CHEMICAL SAFETY REPORT

Part A and Part B

Sections 9 + 10

Public version

Substance:	Annex XIV entry #42: 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylate, covering well-defined substances and UVCB substances, polymers and homologues (Triton™ X-100, Triton™ X-405, Triton™ X-705)
Applicant:	Siemens Healthcare Diagnostics Products GmbH
Site:	Marburg, Germany
Use #4:	Widespread use by professional workers - Use of IVD kit reagents on diagnostic analyser systems
Use #5:	Widespread use by professional workers - Use of IVD wash solutions on diagnostic analyser systems
Generated with Chesar 3.4.1	
Date:	15.10.20

Content

Part A

Part B

LIST OF TABLES

LIST OF FIGURES

Part A

1. SUMMARY OF RISK MANAGEMENT MEASURES

The risk management measures for the use of OPE as detergent in protein cell extraction and formulation of IVD kits and IVD wash solutions are described in the document “succint_summary_rmm_oc_uses 1-2-3”. The risk management measures for the use of IVD kit reagents and IVD wash solutions are described in the document “succint_summary_rmm_oc_Mar use 4,5”.

2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

The risk management measures for workers and the environment as described in the “succint_summary_rmm_oc_uses 1-2-3” are implemented at Siemens Healthcare Diagnostics Products GmbH.

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_oc_Mar use 4,5” are communicated with the safety data sheet to downstream users.

Part B

9 Introduction

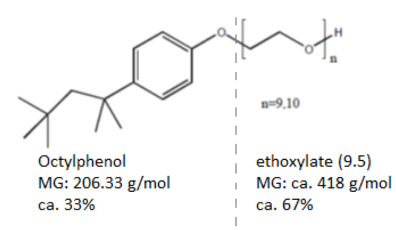
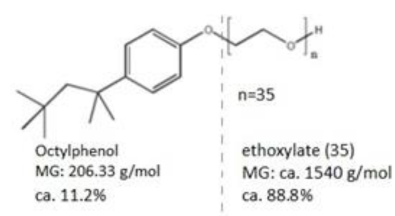
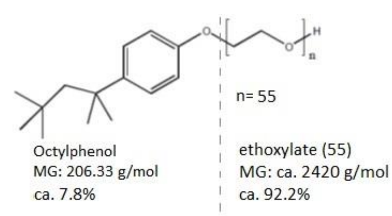
9.1 Substance description

Substance subject to authorisation (REACH Annex XIV, entry #42):

4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated, covering well-defined substances and UVCB substances, polymers and homologues.

Commercial products used in IVD kits by Siemens Healthcare Diagnostic Products GmbH

#	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)
3	Triton™ X-705, used on site as a 70% solution	α-[(1,1,3,3-Tetramethylbutyl)phenyl]-ω-hydroxy-poly(oxy-1,2-ethanediyl)	55 (average)

Triton™ X-100	**Triton™ X-405**	**Triton™ X-705**
OP$_{9.5}$EO	**OP$_{35}$EO**	**OP$_{55}$EO**
MG: ca. 625 g/mol	MG: ca. 1952 g/mol	MG: ca. 2626.33 g/mol
		

Triton™ X-705 is currently used in certain IVD kit reagents (ca. #A[1] kg OP$_{55}$EO/year in 2018), but will be eliminated by 2021. Triton™ X-705 is thus not considered in the following assessment for the year 2021 and beyond.

9.2 Description of use

Uses covered by this CSR:

- Use #4 - Widespread use by professional workers - Use of IVD kit reagents on diagnostic analyser systems
- Use #5 - Widespread use by professional workers - Use of IVD wash solutions on diagnostic analyser systems

[1] The use volume reported in the AoA is #A kg/year referring to a 70% solution of OP$_{55}$EO

9.2.1 Use #4 - Use of IVD kit reagents on diagnostic analyser systems

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.

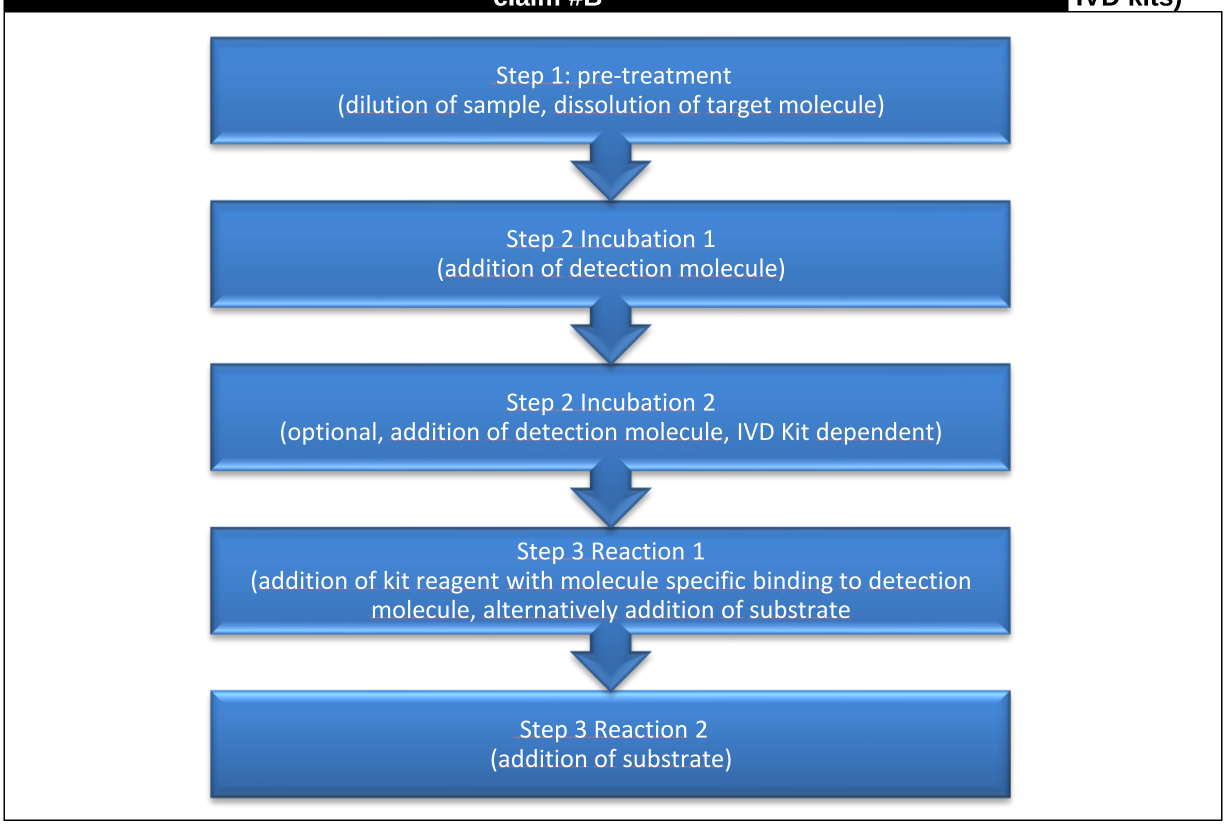
IVD kits are typically supplied in low volumes (in reagents manufactured by Siemens Healthineers volumes are typically <150ml). They typically have low concentrations of OPnEO (in reagents manufactured by Siemens Healthineers the average is ca. [redacted] #A % (range: 0.1 - 1 %). Individual IVD kit reagents 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 11.1.1.

Usually the [redacted] #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 [redacted] claim #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 33 - 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 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 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 #5 - Use of IVD wash solutions on diagnostic analyser systems

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). The highest flow rates related to OPE-throughput are realised on one of the [redacted] platforms with [redacted] ml OPE/hour. Assuming a continuous running of the platform with [redacted] wash solution for a working day, the maximum daily use volume for one platform is calculated with xx g O PE/day (considering the OPE density of 1.07 g/cm³). The throughput rate for the other [redacted] systems is lower (~[redacted] ml OPE/hour for the [redacted], and ~[redacted] ml OPE/hour for [redacted]. Throughput on the other analyser systems in scope of this use are much lower, for example the [redacted] analysers process ~[redacted] ml OPE/hour for one analyser. 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 15 - 100% of the used OPnEO discharged to wastewater. Some customers collect the reagents after use and dispose of it 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

To reduce emissions, Siemens Healthineers (SHS) are **working to eliminate OpnEO, which will reduce potential releases by ~70% within 5 years** of the sunset date.

An analysis was made of existing risk management measures in place at DU sites and what is feasible. This is presented in the response to the Draft Opinion document, and also in the Use 4&5 AoASEA Appendix 3 (p.233).

In summary, SHS understands the following RMM's are in place at DU sites and which do reduce emissions however the amount cannot be quantified -

- 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 comply with the existing EU framework legislation on wastewater and waste that was seen as relevant for these types of fractions. Details on this legislation are shown in Appendix 3 of the AoASEA (p. 233).

In terms of identifying additional RMM's at DU sites an analysis was undertaken of collection and incineration of wastewater from analyser systems. At present there is no 'at the point of discharge' treatment technology available on the market which is compatible with SHS analyser systems, and so incineration was the only route to consider in terms of treatment.

The analysis concluded that it would not make sense for healthcare institutions to implement new drainage networks and collection facilities in parallel to the work by Siemens Healthineers to eliminate OPnEO, to address what will be a continually decreasing impact on the environment. This was due to the significant costs and impracticalities of installing these collection systems, in terms of space, quantity of wastewater in comparison to such low concentrations of OPnEO, also limited access to incinerators in many areas (see details in response to Draft Opinion).

In addition, collection and incineration of wastewater, estimated at >340,000tonnes/annum will have its own environmental impact, resulting in carbon emissions through transport and incineration processes –

- The incineration of wastewater is estimated to cause emissions of CO_2 between 810 – 830 kg/tonne (reference treatment in municipal wastewater treatment 0,3 kg/t), and so when mutlplied with estimated wastewater could be **>270,000tonnes/annum CO_2**

- In addition, transporting this vast quantity of wastewater by road will result in **significant consumption of fuel** (and in consequence CO_2 emissions). We calculate -
-
    - By lorry, 40 t: 5 – 25 kg CO2 per ton liquid waste (in case of no access to incinerators in an area this could be 54 – 70 kg CO_2 per ton liquid waste)
    -
    - By truck, 3.5t-7.5 t: 14 – 68 kg CO2 per ton liquid waste (in case of no access to incinerators in an area this could be 150 – 192 kg CO2 per ton liquid waste)
-
- It must also be taken into account the generation of **additional traffic**, and which also results in impacts such as **noise generation** and increased accident risks.

Other points taken into account included –

- The overall tonnage of OPnEO used by downstream users in 2021 in regard to **Use #4 is** [redacted] **kg (200-400kg)**, and for **Use #5 is 1545kg**.

- The overall tonnage and assumed release to the aquatic environment in 2021 of the substance, **4-tert-OP**, (**26.5% of** OPnEO), in regard to **Use#4 is** [redacted] **kg (50-150kg)** and for **Use #5 is 409kg.**

- In 2021, total potential release of 4-tert-OP from EU Wastewater Treatment Plants (WwTP) is estimated at **less than** [redacted] **kg (200-800kg)** in the **very worst case**, distributed between **thousands of discharge points** across the EU in an **extremely low concentration** within millions of tonnes of dilute wastewater.

- Under Use#4, we estimate for 2021 –
  - Release per downstream user = **< 0.1kg 4-tert-OP/annum**
  - Total Wastewater to collect & incinerate = **107,646 tonnes/annum**
  - Cost to comply with conditions = **~€ 1,050,544 per kg of 4-tert-OP saved**

- Under Use#5, we estimate for 2021 –
  - Release per downstream user = < **0.5kg 4-tert-OP/annum** average (highest hotspot example was 7.9kg/annum in 2017)
  - Total Wastewater to collect & incinerate = **239,021 tonnes/annum**
  - Cost to comply with conditions = **~€525,417 per kg of 4-tert-OP saved**

- Within 5 years of the sunset date, the estimated yearly release volume of **511kg (200-800kg)** of 4-tert-OP **will be reduced to <150kg** (only <8 % of the initial use tonnage of OPnEO) through the vast substitution and phase out efforts for OPE.

- There are [redacted] (5,000 - 25,000) analyser systems in scope of these conditions, located across all Member States and the UK, used every day to diagnose hundreds of different diseases and conditions for millions of patients requiring urgent and non-urgent care.

- We have in this CSR presented an **assumption that there is 100% release** of 4-tert-OP from WwTPs to the aquatic environment (the tonnage is 26.5% of the OPnEO number, with the degradation product 4-tert-OP causing the environmental concern– we felt we had no option but to present this very **worst case scenario** of 100% release despite the fact that **in reality the release will be significantly lower due to solid waste disposal pratices and treatment processes at WwTPs removing some portion of the** OPnEO **–** we have to make this worst case assumption because there is **no way to attribute the correct portion of the overall output of** OPnEO **at a WwTP** to uses covered in our applications and thus measure the effectiveness of the treatment. Also, we cannot know how many of the hundreds of WwTP's within the EEA collect and incinerate sludge or spread it and thus we considered up to 6.5% of the OPnEO may enter agricultural soil as 4-tert-OP, despite knowing that many WwTP´s, especially in urban and industrial areas incinerate their sludge.

- Given that WwTP technologies will remove 4-tert-OP to some level in all cases, it is likely only a small portion of the estimated release of [redacted] **kg (200-800kg)** in 2021, < 150 kg in 2026, will eventually enter the environment.

- We estimate that the costs for EU healthcare institutions to comply with the proposed additional conditions could be in the range of **€599,000 per kg of** 4-tert**-OP** saved to the environment (see calculations in Figure 2).

Further Risk Management Measures -

In addition to the work underway to eliminate OPnEO through reformulation**,** [redacted] **aims to minimise the releases of substances to sewer systems and WwTPs.**

[redacted].

[redacted].

Use of OPE in COVID-19 TESTS – Use#4

In early 2020 when the COVID-19 situation became a global public health emergency, Siemens Healthineers began developing antigen and antibody diagnostic tests. In feasibility testing, some of the antibody tests under development were found to perform most effectively with an existing OPnEO - containing reagent used with several other diagnostic test kits and on analyser systems already described in our Application for Authorisation (Use #4), and which would be used by customers in the same way as is described under this use.

To design a new reagent without OPnEO would have added significant extra time (months, possibly years) on the time to design (please note that registration in countries which typically adds years to commercialising tests is not required in a public health emergency, with 'emergency use' status granted).

We informed ECHA of this as clearly the use of the reagent within the COVID-19 antibody tests could affect the annual volumes of OPnEO used and forecasted in our application. At this time, however, it is not possible to confirm how those volume numbers will be affected, and as such we have not updated the volumes calculated in this CSR.

While clearly the volume of this reagent could increase in line with its use in the COVID-19 test, the demand for our other diagnostic tests which use this same reagent has decreased while healthcare systems focus their diagnostic testing on COVID-19 and associated inflammatory markers. As such, in the near- and intermediate-term it is possible OPE volumes overall will not increase, may stay flat or even be at a lower level than we have forecasted depending how the COVID-19 situation continues to develop. As the need for continued COVID-19 testing evolves, this test and the component reagents will be assessed for future re-design, as described in our Application for Authorisation (Use#4).

The COVID-19 Antibody Tests containing OPE are as follows –

COVID-19 Test	**Analyser System**	**OPE Concentration**
SARS-CoV-2 Total Antibody, SARS-CoV-2 IgG	[redacted]	[redacted] %
SARS-CoV-2 Total Antibody, SARS-CoV-2 IgG	[redacted]	[redacted] %

9.3 Introduction to the assessment for the environment

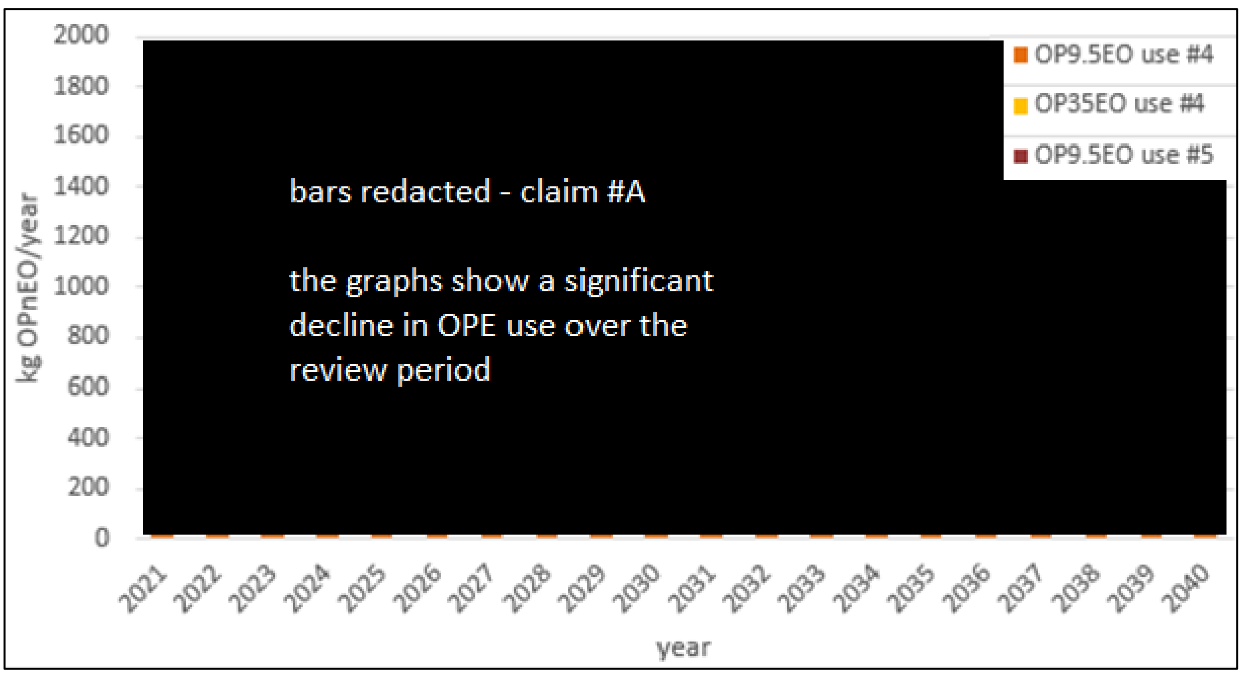
9.3.1 Tonnage

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 #4 - Widespread use by professional workers - Use of IVD kit reagents on diagnostic analyser systems	0.1 - 1		
	- Use of IVD kit reagents on diagnostic analyser systems (ERC 8a)		1 - 10E-7	-
ES2 (PW)	Use #5 - Widespread use by professional workers - Use of IVD wash solutions on diagnostic analyser systems	1 - 10		
	- Use #5 - Use of IVD wash solutions on diagnostic analyser systems (ERC 8a)		1 – 10E-5	-

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 11.2 and separate AoA-document), the use of OPnEO-containing IVD kits will decline year on year, leading to the complete phase-out by 2033 for use #5 wash solutions (with the highest volumes phased out by end [redacted] #B), and 2041 for use# 4 reagents. Due to the use of IVD kits on the [redacted] #B platform, which has an anticipated increasing growth rate in terms of demand, the use figures for OP9.5EO in use #4 will increase until [redacted] #B. This product is thus a major focus of the reformulation effort as defined in the response plan set out in the AoA/SEA and thereafter the OPE consumption for this use will decline dramatically.

Figure 2: Projection of use volumes of OPnEOs in IVD kits (use #4 and #5)



Accordingly, the local and regional release of OP due to use of OPnEOs in in-vitro diagnostic products by Siemens customers will decrease by more than 70% by [redacted] #B (compared to 2021) and finally end in 2041 (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. Only a few customers with specific applications resulting in a high content of other hazardous compounds collect the wastewater and dispose it of as hazardous liquid waste for incineration.

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 and substitution strategy in the AoA-document section 2.2).

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[2]. Since for an individual local scenario 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 and Table 3 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[3] 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 GmbH 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 and 11.2% for Triton™ X-405 (see also section 4.5 of the CSR in a separate document).

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.

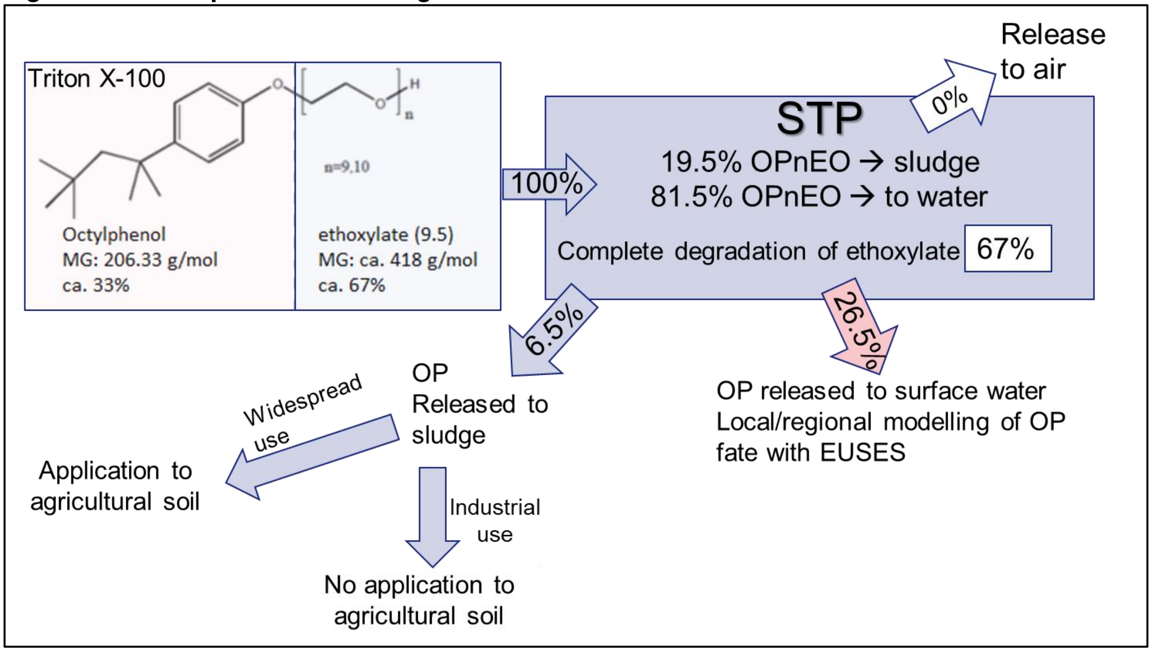
Based on the assumption above OPnEO is partly degraded and 19.5 % is adsorbed to sludge while the remaining OPnEO and degradation products are discharged with the STP effluent. However, since only the OP-part of the molecule is relevant for the environmental risk assessment, the different degradation 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.

---

[2] 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#

[3] 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



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 #4 and #5

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 #4) 2021: #A kg Triton™ X-100	200 - 400 kg $OP_{9.5}EO$			referring to 50-100 kg OP released to the environment
estimated volume used in IVD kits (use #5) 2021: 1000 – 10,000 kg Triton™ X-100	1545 kg $OP_{9.5}EO$			referring to kg OP released to the environment

Table 3: releases of OP after STP for Triton™ X-405 use #4

fate referring to OP in OPnEO in STP	% initial OPnEO	%OP	% EO	compartment
originally released OPnEO	**100**	**11.8**	**88.2**	
release to sludge (considered as OPnEO)	19.5	2.3	17.2	sludge/soil
mineralisation of dissolved OPnEO	71.0	0	71	
OP not adsorbed to sludge and released to water	9.5	9.5	0	water/sediment
calculated efficiency concerning how much OP is released to water from initially discharged OPnEO		90.5		
estimated volume used in IVD kits 2021: #A kg Triton™ X-405 (70%)	#A kg[4] $OP_{35}EO$			referring to #A kg OP released to the environment

For the estimation of environmental OP-concentrations resulting from use #4 the calculated efficiency of 73.5 % for Triton™ X-100 will be applied to the sum of OPnEOs. This way the result (kg OP release for use #4 in 2021) will be an overestimation of about 7%, 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 Healthcare Diagnostics Products 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 used to determine so called "Latest Research Value" (detailed explanation can be found in section 7.4 in the separate CSR-document). These values are not considered no effect levels.

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 Latest Research Value (Table 4) 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 4: Summarised Latest Research Value used for environmental risk characterisation[5]:

compartment	latest research value	based on
Freshwater	**0.034 µg/L**	NOEC of 0.34 µg/l Gastropods, number of new embryos/eggs
Saltwater	**0.0034 µg/L**	based on AF 10 freshwater /marine water
Sediment	**0.028 mg/kg (dry weight)**	calculated (EPM)
Marine sediment	**0.0028 mg/kg (dry weight)**	based on AF 10 freshwater /marine water
Soil	**0.0056 mg/kg (dry weight)**	calculated (EPM)

[4] This figure is already considered in the release rate of 200 – 400 kg/year (see table 2)

[5] Source: 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

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 5: Substance key phys-chem and fate properties of OP[6]

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

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

For the local exposure estimation due to use #4 – the use of IVD kits - the default values of the EUSES tool have been applied.

For use #5 – the use of wash solutions – the default value of 1.1 g/day is proposed by the model, but this might lead to an underestimation of local exposure in some places, since the hourly throughput of OPE on one of the [redacted] platform is already [redacted] ml /[redacted] g OPE (see annex 11.3). These systems represent the highest volume of OPnEO used on any system in the impacted Siemens Healthineers portfolio, with [redacted] wash products, representing >[redacted] % of the volume of OPEs used by Siemens Healthineers customers in 2021. These wash solutions are planned to be completely phased-out by [redacted], which results in the significant decline of OPnEO releases due to use #5 (see Figure 2).

Assuming this platform runs continuously up to 8 hours per day, the daily local use sums up to [redacted]g OPnEO (see Table 6). For other platforms with lower OPE-throughput and users with shorter use durations, the use amount and local releases would be much lower. After phase-out of [redacted] the default values of the model are considered sufficiently conservative to determine the local release (see Figure 4).

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

The daily use amount would also cover the use of other platforms with lower OPE-throughput and users with shorter use durations, although the local releases from these sites would be much lower.

Table 6: Local daily tonnage for uses #4 and #5

ES#	Exposure scenario (ES) name and related environmental contributing scenarios	year	source	Daily local use (g/day)
ES 1 (PW)	Use # 4 - use of IVD kit reagents (ERC 8a)	2021	default	#A
ES 1 (PW)	Use # 4 - use of IVD kit reagents (ERC 8a)	2027	default	#A
ES 2 (PW)	Use of IVD wash solutions (ERC 8a)	2021	Maximum daily use related to [redacted] #claim #B [redacted]	#A
ES 2 (PW)	Use #5 - Use of IVD wash solutions (ERC 8a)	2027	default	#A

These values are considered sufficiently conservative for most of the Siemens users. The biggest Siemens customers for OPnEO-containing wash solutions will, however, exceed the above daily use volumes. These \`power users´ use several OPE-dependent platforms in parallel and have thus higher daily use volumes and consequently higher release rates. As an example the 3 biggest individual consumers of #B #B [redacted] wash solutions are listed in Table 7. Assuming a continuous steady use over 250 days per year or more by these power users, the local environmental release due to use #5 will be up to 6 fold higher than the value used in the assessment.

On the other hand, these bigger hospitals and labs are usually located in urban areas with a higher number of inhabitants (see right column) as used in the model, which is a town of 10,000 inhabitants. Here, the local STP-capacities and related flow rates of the receiving waters will be also higher and local releases will be diluted accordingly. An individual local exposure assessment would thus not result in higher PECs than calculated by the model. 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 towns. Even industrial and commercial areas far off cities, where service labs might also be located, would have to install adequate STP-capacities.

Table 7: Siemens customers with highest yearly consumption of OPnEO-containing wash solutions

#B	#B [redacted]	#B [redacted]	#A [redacted]	#A [redacted]	#A [redacted]	#A [redacted]	#A [redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Based on this the calculated local environmental concentrations due to use #5 in sections 9.5.1.3 and 10.1.1. are considered sufficiently conservative.

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). The regional assessment includes also emissions from the industrial uses at Siemens Marburg use #1 (cell extraction) and uses #2 and #3 (formulation) (see separate CSR-document section 9+10 for uses # 1,2 and 3).

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 4: Widespread use by professional workers – Use #4 - 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 kit reagents 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

Amount used, frequency and duration of use (or from service life)
• Daily local widespread use amount: <= 1 – 10E-7 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 8: Local releases to the environment

Release	Release estimation method	Explanations
Water	ERC	**Release factor before on site RMM: 33 - 100%** **Release factor after on site RMM: 33 - 100%** **Local release rate: #A g OP/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 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 9: Exposure concentrations and risks for the environment

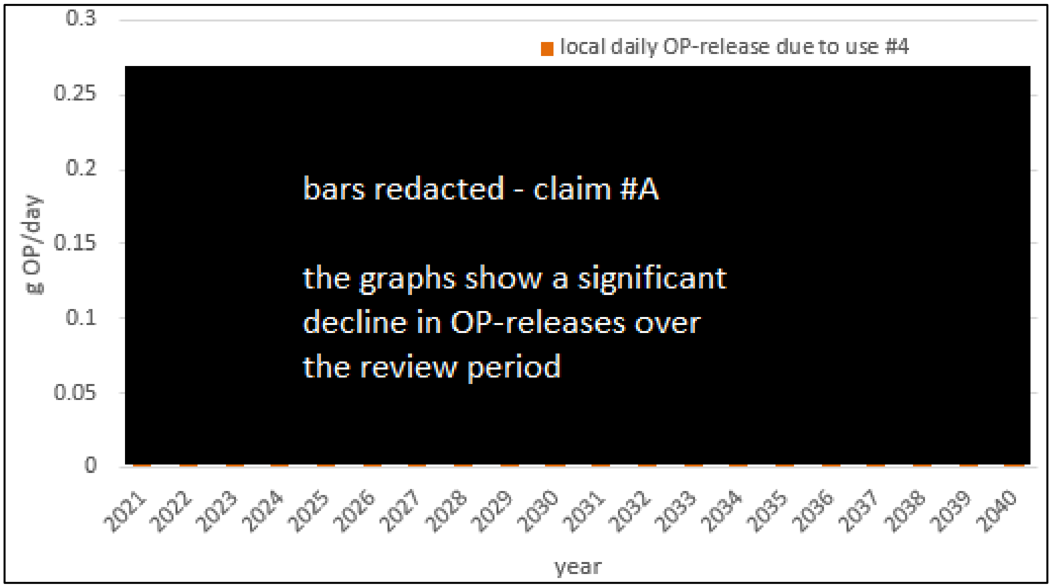
Protection target	**PEC local**	**Latest Research Value** (see Table 4)	**qualitative risk characterisation**
Fresh water	**Local PEC:** 0.0030 µg/L	**0.034 µg/L**	calculated local freshwater concentration of OP is below Latest Research Values, but risks for the environment cannot not be excluded.
Sediment (freshwater)	**Local PEC:** 0.00076 mg/kg dw	**0.028 mg/kg dw**	calculated local freshwater sediment concentrations of OP are below the Latest Research Values, but risks for sediment organisms cannot be excluded
Marine water	**Local PEC:** 0.00029 µg/L	**0.0034 µg/L**	calculated marine water concentration of OP is below Latest Research Values, but risks for the environment cannot be excluded.
Sediment (marine water)	**Local PEC:** 0.000075 mg/kg dw	**0.0028 mg/kg dw**	calculated marine sediment concentrations of OP are below latest research value, but risks for sediment organisms cannot be excluded.
Agricultural soil	**Local PEC:** 0.000039 mg/kg dw	**0.0056 mg/kg dw**	compared to the Latest Research Value the calculated concentration of OP in soil in the regional scenario is low. Although risks for soil organisms not be entirely excluded they are considered unlikely.

Critical values are marked in in orange.

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 2041. The temporary increase of OPnEO use until #B is caused by the anticipated increased demand for the #B platform before the reformulation is completed (see 9.3.1). Accordingly, the yearly local release of OP by customers using Siemens IVD kits will initially increase and thereafter decline significantly (Figure 4). The calculated PECs will follows this development (Figure 5).

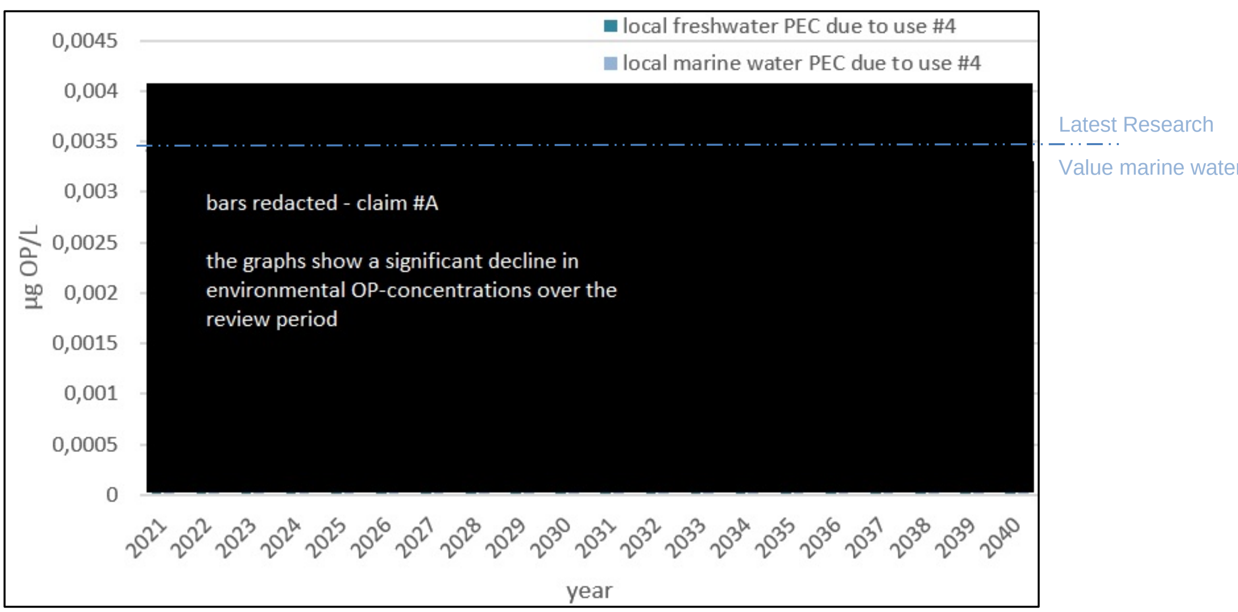
Figure 4: Estimated development of local OP-release rates related to use #4



remark:

Considering the lower OP-Content in the used Triton™ X-405 ($OP_{35}EO$) the actual OP-releases to the environment from use #4 will be lower (about 7% lower in 2021), but since the use of $OP_{9.5}EO$ increases until #B, the proportion of $OP_{35}EO$ decreases during this phase (see Figure 2) and this way also the relevance of this effect.

Figure 5: Estimated development of local aquatic PECs of OP related to use #4



The Latest Research Value for freshwater of 0.034 µg/L lies out of this scale

The local PECs for sediment and soil are considerably below the related Latest Research Values. Analogue to the aquatic PECs above these will increase in the years #B before the decline in #B and the following years (no figure).

9.5 Exposure scenario 5: Widespread use by professional workers - Use #5 - Use of IVD wash solutions 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 wash solutions on diagnostic analyser systems	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

Amount used, frequency and duration of use (or from service life)
• Daily local widespread use amount: <= 1 – 10E-5 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.*

9.5.1.2 Releases

The local releases to the environment are reported in the following table. The biggest Siemens customers will exceed the local release rates, but these are located in urban areas 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 10: Local releases to the environment

Release	**Release estimation method**	**Explanations**
Water	ERC	**Release factor before on site RMM:** 15 - 100% **Release factor after on site RMM:** 15 - 100% **Local release rate:** #A 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 unless stated otherwise.

Table 11: Local Exposure concentrations and risks for the environment 2021

Protection target	**PEC local**	**Latest Research Value** (see Table 4)	**qualitative risk characterisation**
Fresh water	**Local PEC:** 0.19 µg/L	**0.034 µg/L**	calculated local freshwater concentration of OP is above Latest Research Value (factor 6), indicating a potential risk for the environment.
Sediment (freshwater)	**Local PEC:** 0.047 mg/kg dw	**0.028 mg/kg dw**	calculated local freshwater sediment concentrations of OP is above Latest Research Value (factor 2), indicating a potential risk for the environment.
Marine water	**Local PEC:** 0.019 µg/L	**0.0034 µg/L**	calculated local freshwater concentration of OP is above Latest Research Value (factor 6), indicating a potential risk for the environment.
Sediment (marine water)	**Local PEC:** 0.0047 mg/kg dw	**0.0028 mg/kg dw**	Calculated local freshwater sediment concentrations of OP is above Latest Research Value (factor 2), indicating a potential risk for the environment.
Agricultural soil	**Local PEC:** 0.0028 mg/kg dw	**0.0056 mg/kg dw**	Calculated marine water concentration of OP is similar to Latest Research Value, risks for the environment can thus not be excluded.

Most critical values are marked in red other critical values in orange.

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 2033 (see Figure 2). Since the maximum daily use was determined for a full day running one of the [redacted] System analysers, this value remains stable until phase out of the system in [redacted]. In [redacted] the local daily use for the remaining systems will drop down and this way also the local releases of OP (see Figure 6). Consequently the calculated local environmental concentrations fall below the Latest Research Values (see Figure 7).

Calculated local PECs for sediment and soil are also above the related Latest Research Values. After the phase-out of the [redacted] wash solution these PECs will also fall below these indicative values (no figure).

Figure 6: Estimated development of local daily OP-release with STP-effluent related to use #5

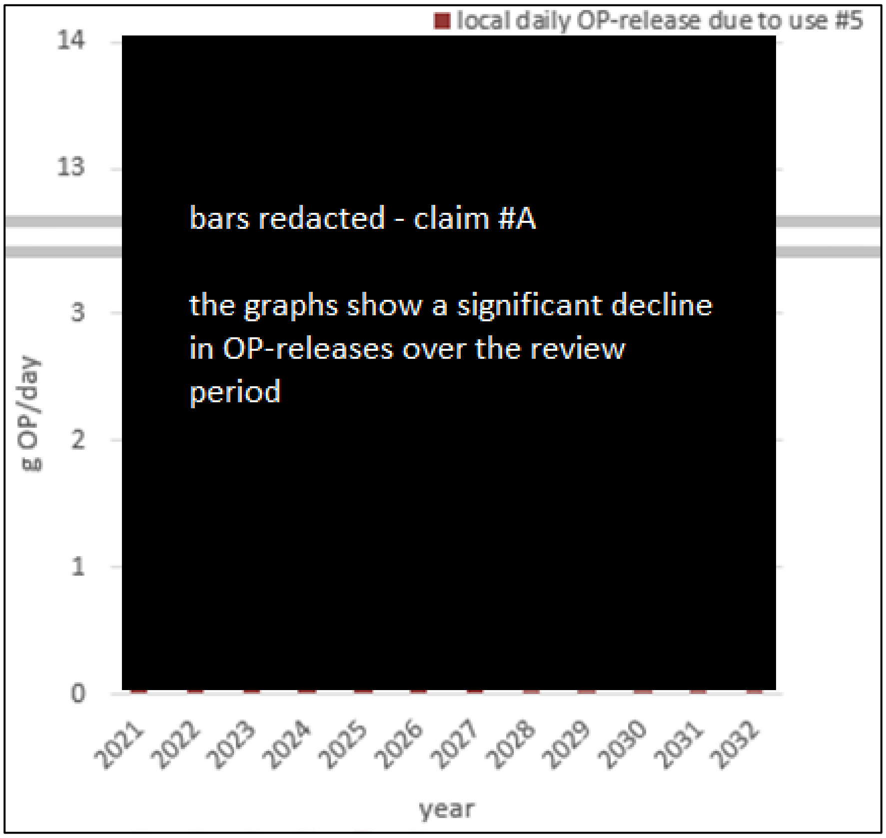
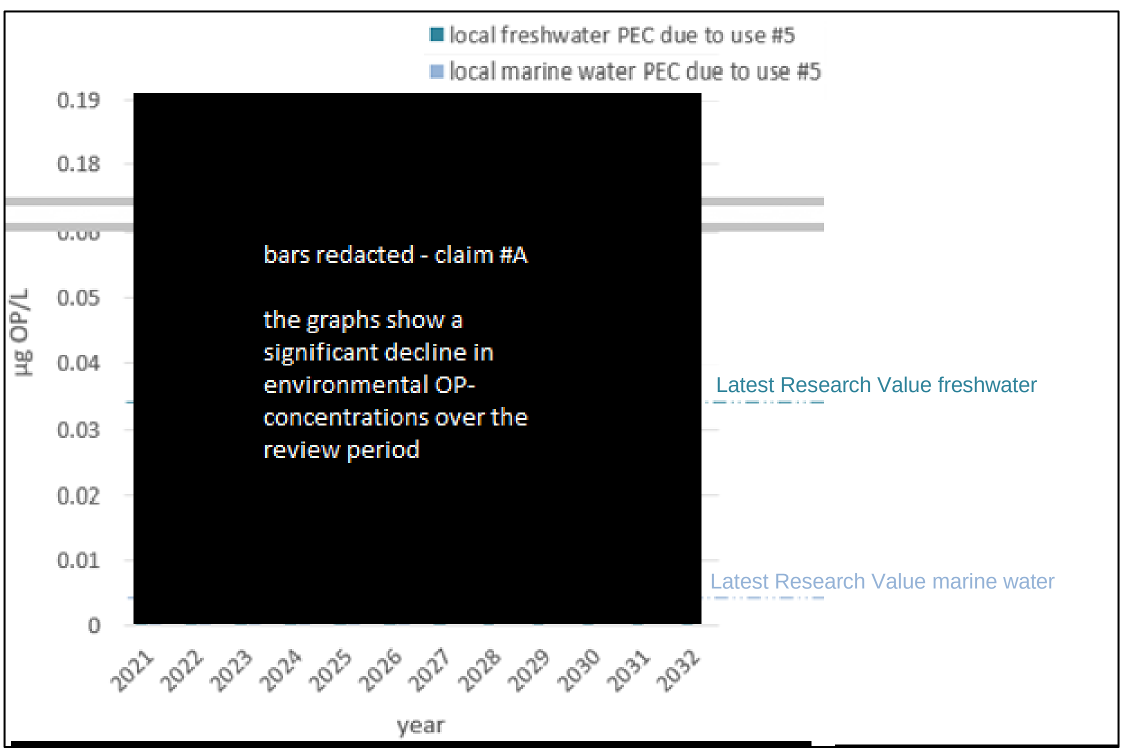


Figure 7: Estimated development of local aquatic PECs of OP related to use #5



10 RISK CHARACTERISATION RELATED TO COMBINED EXPOSURE

10.1 Environment (combined for all emission sources)

10.1.1 Local exposure due to all widespread uses

Table 12: Total releases to the local environment from all widespread uses

Release route	Total releases per year (2021)
Water	1750 - 1950 kg/year
Air	0 kg/year
Soil	0 kg/year

The predicted local environmental concentrations (PEC local) based on the releases from both widespread uses (uses #4 and #5) are reported in the table below. The exposure estimates have been obtained with EUSES 2.1.2.

Table 13: Predicted exposure concentrations and risks for the environment due to uses #4 and #5

Protection target	PEC local due to all widespread uses	Latest Research Value (see Table 4)	qualitative risk characterisation
Fresh water	**Local PEC:** 0.19 µg/L	**0.034 µg/L**	calculated local freshwater concentration of OP is above Latest Research Value (factor 6), indicating a potential risk for the environment.
Sediment (freshwater)	**Local PEC:** 0.048 mg/kg dw	**0.028 mg/kg dw**	calculated local freshwater sediment concentrations of OP is above Latest Research Value (factor 2), indicating a potential risk for the environment.
Marine water	**Local PEC:** 0.019 µg/L	**0.0034 µg/L**	calculated local freshwater concentration of OP is above Latest Research Value (factor 6), indicating a potential risk for the environment.
Sediment (marine water)	**Local PEC:** 0.0048 mg/kg dw	**0.0028 mg/kg dw**	Calculated local freshwater sediment concentrations of OP is above Latest Research Value (factor 2), indicating a potential risk for the environment.
Agricultural soil	**Local PEC:** 0.0029 mg/kg dw	**0.0056 mg/kg dw**	Calculated marine water concentration of OP is similar to Latest Research Value, risks for the environment can thus not be excluded.

Most critical values are marked in red other critical values in orange.

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 #4 and #5 (Figure 2) show, that OP-emissions in the years 2021 to [redacted] are clearly dominated by the use of wash solutions (use #5), which, as a result of the Siemens substitution strategy, will significantly decline. A reduction of more than 70% in OP-emissions is expected from [redacted] onwards, mainly due to the phase out of the [redacted] wash solutions, and emissions will further decline and finally end in 2040.

The local environmental concentrations will decrease accordingly

10.1.2 **All uses (regional scale) – uses #1, #2, #3, #4 and #5**

10.1.2.1 Total releases

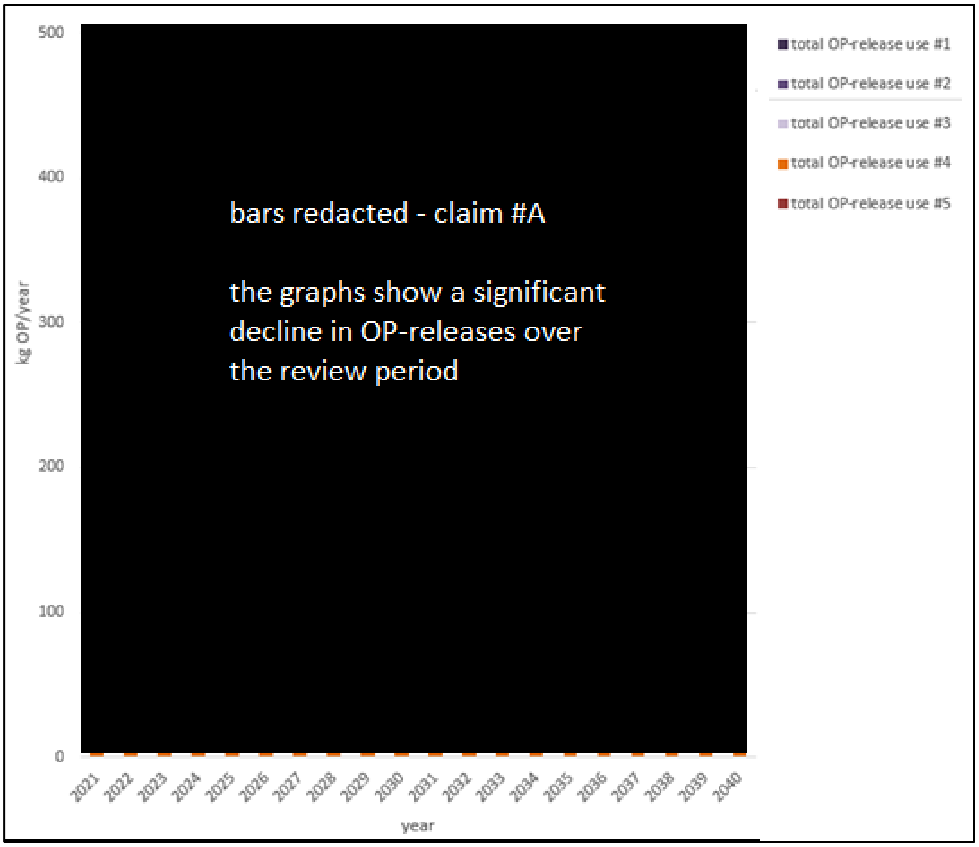
The total releases to the environment from all the exposure scenarios covered by this CSR are presented in the table below. This is the sum of the releases to the environments from all exposure scenarios addressed. The release due to the industrial uses #1, #2 and #3 in Marburg do not contribute significantly to the regional environmental concentration.

Table 14: Total releases to the environment per year from all life cycle stages 2021

use	OPnEO applied/year #A	OPnEO released/year #A	OP released to water/year #A
use #1	1,000 - 10,000 g	61 g	17 g
use #2	1,000 - 10,000 g	1 g	0 g
use #3	100,000 - 1,000,000 g	2,493 g	661 g
use #4	100,000 - 1,000,000 g	200,000 – 400,000 g	53,000 – 106,000 g
use #5	1,000,000 - 10,000,000 g	1,545,000 g	409,000 g
sum of all uses	1,000,000 - 10,000,000 g	1,750,000 - 1,950,000 g	463,000 - 515,000 g

Release route	**Total releases per year (2021)**
Water	1750 - 1950 kg/year
Air	0 kg/year
Soil	0 kg/year

Figure 8: Development of total OP-releases from all uses



10.1.3 **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.

Table 15: Predicted regional exposure concentrations (Regional PEC) and risks for the environment

Protection target	**Exposure concentration**	**Latest Research Value**	**qualitative risk characterisation**
Fresh water	**Regional PEC:** 0.00044 µg/L	**0.034 µg/L**	calculated local freshwater concentration of OP is below Latest Research Value, however, risks for aquatic organisms cannot be excluded
Sediment (freshwater)	**Regional PEC:** 0.18 µg/kg dw	**28 µg/kg dw**	compared to the Latest Research Value the calculated concentration of OP in freshwater sediment in the regional scenario is low. Although risks for sediment organisms cannot entirely excluded they are considered unlikely
Marine water	**Regional PEC:** 0.000040 µg/L	**0.0034 µg/L**	calculated marine water concentration of OP is below Latest Research Value, but risks for marine organisms cannot be excluded.

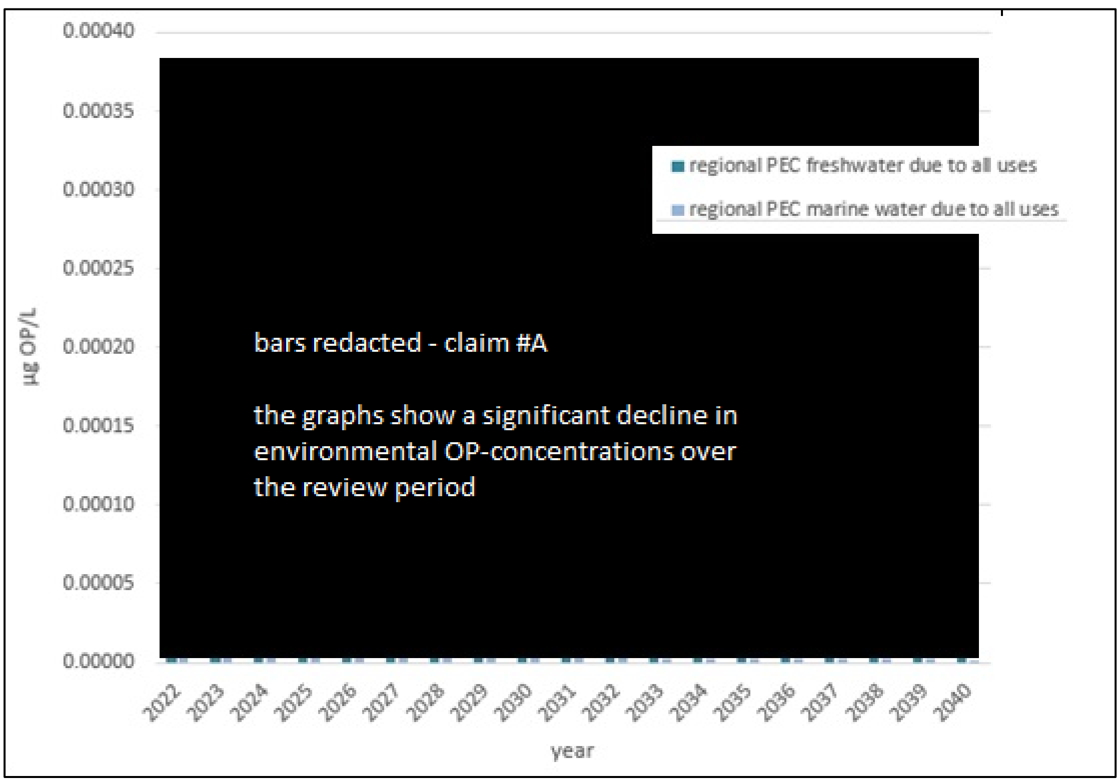
Protection target	Exposure concentration	Latest Research Value	qualitative risk characterisation
Sediment (marine water)	**Regional PEC:** 0.014 µg/kg dw	**2.8 µg/kg dw**	compared to the Latest Research Value the calculated concentration of OP in marine water sediment in the regional scenario is low. Although risks for sediment organisms cannot be entirely excluded they are considered unlikely
Agricultural soil	**Regional PEC:** 0.0001µg/kg dw	**5.6 µg/kg dw**	compared to the Latest Research Value the calculated concentration of OP in soil in the regional scenario is low. Although risks for soil organisms not be entirely excluded they are considered unlikely

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 lower. The regional concentrations are dominated by the emissions from wide dispersive uses, particularly use #5. The local use #3 applied at the Marburg site (#A kg in 2021) contribute with <1% to the regional PECs.

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 70% OP-emissions compared to 2021. A decline of IVD reagents use is expected in 2029, but this use will still dominate the regional PECs, since use #1 is terminated in 2030 and uses #2 and #3 will be also further reduced and phased-out in 2033. From 2033 onwards only imported OPnEO-containing IVD kits will be supplied.

At any time the regional environmental concentrations are dominated by the emissions resulting from wide dispersive uses. The related figures are thus consistent with the release figures for uses #4 and #5.

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



The latest research value for freshwater and marine water lie outside this scale

10.2 Summary of risk conclusions

Environmental OP-concentrations calculated for the local scenarios due to the wide dispersive use #4 are below the Latest Research Values used as indicative values for risk characterisation. For use #5 the calculated local PECs are much higher and exceed related Latest Research Values indicating a potential risks for aquatic and sediment organisms.

At regional scale the calculated aquatic PECs due to all uses are factor 50 below the related Latest Research Values, while the PECs for sediment and soil are more than two orders of magnitude below these indicative 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 OPnEO uses in IVD kits and wash solutions. In the first instance the use of OPE-dependent IVD kits will increase in the years 2022 to [redacted], while the overall emissions of OP to the environment will decrease (see Figure 2 and Figure 9). A continuous decrease of OP-emissions is expected until complete phase-out in 2041.

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:

- Local release figures refer to intensive use with highest OPE-concentrations and OPE-consumption related to wash solutions (Use#5) used on [redacted]-analysers. Less intensive uses and use of other analyser systems [redacted]) will result in much lower use and local release values.
- 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 #4 and #5 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 #4 represent thus a slight overestimation;
- Even if power users of [redacted] wash solutions may exceed the daily release figure used in the calculation, these hospitals or service labs are usually located in urban areas or professional/industrial areas. The local STP-capacities and flow rates will thus be much higher than the standard figures used in the model. It is thus very unlikely, that an individual local assessment would result in higher local PECs.
- 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 EU-wide only 53% of STP-sludge is applied to agricultural soil.

Overall, even if local and regional PECs are below the Latest Research Values, risks for the local and the regional environment cannot be excluded. According to the review of available data (see section 7 of the separate CSR-document) the most sensitive endpoints describing effects on OP have been observed for gastropods and the number of new embryos/eggs. While the Latest Research Values (Table 4) have been derived based on the related NOEC, this cannot be considered a no effect concentration 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 Latest Research Value.

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

The stepwise phase-out of OPnEO-use as planned by Siemens Healthcare Diagnostic Products GmbH 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 OPnEO uses by Siemens Healthcare Diagnostic Products GmbH.

11 Annex

11.1.1 Example of an analyser system

[redacted] Claim #B

Figure 10: [redacted] #B

[redacted] Claim #B

Figure 11: Top view of an [redacted] #B System and the various sample and IVD kit reagent handling sections

11.2 Projections of OPE-uses [kg/year]

Year	Use 4			Use 5
	Triton™ X-100	Triton™ X-405	Triton™ X-705	Triton™ X-100
2017	[redacted]			
2018				
2019				
2020				
2021				
2022				
2023				
2024				
2025		Claim #A		
2026				
2027				
2028				
2029				
2030				
2031				
2032				
2033				
2034				
2035				
2036				
2037				
2038				
2039				
2040				

11.3 Determination of local daily use volumes for wash solution in use #5

[redacted] claim #A and #B [redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[7] Includes 0.18mL used in daily shutdown wash (WASH 2)

11.4 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[8]*
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
ww	Wet weight
WHO	World Health Organisation
WWTP	Wastewater treatment plant

[8]* 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

11.5 Justification for confidentiality claims

Table 16: justification for confidentiality claims

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