Application for Authorisation
UK REACH

CHEMICAL SAFETY REPORT

Part A and Part B

Sections 9 + 10

Public version

Legal name of applicant(s):	Siemens Healthcare Diagnostics Products GmbH (Marburg Germany)
Submitted by:	Siemens Healthcare Diagnostics Products Ltd. (Llanberis UK, Only Representative
Substance:	Entry #12: 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated, covering well-defined substances and UVCB substances, polymers and homologues (Triton™ X-100, Triton™ X-405)
Use title:	#1: Use of IVD kit reagents on diagnostic analyser systems by professional users #2: Use of IVD wash solutions on diagnostic analyser systems by professional users

Note

This complete version of this document includes some text and figures that are redacted.

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Part A

1. SUMMARY OF RISK MANAGEMENT MEASURES

The risk management measures for the use of IVD kit reagents and IVD wash solutions are described in the document “succint_summary_rmm_OPE_UK”.

2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

The risk management measures for workers and the environment as described in the “succint_summary_rmm_OPE_UK” are implemented at Siemens Healthcare Diagnostics Products Ltd.

3. DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED

Risk management measures related to the use of OPE containing IVD kits and IVD wash solutions as described in the document “succint_summary_rmm_OPE_UK” are communicated with the safety data sheet to downstream users.

Part B

9 Introduction

9.1 Substance description

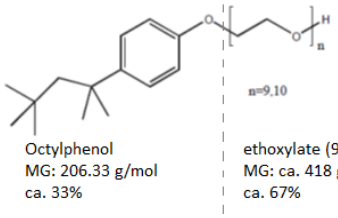
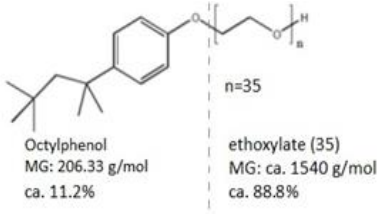
Substance subject to authorisation (UK REACH, entry #12):

The substance 4-(1,1,3,3-Tetramethylbutyl) phenol, ethoxylated is a UVCB (organic) having the following characteristics and physical–chemical properties:

CAS number:	9002-93-1
CAS name:	Octoxynol 9
IUPAC name:	4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated
Synonyms:	CAS number: 9036-19-5 IUPAC name: 2-[4-(2,4,4-trimethylpentan-2-yl)phenoxy]ethanol IUPAC name: 26-(4-Octylphenoxy)-3,6,9,12,15,18,21,24-octaoxahexacosan-1-ol IUPAC name: Polyethyleneglycol p-(1,1,3,3-tetramethylbutyl) phenyl ether common name: Octylphenol ethylene oxide condensate
Molecular formula:	(C2-H4-O)mult-.C14-H22-O
Molecular weight range:	see 1.2 for molecular weights of commercial products

The following public name is used in the assessments: OPnEO or OPE used in IVD kits by Siemens Healthcare Diagnostic Products GmbH (“Siemens Marburg”)

#	Common trade name	Chemical name	Degree of ethoxylation (EO units)
1	Triton™ X-100	(4-(1,1,3,3-Tetramethylbutyl) phenylpolyethylene glycol	9.5 (9 or 10)
2	Triton™ X-405, used on site as a 70% solution	Oxirane, 2-methyl-, polymer with oxirane, bis(2-oxiranylmethyl) ether	35 (average)

Triton™ X-100	**Triton™ X-405**
$OP_{9.5}EO$	**$OP_{35}EO$**
MG: ca. 625 g/mol	MG: ca. 1952 g/mol
	

Triton™ X-405 is currently used in certain IVD-kit reagents, but Triton™ X-100 is by far the most dominant source of releases of octylphenol (OP) to the environment. Any Triton™ X-405 would release less OP per kg OPE unit. All OPE applied in Siemens Marburg IVD-kits is thus considered Triton™ X-100.

(A third substance (Triton™ X-705, CAS No. 9081-99-6) was considered in the EU REACH application, even though its use in the EU would cease before the Sunset Date.)

9.2 Description of use

Uses covered by this CSR:

- Use #1 - Widespread use by professional workers - Use of IVD kit reagents on diagnostic analyser systems by professional users
- Use #2 - Widespread use by professional workers - Use of IVD wash solutions on diagnostic analyser systems by professional users

9.2.1 Use #1 - Use of IVD kit reagents on diagnostic analyser systems by professional users

In REACH terminology, an IVD reagent is a formulated mixture that contains a number of chemicals that enables a certain function when used in an assay.

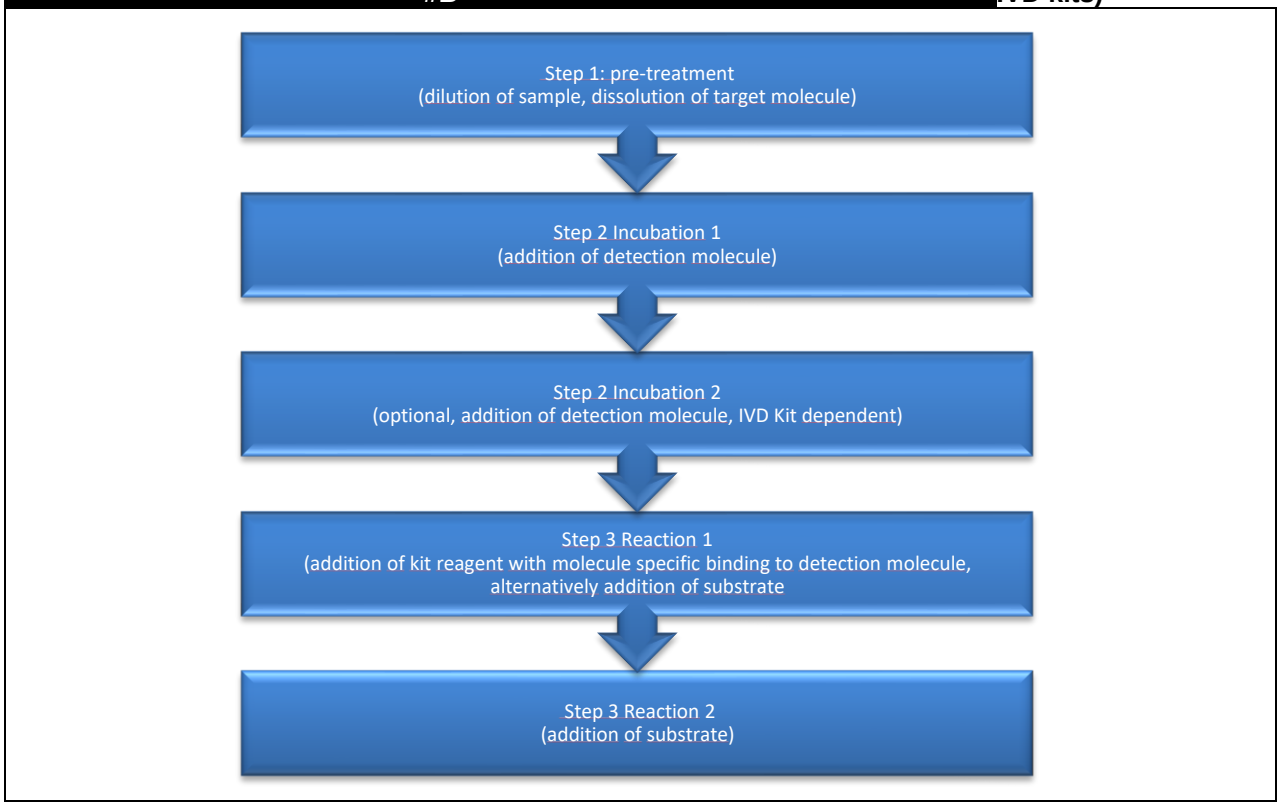
IVD kits are typically supplied in low volumes (in reagents manufactured by Siemens Marburg volumes are typically <150ml). They typically have low concentrations of OPnEO (in reagents manufactured by Siemens Marburg the average is ca. #A, J % (range: 0.1 - 1 %). Individual IVD kit reagents can either be bought as an IVD kit that contains all reagents needed or individually, for example if a single reagent within a kit needs to be replenished. The number of different reagents in the IVD kit can vary. If an IVD kit contains OPnEO, in some cases it will be present in only one of the reagents, in other cases it will be in multiple reagents contained within that kit.

To perform an assay for a specific disease or condition, the IVD customer is essentially running a 'ready to use' IVD kit on a compatible analyser system. While some IVD kit reagents are concentrates and have to be pre-diluted before they can be used, no other manual steps are required apart from subjecting the sample to the test. Following a specific protocol, the other IVD kit reagents are added to the sample and the detection occurs. Many analysers can handle several assays in a row, additional core functionalities for the application of IVD kits are the automated sample processing and unique identification (e.g. by a bar code system) and the documentation of results. In some cases, different analysers are also connected with each other to measure a broad range of parameters in one sample – each by the application of a different IVD kit.

The typical layout of an analyser system is shown in Figure 10 and Figure 11 in annex 11.1.

Usually the #B IVD kit consists of the steps set out in Figure 1.

Figure 1: Steps to perform an IVD kit assay on an automated analyser (only applies to #B IVD kits)



IVD kit operations are performed by trained healthcare staff (WCS 1: PROC 15). Siemens Healthineers provide training courses for workers that include handling of IVD kits and the operation of the analyser systems, often performed at the point of work at customer sites. Courses also include training on the maintenance of the instrument and the disposal of consumables (the kit components and the patient samples).

In most cases the consumed reagents from laboratory use are usually discharged to the communal wastewater and treated in local STPs. This applies also to OPnEO containing solutions and thus the assessment considers 100% of the used OPnEO discharged to wastewater. Some customers collect the reagents after use and dispose them of as waste (WCS 2: PROC 8b). This is especially the case, if the waste solutions are contaminated with a high content of other hazardous material. The amount not released via wastewater can, however, not be quantified.

A small proportion of the applied OPnEO (assumption: < 0.1%) adheres to solid waste like pipettes, gloves, wipes or containers, which are collected as solid laboratory waste (WCS 3: PROC 21) for incineration. Since this volume cannot be quantified adequately, it was not considered in the calculation of emissions to wastewater.

It is assumed that any disposable materials like gloves, lab coats, pipettes, one-time pipes, which may be contaminated with OPnEO, is disposed of as solid waste for incineration.

9.2.2 Use #2 - Use of IVD wash solutions on diagnostic analyser systems by professional users

IVD wash solutions are not usually provided as part of an IVD kit, but as a separate product. Each wash solution design is specific to the analyser system it can be used on. IVD wash solutions are used with every IVD kit on an analyser system to clean and flush the internal parts which have come into contact with the IVD kit reagents and/or patient sample as part of the liquid-handling operation.

Their technical function is to maintain a clean status between single measurements on the analyser system, which is vital for the accuracy of high-throughput testing since any impurities carried over from one sample or reagent to another can affect the diagnostic result.

IVD wash solutions are typically supplied in plastic bottles and in larger volumes than IVD reagents, up to 2000ml. They are typically supplied as a concentrated solution and then diluted at the customer site (WCS 1: PROC 5, PROC 8a). Following this dilution step, the wash solution is normally placed on or by the machine and is automatically pumped into the relevant parts of the analyser (WCS 2: PROC 15). In most cases the consumed wash solutions together with the reagents are flushed to the drain and end up in the communal wastewater. This applies also to OPnEO containing solutions and thus the assessment considers 100% of the used OPnEO discharged to wastewater. Some customers collect the reagents after use and dispose it of as waste (WCS 3: PROC 8b). This is especially the case, if the waste solutions are contaminated with a high content of other hazardous compounds. The amount not released via wastewater can, however, not be quantified.

A small proportion of the applied OPnEO (assumption: < 0.1%) adheres to solid waste like pipettes, gloves, wipes or reagent containers, which are collected as solid laboratory waste (WCS 4: PROC 21) for incineration. Since this volume cannot be adequately quantified, it was not considered in the calculation of emissions to wastewater.

It is assumed that any disposable materials like gloves, lab coats, pipettes, one-time pipes, which may be contaminated with OPnEO, is disposed of as solid waste for incineration.

Additional Risk Management Measures

A detailed analysis was made of existing risk management measures in place at DU sites.

Significant efforts were made to engage with many DU‘s in the EEA including UK before the Brexit. Appendix 1 (Section 9) to the Use 1-2 AoA-SEA document presents the consultations undertaken.

We understand the following RMM’s are in place at DU sites, resulting in lower emissions than those estimated in this CSR, however, are not quantifiable –

- Collection of any physical materials which may be contaminated with OPnEO, subsequent disposal and incineration of these items as solid waste as described above.
- Customers complied with the existing EU framework legislation on wastewater and waste respectively the corresponding UK legislation that was seen as relevant for these types of fractions. Furthermore, some examples of the national legislation in the UK, were analysed, to see if these legal acts might lead to additional treatment requirements.

To reduce emissions, Siemens Marburg is **working on a REACH Response Plan to eliminate 4-tert-OpnEO, which will reduce potential releases of OPE by ~90% within 4 years** of submission of the application.

In terms of identifying additional RMM’s at DU sites we consider it would **not make sense for healthcare institutions to implement new drainage networks and collection facilities** in parallel to this effort and to address what will be a continually decreasing impact on the environment as described in this CSR. Therefore, we believe the logical choice for the benefit of the environment and for the EU healthcare system would be to eliminate OPE emissions as opposed to collection of wastewater and treatment.

9.3 Introduction to the assessment for the environment

9.3.1 Tonnage

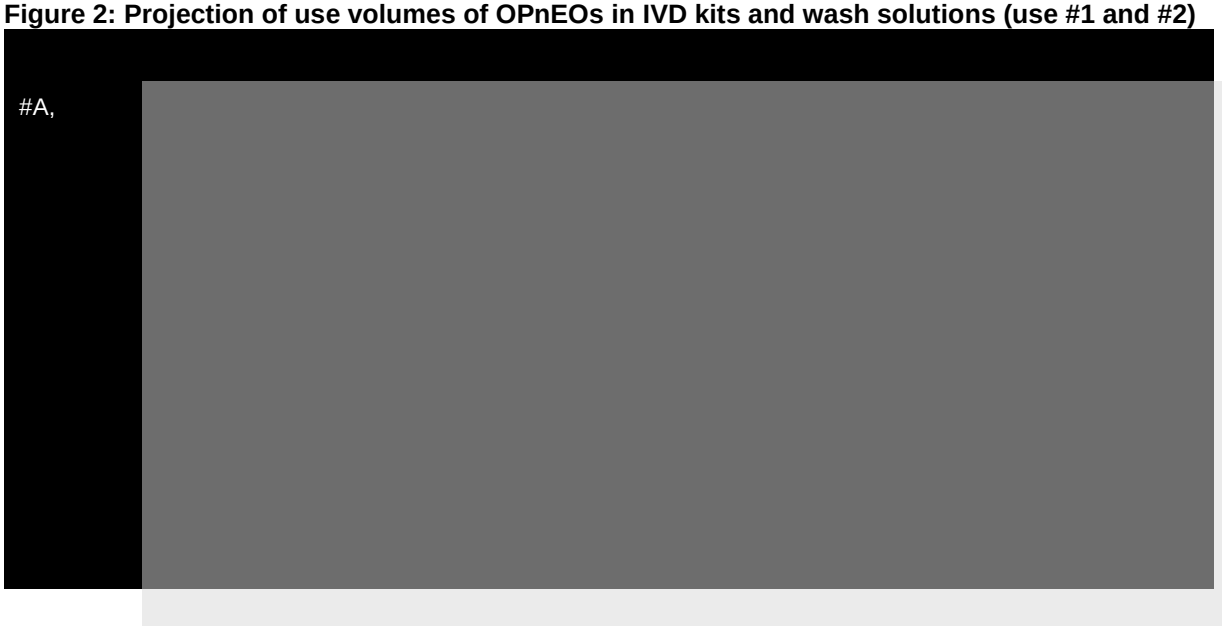
Table 1: Tonnage for assessment (2021)

ES#	Exposure scenario (ES) name and related environmental contributing scenarios	Tonnage per use (t/year)	daily local tonnage (t/day)	annual local tonnage (t/year)
ES1 (PW)	Use #1 - Use of OPE by UK Customers - IVD reagents (2021)	#A table		
	- Use of IVD kit reagents on diagnostic analyser systems by professional users (ERC 8a)		-6	-
ES2 (PW)	Use #2 - Use of OPE by Customers - Wash Solutions			
	- Use #2 - Use of IVD wash solutions on diagnostic analyser systems by professional users (ERC 8a) (2021		-5	-

Daily local tonnages above have been modelled using different approaches for use #1 and use #2. For use number #1 the default values of EUSES tool for wide dispersive uses have been applied, while for use #2 the daily local use has been estimated for a typical power user (see chapter 9.3.5 for details).

In line with the substitution strategy for phase-out of OPnEO through reformulation of IVD kit reagents and wash solutions along with phase-out of certain analyser systems (see section 0 and separate AoA-document), the use of OPnEO-containing IVD kits will decline year on year, leading to the complete phase-out by 2025 for use #2 wash solutions, and 2033 for use# 1 reagents.

Figure 2: Projection of use volumes of OPnEOs in IVD kits and wash solutions (use #1 and #2)



Accordingly, the local and regional release of OP due to use of OPnEOs in in-vitro diagnostic products by Siemens Marburg customers will decrease by more than 90% by #A, C (compared to 2021) and finally end in 2033 (see 9.4.1.2.).

9.3.2 Summary of risk management measures and operational conditions to reduce environmental releases

OPnEO containing reagents and wash solutions are handled exclusively by professional users in standardised procedures at laboratory scale. OPnEO containing wastewater from laboratory use is usually discharged to the communal wastewater and treated in local STPs as far as this complies with the wastewater requirements. An unknown number of customers collect the wastewater and dispose it

of as hazardous liquid waste for incineration, where this is required due to specific local requirements or a high content of other hazardous substances.

Since not all IVD reagents and wash solutions used on an IVD platform contain OPnEO its concentration in the solutions after use is low (< 0.01% g OPnEO per litre) even for the platforms with the highest throughput. Further separation and treatment of the OPnEO-containing wastewater is thus considered unsuitable as a general measure to reduce OP-emissions to the environment from wide dispersive use (see separate AoA-document section 10.3.1). The most effective measure to reduce the OPnEO-release and thus the OP environmental concentration is the stepwise phase-out of OPnEO containing IVD kits and the substitution of OPnEO in wash solution (see 9.3).

The STP-sludge may or may not be incinerated, disposed as waste for landfill or reused as fertiliser in agriculture. On average, 53% of sewage sludge in the EU is disposed as fertiliser to agricultural soils or as compost[1]. Since for an individual local scenario in the UK the further treatment of the STP-sludge is not known, 100% application to agricultural soils is assumed as reasonable worst-case. The regional PECs for agricultural soil may thus be an overestimation. On the other hand OP-concentrations in sludge may be higher than expected acc. to Table 2 due to longer retention times of the wastewater in the STP and this way higher proportions of adsorbed OP.

9.3.3 Assumed fate and behaviour of OPnEO during use and wastewater treatment

The RAC Q&A-paper[2] related to the application for authorisation OPnEO and NPnEO answers the questions on which substances and/or degradation products should be addressed in the chemical safety assessment in application for authorisation for OPnEO and NPnEO (question 1). It states that the assessment should focus solely on the degradation product OP and the identified endocrine disrupting properties. In its application Siemens Healthcare Diagnostics Products Ltd follows the approach to consider the degradation of OPnEO in the aquatic compartment after anaerobic wastewater treatment, taking into account, that the average proportion of OP in the applied OPnEO commercial product is 33% for Triton™ X-100.

Ethoxylated alkylphenols are enzymatically degraded in wastewater by shortening the polyethoxylate chains and hydrophobic alkyls. With the decreasing chain length, the water solubility of the molecule decreases while it´s tendency to adsorb to sludge and organic matter increases.

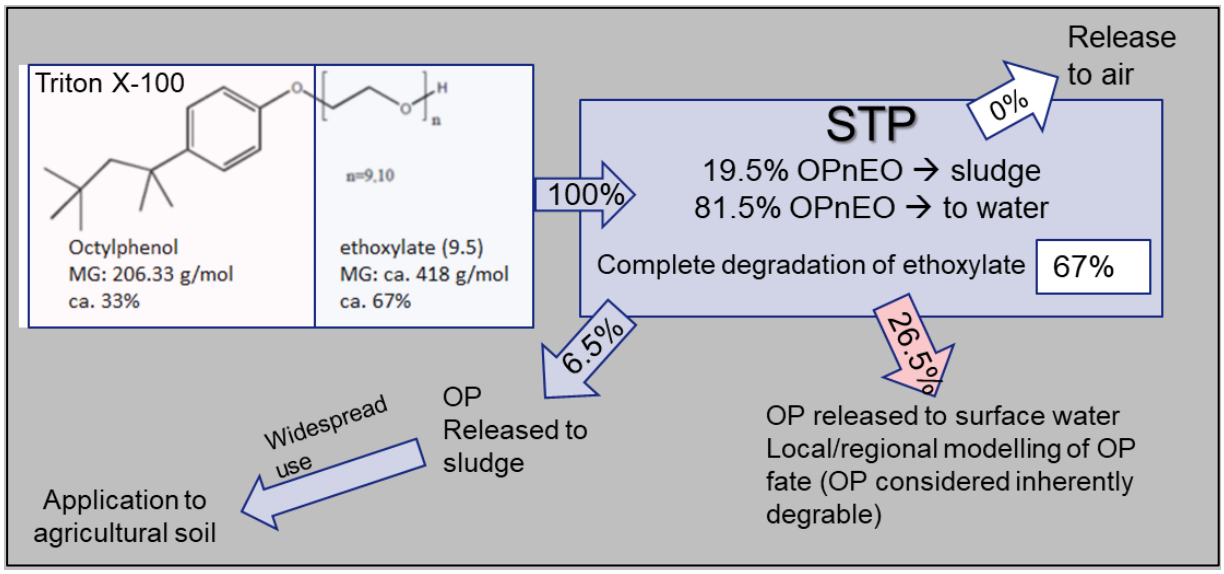
According to the European Risk Assessment Report on Nonylphenolethoxylates (NPnEO), it may be predicted that the major amount of undegraded NPnEO is directed to the effluent (25 %), and the sewage sludge represents the secondary sink, receiving 19.5 % of the initial amount of NPnEO (reasonable worst-case assumptions for the fate of NPnEO during anaerobic wastewater treatment). It is assumed that OPnEO behaves in the same way.

Based on the assumption above OPnEO is partly degraded and 19.5 % is adsorbed to sludge while the remaining OPnEO and degradation products are discharged with the STP effluent. However, since only the OP-part of the molecule is relevant for the environmental risk assessment, the different degradation products are not further considered in the model and it is assumed that all OPnEO released to the environment is finally degraded to OP, which represents 12-33% of the molar mass of OPnEO depending on the ethoxylate chain length.

[1] Also discussed in ANNEX XV RESTRICTION REPORT on intentionally added microplastics; ECHA; 11. January 2019; data gained from Eurostat: https://ec.europa.eu/eurostat/data/database?node_code=env_ww_spd#

[2] Committee for risk assessment, 2017: Risk related considerations in application for authorisation for endocrine disrupting substances for the environment, especially OPnEO and NPnEO, Agreed at RAC-43

Figure 3: Assumptions on the degradation and behaviour of Triton™ X-100 in STP



Under typical use conditions in laboratories, in the absence of bacteria OPnEO is regarded as stable. Thus, OPnEO will not be degraded during formulation and application of reagents or wash solutions, nor during collection of wastewater. No release to air is assumed, since OPnEO is not volatile and the formation of aerosols during use can be excluded.

The following distribution of OP-molecules after STP is considered a reasonable worst-case estimation for use of OPnEO.

Based on the worst-case assumption described in section 4.5 of the CSR (Degradation and fate of OPnEO used for modelling of environmental exposure) a theoretical complete mineralisation of the ethoxylate chain and the following distribution of OP-molecules after STP (Table 2) is considered a reasonable worst-case estimation for the fate of OPnEO.

Table 2: releases of OP after STP for Triton™ X-100 uses #1 and #2 in 2021

fate referring to OP in OPnEO in STP	% initial OPnEO	%OP	% EO	compartment
originally released OPnEO	**100**	**33**	**67**	
release to sludge	19.5	6.5	13.0	sludge/soil
mineralisation of dissolved OPnEO	54.0	0	54.0	
OP not adsorbed to sludge and released to water	26.5	26.5	0	water/sediment
calculated efficiency concerning how much OP is released to water from initially discharged OPnEO		73.5		
estimated volume used in IVD kits (use #1) 2021: #A kg Triton™ X-100	#A kg $OP_{9.5}EO$			referring to #H kg OP released to the environment
estimated volume used in IVD kits (use #5) 2021: #A kg Triton™ X-100	#A kg $OP_{9.5}EO$			referring to #H kg OP released to the environment

For the estimation of environmental OP-concentrations resulting from use #1 the calculated efficiency of 73.5 % for Triton™ X-100 regarding releases to water is applied to the sum of OPnEOs. This way the result (#H kg OP release for use #1 in 2021) will be a slight overestimation since the lower OP-content of Triton™ X-405 is not taken into account.

9.3.4 Scope and type of assessment for the environment

The RAC Q&A-paper states, that RAC will not develop reference PNEC values or dose-response relationships for OPnEO. An applicant may choose to assume that OPnEO is a non-threshold substance

for the purpose of the AfA (question 5). Based on this and the conclusions in the report by Ramboll Siemens Marburg assumes that OPnEO is a non-threshold substance for the purpose of this AfA. The risk assessment is thus qualitative.

However, in order to get indicators for potential environmental risks related to the predicted environmental concentrations and the assumed decrease after phase-out and substitution, the available data on effects and existing environmental thresholds have been screened for suitable standards for risk characterisation. The Environmental Quality Standards (EQS) as defined under the EU Water Framework Directive (2000/60/EC) are considered appropriate to characterise the risk of environmental emissions, even though these values are not considered "no effect concentrations". In the UK the same values are used for the assessment of water quality and with regard to discharge permits to market actors[3].

As requested by the RAC Q&A paper, the releases are calculated based on reasonable worst-case assumptions for the release of OP from the use of OPnEO (see section 9.3.5). Environmental exposure is calculated by using the Chesar/EUSES tool for the degradation product OP. The resulting PECs are compared with the EQS values (Table 3) in order to get a better understanding on the risk level related to the exposure levels and the effects of the intended emission reduction.

Table 3: Summarised EQS used for environmental risk characterisation:

compartment	latest research value	based on
Freshwater	**0.1 µg/L**	AA-EQS for inland surface water (according to EU Directive 2008/105/EC, Entry No. 25)
Marine water	**0.01 µg/L**	AA-EQS for other surface water (according to EU Directive 2008/105/EC, Entry No. 25)
Sediment	**0.082 mg/kg (dry weight)**	Extrapolated from AA-EQS
Marine sediment	**0.0082 mg/kg (dry weight)**	Extrapolated from AA-EQS
Soil	**0.017 mg/kg (dry weight)**	Extrapolated from AA-EQS

Physicochemical properties used for exposure estimation

The following substance properties are used in the fate estimation done by EUSES. They correspond to the degradation product of OPnEO.

Table 4: Substance key phys-chem and fate properties of OP[4]

Substance property	**Value**
Molecular weight	≥ 206.3
Molecular weight used for the assessment	206.3
Melting point at 101 325 Pa	85 °C
Vapour pressure	2 Pa at 38 °C
Partition coefficient (Log Kow)	4.8 at 22 °C
Water solubility	7 mg/L at 20 °C
Henry's law constant (in Pa m3/mol)	574 at 278 K
Biodegradation in water: screening tests	inherently biodegradable
Half-life in freshwater	5 d
Bioaccumulation: BCF (aquatic species)	740 L/kg ww
Adsorption/Desorption: Koc at 20 °C	2.51E3

[3] See also http://www.environmentlaw.org.uk/rte.asp?id=291

[4] Source: ECHA dissemination https://echa.europa.eu/de/brief-profile/-/briefprofile/100.004.934 (status: September 2018)

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

In a standard (modelled) biological STP, the emissions are distributed in the following way:

Release to water	26.5%
Release to air	0%
Release to sludge	6.5%
Release degraded	67.0%

9.3.5 Comments on assessment approach for the environment – local and regional scenario

The local scenario for use #1 is considered a wide dispersive use of OPE in IVD-kits. In 2021 OPE is contained in #D different reagents used by customers on #D installed Siemens analysers in the UK. Local use volumes are thus low and the application of the EUSES modelling tool for wide dispersive use is considered sufficiently conservative for use #1. With the decreasing number of sold OPE-containing IVD-kits, the local OPE-release will decrease too, while the customer apply other non-OPE-containing kits at the same platforms.

Although use #2 is described as a professional use too, the situation is different, as the number of installed analysers in the UK is #D (2021) and thus the number of potentially OPE-releasing sites for this use < 100. The default values of the EUSES tool for wide dispersive uses did not seem appropriate for the application of OPE-containing wash solutions for the following reasons:

- Due to the lower number of installed analysers the number of sites applying OPE solutions is much lower than the default in the EUSES model, which may result in an underestimation of local concentrations;
- Some sites (in the following `power users´) have up to 4 analysers in use and thus the maximum daily use of OPE is much higher than the default in the EUSES model, which may also underestimate local concentrations;
- Hospitals and research labs are typically located in urban areas with a higher number of inhabitants, related STP loads and receiving surface waters. These are by far bigger than the default receiving water used in the EUSES model, which would here overestimate local concentrations;

For use #2 – the use of wash solutions – a default value of #A g OPE/day is proposed by the EUSES model, but this is an underestimation of local uses in most places. These wash solutions are planned to be completely phased-out by #D, which results in the significant decline of OPnEO releases due to use #2 (see Figure 2).

In order to define the local exposure scenarios as realistic as possible, the maximum daily use has been calculated based on the yearly volume, the number of analysers (#D) and the number of application days per year (300):

Estimation of maximum daily use volumes for 2021:

use	volume of OPE per year	volume of OPE per analyser per year	Daily volume of OPE per analyser (300 days per year)	Maximum daily volume of OPE by power users with up to 4 platforms used in parallel
Use#2	#A,J kg/year	#A,J kg	#A,J g/day	#A,J g/day

In the case of use #2 the OPE-containing wash solution is the #D platform depending on these wash solutions that is phased out by #D. The number of platforms will decrease in the coming years and thus also the yearly use volume of wash solution. As a worst case it is, however, assumed, that the local use per analyser remains constant and that any power users applies up to 4 analysers in parallel until the final phase-out. Thus, the local release by such a power user is considered constant until #D.

To calculate a local worst case PEC a local scenario for a known power user has been created with the following environmental parameters:

Table 5: Parameters considered for the local scenarios of a typical power user

		Source of information
Name of the power user	#C,I	Siemens internal
Number of installed #C,I platform		Siemens internal
located	#C,I	Siemens internal
Number of inhabitants relevant for water management	#J	#C,I
STP effluent	#J	Assuming wastewater of minimum 150 l/day per inhabitant
Receiving water	#J	
Volume of receiving water	1.3 mio m³ /day	#I)

This represents a typical power user of Siemens Marburg, being located in an urban area with more than 100.000 inhabitants and related local STP-capacities and flow rates of the receiving waters. The individual local assessment (see below) results in environmental PECs below the EQS values used for orientation. Users with 1 – 3 analysers will have lower release rates but are still located in urban areas.

A remaining uncertainty relates, however, to power users not known to Siemens (due to indirect supply), but it is considered unlikely that these are located in rural areas or small villages. Even industrial and commercial areas far off cities, where service labs might also be located, would have to install adequate STP-capacities.

Table 6: Local daily tonnage for uses #1 and #2 in 2021 and before phase-out

ES#	Exposure scenario (ES) name and related environmental contributing scenarios	year	source	Daily local use (g/day)
ES 1 (PW)	Use # 1 - use of IVD kit reagents (ERC 8a)	2021	default	#D,A,I table
ES 1 (PW)	Use # 1 - use of IVD kit reagents (ERC 8a)	[redacted]	default	[redacted]
ES 1 (PW)	Use # 1 - use of IVD kit reagents (ERC 8a)	[redacted]	Phase-out	[redacted]
ES 2 (PW)	Use #2 - Use of IVD wash solutions (ERC 8a)	2021	Power user	[redacted]
ES 2 (PW)	Use #2 - Use of IVD wash solutions (ERC 8a)	[redacted]	Power user	[redacted]
ES 2 (PW)	Use #2 - Use of IVD wash solutions (ERC 8a)	[redacted]	phase-out	[redacted]

The regional concentrations are reported in section 10.2.1.1. The local Predicted Exposure Concentrations (PECs) reported for each contributing scenario correspond to the sum of the local concentrations and the regional concentrations (PEC regional).

9.3.6 Scope and type of assessment for man via environment

The scope of exposure assessment and type of risk characterisation required for man via the environment are not considered, since human health hazards are not covered by this assessment.

9.3.7 Introduction to the assessment for workers

With regard to human health effects OPnEO is classified as harmful if swallowed (H302), skin irritating (H315) and serious eye damage (H318). No DNELs have been derived for the substance.

The customers use OPnEO containing IVD reagents and wash solutions as laboratory chemicals at laboratory scale for in vitro diagnostics. Only laboratory workers with related training apply these IVD reagents and wash solutions according to related and laboratory procedures and under high laboratory hygienic standard. Workers may use the IVD kits and wash solutions on diagnostic analyser systems up to 8 h per day and 5 days per week. The use of laboratory personal protection equipment is recommended (gloves, goggles, coats and shoes).

Under these conditions no health risks for workers related to the use of OPnEO are expected

9.3.8 Introduction to the assessment for consumers

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

9.4 Exposure scenario 1: Widespread use by professional workers – Use #1 - Use of IVD kit reagents on diagnostic analyser systems

Product category used: PC 21: Laboratory Chemicals

Sector of use: SU 20: Health services

Environment contributing scenario(s):		
ECS 1	use of IVD kit reagents on diagnostic analyser systems	ERC 8a
Worker contributing scenario(s):		
WCS 1	use of IVD Kits on diagnostic analyser systems	PROC 15
WCS 2	collection of OPE-containing wastewater and discharge to communal waste water	PROC 8b
WCS 3	collection and handling of solid waste	PROC 21

Further description of the use:

IVD kits are applied to diagnostic platforms by automated process,

used by Hospitals, Commercial labs, blood Banks, Research centres.

9.4.1 Env CS 1: Use of IVD kit reagents on diagnostic analyser systems (ERC 8a)

9.4.1.1 Conditions of use (2021)

Amount used, frequency and duration of use (or from service life)
• Daily local widespread use amount: <= [redacted]-9 tonnes/day
Conditions and measures related to biological sewage treatment plant
• Biological STP: Standard [Effectiveness Water: 73.5%]
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: No (low risk) *Low risk assumed for waste life stage. Solid waste is incinerated and any adhering OPnEO is completely destroyed. Waste disposal according to national/local legislation is considered sufficient.*

9.4.1.2 Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 7: Local releases to the environment

Release	Release estimation method	Explanations
Water	ERC	**Release factor before on site RMM: 100%** **Release factor after on site RMM: 100%** **Local release rate:** [redacted]-6 kg/day
Air	Estimated release factor	**Release factor before on site RMM:** 0% **Release factor after on site RMM:** 0% **Explanation:** based on low volatility of OPnEOs
Non agricultural soil	Estimated release factor	**Release factor after on site RMM:** 0% No release to soil, all OPE is discharged via

Release	Release estimation method	Explanations
		wastewater or disposed of as waste for incineration

Releases to waste

Release factor to external waste: 0.1 %: solid waste from used gloves and empty containers/wedges adhering OPnEO (see section 9.2.1).

9.4.1.3 Exposure and risks for the environment

The exposure concentrations are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 8: Exposure concentrations and risks for the environment for use #1 (2021)

Protection target	**PEC local**	**EQS** (see Table 3)	**qualitative risk characterisation**
Fresh water	Local PEC: #H,J E-7 mg/L	**1E-4 mg/L**	Compared to the EQS values the calculated concentration of OP in the related compartments are low (> factor 100 lower). Expected exposure thus remains below current regulatory action thresholds. Due to the endocrine mode of action, harmful effects can nevertheless not be excluded.
Sediment (freshwater)	Local PEC: #H,J E-5 mg/kg dw	**8.2E-2 mg/kg (dw)**	
Marine water	Local PEC: #H,JI E-8 mg/L	**1E-5 mg/L**	
Sediment (marine water)	Local PEC: #H,J E-6 mg/kg dw	**8.2E-3 mg/kg (dw)**	
Agricultural soil	**Local PEC:** #H,J E-6 mg/L	**1.7E-2 mg/kg (dw)**	

9.4.2 **Estimated development of local releases and environmental concentrations**

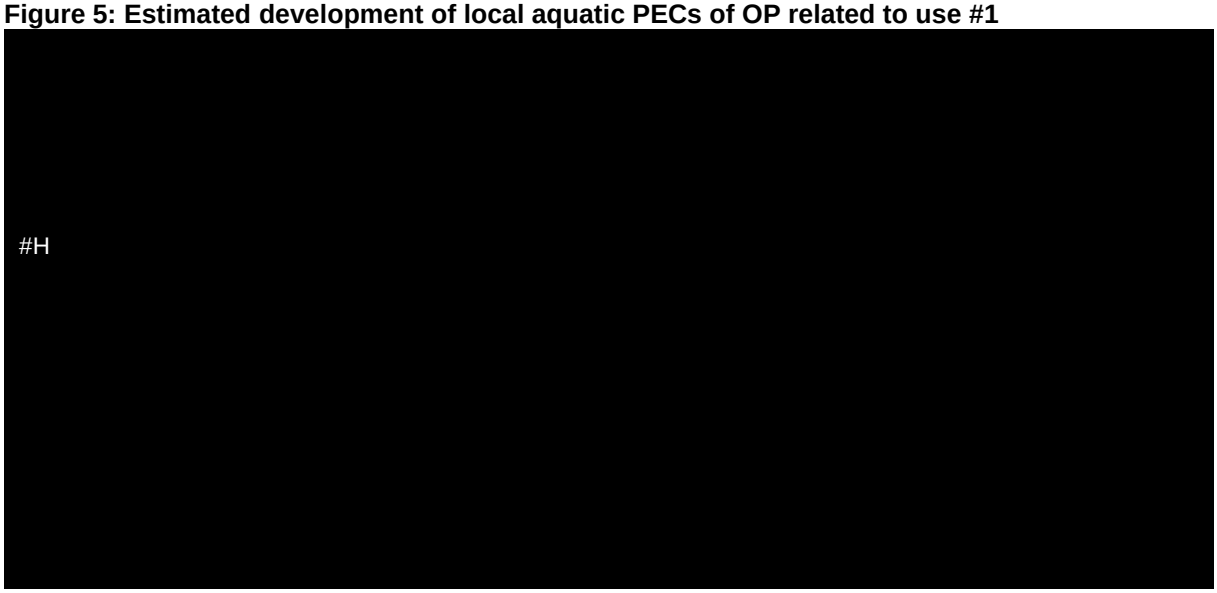
In line with the phase out of the use of OPnEO in IVD kits (see separate AoA-document), the use of IVD reagents containing OPnEO will decline, leading to the complete phase out in 20 #D . Accordingly, the yearly local release of OP by customers using Siemens IVD kits will decline (

Figure 4). The calculated PECs will follow this development (

Figure 5).

Figure 4: Estimated development of daily local OP-release rates to water related to use #1

Figure 5: Estimated development of local aquatic PECs of OP related to use #1



The EQS for freshwater of 0.1 µg/L lies out of this scale

The local PECs are considerably below the related EQS. All will decrease in the years #D before the phase-out in #D .

9.5 Exposure scenario 2: Widespread use by professional workers - Use #2 - Use of IVD wash solutions on diagnostic analyser systems by professional users

Product category used: PC 21: Laboratory Chemicals

Sector of use: SU 20: Health services

Environment contributing scenario(s):		
ECS 1	Use of IVD wash solutions on diagnostic analyser systems by professional users	ERC 8a
Worker contributing scenario(s):		
WCS 1	dilution of wash solution	PROC 5, PROC 8a
WCS 2	Use of IVD wash solutions on diagnostic analyser systems	PROC 15
WCS 3	collection of OPE-containing wastewater and discharge to communal waste water	PROC 8b
WCS 4	collection and handling of solid waste	PROC 21

9.5.1 Use #5 - Use of IVD wash solutions on diagnostic analyser systems (ERC 8a)

9.5.1.1 Conditions of use (2021)

Amount used, frequency and duration of use (or from service life)
• Daily use amount at site: <= #H,J -5 tonnes/day
• Annual use amount at site: <= #H,J tonnes/year
Conditions and measures related to biological sewage treatment plant
• Biological STP: Site specific [Effectiveness Water: 73.5%]
• Discharge rate of STP: >= 9.9E4 m3/day (see Table 5)
• Application of the STP sludge on agricultural soil: Yes
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: No (low risk) *ERC based assessment demonstrating control of risk with default conditions. Low risk assumed for waste life stage. Waste disposal according to national/local legislation is sufficient.*
Other conditions affecting environmental exposure
• Receiving surface water flow rate: >= 1.3E6 m3/day *mean flow rate of river* #J

9.5.1.2 Releases

The local releases to the environment are reported in the following table. The example power user is located in an urban area with high STP-capacity (see 9.3.5).

Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9: Local releases to the environment

Release	Release estimation method	Explanations
Water	ERC	**Release factor before on site RMM:** 100% **Release factor after on site RMM:** 100% **Local release rate:** #H g/day
Air	Estimated release factor	**Release factor before on site RMM:** 0% **Release factor after on site RMM:** 0%
Non agricultural soil	ERC	**Release factor after on site RMM:** 0% No release to soil, all OPnEO-containing solutions are discharged via wastewater or disposed of as waste

Releases to waste

Release factor to external waste: 0.1 %: solid waste from pipettes, gloves and wipes with adhering OPnEO (see section 9.2.2 for further explanation).

9.5.1.3 Exposure and risks for the environment

The exposure concentrations are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 taking into consideration the parameters in Table 5unless stated otherwise.

Table 10: Local Exposure concentrations and risks for the environment 2021

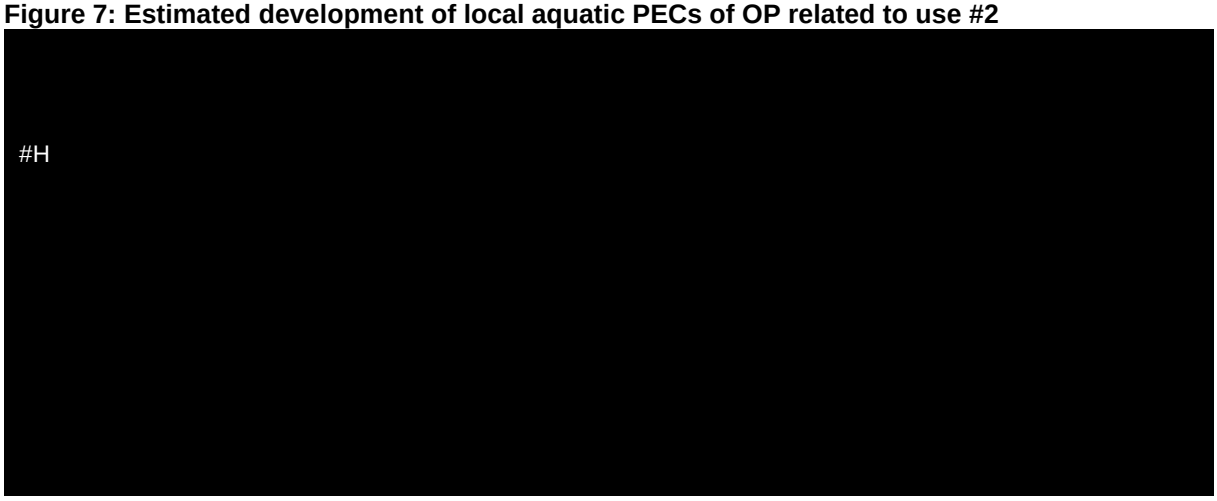
Protection target	PEC local	EQS (see Table 3)	qualitative risk characterisation
Fresh water	**Local PEC:** #H E-6 mg/L	**1E-4 mg/L**	The calculated concentration of OP in the related compartments are below the EQS values. Highest risk can be assumed for marine water, where the PEC is factor 7 below the EQS-value. Expected exposure thus remains below current regulatory action thresholds. Due to the endocrine mode of action, harmful effects can nevertheless not be excluded.
Sediment (freshwater)	**Local PEC:** #H E-3 mg/kg dw	**8.2E-2 mg/kg (dw)**	
Marine water	**Local PEC:** #H E-6 mg/L	**1E-5 mg/L**	
Sediment (marine water)	**Local PEC:** #H E-4 mg/kg dw	**8.2E-3 mg/kg (dw)**	
Agricultural soil	**Local PEC:** #H E-4 mg/kg dw	**1.7E-2 mg/kg (dw)**	

9.5.2 **Estimated development of local releases and environmental concentrations**

In line with the substitution strategy for OPnEO in regard to wash solutions (see separate AoA-document), the use of wash solutions containing OPnEO will decline year on year, leading to the complete phase out in #D (see Figure 2). However, since it is actually the #D platform that is phased out by #D, the local consumption of wash solutions is considered stable per analyser as a worst case. Assuming that a typical power user applies up to 4 analysers in parallel until the final phase-out, the local PECs will stay at those levels reported in Table 10 until #D.

Figure 6: Estimated development of local daily OP-release with STP-effluent related to use #2

Figure 7: Estimated development of local aquatic PECs of OP related to use #2



10 RISK CHARACTERISATION RELATED TO COMBINED EXPOSURE

10.1 Environment (combined for all emission sources)

10.1.1 Total releases

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

Release route	Total releases of OP per year (2021)
Water	0.099 kg/year
Air	0 kg/year
Soil	0 kg/year

10.1.2 Local exposure due to all widespread uses

The predicted local environmental concentrations (PEC local) based on the releases from both widespread uses (uses #1 and #2) are reported in the table below. The exposure estimates have been obtained with EUSES 2.1.2.

Table 11: Predicted exposure concentrations and risks for the environment due to uses #1 and 2 (2021)

Protection target	PEC local due to all widespread uses	EQS (see Table 3)	qualitative risk characterisation
Fresh water	**Local PEC:** #H E-5 mg/L	**1E-4 mg/L**	The calculated concentration of OP in the related compartments are below the EQS values. Highest risk can be assumed for marine water, where the PEC is factor 6 below the EQS-value. Expected exposure thus remains below current regulatory action thresholds. Due to the endocrine mode of action, harmful effects can nevertheless not be excluded
Sediment (freshwater)	**Local PEC:** #H E-3 mg/kg dw	**8.2E-2 mg/kg (dw)**	
Marine water	**Local PEC:** #H E-6 mg/L	**1E-5 mg/L**	
Sediment (marine water)	**Local PEC:** #H E-4 mg/kg dw	**8.2E-3 mg/kg (dw)**	
Agricultural soil	**Local PEC:** #H E-4 mg/kg dw	**1.7E-2 mg/kg (dw)**	

Since OP-containing IVD kits and OP-containing wash solutions may be used in parallel at the same site, combinations of both uses should be considered for the local scenarios. However, the combined release rates of uses #1 and #2 (Figure 2) show, that OP-emissions in the years 2021 to #D are clearly dominated by the use of wash solutions (use #2). A reduction of more than 90% in OP-emissions is expected from #D onwards, mainly due to the phase out of the #D analyser platforms, and emissions will further decline and finally end in #D.

The local environmental concentrations will decrease accordingly

10.1.3 **All uses (regional scale) – uses #1, #2**

10.1.3.1 Total releases

The total releases to the environment from all the exposure scenarios covered by this CSR are presented in the table below. This is the sum of the releases to the environments from all exposure scenarios addressed.

Table 12: Total releases to the environment of OP per year from all life cycle stages 2021

use	OPnEO applied	OP released to water	OP released to sludge
use #1	#A, H Table	[redacted]	[redacted]
use #2	[redacted]	[redacted]	[redacted]
sum of all uses	[redacted]	[redacted]	[redacted]

Figure 8: Development of OP-releases to water from all uses

10.1.4 **Regional assessment**

The regional predicted environmental concentration (PEC regional) are presented in the table below.

The exposure estimates have been obtained with EUSES 2.1.2. considering local conditions of the power user

Table 13: Predicted regional exposure concentrations (Regional) and risks for the environment 2021

Protection target	**Exposure concentration**	**EQS** (see Table 3)	**qualitative risk characterisation**
Fresh water	**Regional PEC**: #H, J E-8 mg/L	**1E-4 mg/L**	Compared to the EQS values the calculated concentration of OP in the related compartments are low (> factor 100 lower).
Sediment (freshwater)	**Regional PEC**: #H, J E-5 mg/kg dw	**8.2E-2 mg/kg (dw)**	Expected exposure thus remains below current regulatory action thresholds.
Marine water	**Regional PEC:** #H, J E-9 mg/L	**1E-5 mg/L**	Due to the endocrine mode of action, harmful effects can nevertheless not be excluded

Protection target	Exposure concentration	EQS (see Table 3)	qualitative risk characterisation
Sediment (marine water)	**Regional PEC**: #H,J E-6 mg/kg dw	**8.2E-3 mg/kg (dw)**	
Agricultural soil	**Regional PEC:** #H,J E-8 mg/kg dw	**1.7E-2 mg/kg (dw)**	

The calculated regional concentrations are lower and thus risks for the environment at regional scale due to the release of OP from all uses are considered low.

After phase-out of certain wash solutions in 2026 OP-emissions are caused mainly by the use of IVD kits leading to a reduction of 90% OP-emissions compared to 2021.

Figure 9: Estimated development of regional freshwater PECs for OP due to all uses

The EQS-value for freshwater lies outside this scale.

10.2 Summary of risk conclusions

Predicted environmental OP-concentrations for the local scenarios in 2021 are below EQS-values of the EU Water Framework Directive (2000/60/EC) for this substance, which have been used as guide values in the assessment. As the UK implements comparable water regulations, the uses subject to this application will not result in environmental concentrations exceeding current regulatory action thresholds.

Predicted local OP-concentrations due to the application of OPE-containing IVD-kits (use #1) are factor 100 below EQS-values. Highest local OP-concentrations are predicted for use#2 and the so-called power users of OPE-containing wash solution having up to #D analyser platforms in operation. As these power users are located in urban areas with accordingly high STP capacities, predicted concentrations for combined uses result in PECs still considerably lower than the respective EQS-values. Due to the endocrine mode of action, harmful effects can nevertheless not be excluded especially for marine water organisms, where the highest PEC/EQS ratio is observed (0.14).

At regional scale the calculated PECs due to all uses are more than factor 100 below the related EQS-values. Thus, adverse effects for water and sediment organisms are less probable than in the local scenario.

Relevant reduction of OP-emissions will be achieved by stepwise phase-out of OPE uses in IVD kits and wash solutions. In the first instance the #D analyser platforms will be phase-out in 2026 and thus use #2 of OPE containing wash solutions will become obsolete. Use #1 of OPE-dependent IVD kits will decrease continuously and phased out in #D, accordingly the overall emissions of OP to the environment will drop down #D and then decrease continuously at a lower level till #D (see Figure 2 and Figure 9).

The estimated release and the calculation of environmental concentrations above are considered reasonable worst-case. Based on the following aspects the exposure is considered to be an overestimation rather than an underestimation:

- Residual reagents and wash solutions remaining in the vials after use of the IVD kits are disposed of as solid waste. The volume of these waste solutions cannot be quantified but is probably in the range of 0.5 - 1% of all wide dispersive uses. The release figures from uses #1 and #2 can thus be considered a slight overestimation;
- In some IVD reagents Triton™ X-405 is used, which has a lower OP-content. The release figures for use #1 represent thus a slight overestimation;
- The example of a power user in the local scenario for use#2 and the related environmental parameters represent a typical power user of Siemens Healthcare Diagnostic Products in the UK. Most high consuming users are located in even bigger cities. A remaining uncertainty relates, however, to power users not known to Siemens (due to indirect supply), but it is considered unlikely that these are located in rural areas or small villages. Even industrial and commercial areas far off cities, where service labs might also be located, would have to install adequate STP-capacities and therefore the example is considered sufficiently conservative.
- Microorganisms present in urban and industrial STPs are probably adapted to OP and thus environmental degradation may happen faster than considered in the calculation leading to lower OP-concentrations in all environmental compartments;
- In modern STPs longer retention times than considered in the calculation can be assumed and will reduce the OP released from STP, while the OP in the sludge will increase. This may lead to lower OP-concentrations in the aquatic compartment, while the OP-concentration in agricultural soil may increase;

- At the same time the regional PECs for OP in agricultural soil is considered an overestimation, since not all STP-sludge from industrial and urban areas are is applied to agricultural soil but disposed of as waste. In 2019 about 87% of STP-sludge was applied to agricultural soil[5].

Overall, local and regional PECs are below the EQS, nevertheless, risks for the local and the regional environment cannot be excluded. According to the review of available data[6] the most sensitive endpoints describing effects on OP have been observed for gastropods and the number of new embryos/eggs. While the EQS-values derived under the EU Water Framework Directive (Table 3) aim at protecting the pelagic community and preventing the occurrence of endocrine effects, these values cannot be considered no effect concentrations at all. Other endocrine effects on aquatic and sediment organisms at even lower concentrations cannot be excluded. Since OP bound to sludge may enter agricultural soils, it may also pose a risk to terrestrial organisms. Concentrations calculated for this compartment are, however, considerably below the extrapolated quality standards.

Thus, even after significant reduction of OPnEO-releases to the environment and the resulting reduced environmental OP-concentrations from #H, J on, risks for aquatic and sediment organisms due to the use of OPE cannot be excluded until the complete phase-out of the substance.

The stepwise phase-out of OPE-use as planned by Siemens Healthcare Diagnostic Products Ltd is thus considered an appropriate measure to reduce the local and regional risks for the environment effectively. The lack of reliable safe levels for environmental concentrations will question any reduction of emissions without termination. Any activities in this regard will thus focus on complete phase-out of OPE uses by Siemens Healthcare Diagnostic Products Ltd.

[5] https://committees.parliament.uk/writtenevidence/42145/pdf/

[6] Ramboll Environment & Health GmbH, Patricia Janz, Christiane Brandt, Derivation of the PNEC or dose-response relationship for endocrine disrupting properties of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (OPNEO), February 28, 2019

11 Annex

11.1 Example of an analyser system

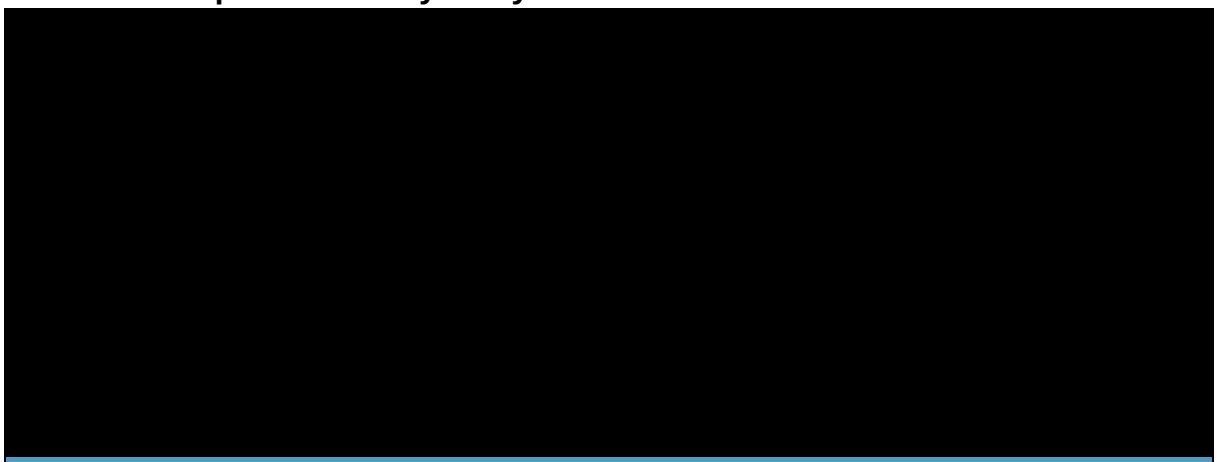


Figure 10: #D

Figure 11: Top view of an #D System and the various sample and IVD kit reagent handling sections

11.2 Projections of OPE-uses [kg/year]

use of Triton™ X-100 (kg/year)

year	use#1	use#2
2021	[redacted]	[redacted]
2022	[redacted]	[redacted]
2023	[redacted]	[redacted]
2024	[redacted]	[redacted]
2025	[redacted]	[redacted]
2026	[redacted]	[redacted]
2027	[redacted]	[redacted]
2028	[redacted]	[redacted]
2029	[redacted]	[redacted]
2030	[redacted]	[redacted]
2031	[redacted]	[redacted]
2032	[redacted]	[redacted]
2033	[redacted]	[redacted]

11.3 List of Abbreviations

Remark: OPnEO, OPE and Triton™ X-100 are used synonymously

AfA	Application for authorisation
AoA	Analysis of Alternatives
AP	Alkylphenol
APERC	Alkylphenols & Ethoxylates Research Council
APEs	Alkylphenol ethoxylates
APnEC (AP1EC, AP2EC)	Alkylphenol carboxylates
APnEO (AP1EO, AP2EO)	Alkylphenol ethoxylates
dw	Dry weight
ECHA	European Chemicals Agency
EDC	Endocrine disrupting chemical
EDS	Endocrine disruptive substance
EQS	Environmental Quality Standard
ERC	Environmental release category within the use descriptor system*
IUCLID	International Uniform Chemical Information Database
MAC-EQS	Environmental Quality Standard expressed as a maximum allowable concentration (short-term EQS)
NP	Nonylphenol
NPnEC (z.B. NP1EC)	Nonylphenol carboxylates
OC	Operation Conditions of use
OP	Octylphenol
OPE	4-(1,1,3,3-Tetramethylbutyl)phenol, ethoxylated
OPnEC	Octylphenol carboxylates
OPnEO	4-(1,1,3,3-Tetramethylbutyl)phenol, ethoxylated

PEC	predicted environmental concentration
PNEC	Predicted no-effect concentration
PROC	Process category within the use descriptor system[7]*
RAC	Risk Assessment Committee
RCR	Risk Characterization Ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RMM	Risk Management Measure
STP	Sewage treatment plant
t-OP	tert-octylphenol
UK	United Kingdom
ww	Wet weight
WHO	World Health Organisation
WWTP	Wastewater treatment plant

[7]* see chapter R.12 in the related ECHA guidance https://echa.europa.eu/documents/10162/13632/information_requirements_r12_en.pdf/ea8fa5a6-6ba1-47f4-9e47-c7216e180197

11.4 Justification for confidentiality claims

Table 14: justification for confidentiality claims

Reference type	Commercial Interest	Potential Harm	Limitation to Validity of Claim
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

Reference type	Commercial Interest	Potential Harm	Limitation to Validity of Claim
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

Reference type	Commercial Interest	Potential Harm	Limitation to Validity of Claim
[redacted]	[redacted]	[redacted]	[redacted]

Reference type	Commercial Interest	Potential Harm	Limitation to Validity of Claim
[redacted]	[redacted]	[redacted]	[redacted]

Reference type	Commercial Interest	Potential Harm	Limitation to Validity of Claim
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]