	1.21E-8	NA	NA	4.51E-9	5.19E-9	1.42E-9	2.09E-9
Sediment (freshwater) mg/kg dw	4-tert-OPnEO		5.06E-5		2.15E-5		NA		1.08E-5		5.96E-6
	4-tert-OP		3.09E-5		1.21E-5		NA		5.12E-6		2.1E-6
Marine water mg/l	4-tert-OPnEO	NA	NA	NA	NA	4.46E-8	1.12E-7	NA	NA	NA	NA
	4-tert-OP	NA	NA	NA	NA	1.55E-10	2.15E-10	NA	NA	NA	NA
Sediment (marine water)	4-tert-OPnEO		NA		NA		6.06E-7		NA		NA
	4-tert-OP		NA		NA		2.162E-7		NA		NA
Sewage Treatment Plant mg/kg dw	4-tert-OPnEO		1.42E-4		3.01E-4		4.46E-6		6.18E-5		4.79E-6
	4-tert-OP		5.01E-7		1.06E-6		1.58E-8		2.18E-7		1.69E-8
Air mg/m³	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	5.68E-10	5.76E-10	3.05E-10	3.13E-10	3.14E-10	3.87E-11	1.98E-10	2.06E-10	1.76E-11	2.55E-11
Agricultural soil mg/kg dw	4-tert-OPnEO	0	0	0	0	0	0	0	0	0	0
	4-tert-OP	5.74E-9	6.15E-9	3.08E-9	3.49E-9	3.08E-9	7.17E-10	2E-9	2.41E-9	1.78E-10	5.83E-10
Predator's prey (freshwater) mg/kg ww	4-tert-OPnEO		8.71E-5		3.16E-5		NA		2.58E-5		1.82E-5
	4-tert-OP		9.16E-6		2.5E-6		NA		1.81E-6		8.93E-7
Predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		1.8E-6		NA		NA
	4-tert-OP		NA		NA		8.74E-8		NA		NA
Top predator's prey (marine water) mg/kg ww	4-tert-OPnEO		NA		NA		1.51E-6		NA		NA
	4-tert-OP		NA		NA		5.29E-8		NA		NA
Predator's prey (terrestrial) mg/kg ww	4-tert-OPnEO		6.78E-9		6.78E-9		6.78E-9		6.78E-9		6.78E-9
	4-tert-OP		1.74E-7		1.7E-7		1.65E-7		1.68E-7		1.64E-7

Appendix Table 6: Predicted regional exposure concentrations (Regional PEC) for the selected ten sites

Protection target	Assessment entity	Regional PEC		
		100% transformation scenario	0% transformation scenario	2.5% transformation scenario
Fresh water	4-tert-OPnEO	0 mg/l	7.11E-7 mg/l	6.93E-7 mg/l
	4-tert-OP	2.78E-8 mg/l	0 mg/l	6.74E-10 mg/l
Sediment (freshwater)	4-tert-OPnEO	0 mg/kg dw	3.52E-6 mg/kg dw	3.43E-6 mg/kg dw
	4-tert-OP	5.21E-5 mg/kg dw	0 mg/kg dw	1.26E-6 mg/kg dw
Marine water	4-tert-OPnEO	0 mg/l	6.89E-8 mg/l	6.71E-8 mg/l
	4-tert-OP	2.46E-9 mg/l	0 mg/l	5.98E-11 mg/l
Sediment (marine water)	4-tert-OPnEO	0 mg/kg dw	3.43E-7 mg/kg dw	3.35E-7 mg/kg dw
	4-tert-OP	4.17E-6 mg/kg dw	0 mg/kg dw	1.01E-7 mg/kg dw
Air	4-tert-OPnEO	0 mg/m³	0 mg/m³	0 mg/m³
	4-tert-OP	3.27E-10 mg/m³	0 mg/m³	7.93E-12 mg/m³
Agricultural soil	4-tert-OPnEO	0 mg/kg dw	0 mg/kg dw	0 mg/kg dw
	4-tert-OP	1.67E-8 mg/kg dw	0 mg/kg dw	4.05E-10 mg/kg dw