CHEMICAL SAFETY REPORT

Public Version

28 October 2022

Legal name of applicant:	CSL Behring AG
Substance:	4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated - covering well-defined substances and UVCB substances, polymers and homologues (Annex 1.17 of ORRChem, entry number: 42)
Use title:	Use of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (as a detergent) for virus inactivation via S/D (Solvent/Detergent) treatment in the plasma-derived medicinal product Rhophylac®
Use number:	1

Note: Confidential information (CBI) is marked in [redacted].

Table of Contents

List of Tables

List of Figures

ABBREVIATIONS

4tOP	4-tert-octylphenol
AfA	Application for Authorisation
AM	Arithmetic mean
ARA	“Abwasserreinigungsanlagen” (sewage treatment plant)
BCF	Bioconcentration factor
DaP	Day after production day
ESI-LC MS/MS	Electrospray Ionization Liquid-Chromatography-Tandem Mass Spectrometry
HPLC	High Performance Liquid Chromatography
Koc	Organic Carbon normalized adsorption coefficient
Kow	Octanol-Water partition coefficient
KVA	“Kehrricht-Verbrennungs-Anlage” (waste incineration plant)
LoQ	Limit of Quantification
MCI	Molecular Connectivity Index
mSTP	Municipal sewage treatment plant
MW	Molecular weight
N/A	Not applicable
N/D	Not determined
OPnEO	Octylphenol ethoxylates
PD	Production day
PEC	Predicted Exposure concentration
PNEC	Predicted No-Effect Concentration
QSAR	Quantitative structure-activity relationship
RCR	Risk Characterisation Ratio(s)

S/D	Solvent/detergent
SMILES	Simplified molecular-input line-entry system
SP	Sampling Point
T1/2	Half-life
TnBP	Tri-n-butyl-phosphate
UV	Ultraviolet
VP	Vapour pressure
WS	Water solubility
WW	Wastewater
WWTP	Wastewater treatment plant

1 SUMMARY OF RISK MANAGEMENT MEASURES

ECS and WCS	Task (ERC/spERC or PROC)	Annual amount per site (tonnes/ year)	Technical RMMs, including: *Containment, *Ventilation (general, LEV…) *customized technical installation, etc.	Organisational RMMs, including: *Duration and Frequency of exposure *OSH management system *Supervision *Monitoring arrangements *Training, etc.	PPE (characteristics)	Other conditions	Effectiveness of wastewater and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Detailed info. in CSR (section)
ECS 1	ERC 4	[redacted] (range 0.1-1)	Not applicable	Not applicable	Not applicable	Not applicable	- Collection of wastewater (WW); - future on site WW treatment for Triton X-100 degradation (min. 90% efficiency); - biodegradation of Triton X-100 in high-load reactor at ARA Region Bern (about 90% efficiency); - treatment of the discharged wastewater in the municipal STP (ARA Region Bern)	Water: [redacted] % [range: 5-50%] Air: 0% Soil: 0%	5.6.1 and 5.7

Abbreviations: WCS=Worker contributing scenario, ECS=Environmental Contributing Scenario,* ERC=Environmental Release Category (or spERC if available), PROC= Process category, LEV=Local Exhaust Ventilation, PPE=Personal Protective Equipment; n.a. = not applicable

2 DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

We, CSL Behring AG, claim the specified information in this report as confidential. We hereby declare that, to the best of our knowledge as of today (28 October 2022) the information is not publicly available, and in accordance with due measures of protection that we have implemented, a member of the public should not be able to obtain or have access to the information without our written consent or, if in respect of a third party, then the consent of that party to disclosure of their confidential information.

By means of this statement, we hereby confirm that the appropriate risk management measures (RMMs) required for safe use of 2-[4-(2,4,4-trimethylpentan-2-yl)phenoxy]ethanol (the main active ingredient in Triton® X-100) as described in detail in section 5 and summarised in section 1 of this Chemical Safety Report for safe use relating to the environment have been implemented at the site in Bern under the control of CSL Behring AG.

DocuSigned by:
Livia Artuso

Signature: Name des Unterzeichners: Livia Artuso
Signiergrund: Ich genehmige dieses Dokument
Signierzeit: 28-Oct-2022 | 2:26:11 AM PDT
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Date/Place: 28-Oct-2022 Bern

Livia Artuso
Site General Manager

DocuSigned by:
Niklaus Krähenbühl

Signature: Signer Name: Niklaus Krähenbühl
Signing Reason: I approve this document
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Date/Place: 27-Oct-2022 Bern

Niklaus Krähenbühl
Site Head Legal Affairs

3 DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED

Not applicable for this Application for Authorisation (AfA). As a downstream user of Triton® X-100 CSL Behring AG does not put on the market the substance and therefore no risk management measures need to be communicated.

4 Summary

CSL Behring AG uses Triton® X-100 for the production of the plasma-derived medicinal product Rhophylac® at its manufacturing plant in Bern, Switzerland. Purified Triton X-100 is used as a virus inactivation agent via solvent/detergent (S/D) treatment.

Triton X-100, which is covered by the group of substances '4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated – comprising well-defined substances and UVCB substances, polymers and homologues (4-tert-OPnEO)' has been included as entry No. 42 in Annex 1.17 of the Swiss Chemical Risk Reduction Ordinance, ORRChem SR814.81 due to its endocrine disrupting properties.

Already in 2017 CSL Behring AG has identified a possible alternative and was investigating the technical feasibility to substitute Triton X-100 with the alternative. Technical feasibility studies have been pushed forward and currently available results indicate that a complete substitution of Triton X-100 should be feasible within 5 years after the sunset date (2 May 2024). Based on the anticipated timeline for the technical implementation and market approval a substitution of Triton X-100 until the sunset date is not feasible. Therefore, CSL is applying for a 5 years bridging authorisation for the

„Use of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (as a detergent) for virus inactivation via S/D (Solvent/Detergent) treatment in the plasma-derived medicinal product Rhophylac®".

The CSR describes the use, the risk minimisation measures, the resulting emissions and the mass balance. The calculations of emissions are based on measurements in the wastewater and predictions on future use, taking into account a gradual substitution considering expected market approvals.

Currently, measures are in place to prevent any release of Triton X-100 into the environment via routes other than wastewater. A relevant proportion of the Triton X-100 required for S/D treatment is already separated within the production process and disposed via waste incineration. The remaining Triton X-100 is currently completely discharged via wastewater. Before the wastewater is fed to the municipal wastewater treatment plant, parts of the wastewater are treated in a bioreactor that efficiently degrades the Triton X-100. However, since not all wastewater can be treated in the bioreactor, CSL Behring AG will implement additional on-site wastewater treatment technology. This will almost completely degrade the Triton X-100 from production before being added to the industrial wastewater and represents a relevant minimisation measure in addition to the gradual substitution of Triton X-100 within the applied for use extension period.

With these minimisation measures, CSL Behring AG contributes significantly to the reduction of environmental emissions of Triton X-100, which is particularly important as the endocrine effects of the substance are relevant to environmental organisms but not to humans. For this reason, hazards to human health are not considered in this CSR. Nevertheless, measures are in place to prevent human exposure as far as possible.

5 EXPOSURE ASSESSMENT (and related risk characterisation)

5.1 Introduction

CSL Behring AG (hereafter referred to as CSL), located in Bern, uses Triton® X-100 ($C_{14}H_{21}$-$[C_2H_4O]_n$-OH) (hereafter referred to as Triton X-100) at their manufacturing plant in Bern, Switzerland. At the plant, purified Triton X-100 is used as a virus inactivation agent in the manufacturing process of the plasma derived protein therapeutics product Rhophylac®, intended[1] for the suppression of rhesus isoimmunization in:

- Pregnancy and obstetric conditions in rhesus (D)-negative women with a rhesus-incompatible pregnancy;
- Incompatible transfusions in rhesus (D)-negative individuals transfused with blood components containing rhesus (D)-positive red blood cells.

Rhophylac® is additionally registered for the treatment of:

- Immune thrombocytopenic purpura (only in the US)

These products are commonly referred to as Rho(D) immune globulin products.

Triton X-100 is covered by the group of substances '4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated – comprising well-defined substances and UVCB substances, polymers and homologues (4-tert-OPnEO)' that have been included in Annex XIV of the EU's REACH Regulation due to their endocrine activities on environmental organisms on 13 June 2017 (see Commission Regulation (EU) 2017/999[2]). Triton X-100 has been included as entry No. 42 in Annex 1.17 of the Swiss Chemical Risk Reduction Ordinance, ORRChem SR814.81 due to its endocrine disrupting properties in Fall 2021[3], with a sunset date on 2 May 2024 and a latest Application Date on 2 November 2022 (18 month before the sunset date).

In 2017 CSL Behring AG has identified [redacted] as possible alternative and was investigating the technical feasibility to substitute Triton X-100 with [redacted]. Technical feasibility studies have been pushed forward, and currently available results indicate that a successful substitution of Triton X-100 should be feasible. CSL will progress with final process setpoint definition in the coming months (end 2022/early 2023). Confirmation runs on full scale will then be performed before entering formal process performance qualification later in 2023. This will be followed by generation of data packages needed for health authority regulatory submissions and approval of the changed manufacturing process. Based on the anticipated timelines, a substitution of Triton X-100 till the sunset date is not feasible. Therefore, CSL is applying for a 5 years bridging authorisation for the „Use of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (as a detergent) for virus inactivation via S/D (Solvent/Detergent) treatment in the plasma-derived medicinal product Rhophylac®.

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[1] https://www.rhophylac.com/

[2] http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1497426084925&uri=CELEX:32017R0999

[3] Chemikalien-Risikoreduktions-Verordnung, version of 1.November 2020; SR 814.81 - Verordnung vom 18. Mai 2005 zur Reduktion von Risiken beim Umgang mit bestimmten besonders gefährlichen Stoffen, Zubereitungen und Gegenständen (Chemikalien-Risikoreduktions-Verordnung, ChemRRV) (admin.ch) accessed 26 November 2021

5.2 Identity of the substance

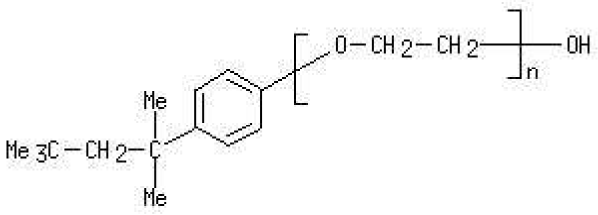
5.2.1 Name and other identifiers of the substance

The substance 2-(2-[4-(1,1,3,3-Tetramethylbutyl)phenoxy]ethoxy)ethanol (the active ingredient in Triton® X-100) is an organic polymer having the following characteristics and physical–chemical properties.

Table 1 **Substance identity**

EC number:	618-541-1
EC name:	2-(2-[4-(1,1,3,3-Tetramethylbutyl)phenoxy]ethoxy)ethanol
CAS number:	9036-19-5
IUPAC name:	2-{2-[4-(2,4,4-Trimethyl-2-pentanyl)phenoxy]ethoxy}ethanol
Synonyms:	Octylphenol polyethoxyethanol, OCTOXYNOL-10
Molecular formula:	$C_8H_{17}C_6H_4(OCH_2CH_2)nOH$
Molecular weight range:	Not applicable, polymer

Structural formula:



5.2.2 Composition of the substance

Name: 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated - covering well-defined substances and unknown or variable composition, complex reaction products or of biological (UVCB) substances, polymers and homologues

The Triton X-100 used by CSL contains ethoxylates (EO) with an average chain length of 9.5 EO units.

The identification of ethoxylated 4-(1,1,3,3-tetramethylbutyl)phenol as a substance of very high concern (SVHC) and its inclusion in Annex XIV of the REACH Regulation has been justified with the known endocrine disrupting (ED) properties of its degradation product 4-tert-octylphenol (4tOP) which causes '*probable serious effects to the environment*' (ECHA, 2012). There is evidence that other degradation products of Triton X-100, like short chain ethoxylates with only one or two ethoxy groups (OP1EO and OP2EO), could cause endocrine effects as well. ECHA states that the potency of the ethoxylates is '*nearly as high (factor 10) or similar*' as the potency of 4tOP (ECHA, 2012) based on findings for nonylphenol ethoxylates. However, in the absence of tests on adverse endpoints it was impossible to conclude whether or not OP1EO and OP2EO are endocrine disruptors themselves (ECHA, 2012).

Due to the degradation of Triton X-100 to the endocrine active 4tOP, the hazard assessment (see Annex 2 for the derivation of PNEC and related values) is based on data for 4tOP and structural analogues, especially nonylphenol. This approach is regarded as sufficiently conservative and protective with respect to the group of Triton X-100 degradation products. This procedure is in accordance with the procedure of the Annex XV Dossier for the group of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated - covering well-defined substances and UVCB substances, polymers and homologues (ECHA, 2012).

In order to consider the fact that the ethoxylates contained in Triton X-100 are ultimately degraded to 4tOP, a conversion of OPnEOs to 4tOP EQV is performed for the exposure assessment, taking into account the corresponding molecular weights. This approach is considered sufficiently conservative for the assessment. For easier readability, abbreviations are used to describe the different octylphenol ethoxylates, their mixtures and degradation products (Table 2).

Table 2 Terminology used in this report

4tOP	4-tert-octylphenol; 4-(1,1,3,3-tetramethylbutyl)phenol (CAS No. 140-66-9)
4tOP EQV	4-tert-octylphenol equivalents; calculated from concentrations or amounts of individual substances using conversion factors
OP9.5EO	Octylphenol ethoxylates with an average of 9.5 EO units (other species with different numbers of EO units accordingly)
OPnEO	General abbreviation for octylphenol ethoxylates with an undefined number of EO units; 'x' may be substituted with specific numbers, *e.g.* OP1EO for the monoethoxylate, or ranges, e.g OP6-11EO, octylphenol ethoxylates with 6-11 EO units
Triton X-100	2-(2-[4-(1,1,3,3-Tetramethylbutyl)phenoxy]ethoxy)ethanol (the main active ingredient in Triton X-100)

Degree of purity: 100%

Table 3 Constituents of Triton X-100

Constituent	Typical concentration	Concentration range	Remarks
2-(2-[4-(1,1,3,3-Tetramethylbutyl)-phenoxy]ethoxy)ethanol	No information available	90.0 – 100.0 %	---

Table 4 Impurities of Triton X-100

Impurities	Typical concentration	Concentration range	Remarks
No information available	---	---	---

Table 5 Additives of Triton X-100

Constituent	Typical concentration	Concentration range	Remarks
No information available	---	---	---

5.3 Process description

5.3.1 Rhophylac manufacturing process

As outlined in section 5.1 the detergent Triton X-100 is used by CSL during production of a plasma derived protein therapeutic (Rhophylac®). Triton X-100's primary role is virus inactivation [redacted] The highly automated manufacturing process of Rhophylac® with special focus on the contribution of Triton X-100 and its fate in the process and the environment is described in the following section.

Triton X-100 is used as part of a solvent/detergent (S/D) treatment.

S/D treatment

Within the S/D treatment, a 1:1 mixture of Triton X-100 and the organic solvent tri-n-butyl phosphate (TnBP) is used as a potent agent for disrupting the lipid membrane of viruses, which leads to the inactivation of viruses. This method is approved worldwide by authorities (*e.g.*, Swissmedic, EMA, FDA, WHO).

Triton X-100 is purchased as a pure (100%) substance in [redacted] glass bottles. For each batch, [redacted] Triton X-100 and [redacted] TnBP are pre-mixed in a bucket. About [redacted] Triton X-100/TnBP (exact amount depending on lot size) is added to the production stream by transfer via bucket(s) to stainless steel tank FT2, where S/D treatment and inactivation of lipid enveloped viruses takes place. The excess amount of approximately [redacted] kg S/D solution is collected in bottles and forwarded to waste incineration. Subsequently, the intermediate production stream is transferred via closed lines to stainless steel tank FT3. [redacted], about [redacted] of Triton X-100 is separated from the process, collected in plastic cubitainers, and sent for off-site waste incineration by a hazardous waste contractor. The remaining intermediate product containing approximately [redacted] of Triton X-100 is automatically transferred via closed lines to chromatography column CM1.

Chromatography CM1

Chromatography column CM1 is loaded with the intermediate product. During the chromatography process, the intermediate product is washed with buffer, which results in purification and to a great extent removal of Triton X-100 from the intermediate product.

Washing liquids containing Triton X-100 are sent to wastewater (see below). After elution from column CM1, the intermediate product undergoes further process steps. In the final product, Triton X-100 specific limit is set to [redacted] [redacted]. Based on a dataset of [redacted] batches, Triton X-100 concentrations in the final product were on average

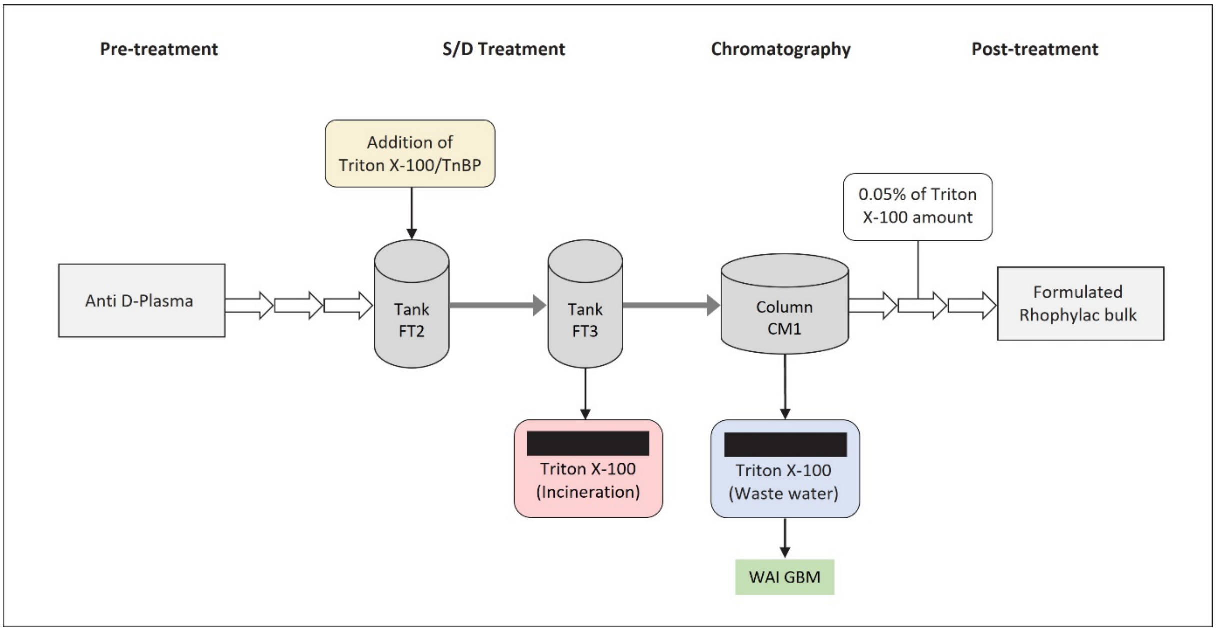


Figure 1 **Scheme of Rhophylac® production focussing on Triton X-100 process flow.**

5.3.2 Triton X-100 Waste

Liquid waste containing Triton X-100 sent to incineration

During the preparation of the S/D solution (Triton X-100/TnBP), an excess of approximately [redacted] kg, which is not added to the production process, is gathered in bottles, and sent to waste incineration.

[redacted] This liquid waste contains approximately [redacted] of the amount of Triton X-100 used and is collected in plastic cubitainers, which are sent to waste incineration.

Waste incineration is carried out by an external waste management partner (SOVAG-Veolia) under consideration of the current legislation (VeVa; Ordinance on the transport of waste SR.814.610; waste code 16 05 08 “used organic chemicals consisting of or containing dangerous substances”). Based on the technical data of the high temperature incineration plant (temperature in rotary furnace: 1100 °C; temperature in post combustion: 1150 °C; dwell time of flue gas: 6 sec in total; it should be noted that in accordance with Swiss requirements the temperatures are higher and the dwell time is longer than in specifications of similar EU plants) a complete combustion of Triton X-100 to carbon dioxide and water can be assumed.

Wastewater emissions

Triton X-100 containing wastewater can arise from the following sources:

- Washing steps during chromatography CM1
- Rinsing water from cleaning buckets used for mixing and transferring S/D solution
- Residue in tanks FT2, FT3 and associated piping
- Further purification steps after Triton X-removal

All wash/eluate water (including rinsing water from cleaning buckets and residues in tanks FT2 and FT3) that arises during pre-treatment, loading, and washing of column CM1 and the following purification steps is currently discharged to the on-site wastewater collection system (for further details see below). More than 99% of Triton X100 discharge to wastewater stems from column CM1. Per batch a total amount of approximately [redacted] wastewater are generated by the CM1 operation. Highest concentrations of Triton X-100 are present in the first [redacted] (about [redacted] of total Triton X-100 loaded to / washed from column CM1). The remaining [redacted] of the total Triton X-100 loaded to / eluted from column CM1.

The wastewater from the Rhophylac® production process is first gathered in a wastewater collecting tank located at the GBM production facility. From there, it is further routed via a collection basin in the PRO building to the GBB collection basin. These basins also receive wastewater from other – non Rhophylac® production – sources (see scheme below). Afterwards, the wastewater is discharged into a large stacking basin (ARA Stapelbecken Sempachpark), which is located directly outside the plant premises. This basin is connected to the stacking basin MAB at ARA Region Bern, the municipal wastewater treatment plant (WWTP), via an approximately 4 km long pressure line used exclusively for CSL industrial wastewater. The daily discharge from CSL to ARA Region Bern is about [redacted] m^3. The stacking basin MAB only contains wastewater discharged by CSL. Wastewater is fed from the MAB basin into a mixing tank for neutralisation with CO_2 (waste product from biogas treatment plant at ARA Region Bern) and, if necessary, subsequently with hydrochloric acid. Afterwards, the CSL wastewater enters the anaerobic reactor, the so called "High-Load Reactor", for carbon (COD) degradation. Wastewater from the high-load reactor is pumped to the wastewater treatment plant intake and further purified with the raw wastewater from the public sewer system. Afterwards, the treated wastewater is discharged into the river Aare.

Wastewater not sent via the high-load reactor to the municipal STP ARA Region Bern due to technical reasons can be directly discharged from the stacking basin MAB into the municipal STP ARA Region Bern (see section 5.3.2.2 for further details).

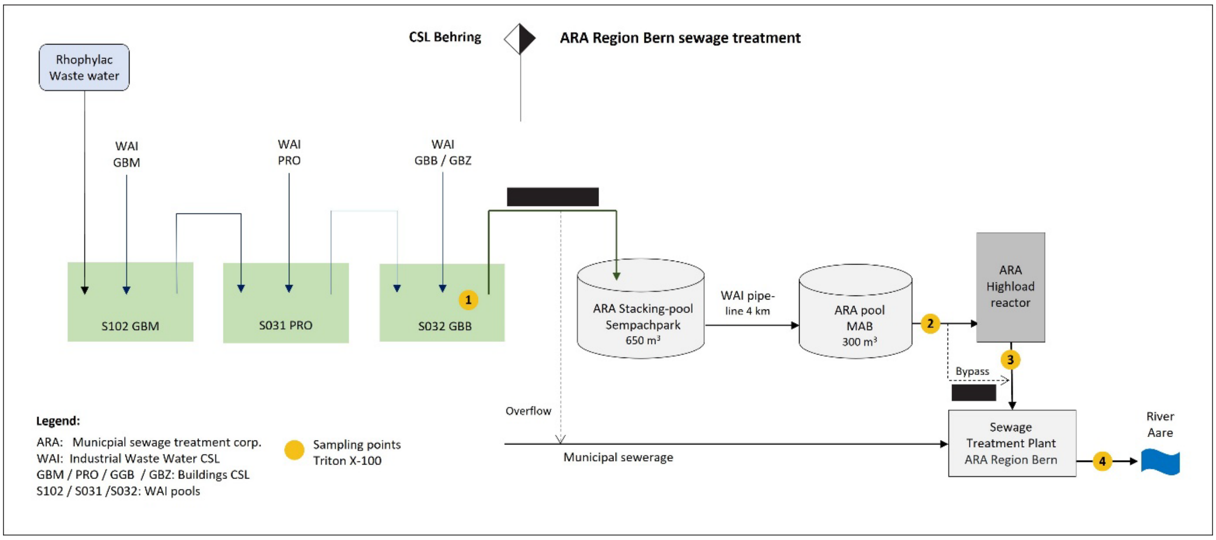


Figure 2. Triton X-100 wastewater streams and sampling points for wastewater monitoring

5.3.2.1 Wastewater Monitoring

CSL has initiated Triton X-100 monitoring in the wastewater to generate representative and reliable data as basis for the environmental assessment.

On the one hand, CSL investigated how much of the Triton X-100 is released from the Rhophylac® manufacturing process to the production washwaters.

On the other hand, CSL measured Triton X-100 concentrations at different points along the waste-water route from the CSL plant to the exit of the municipal STP to the river Aare. Based on those measurements

a) the amount of Triton X-100 released from the Rhophylac® manufacturing process to production washwaters could be quantitatively confirmed in CSL's industrial wastewater.
b) degradation of Triton X-100 could be demonstrated on its way via the municipal STP (ARA Region Bern) to the river Aare, particularly, via biodegradation and mineralisation of Triton X-100 in the high-load reactor.
c) no quantifiable amounts of Triton X-100 were found in the discharge from the municipal STP into the river Aare.

Suitable Triton X-100 analytics first needed to be developed. For the Triton X-100 determination in the Rhophylac® production washwaters containing relatively high concentrations of Triton X-100, an established in-house analytical method was used for the determination of Triton X-100 (Reversed-phase HPLC with UV detection at 223 nm; LoQ < 1 mg/L). Using this method, the individual washwater fractions were monitored and the total amount of Triton X-100 entering the industrial wastewater from the Rhophylac® production was determined on the basis of the measured concentrations and volumes.

Since the wastewater from the Rhophylac® production is mixed and diluted with other industrial wastewater from CSL on its way to the municipal STP (see Figure 2), a more sensitive method with a lower limit of quantification was developed in cooperation with an external laboratory. Furthermore, this method is able to specifically measure the ethoxylates of different lengths. This ESI-LC-MS/MS (Electrospray Ionization Liquid-Chromatography-Tandem Mass Spectrometry) method can quantitatively determine 4tOP and all ethoxylates (from OP1EO to OP17EO).

During three independent monitoring campaigns (one each in 2017, 2018 and 2022), the Triton X-100 amount discharged per Rhophylac® batch to production washwaters was determined (see Table 6) at the outflow of column CM1. The amount of 4tOP EQV discharged per batch was [redacted] g, [redacted] g, and [redacted] g in 2017, 2018 and 2022, respectively (mean value: [redacted] g 4tOP EQV). These measured values show a very high level of consistency and show that only approximately [redacted] of the added Triton X-100 quantity ([redacted] g 4tOP EQV) ends up in the wastewater, while about [redacted] of the added Triton X-100 quantity is separated before column CM1 and sent to incineration with the other process waste generated during Rhophylac® production.

Table 6 Total amount of Triton X-100 in production washwaters on production days (measured at the outflow of column CM1)

	2017	2018	2022
g 4tOP EQV*	[redacted]	[redacted]	[redacted]
Mean	[redacted]		

*: based on measurements of total Triton X-100; rounded values given in the table, but the calculations were made with the non-rounded values.

Triton X-100 measurements in wastewater were also carried out at three different times. The results of the measurement campaigns are documented in Annex 3.

In a first measurement campaign in November 2021, 24 h collection samples were taken at the outlet of the MAB stacking basin upstream to the inlet to the high-load reactor (sampling point 2; see Figure 2) and at the outlet of the high-load reactor (sampling point 3) by autosamplers. The samples were analysed for the content of 4tOP and all ethoxylates from OP2EO to OP17EO. An analysis of OP1EO was not possible at that time due to the lack of sensitivity of the method.

In April 2022, another measurement campaign was carried out on samples from all 4 sampling points shown in Figure 2, *i.e.* including sampling point 1 in the GBB collection basin and sampling point 4 at the effluent of the municipal STP. The measurement campaign in June 2022 including manual and autosampler samples from sampling point 1 served primarily to investigate open questions regarding the results obtained from sampling point 1 within the April 2022 campaign.

All concentrations for OPnEO were converted to 4tOP EQV concentrations. Measured values that were below the limit of quantitation were considered with LoQ/2, except for OP1EO. In this particular case, the LoQ of OP2EO was used instead of LoQ/2 for OP1EO. This procedure was chosen to avoid a bias in the evaluation caused by the LoQ for OP1EO (194 or 380 µg/L), which is two orders of magnitude higher than for all other OPnEOs (0.1 to 1.3 µg/L). This approach is supported by scientific literature on nonylphenol ethoxylates indicating that summed-up concentrations of 4tOP and OP1EO are expected to be comparable to the OP2EO concentration (see box on metabolite distribution data for STP effluents below). Still, in a conservative way, 4tOP was evaluated based on its respective LoQ/2.

Metabolite distributions from STPs to judge on the relative amounts of 4tOP, OP1OE, and OP2OE

The most comprehensive analysis of metabolite formation, partitioning to sludge and final extent of degradation was performed by Ahel et al. (1994) investigating 11 different STPs in Switzerland. While these analyses focused on nonylphenol ethoxylates (NPnOE), results are regarded to be well transferrable to OPnOE and assumed to be rather worst case for OPnOE due to the higher hydrophobicity and therefore higher adsorption potential of NPnOE. This is because compounds adsorbed to particulate matter usually are degraded at a slower rate compared to compounds that are freely dissolved. From comparative analysis of commercial nonylphenol ethoxylate (NPnEO) mixture, wastewater, mechanically treated wastewater (primary effluent) as well as biologically treated wastewater (secondary effluent) distinct distributions of NPnEO became obvious. Commercial mixtures contained only very low fractions of 1-3 EO groups. On a molar scale, primary effluent had nearly equal amounts of NP, NP1EO and NP2EO (local minimum at NP3EO). Most pronounced, however, is the impact of the aeration basin, leading to an effluent dramatically depleted in total NP derivatives, missing longer chain derivatives >8 EO and being largely constituted **by NP2EO (ca. 50 %) and NP / NP1EO (ca. 25 % each)**.

By multiplying 4tOP EQV concentrations with the corresponding wastewater amounts, 4tOP EQV in grams (g) were obtained. The data shown in following Table reveal that even on days without production, small amounts of Triton X-100 can still be detected in the wastewater. This is due to the buffering volume of the basins along the wastewater route from the Rhophylac plant to the ARA. To determine the total amount of Triton X-100 released per production day (per batch), the determined masses of 4tOP EQV in the wastewater of a production day and the day after production were added together.

A very high level of agreement between the results of different campaigns is observed, see November 2021 and April 2022 results of sampling point 2 and June 2022 results of sampling point 1 in Table 7. The mean 4tOP EQV amount fed to the municipal sewage treatment plant (mSTP) ARA Region Bern ([redacted] g 4tOP EQV, see Table 7; individual values obtained by adding up analytically determined 4tOP EQV amounts of production days (PD) and the days after production (DaP)) is practically identical to the mean 4tOP EQV amount determined in the column CM1 washwater of the Rhophylac® plant ([redacted] g 4tOP EQV). Based on these data, it can be concluded that the total amount of Triton X-100 from the Rhophylac® production that enters the wastewater is also practically completely discharged to the mSTP. Emission via sludge residues that accumulate in the water collection basins over time and are then fed via waste disposal through specialised companies is therefore not to be considered in the context of this AfA. This conclusion is further supported by the fact that even under worst-case assumptions, the amount of Triton X-100 in the sludge does not exceed 0.0028%, *i.e.* is below the concentration to be considered in an AfA (for details see Annex 4).

Table 7 Total amount of Triton X-100 discharged via wastewater on production days (PD) and days after production days (DaP) expressed as g 4tOP EQV

	PD	DaP	PD	DaP	PD	DaP	PD	DaP	PD	DaP	PD	DaP	PD	DaP
	November 2021						April 2022						June 2022	
Sampling point 1 [g 4tOP EQV*]	N/D	N/D	N/D	N/D	N/D	N/D	invalid	invalid	invalid	invalid	invalid	invalid	[redacted]	[redacted]
	N/D	N/D	N/D	N/D	N/D	N/D	invalid		invalid		invalid		[redacted]	
Sampling point 2 [g 4tOP EQV*]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	N/D	N/D
	[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		N/D	N/D
Mean value for (PD + DaP) [g 4tOP EQV]	[redacted]													

*: based on measurements of total Triton X-100; rounded values given in the table, but the calculations were made with the non-rounded values.

Results obtained on sampling point 1 in the April 2022 campaign were invalidated. Amounts were almost twice as high as those expected based on analyses of column CM1 outlet and also twice as high as those found at sampling point 3 in the same measuring campaign. These invalid results at sampling point 1 were probably due to a systematic error of the used autosampler. In June 2022, sampling was repeated at sampling point 1 using both, the autosampler and manual sampling (see Appendix 3 for the individual values). Furthermore, a re-analysis of column CM1 outlet was performed. The June 2022 analyses of sampling point 1 were in agreement with both, the total mass of 4tOP EQV after column CM1 and also the total masses of 4tOP EQV as measured in November 2021 and April 2022 at sampling point 2.

5.3.2.2 Triton X-100 minimisation in high-load reactor

As described in section 5.3.2, parts of CSL wastewater are discharged to ARA Region Bern directly, and parts of the wastewater enter the anaerobic reactor, the so called “High-Load Reactor”, before being fed to the public sewer system.

The high-load reactor has been built in cooperation between ARA Region Bern and CSL as an efficient measure to destroy organic pollutants. The monitoring values from April 2022 show that Triton X-100 is efficiently degraded in the high-load reactor. While at sampling point 2, values above the LoQ were measured for almost all OPnEOs, significantly lower concentrations were measured for the individual OPnEOs at the outlet of the high-load reactor, often below the limit of quantification (for details see Annex 3, Table 29). As shown in the table below for production days, the concentration (µg 4tOP EQV/L) at sampling point 3 (SP3) is no more than 10% of the concentration before the high-load reactor treatment at sampling point 2 (SP2), *i.e.* there is a minimisation of at least 90%. Treatment of the wastewater in the high-load reactor is therefore an efficient minimisation measure. Overall, this is a conservative estimate of the efficiency of the high-load reactor, as the "measured" concentrations at sampling point 3 are strongly influenced by the limits of quantification of the individual components and overall minimisation is probably higher. For the same reason, the minimisation coefficient cannot be determined on the days after production, as the total concentrations at sampling point 3 are mostly determined by the LoQs (see Annex 3).

Table 8 Degradation of Triton X-100 in the high-load reactor on production days

	SP 2	**SP 3**	**SP 2**	**SP 3**	**SP 2**	**SP 3**
Date	04.04.2022	04.04.2022	06.04.2022	06.04.2022	08.04.2022	08.04.2022
Concentration (µg/L 4tOP EQV)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
% Reduction	**N/A**	**90.5**	**N/A**	**94.7**	**N/A**	**93.8**

However, for reasons unrelated to this application, the high-load reactor cannot be used to its full capacity at present. The following figure with the monthly average values from August 2019 to July 2022 for the proportion of wastewater that is routed via the high-load reactor shows that on average [redacted]% [range: 10-100%] of the CSL wastewater is routed via the high-load reactor, [redacted]

[redacted]

Figure 3 Proportion of wastewater that is routed via the high-load reactor (confidential information)

5.4 Overview of Uses and Exposure Scenarios

5.4.1 Tonnage information

Tonnage supplied per market sector:

The following table lists all the exposure scenarios (ES) assessed in this CSR.

Table 9 Overview of exposure scenarios and contributing scenarios

Identifiers*)	Titles of exposure scenarios and the related contributing scenarios	Tonnage (tonnes per year)
ES-1 (IW-1*)	**Exposure scenario 1**: Use of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (as a detergent) for virus inactivation via S/D (Solvent/Detergent) treatment in the plasma-derived medicinal product Rhophylac® **Environmental contributing scenario (EnvCS):** EnvCS 1: Use of Triton X-100 as a process chemical (ERC 4) **Worker contributing scenarios (WCS):** Not relevant	[redacted] Triton X-100 (range: 0.1-1) Corresponding to [redacted] 4tOP EQV (range: 0.033-330)

*: Industrial end use at site

Based on past consumption data (2012-2020), CSL used an average of [redacted] (range: 0.1-1 tonnes/year). Future consumption could be higher, but higher estimates do not currently consider any reductions in the consumption of Triton X-100 due to its substitution for markets where health authorities will have approved the new Rhophylac ® manufacturing process without Triton X-100. Consumption of Triton X-100 is directly related to the number of batches manufactured per year. The plants maximum capacity is [redacted] batches per annum. Each batch uses [redacted] kg of Triton X-100, therefore the maximum plant capacity of [redacted] batches would use [redacted] kg of Triton X-100. In 2023 and 2024 a total of batches are anticipated per year, resulting in a total Triton X-100 tonnage of kg/year (range: 100-1000 kg/year). This amount corresponds to [redacted] kg 4tOP EQV/year) (range: 33-330 kg 4tOP EQV /year).

If the implementation plan for an identified alternative adheres to its envisaged timeline, consumption of Triton X-100 will start decreasing from Q4/2024 onwards and, from that point in time, it will be lower than assumed here (for details see AoA/SEA report).

Table 10 Mass balance

Parameter	**kg Triton X-100/year**	**kg 4tOP EQV/year**
Amount used	[redacted] [100-1000]	[redacted] [33-330]
Excess amount of approximately [redacted] kg S/D solution per batch containing approximately [redacted] kg Triton X-100 is collected in bottles and INCINERATED	[redacted]	[redacted]
Triton X-100 separated [redacted] and INCINERATED ([redacted] of amount used)	[redacted]	[redacted]
Released to wastewater (based on monitoring of the outflow of the column CM1, see Table 6)	[redacted]	[redacted]
of which are removed in the high load reactor by anaerobic biodegradation (monitoring data)	---	[redacted]
of which are removed in the mSTP by adsorption to sludge and biodegradation (EUSES modelling, Scenario 2a)	---	[redacted]
emitted to surface water	---	6.8

*not considered as the release to WW is based on monitoring data

The emission to wastewater summarised in Table 10 is based on the measurements at the outflow of column CM1 (see Table 6). Approximately [redacted]% of the total Triton X-100 in the wastewater is degraded in the high-load reactor. This estimate is based on the average fraction of CSL wastewater processed by the high-load reactor ([redacted]%) and a Triton X-100 biodegradation efficiency of at least 90% of Triton X-100, see monitoring data in section 5.3.2.1. Furthermore, adsorption and biodegradation in the mSTP (EUSES modelling, Tier Scenario 2a) results in a degradation of at least 72%.

5.5 Technical and organisational risk management measures

With regard to risk management measures two different situations are distinguished:

a) the current situation until the sunset date and

b) the future situation, possibly in place at a date around the sunset date (for details see Annex 5).

As a basic risk management measure CSL has decided to substitute Triton X-100 and has started in 2017 research and development activities to identify a possible alternative.

While the alternative was identified relatively quickly, the technical implementation proved to be challenging and took longer than initially planned. The original plan of switching production to the alternative by the sunset date was not technically possible. After further research and development, the alternative is now assessed as feasible and work for technical implementation is underway. However, an immediate switch to the alternative is not feasible due to remaining development and process confirmation work, and generation of data packages needed for health authority regulatory submissions and approvals. Before implementing the alternative manufacturing process without Triton X-100, approval for the modified production must first be obtained in the individual countries. A step that can take longer or shorter, depending on the country and the requirements for approval.

Currently, measures are in place to prevent any release of Triton X-100 into the environment via routes other than wastewater. Strict handling procedures are in place, and operators have been trained to carefully handle and transport process raw materials (including Triton X-100) to protect the integrity of the raw materials and to prevent accidental releases. Operator training has also been completed to prevent the release of the substance.

Spill and emergency procedures are in place, spill kits are available in the warehouse and process areas, and relevant operator training has been completed. In the unlikely event of a spill of Triton X-100, it is contained and cleaned up quickly, and the clean-up material is safely packaged as hazardous waste and incinerated in accordance with the requirements of Swiss waste management regulations (*e.g.* “Verordnung 814.600 über die Vermeidung und die Entsorgung von Abfällen (Abfallverordnung, VVEA)”), preventing any release into the environment.

The potential release of Triton X-100 to air during handling and use at the site is excluded due to both, the operating conditions under which Triton X-100 is used at the site and the physical and chemical properties of the substance. Triton X-100 is stored at room temperature in sealed containers so that volatile losses of the substance to air during on-site storage can be excluded. In addition, further handling (*e.g.* preparation of stock solution) takes place at room temperature, so that potential losses of Triton X-100 to air throughout the process can be considered insignificant.

A list of RMM is in place to minimise unintended exposure to the environment:

- Triton X-100 is delivered and stored in closed glass containers, which are stored in the warehouse under conditions which prevent leakages into the environment (sealed floors, which in emergencies prevent the seepage of leaked chemicals);
- Transport of the glass bottles in a second container;
- Preparation of the S/D solution under conditions that avoid contamination of the environment (careful handling of the solution, adding the wash water of the buckets to the general wastewater stream with subsequent minimisation treatment, incineration of the solid waste generated during preparation of the SD solutions);
- Process use of the S/D solution under controlled conditions (careful manual addition to the process; collection and incineration of the excess amount of S/D solution);
- Removal of Triton X-100 from the production process: approximately [redacted] separated from the process, which is collected and sent to incineration; only about [redacted] of the Triton X-100 used is discharged to the wastewater during the purification of the product (see figure below);
- The wastewater is collected and transported in closed pipes and containers and discharged to the municipal sewage treatment plant (mSTP; ARA Region Bern);
- Before the wastewater is added to the rest of the wastewater in the mSTP, the wastewater from CSL is collected in a stacking basin.
- In cooperation with the mSTP, CSL has developed and built a high-load reactor in which CSL's wastewater is subjected to biological treatment, which on the one hand leads to

the decomposition of organic materials (and thus also to the degradation of Triton X-100) and on the other hand generates biogas for heat generation as decomposition products (see. section 5.3.2.2 on efficiency).

- A new wastewater treatment system will be installed at the CSL site with which the wastewater fraction containing about [redacted] of the Triton X-100 fed to the wastewater will be treated. This additional treatment step will efficiently minimise the Triton X-100 emissions (for details see Annex 5).

[redacted]

Figure 4 Simplified Triton X-100 wastewater streams (confidential information)

5.6 Introduction to the assessment

5.6.1 Environment

Scope and type of assessment

The following Environmental Quality Standards (EQSs) and Predicted No-Effect Concentrations (PNECs) values are used in section 5.7.1.1.7 to calculate Risk Characterisation Ratios (RCRs). Their detailed derivation and justification is given in Annex 2.

Regarding the PNEC for freshwater sediment, a sediment quality criterion (SQC, = EQS_{sed}) of 12.1 µg/kg sediment dry weight was recently derived for Switzerland by the equilibrium partitioning method (EPM) from the Environmental Quality Standard (EQS) for freshwater of 0.122 µg/L (Kroll and Casado-Martinez, 2020). As outlined in detail in Annex 2, this value relates to an organic carbon (OC) content for sediment of only 1%. Due to the low OC content assumed for sediment in Switzerland, less 4tOP will partition into the sediment and correspondingly, less of the 4tOP present in the sediment will be in the adsorbed (non-bioavailable) state. This is the reason for the higher PNEC sediment from EPM compared to the freshwater EQS. In the EU, the PNEC for sediment is given in relation to the local assessment for which by default 10% OC is assumed (like for suspended matter). However, for any EPM-based sediment assessment, the exact OC content assumed for the sediment is not relevant for the resulting $RCR_{sediment}$ as long as

- the same Koc is used for the exposure assessment in EUSES and the derivation of the PNEC using EPM
- EPM is performed using the same OC content for sediment as assumed for sediment in the environmental exposure assessment.

Correspondingly, recalculating the Swiss EPM-derived SQC (1% OC) of 12.1 µg/kg for sediments with 10% OC, a value of 119.2 µg/kg dw results, which is in support of the value used for this assessment of 100 µg/kg dw (see Table 11 and Annex 2 for more details).

Of note,RCRs were only used to demonstrate low exposures against an existing benchmark, but this approach is not intended to imply adequate control of all risks.

Table 11 Type of risk characterisation required for the environment

Protection target	**Type of risk characterisation**	**Hazard conclusion**
Freshwater	Quantitative	EQS: 0.1 µg/L*
Sediment (freshwater)	Quantitative	PNEC: 100 µg/kg dw
Sewage treatment plant	Quantitative	PNEC: 100 µg/L
Air	Qualitative	No hazard identified
Agricultural soil	Quantitative	PNEC: 2 300 µg/kg dw
Predator	Quantitative for freshwater and terrestrial compartments (top predators,	PNEC: 2 360 µg/kg food

*) EQS value rounded to one significant figure.

5.6.2 Man via environment

Not within the scope of this AfA.

An assessment of human exposure via the environment (HvE assessment) is not required for this substance, as OPnEO was listed in Annex XIV of the REACH Regulation on the basis of endocrine disrupting properties for the environment. This interpretation is confirmed by RAC in its “Risk related considerations in applications for authorisation for endocrine disrupting substances for the environment, specifically OPnEO and NPnEO”[4] where it is stated that “risks to human health do not need to be assessed in the CSR included in an application for authorisation for OPnEO”.

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[4] https://echa.europa.eu/documents/10162/17229/npneo_and_opneo_for_agreement_final_en.pdf/026cbafc-6580-1726-27f3-476d05fbeef0; accessed 14 September 2022

5.6.3 Workers

Not within the scope of this AfA.

Whilst a worker contributing scenario is not required for this substance, as it was listed in Annex XIV of the REACH Regulation on the basis of endocrine disrupting properties for the environment, the Operational Conditions in place ensure worker exposure risk is low. Primarily from an exposure assessment perspective, Triton X-100 is a non-volatile liquid, which can cause eye damage & skin irritation. Triton X-100 is used predominantly in a closed system. Opening of vendor supplied glass bottle takes place within a flowbooth and potential dermal exposure is controlled with PPE.

5.6.4 Consumers

Not within the scope of this AfA.

Due to OPnEO’s inclusion in Annex XIV of the REACH Regulation on the basis of endocrine disrupting properties for the environment no assessment of consumer exposure is required.

5.7 Exposure Scenario 1: Use of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (as a detergent) for virus inactivation via S/D (Solvent/Detergent) treatment in the plasma-derived medicinal product Rhophylac®

Sector of use: SU0: Other (NACE C21: Manufacture of basic pharmaceutical products and pharmaceutical preparations)

Article categories: Not applicable

Environment contributing scenario(s): Use of Triton® X -100 as a process chemical (ERC 4)

Worker/Consumer contributing scenario(s): Not applicable

Subsequent service life exposure scenario(s): Not applicable

Exposure scenario(s) of the uses leading to the inclusion of the substance into the article(s): Not applicable

5.7.1 Environmental contributing scenario 1: Use of Triton® X-100 as a process chemical (ERC 4)

Table 12 Conditions of use

Product (article) characteristics
Liquid
Amount used, frequency and duration of use (or from service life)
Amount used: [redacted] [0.1-1] t/a Triton X-100 (= [redacted] t/a 4tOP EQV [0.033-0.33]), corresponding to [redacted] [1 – 10] kg/d Triton X-100 (= [redacted] kg/d 4tOP EQV [0.1-2]) Frequency of use (release days per year): [redacted] d/a
Technical and organisational conditions and measures
Collection of wastewater (WW); future on site wastewater treatment for Triton X-100 degradation (min. 90% efficiency); biodegradation of Triton X-100 in high-load reactor at ARA Region Bern (about 90% efficiency); Treatment of the discharged wastewater in the municipal STP (ARA Region Bern)
Conditions and measures related to sewage treatment plant
Discharge from the site into public sewer: ca. [redacted] m^3/d (AM value over 6 days in April 2022 and 6 days in November 2021) Municipal STP: 65 000 m^3/d (lower limit for ARA Region Bern, confirmed Sept. 2021) River flow rate: 6 480 000 m^3/d (River surveillance station Schönau 1935-2018: based on 4-month period with lowest average flow (Jan-April; annual average flow: 10 540 800 m^3/d)

Conditions and measures related to treatment of waste (including article waste)
Incineration of the solid waste according to national legislation Sludge from the high-load reactor as well as the surplus sludge from the municipal STP is dried and supplied to cement works as fuel and mineral material. Organic pollutants are destroyed in the process.
Other conditions affecting environmental exposure
Relevant reduction of Triton X-100 by the high-load reactor; not considered in EUSES modelling [redacted] fraction of ([redacted]% [10-100%]) wastewater treated by the high-load reactor

5.7.1.1 Exposure and risks for the environment

Analytical monitoring was performed to quantify 4tOP EQV in the wash water, in the wastewater leaving the plant, after the high-load reactor and at the discharge point of the mSTP (see section 5.3.2.1). These data allow for conclusions on a) the amount of Triton X-100 released per production day, b) elimination extent in the high-load reactor, and c) a worst case estimate for the release of Triton X-100 from the mSTP based on ½ LoQ values for the different analysed contributing species.

The estimated 4tOP EQV amount discharged from the mSTP into the river based on ½ LoQ values is certainly too high

A two-tier assessment was performed to estimate more realistic amounts:

- The Tier 1 assessment estimates exposure without any consideration of biodegradation and adsorption to sewage sludge in the mSTP to specifically address the impact of dilution on concentrations in the mSTP effluent and the river water. This assessment is done by simple spread-sheet calculations based on measured values for the wastewater flow, the STP discharge rate as well as concentrations of 4tOP EQV in wastewater entering the mSTP.
- The impact of adsorption to sludge and biodegradation in the mSTP is considered in the Tier 2a assessment (adsorption and biodegradation) as well as the Tier 2b assessment (only adsorption). Full scale EUSES modelling is performed focussing on 4tOP for reasons discussed below. These Tier 2 assessments are considered to be most relevant and to give a conservative estimate for the range of exposure to be expected depending on the extent of biodegradation actually occurring.

5.7.1.1.1 Used 4tOP EQV Amounts

The monitoring data revealed that even on days without Rhophylac® production small amounts of Triton are detectable in the wastewater (see section 5.3.2.1 and Annex 3). For the calculation of the release per production day to be used within the EUSES exposure assessment, the mean release per production day and the mean release per day after production were added. This is a conservative way to account for the Triton X-100 still being present on the day after production. Accordingly, the results from the April 2022 measurement campaign spanning six days (4 April to 9 April 2022) are evaluated as if the total release during these six days would have occurred during the three production days. This leads to a higher calculated local peak exposure.

Table 13 Measurement results for 4tOP EQV in wastewater as a basis for calculation of the release per production day used in the EUSES exposure assessment

Day of measurement (2022)	**4 April**	**5 April**	**6 April**	**7 April**	**8 April**	**9 April**	**AM**	**AM**
Prod. Day (PD) or Day after Prod. (DaP)	**PD**	**DaP**	**PD**	**DaP**	**PD**	**DaP**	**PD**	**DaP**
Measured concentration in wastewater before mSTP* (4tOP EQV) [µg/L]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Measured wastewater flow [m^3/d]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Resulting release of 4tOP EQV [g/d]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Mean release PD and DaP [g/d], taken as release per release day for EUSES exposure assessment (Tier 2 assessment):								[redacted]

*: sampling point 2; rounded values given in the table, but the calculations were made with the non-rounded values

5.7.1.1.2 Releases

Based on the amount of Triton X-100 used per batch ([redacted] kg 4tOP EQV [0.1-2]). and the amount of Triton X-100 measured per batch in the wastewater ([redacted] g 4tOP EQV, see table above), a release fraction into the wastewater of [redacted] [0.05-0.50] can be calculated. Below release factors and amounts (expressed as 4tOP EQV) were used for scenario Tier 2 (a and b; full EUSES modelling). Based on the low volatility of Triton X-100 as well as 4tOP (see Annex 1) and because there are no elevated temperatures applied within this scenario, emissions to air are judged to be negligible.

For scenario Tier 1 (only dilution, no adsorption, no biodegradation) specific measured values for six representative days in April 2022 were used (for details, see Table 17).

Table 14 Local releases to the environment

Release	Release factor estimation method	Explanation / Justification
Water	Measured data	Release factor: [redacted] % [range: 5-50 %] Local release rate: [redacted] g/d Explanation / Justification: See section 5.7.1.1.2
Air	Derived from physico-chemical data and process temperature	Release factor: 0.00 % Local release rate: 0.00 g/d Explanation / Justification: See data on volatility presented in Annex 1
Soil	N/A	Final release factor: 0 % Explanation / Justification: No direct releases to soil; incineration of sewage sludge (KVA) or thermic destruction during cement production

Releases to waste other than wastewater

Release factor to waste from the process: for the environmental exposure assessment, release to waste other than wastewater does not need to be considered for the following reasons:

- Vessels that come into contact with Triton X-100 are rinsed out, residual amounts of S/D solution are collected and incinerated.
- A considerable fraction of 4tOP EQV initially used for the process is separated [redacted] and sent to incineration. This fraction will therefore not contribute to any environmental release.

Release factor to waste from sludge recovered from collection basins in the wastewater stream and treatment in the mSTP:

From mass balancing it is concluded that no relevant amounts of 4tOP EQV are lost with sludges evolving from collection basins in the wastewater stream towards the high-load reactor and/or the mSTP. Details are given in Annex 4.

Regarding the mSTP, as much as about 72% of the amount directed to the mSTP may be removed during sewage treatment (see Tier 2a assessment below). Removal will be due to biodegradation and adsorption to sludge. However, both processes cannot be separated for a quantitative estimate, and a fraction directed to sewage sludge cannot be given. The same may apply to sludges from the high-load reactor. Sludges from the high-load reactor are incinerated. Sludges from the mSTP are first used for bio-gas production and then incinerated either in KVA or cement plant. Therefore, no direct releases to soil have to be considered.

5.7.1.1.3 Used Flow Rates

Used flow rates for the Tier 1 and Tier 2 assessments are given in Table 15. The river Aare flow rate was set to the average flow rate (1935-2018) for the 4-month period with lowest average flow (Jan-April; 6 480 000 m3/d) for Tier 1 and Tier 2. For the Tier 2 assessment, a conservative low mSTP discharge rate (lower limit of mSTP) was used instead of the measurement results from the specific days of analytical sampling used for the Tier 1 assessment.

Table 15 Summary of flow rates used in the two scenarios addressed

Scenario number	**Tier 1 assessment (spreadsheet)**	**Tier 2 assessment (EUSES)**
River flow rate (Aare)	River surveillance station Schönau 1935-2018: based on 4-month period with lowest average flow (Jan-April: 75 m^3/s corresponding to **6 480 000 m^3/d**); annual average flow: 122 m^3/s corresponding to 10 540 800 m^3/d	
Discharge from site	[redacted] m^3/d (AM flow rate based on measurements performed at the specific days of analytical sampling)	--*
Discharge from mSTP	[redacted] m^3/d (AM flow rate based on measurements performed at the specific days of analytical sampling)	65 000 m^3/d (lower limit ARA Region Bern) **

*: Discharge from site only used to calculate the release of tOP EQV into wastewater (mass per day) from analytical quantifications performed to derive the release fraction to wastewater.; **: based on information provided by ARA Region Bern

5.7.1.1.4 Properties of 4tOP relevant for the Tier 2 assessment

The Tier 2 assessment requires input data for 4tOP that affect partitioning during wastewater treatment (including adsorption to sludge) as well as biodegradation. The partitioning behaviour of a substance during wastewater treatment depends on its physico-chemical properties. While the Koc (organic carbon-water partition coefficient) value is relevant for the adsorption to sludge, other physico-chemical properties (Henry's Law constant, often calculated from vapour pressure and water solubility) also have an impact on overall partitioning.

For the purpose of the Tier 2 assessment, available data were reviewed and values derived for use in the assessment (see Annex 1-1). The following physico-chemical properties are used in the Tier 2 assessment to model the behaviour of 4tOP in the m-STP (see Table 16, see Annex 1-1 for details).

Table 16 Key physico-chemical and fate properties of 4tOP used in the Tier 2 assessment

Parameter	Unit	Value	T [°C]	Rationale
Melting point	°C	80.5	-	Considered representative in Brooke et al. (2005)
Boiling point	°C	281.5	-	Considered representative in Brooke et al. (2005)
Vapour pressure	Pa	0.21	20	Preferred value in Brooke et al. (2005), see Annex 1-1
Water solubility	mg/L	19	22	Preferred value in Brooke et al. (2005), see Annex 1-1
Log Kow	-	4.12	20.5	Preferred value in Brooke et al. (2005), see Annex 1-1
Henry's Law Constant	Pa.m^3/mol	0.52	24.85	Preferred value in Brooke et al. (2005), see Annex 1-1
Koc	L/kg	9 979	-	Valid QSAR model, supported by field data (see above and Annex 1-1)
BCF (fish)	-	634	-	Preferred value in Brooke et al. (2005), see Annex 1-1
BCF (earthworm)	-	159	-	Calculated by EUSES
BMF (fish)	-	1	-	Default based on ECHA (2016)*

* Applies to both BMF_1 for fish-eating predators and BMF_2 for marine top predators according to ECHA (2016) at log Kow < 4.5.

Biodegradation

The Environmental Risk Evaluation Report by the UK Environmental Agency (Brooke et al., 2005) assumed that 4tOP '*is inherently biodegradable, not fulfilling the criteria for the purposes of the assessment of WWTP. There is evidence for a greater degree of removal in treatment plants than is estimated by sorption only*', which led the authors to suggest *'that some removal by degradation is possible. The effect of assuming inherent degradability meeting the criteria is therefore considered further in the risk characterisation*'. Inherent biodegradation fulfilling the criteria translates into a rate constant for biodegradation in the WWTP of 0.1/h (ECHA, 2016). The criteria referred to in that report are the specific criteria defined in EC (2003). The SVHC Support Document (ECHA, 2011a) stated that 4tOP '*is not readily biodegradable with some indications for a certain degree of biodegradation following a period of adaption*'. For modelling the distribution in an STP, these authors also assumed a rate constant of 0.1/h.

Based on these considerations, the Tier 2 assessment considers (a) a scenario assuming some biodegradation (inherently biodegradable (fulfilling criteria)) as proposed by Brooke et al. (2005) and performed in the SVHC Support Document (ECHA, 2011a)) as well as (b) a scenario assuming no biodegradation, reflecting the uncertainty of this parameter.

5.7.1.1.5 Used Simulation Software

Apart from substance-specific input parameters, many parts of the EUSES software (version 2.1.2), which is considered a standard tool for environmental exposure assessment (ECHA, 2016), were not updated for a long time. Consequently, an ECHA-sponsored study identified several update needs of the software (RIVM, 2014). Among them, the sewage treatment plant model within EUSES (called SimpleTreat; version 3.1 implemented in EUSES) has received some attention. A more recent stand-alone version of SimpleTreat (version 4.0, not yet implemented in EUSES) is available (Struijs, 2014; 2015) and recommended to be implemented in EUSES (RIVM, 2014). This issue was also discussed at a recent workshop where an update of the SimpleTreat model within EUSES to version 4.0 was considered very important[5].

The differences between SimpleTreat 3.1 (EUSES) and SimpleTreat 4.0 are related to several changes in the most recent versions, *e.g.* adaptations of default values for some parameters to more recent knowledge and technological advancements introduced within the last 25 years in wastewater treatment. This involved *e.g.* changes in the default values for the sludge loading rate and the concentration of suspended solids in the effluent. The latter value was changed from 30 mg/L in SimpleTreat 3.1 to 7.5 mg/L in SimpleTreat 4.0, since this lower value better reflects current wastewater treatment technology in Europe according to the developers of the tool (Struijs, 2014; 2015).

Because the relevant mSTP for this site-specific assessment implements most recent technologies in wastewater treatment, it was judged to be better represented by SimpleTreat 4.0 compared to SimpleTreat 3 released in the 1990s. As a consequence of these considerations, SimpleTreat 4.0 was used to estimate the fractions directed to different media (air, water, sludge as well as fraction degraded) during wastewater treatment in the mSTP using the new default value for the concentration of suspended solids in the effluent of 7.5 mg/L. These fractions were used in the Tier 2 assessment and were manually entered in EUSES for full-scale EUSES modelling.

Both in SimpleTreat 4.0 and in full-scale EUSES modelling, the following parameters were set to reflect the characteristics of the mSTP:

Sewage flow of 65 000 m^3/d (instead of default: 2 000 m^3/d), see Table 15[6]

Overall, the following two scenarios are addressed in the Tier 2 assessment (modelling environmental exposure with EUSES):

Tier 2a assessment:

EUSES modelling based on 4tOP, adsorption-based elimination of 4tOP EQVs in the STP, assumption of low biodegradation rate of 0.1/h in STP (corresponding to *inherently biodegradable fulfilling specific criteria*);

Tier 2b assessment:

EUSES modelling based on 4tOP, adsorption-based elimination of 4tOP EQVs in the STP but no biodegradation.

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[5] https://echa.europa.eu/de/-/workshop-on-euses-update-needs, accessed September 2018.

[6] Technically, this is implemented in SimpleTreat 4.0 by entering a number of inhabitants of 836 510, which results in the indicated flow rate under the default assumption of a default sewage flow of 0.2 m^3/(d x PE); PE: population equivalents.

5.7.1.1.6 Tier 1 assessment

Based on the observation that in the discharge of the mSTP all concentrations found for the analytes measured (4tOP; OP1EO to OP17EO) were below the LoQ, it is not a priori clear, whether efficient elimination occurs within the mSTP, or if dilution alone yields concentrations below the LoQ in the mSTP discharge. The Tier 1 assessment estimates the concentrations in the mSTP discharge as well as in the river Aare under the theoretical assumption of no elimination in the mSTP. Accordingly, these results may be taken as a theoretical benchmark against which the results from EUSES modelling considering elimination in the mSTP to differential degrees (in Tier 2a and Tier 2b, see below) can be compared.

For the Tier 1 assessment, measured results for 4tOP EQV in wastewater, measured wastewater flow, and measured mSTP discharge rates obtained for six consecutive days between April 4th and April 9th 2022 were used, together with a conservative assumption for the river Aare flow rate (values given in Table 17 below). The Tier 1 assessment is based on simple spreadsheet calculations on a local level, restricted to the pathway wastewater – mSTP – river Aare.

As described above, the Tier 1 assessment is performed under the following assumptions:

- No biodegradation occurs in the mSTP
- No adsorption-based elimination occurs in the mSTP
- Effect of high-load reactor not considered

The following table shows the Tier 1 calculations. All values for amounts and concentrations are shown as 4tOP EQV.

Table 17 Theoretical 4tOP-EQV concentration in the mSTP discharge and river Aare, based on measured 4tOP-EQV-concentrations in WW and subsequent dilution

	Date of WW sampling						**Mean value (AM)**		
	4 Apr 2022 (PD)	5 Apr 2022 (DaP)	6 Apr 2022 (PD)	7 Apr 2022 (DaP)	8 Apr 2022 (PD)	9 Apr 2022 (DaP)	PD (AM, n= 3)	DaP (AM, n= 3)	Sum (PD, DaP)
Triton X-100 concentration **measured in the WW** at the outlet of the mSTP basin MAB (sampling point 2)									
4tOP-EQV [µg/L]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
WW-volume flow inlet mSTP [m^3/d]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]			
4tOP-EQV in WW [g/d]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Discharge rate of mSTP (m^3/d)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]			
Theoretical (dilution only) Triton X-100 concentration in the mSTP discharge									
4tOP-EQV [µg/L]	3.53	0.673	4.66	0.472	2.54	0.411	3.58	0.518	**4.09**
River flow rate Aare [m^3/d]: 6480000									
Theoretical (dilution only) Triton X-100 concentration in the river Aare									
4tOP EQV [µg/L]	4.91E-02	6.98E-03	5.67E-02	7.19E-03	4.59E-02	6.46E-03	5.06E-02	6.88E-03	**5.74E-02**

As result of the Tier 1 assessment, a dilution-based theoretical worst-case concentration of 4tOP EQV in the mSTP effluent (STP discharge) of 4.09 µg/L was derived. This concentration is about half the analytically derived concentration of 8.3 µg/L based on ½ LoQ for the respective analytes. The latter is mainly determined by the LoQ for 4tOP of 10.3 µg/L. If the LoQ of 1.1 µg/L from OP2EO is used for 4tOP an analytically derived concentration of 4.25 µg/L results, which is nearly equal (slightly lower) than the theoretical concentration of 4.09 µg/L resulting from dilution. Accordingly,

- the theoretical approach of Tier 1 corroborates the analytical result that concentrations of Triton X-100 metabolites in the mSTP are analytically not accessible.
- due to the insufficient analytical sensitivity, analytical measurements in the mSTP effluent cannot indicate any elimination extent of the mSTP.

5.7.1.1.7 Tier 2 assessment

The Tier 1 assessment presented above assumed that neither biodegradation nor adsorption to sludge occurred in the mSTP. This is a highly unlikely worst-case assumption. For more realistic estimates of environmental exposure, full EUSES modelling was performed considering adsorption and biodegradation in the Tier 2a assessment and adsorption only in the (Tier 2b) assessment.

Input values required for an assessment of adsorption to sludge (partition coefficients and physico-chemical properties) and biodegradation are available only for 4tOP. It is noted that even the biodegradation of 4tOP in wastewater or STPs shows some variability, and some uncertainty exists with respect to Koc values. For all other compounds, experimental data are generally lacking. Values predicted by QSAR models would need to be used, which are associated with a high degree of uncertainty.

Therefore, the impact of adsorption and biodegradation in the mSTP is evaluated for 4tOP only. Other substances may show a different behaviour (*e.g.* less adsorption of OPnEO to sludge). The Tier 1 assessment above represents the worst-case benchmark by assuming no biodegradation and no adsorption in the mSTP at all. The Tier 2b assessment represents the worst-case benchmark by assuming no biodegradation.

The fractions directed to different pathways in the mSTP were estimated with SimpleTreat 4.0. Table 18 shows the results of these estimates under the assumption of

- Tier 2a: adsorption and inherent biodegradability
- Tier 2b: adsorption but no biodegradation
- Tier 2a and Tier 2b: Effect of high-load reactor not considered

Table 18 Fractions (in %) of emissions directed to different pathways during treatment in the mSTP: SimpleTreat 4.0 results

Biodegradation assumed	**Inherent biodegradability (Tier 2a)**	**None (Tier 2b)**
Fraction directed to air*	0.3349 %	0.4763 %
Fraction directed to water	**28.26 %**	**41.76 %**
Fraction directed to sludge	51.55 %	57.76 %
Fraction emission degraded	19.85 %	0 %
Total	100 %	100 %

*) While it was argued in section 5.7.1.1.2 that release to air from the mSTP are unlikely to occur, the values modelled by SimpleTreat 4.0 are reported here and were also used in the Tier 2 calculations reported below.

The data demonstrate that consideration of adsorption alone results in a decrease of emissions to water by almost 58 %. Assuming both adsorption and inherent biodegradability leads to an overall removal in the mSTP of about 72%. The fraction estimated to be released to air is small (<0.5 %) in both scenarios.

These fractions are used in the Tier 2 calculations and full EUSES modelling.

Full EUSES modelling

Scenarios and input data

Modelling with EUSES (v. 2.1.2) was performed for the two scenarios Tier 2a and Tier 2b described above. EUSES modelling requires several input data on physico-chemical and environmental fate properties. As discussed above, the data for 4tOP have to be used due to lacking information for other substances. Such a modelling approach may underestimate 4tOP EQV concentrations in the receiving river, since a relatively high removal by adsorption to sludge in the mSTP is predicted based on the comparatively high Koc for 4tOP.

Analytical data presented above for evaluation of the degradation extent in the high-load reactor have shown that ca. 90% of 4tOP EQV are degraded and the remaining 10% of 4tOP EQV are more or less evenly distributed over the full spectrum of EO chain length. It must be considered here that adsorption increases steadily with decreasing EO chain length (see QSAR based estimates for Koc given in Annex 1-2) down to OP1EO (Koc ca. 795 L/kg). In contrast, there is a dramatic increase of Koc from OP1EO to 4tOP by ca. factor 12 (Koc 9979 L/kg), such that analytical data especially for 4tOP will only show the very minor dissolved fraction, while the major amount must be distributed between the fraction adsorbed to sludge and the fraction fully mineralized. While monitoring data do not allow to quantify these fractions, one can reasonably assume that observed 90% degradation efficiency in the high-load reactor is due to degradation via shortening of EO chain down to OP1EO and, predominantly, 4tOP, and those species then being efficiently removed from solution via adsorption and most probably also degradation. If this is the case, the EUSES assessment for 4tOP EQV based on substance properties for 4tOP would be adequate, because this last transformation product of Triton X-100 determines the environmental fate of 4tOP equivalents most pronouncedly. Finally, assuming that environmental emissions are solely in the form of 4tOP is worst case considering its endocrine activity.

The fact that the remaining 10% of 4tOP EQV in the effluent from the high-load reactor are distributed more or less evenly over the full spectrum of EO chain length indicates that there are longer EO chain derivatives with low binding potential to STP sludge and by that prone to escape to the environment. Even if this constitutes the very minor fraction from Triton X-100 not yet fully degraded to 4tOP or mineralized, this fraction will largely leave the high-load reactor with the effluent.

While these considerations are based on measured values for the high-load reactor only, they probably can be at least qualitatively transferred to the mSTP as well. This is supported by the data summarised in Ahel et al. (1994) for nonylphenol ethoxylates, suggesting that 60 % of the inflow load is removed in the mSTP due to adsorption and degradation.

Altogether, EUSES modelling of Triton X-100 derived 4tOP EQV exposure based on substance properties of 4tOP is concluded to be the most reliable and relevant approach.

Input data for modelling scenarios Tier 2a and Tier 2b are given in Table 12 and Table 14 above. In scenario Tier 2a, inherent biodegradability fulfilling specific criteria

(biodegradation rate constant of 0.1/h) is assumed based on the data outlined above. For both scenarios distribution of STP sludge on agricultural soil can be excluded.

Some technical adaptations in EUSES are required, since the software was not developed for site-specific assessments (RIVM, 2004). For example, the default assumption in EUSES that 80 % of the regional emissions are directed to wastewater (and therefore treated in a hypothetical STP) while the remaining 20 % are directly discharged to surface water was changed to 100% of the wastewater emissions directed to the mSTP[7].

Results of the Tier 2 exposure assessment

Table 19 shows the results of the assessment in EUSES for the two Tier 2 scenarios described above. For comparison, also the Tier 1 results are shown. All concentrations are given as 4tOP EQV. Since the site does not release the substance to marine environments, no exposure and risk assessment is presented for marine water and sediment.

The PEC_mSTP from the Tier 2b scenario (worst case) is 2.43 µg/L (data not shown) and thus pronouncedly below the PNEC_STP (100 µg/L; see Table 11). This comparison demonstrates that the releases do not contribute to any toxicity towards the microorganisms in the mSTP and no further details are shown below.

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[7] Note that these changes are technical adaptations to perform a site-specific assessment with EUSES (which was not developed to perform such site-specific assessments). Thus, a hypothetical regional STP has to be considered to address regional (*i.e.* background) concentrations, while such a regional STP does not exist in reality.

Table 19 Tier 2 assessment in EUSES: local and regional concentrations (as 4tOP EQV) in the environment

Protection target	Unit	Tier 2a	Tier 2b	Tier 1 (dilution)
Local Assessment				
Annual average local PEC in air (total)	ng/m^3	0.110	0.157	--
Local PEC in surface water during emission episode (dissolved)	**ng/L**	**16.2**	**23.9**	**57.4***
Annual average local PEC in surface water (dissolved)	ng/L	5.14	7.61	17.9*
Local PEC in fresh-water sediment during emission episode	µg/kg dw	16.2	24.0	--
Local PEC in agric. soil (total) averaged over 30 days	µg/kg dw	0.00124	0.00298	--
Local PEC in agric. soil (total) averaged over 180 days	µg/kg dw	0.00125	0.00303	--
Local PEC in grassland (total) averaged over 180 days	µg/kg dw	0.00214	0.00552	--
Regional Assessment				
Regional PEC in air (total)	ng/m^3	4.04E-04	6.69E-04	--
Regional PEC in surface water (total)	ng/L	0.123	0.195	--
Regional PEC in sediment (total)	µg/kg dw	0.227	0.361	--
Regional PEC in agricultural soil (total)	µg/kg dw	4.4E-05	3.23E-04	--
Secondary poisoning				
Concentration in fish for secondary poisoning (freshwater)	mg/kg ww	1.67E-03	2.47E-03	--
Concentration in earthworms from agricultural soil	mg/kg ww	5.22E-07	1.35E-06	--
Concentration in fish for fish-eating marine top-predators	mg/kg	1.14E-03	1.14E-03	--

*) The spreadsheet-based concentrations from the Tier 1 assessment cannot take account of the regional background concentration but which is of very low magnitude (see Tier 2 scenarios).

Comparing the local PEC in surface water during emission episode between the scenarios assessed shows that – in comparison with dilution alone (Tier 1) – the adsorption based elimination (Tier 2b) in the mSTP results in a PEC lower by a factor of 2.4. Considering in addition a low biodegradation rate in scenario Tier 2a, this results in a PEC lower by a factor of 1.48 compared to scenario Tier 2b and a factor of 3.54 lower compared to dilution alone (Tier 1). This is equivalent to an elimination extent in the mSTP by 72% due to the combination of adsorption and biodegradation.

Environmental risk characterization

The exposure estimates derived in this CSR are reported in Table 20 together with their corresponding RCRs resulting from the comparison with respective PNECS/EQS values. PNEC/EQS values used are summarized in Table 11, with details on derivation and justification given in Annex 2. This comparison is not intended to demonstrate adequate control of risks, but only serves the purpose of demonstrating low exposures against an existing benchmark and informs comparisons across compartments.

The following tables summarise the exposure concentrations and risk characterisation ratios (RCRs) for the local (Table 20) and regional (Table 21) scale[8]. No risk characterisation is performed for the air compartment because of the extremely low concentrations (<0.2 ng/m^3; see Table 19). This approach is in agreement with the one by Brooke et al. (2005), who also performed no risk assessment for this compartment. Finally, human exposure via the environment is not assessed since this is not a matter of concern in the context of this report. The assessment for predators is included in the table for the local assessment, since EUSES estimates exposure of predators at a combined scale considering the predation pattern (local/regional) of the specific predators.

Table 20 Exposure concentrations and risks for the environment – local scale

Protection target	**Unit**	**Exposure concentration**			**Risk characterisation ratio (RCR)**		
		Tier 2a	**Tier 2b**	**Tier 1**	**Tier 2a**	**Tier 2b**	**Tier 1**
Freshwater	µg/L	1.62E-02	2.39E-02	5.74E-02	1.62E-01	2.39E-01	5.74E-01
Sediment (freshwater)	µg/kg dw	16.2	24.0	--	1.62E-01	2.40E-01	--
Agricultural soil	µg/kg dw	1.24E-03	2.98E-03	--	5.39E-07	1.30E-06	--
Predator freshwater	mg/kg food	1.67E-03	2.47E-03	--	7.08E-04	1.05E-03	--
Predator terrestrial	mg/kg food	5.22E-07	1.35E-06	--	2.21E-07	5.72E-07	--

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[8] see EUSES background report by RIVM (2004) for definition of local and regional scale

Table 21 Exposure concentrations and risks for the environment – regional scale

Protection target	Unit	Exposure concentration		Risk characterisation ratio (RCR)	
		Tier 2a	Tier 2b	Tier 2a	Tier 2b
Freshwater	µg/L	1.23E-04	1.95E-04	1.23E-03	1.95E-03
Sediment (freshwater)	µg/kg dw	2.27E-01	3.61E-01	2.27E-03	3.61E-03
Agricultural soil	µg/kg dw	4.40E-05	3.23E-04	1.91E-08	1.4E-07

The data can be summarized as follows (focus on local assessment):

- Because no sewage sludge is spread on agricultural soils, the terrestrial compartments including terrestrial predators show lower PECs than PECs for respective water and sediment compartments. The local aquatic PEC directly transforms to the PEC for the local sediment. The focus of discussion is therefore on the aquatic PECs/RCRs.
- The highest RCR of 0.57 is obtained from the Tier 1 assessment for freshwater considering only dilution but neither elimination by adsorption nor biodegradation in the mSTP. This scenario is unrealistic but meant as a benchmark for the PEC (water) to be expected under those theoretical assumptions, given that actual concentrations are analytically not accessible in the mSTP effluent.
- The next highest RCR of 0.24 is obtained in scenario Tier 2b for water (sediment) assuming adsorption to sludge in the mSTP based on the properties of 4tOP. No biodegradation of 4tOP EQV is assumed in this scenario. While the adsorption potential of OPnEO decreases with each EO unit, from the analytical results obtained before and after the high-load reactor as well as from the results summarized for nonylphenol ethoxylates by Ahel et al. (1994) it can be concluded that the ethoxylate chain is efficiently degraded during mSTP passage (for details, see above). Therefore, distribution assumptions based on 4tOP may somewhat overestimate adsorption-based elimination in the mSTP but are still assumed to be the most realistic and meaningful way for modelling. Removal via adsorption amounts to ca. 58%.
- Scenario Tier 2a results in the lowest RCR of 0.162 for freshwater (sediment) out of the three scenarios. This scenario addresses the combined effect of adsorption to sludge and some ultimate biodegradation in the mSTP, leading to a total elimination in the mSTP by 72%. This scenario can be regarded as the most realistic one. While results of the high-load reactor cannot be transferred 1:1 to the mSTP, at least 90% elimination could be confirmed for the treatment in the high-load reactor via detailed analytical measurements of 4tOP(0-17)EO. Further, the data summarised in Ahel et al. (1994) for nonylphenol ethoxylates allow concluding that 60 % of the inflow load is removed in the mSTP due to adsorption and degradation.

Scenarios Tier 2a and Tier 2b addressed above did not consider the elimination extent of about [redacted] % achieved on average by the high-load reactor (outlined in detail in section 5.3.2.2). In Table 22 below this additional removal was taken into account by multiplication of PEC-values derived from Tier 2a assessment with the fraction remaining after the high-load reactor ([redacted])9. Accordingly, all RCRs including the most critical RCR for fresh water are still considerably reduced.

Table 22 Impact of the activity of the high-load reactor on PECs and RCRs compared to scenario Tier 2a results

Protection target	Unit	Tier 2a	RCR	Tier 2a & high load reactor	RCR
Local Assessment					
Annual average local PEC in air (total)	ng/m³	0.11	--	[redacted]	[redacted]
Local PEC in surface water during emission episode (dissolved)	ng/L	16.2	1.62E-01	[redacted]	[redacted]
Local PEC in fresh-water sediment during emission episode	µg/kg dw	16.2	1.62E-01	[redacted]	[redacted]
Local PEC in agric. soil (total) averaged over 30 days	µg/kg dw	1.24E-03	5.39E-07	[redacted]	[redacted]
Regional Assessment					
Regional PEC in surface water (total)	ng/L	0.123	1.23E-03	[redacted]	[redacted]
Regional PEC in sediment (total)	µg/kg dw	0.227	2.27E-03	[redacted]	[redacted]
Regional PEC in agricultural soil (total)	µg/kg dw	4.40E-05	1.91E-08	[redacted]	[redacted]
Secondary poisoning					
Concentration in fish for secondary poisoning (freshwater)	mg/kg ww	1.67E-03	7.08E-04	[redacted]	[redacted]
Concentration in earthworms from agricultural soil	mg/kg ww	5.22E-07	2.21E-07	[redacted]	[redacted]

5.7.1.2 Conclusion

The results outlined above demonstrate that even for the unrealistic theoretical scenario Tier 1 (dilution only; neither adsorption nor biodegradation) all RCRs are pronouncedly below one. According to the more realistic scenarios Tier 2a and Tier 2b the highest RCR (local water during emission episode) is between 0.162 and 0.239. The lower value is considered most realistic implicating moderate biodegradation (rate constant 0.1/h) in addition to elimination by adsorption, the only removal mechanism considered in scenario Tier 2b.

As indicated above, modelling partitioning in the mSTP based on physico-chemical and fate data for 4tOP bears the risk of underestimating the mobility especially of OP(≥3)EO. This fraction is deemed to be low based on the removal data for Triton X-100 obtained for the biological treatment in the high-load reactor and supported by data from Ahel et al. (1994) on removal of nonylphenolethoxylates in mSTPs of Switzerland. However, the Triton X-100 molecules not sufficiently shortened due to the biological activity in the activated sludge plant

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[9] Due to the linear relationship between the amount released to waste water and the resulting PECs, this simple adaption yields correct results.

during their hydraulic residence time will predominantly not be retained by adsorption to sludge, but will largely escape with the mSTP effluent due to their significantly lower Koc.

Since these compounds are not considered to possess endocrine disruptive properties, the occurrence of any endocrine disruptive effects close to the discharge point of the mSTP is highly unlikely. Such effects will only occur if these compounds are further degraded to 4tOP in the freshwater compartment. As a consequence, 4tOP may only be generated further away from the discharge point of the mSTP after additional dilution has occurred.

Finally, both Tier 2 scenarios are worst-case because the efficient elimination of more than 90% of 4tOP EQV of the influent by the high-load reactor has not been considered (see section 5.3.2.2 for details). [redacted] Considering the analytically determined 90% depletion efficiency of the high-load reactor, between [redacted] wastewater passing the reactor) and [redacted] wastewater passing the reactor) of total 4tOP EQV emitted by the plant will be removed before entering the mSTP. To account for this in relation to PECs and RCRs, those values are given in Table 22 assuming an average wastewater flow of [redacted] through the high-load reactor.

Future perspectives

Based on the observation that under the current situation [redacted] and in awareness of the responsibility over the ecological fingerprint of the Rhophylac® production, CSL is currently investigating the feasibility of various Triton X-100 on-site degradation options (for details see Annex 5). With the implementation of such an on-site treatment plant, an efficient (ca. 88%) reduction of Triton X-100 in the wastewater coming directly from the Rhophylac® production is anticipated prior to discharge to the mSTP. As a consequence the release factor will be reduced to approximately [redacted] [range 0.5 - 5%] after implementation of this measure. In the combination of these different measures,

a) (future) on site wastewater treatment plant,
b) anaerobic degradation in the high-load reactor ([redacted]),
c) reduction of Triton X-100 amount needed by stepwise substitution (depending on the stepwise market approvals)

efficient measures will be taken to minimise the amount of Triton X-100 to be released to the communal part of the mSTP and to the environment until a complete substitution will be possible due to granted approvals (see table below).

Table 23 Predicted mass balance considering the impact of the on-site WW treatment

Parameter	**kg 4tOP EQV/year**	
	[redacted]	[redacted]
Amount used	[redacted] [33-330]	[redacted] **[33-330]**
Excess amount of [redacted] kg S/D solution per batch containing [redacted] kg Triton X-100 is collected in bottles and INCINERATED	[redacted]	[redacted]
Triton X-100 separated [redacted] and INCINERATED ([redacted] of amount used)	[redacted]	[redacted]
Released to wastewater (based on monitoring by the outflow of the column CM1, see Table 6)	[redacted]	
Released to wastewater considering about 88% minimisation in the future on site WW treatment plant		[redacted]
of which are removed in the high load reactor by anaerobic biodegradation	[redacted]	[redacted]
of which are removed in the mSTP by adsorption to sludge and biodegradation (Scenario 2a)	[redacted]	[redacted]
emitted to surface water	6.8	**0.84**

*not considered as the release to WW is based on monitoring data

The current PEC for surface water (during emission episode) derived from the most relevant Tier 2a exposure assessment and the reduced PECs considering the effect of the high-load reactor and the anticipated minimisation of about 88% by the future on-site wastewater treatment are shown in the following figure. This illustration shows, how efficiently the future emission will be minimised by the planned wastewater treatment, even without considering the stepwise substitution of Triton X-100. [redacted]

[redacted]

Figure 5 Impact of minimisation measures on the PEC surface water during an emission period (confidential information)

Note that an impact assessment is presented in the context of the combined AoA & SEA report.

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Annex 1 Physico-chemical data

Annex 1-1 Evaluation of data for 4tOP

The table at the end of this annex summarises data for the most relevant physico-chemical properties of 4tOP (as used in the Tier 2 assessment) based on a selected number of sources:

- Dossier: REACH registration dossier for 4tOP, https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15074/1, accessed 21 September 2022
- SVHC doc.: ECHA (2011)
- UK-EA: Brooke et al. (2005)
- US HPVIS: https://ofmpub.epa.gov/oppthpv/quicksearch.display?pChem=100234, accessed October 2018
- IUCLID 2000: European Chemicals Bureau, 2000. IUCLID, International Uniform Chemical Information Database. Edition II. EUR 19559 EN, European Commission

With respect to the adsorption behaviour of 4tOP during sewage treatment, application of the most reliable Koc value is critically important. As a consequence, this value is discussed here in more detail.

Koc value

For the Koc value (and derived partition coefficients relevant for the adsorption to sewage sludge) Brooke et al. (2005) simply used a value of 2 740 L/kg that is predicted in EUSES software using the QSAR model for ‘predominantly hydrophobic’ compounds based on a log Kow of 4.12. A justification for using this QSAR model is not provided.

The algorithms for predicting Koc from log Kow in EUSES were derived by Sabljić et al. (1995). According to this publication, the model for ‘predominantly hydrophobics’ was developed almost exclusively on data for halogenated or alkylated aromatics and alkanes without any contribution from phenols. In contrast, these authors noted that substituted phenols (which they considered to be among the ‘nonhydrophobics’) and similar compounds showed a different trend for the relationship between log Kow and log Koc. For phenol-type chemicals, they derived a different algorithm that is based on substituted phenols (Cl, Br, CH_3, OH, NO_2, CH_3O) and similar compounds (Sabljić et al., 1995). These authors derived the following algorithms that are implemented in EUSES (naming refers to the QSAR models implemented in EUSES):

Predominantly hydrophobics:	$\log Koc = 0.1 + 0.81 \times \log Kow$
Phenols, anilines, benzonitriles, nitrobenzenes:	$\log Koc = 0.90 + 0.63 \times \log Kow$

With the log Kow of 4.12, the first algorithm results in a Koc value of 2 740 (as used in Brooke et al. (2005)), while the second algorithm results in a log Kow value of 3 130 L/kg. It must be noted that the terms ‘hydrophobic’ and ‘nonhydrophobic’ in the development of these algorithms is less based on log Kow values, but rather on functional groups being absent or present. For example, some substances used in the development of the first algorithm have log Kow values below 3 (*e.g.* most of the halogenated alkanes), while some of those used in the development of the second algorithm have log Kow values above 3, *e.g.* the higher chlorinated phenols (Sabljić et al., 1995). These authors also noted that Koc estimates for predominantly hydrophobic chemicals based on log Kow have large uncertainties, particularly at log Kow values in the range of 4-7.5. This observation in fact led them to develop a model based on the molecular connectivity index (MCI), which, however, is not implemented in EUSES.

The EPI Suite™ (version 4.11) of the US Environmental Protection Agency (US EPA, 2011) includes the KOCWIN module (v2.00), which allows estimating Koc by two models: (a) a model based on log Kow and (b) a model based on the MCI (independent of log Kow), similar to the one referred to above, but largely based on another publication (Meylan et al., 1992). The model based on log Kow results in a Koc of 2 349 L/kg (based on a log Kow of 4.12; details not shown), while the MCI-based model results in a considerably higher Koc of 9 979 (see Annex 1-2).

Even higher Koc values of up to 18 000 L/kg in river bed sediment and up to 390 000 L/kg in suspended sediment were observed in experimental studies in the UK (Johnson et al., 1998; Jürgens et al., 2009). Additional studies in urban freshwater (Japan) and estuarine environments (USA) also indicate Koc values well above 10 000 L/kg (Ferguson et al., 2001; Isobe et al., 2001). The Japanese study also derived Koc values for four municipal STPs, with average Koc values of 10 223 in the primary effluent and 25 704 L/kg in the secondary effluent (Isobe et al., 2001). These studies consistently noted that Koc values measured in the field were higher (by about one order of magnitude) than those obtained from laboratory studies and those predicted from log Kow (Ferguson et al., 2001; Isobe et al., 2001; Jürgens et al., 2009). These studies are presented in some more detail in Annex 1-1. Some of the UK data are also discussed in Brooke et al. (2005) and the SVHC Support Document (ECHA, 2011a) and taken as an indication of a strong sorption potential of 4tOP to soil, sludge and sediment. Nonetheless, Brooke et al. (2005) used the lowest of the Koc values discussed (*i.e.* the value of 2 740 L/kg predicted in EUSES) in their risk assessment. Within the SVHC Support Document (ECHA, 2011a), it remains somewhat unclear, which Koc was actually used in the distribution modelling.

Overall, the Koc of 9 979 L/kg is used in the exposure assessment, since it

- is based on a more appropriate QSAR model than the one used in Brooke et al. (2005)) and reduces the uncertainty associated with estimates based on log Kow (Meylan et al., 1992; Sabljić et al., 1995);
- is strongly supported by experimental and field data that consistently showed Koc values of 10 000 L/kg or above.

Parameter	**Unit**	**Value**	**T [°C]**	**Type of study**	**Comment**	**Source**
Vapour pressure	Pa	2	38	EXP, ASTM-D 2879 (isoteniscope), non-GLP; no further data	Original value 0.02 mbar; unpublished report (2010); RL 1	Dossier
		1	20	non-GLP; no further data; cited from SIDS (1993)	Possibly based on safety data sheet (1988)	SVHC doc, UK-EA, IUCLID 2000
		0.21	20	EXP, non-GLP; no further data; measurement results for 6 different temperatures reported	Extrapolated from 6 measured values (at 150-276.9 °C); **preferred value in UK-EA**	UK-EA, US HPVIS, IUCLID 2000
		0.091	--	QSAR (MPBWIN v1.30)	no temperature given, probably 25°C (default)	US HPVIS
		<1.0	20	non-GLP; no further data	Based on safety data sheet (1993)	IUCLID 2000
Water solubility	mg/L	17-19	22	EXP, GLP, generator column	Analytical Bio-Chemistry Laboratories, Inc, unpublished, report No. 31914, 1984; 17 mg/L for deionized water; 19 mg for aquatic test water; 19 mg/L **preferred value in UK-EA**	SVHC doc, UK-EA, US HPVIS, IUCLID 2000
		12.6	20.5	EXP, generator column technique	± 0.5 mg/L; N=3	UK-EA; IUCLID 2000; Literature (Ahel and Giger, 1993)
		10	25	Original reference unknown	Reported by Waern (2000)	UK-EA

Parameter	Unit	Value	T [°C]	Type of study	Comment	Source
		7	20	EXP, ASTM E 1148 – 02 (flask method), non-GLP	Arithmetic mean of triple determination (24h: 6.0 mg/L; 48 h: 6.6 mg/L; 72 h: 8.6 mg/L); unpublished report (2009), RL1	Dossier
		4.82	--	QSAR (WSKOW v1.33)	no temperature given, probably 25°C (default)	US HPVIS
Log Kow	--	5.3	--	QSAR, MedChem-Programme (Leo, Hansch) version 1989		UK-EA, IUCLID 2000
		5.28	--	QSAR (KOWWIN v1.63, EPI Suite)		UK-EA, US HPVIS
		4.8	22	EXP, OECD 117 (HPLC-method), non-GLP	pH 6.6; unpublished report (2009), RL 1	Dossier
		4.5	23	EXP, OECD 107 (shake flask), non-GLP	Unpublished report (1989)	UK-EA, IUCLID 2000
		4.12	20.5	EXP, OECD 107 (shake flask), non-GLP	Ahel and Giger, 1993; **preferred value in UK-EA**	UK-EA, IUCLID 2000, US HPVIS
		3.7	--	EXP, non-GLP; HPLC method (analytics by UV absorbance); cited from SIDS (1994)	McLeese et al, 1981	SVHC doc., UK-EA, IUCLID 2000
Henry's Law Constant	$Pa.m^3/mol$	2.3	20-22	Calculated from WS (19 mg/L), VP (0.21 Pa) and MW (206.33 g/mol)		UK-EA, Dossier

Parameter	Unit	Value	T [°C]	Type of study	Comment	Source
		0.58	25	QSAR, HENRYWIN (EPI Suite, 2004)	Average between predictions of 0.46 and 0.70 Pa.m^3/mole	UK-EA, Dossier
		0.52	24.85	EXP, dynamic equilibrium system; sea water	Orig. value: 195 M/atm ± 68 at 298 K; **preferred value in UK-EA**	Dossier, UK-EA, SVHC doc,
		0.079	13.85		Orig. value: 1277 M/atm ± 447 at 287 K	Dossier, UK-EA
		0.050	4.85		Orig. value: 2008 M/atm ± 703 at 278 K	Dossier, UK-EA
Koc	L/kg	3 500-18 000 (bed sediments) 82 000-390 000 (suspended sediments except Thames river)	20	EXP, similar to OECD 106; river sediment samples (8 sampling sites from three rivers) were used to study adsorption-desorption of OP	Adsorption was positively correlated with small particle size, high carbon, silt and clay content; suspended sediments (mainly organic aggregates) adsorbed much higher quantities of OP compared to respective bed sediments with exception of Thames samples consisting largely of algae with much lower Koc (3 281 L/kg) determined.	Dossier; UK-EA; SVHC doc, Literature (Johnson et al., 1998)
		≥ 17 400	-	EXP, similar to OECD 106; based on re-diluted river Calder susp. sediment (270 mg/L)	Calculated from Kd 1427 L/kg (8.2% OC); 2 further suspended sediment samples showed higher Kd	Literature (Jürgens et al., 2009)
		25 704	-	EXP, 4 STPs in the Tokyo metropolitan area, secondary effluent	Calculated by authors from concentrations in particulate matter and water; additional values: 10 233 (primary effluent) and 44 668 (river)	Literature (Isobe et al., 2001)

Parameter	Unit	Value	T [°C]	Type of study	Comment	Source
		151 356	-	EXP, urbanised estuarine sediments in New Jersey, USA	Calculated by authors from concentrations in sediment and water	Literature (Ferguson et al., 2001)
		2 740	-	Based on EUSES QSAR (log Kow 4.1)	QSAR Model: ‘predominantly hydrophobics’; **preferred value in UK-EA**	UK-EA; SVHC doc.
		9 979	-	QSAR (see Annex 1-2 below)	MCI-based model implemented in the EpiSuite™, **preferred value (see discussion above)**	
BCF (fish)	--	740	--	EXP, ASTM 1993, GLP not specified; RA from nonylphenol	Time of plateau: 14 days; flow-through conditions	Dossier
		634	--	QSAR, calculated within EUSES from Kow (log Kow 4.12)	Equation according to Veith et al., 1979; **preferred value in UK-EA**	SVHC doc, UK-EA
		46 - 297	--	EXP, Field study involving 8 rivers and 6 species	Water concentrations were compared with fish tissue concentrations (Tsuda et al., 2000)	UK-EA; SVHC doc.
		261 (±62, n= 4) – 297 (±194, n= 3)	--	EXP, Laboratory (Oryzias latipes) and field study (Plecoglossus altivelis) on 3 rivers, respectively	Water concentrations were compared with whole fish concentrations (Tsuda et al., 2001); no regulatory protocols followed	UK-EA, SVHC doc.
		471	--	EXP, Laboratory study (Oncorhynchus mykiss) with focus on metabolism	Whole fish after 10 days exposure (Ferreira-Leach and Hill, 2001)	UK-EA; SVHC doc.
		3291	--	QSAR, based on experimental values for a group of alkylphenols	McLeese et al. (1981); according to UK-EA, non-reliable due to inadequacies in study design	UK-EA

Parameter	**Unit**	**Value**	**T [°C]**	**Type of study**	**Comment**	**Source**
		113-469	--	EXP, no data on GLP	MITI-List, 2002; Cyprinus carpio, 100 µg/L 4-tert-OP; at 10 µg/L, BCF of 12-135 determined	SVHC doc.

Annex 1-2 Predicted data for 4tOP; OPnEO and OPnEC

Physico-chemical data were predicted using US EPA's EpiSuite™ (version 4.1). The EpiSuite™ contains several models to predict physico-chemical (and environmental fate) properties. Full documentation for the models described below is available in the help file of the software. Since CAS numbers are not available for most of the chemical species of interest, data predictions were based on SMILES notations created for each chemical. Correct structures were verified after insertion of the SMILES notation in the EpiSuite™. For 4tOP, reliable experimental data are available for most physico-chemical properties (see Annex 1-1 above) that were used in the Tier 2 assessment. The data presented for 4tOP in this Annex 1-2 are the ones predicted by the models in the EpiSuite™.

Values for the following parameters were predicted:

Parameter	**Prediction model**
Molecular Formula	Automatically assigned based on SMILES
Molecular weight [g/mol]	Automatically assigned based on SMILES
Conversion factor	Factor used for converting masses of substances to mass of 4-t-OP
Vapour pressure (25 °C) [Pa]	MPBPWIN, v1.43 (estimated vapour pressure from estimated melting/boiling point)
Log Kow	KOWWIN, v1.68
Water solubility (25 °C) [mg/L]	WSKOWWIN, v1.42, WATERNT, v1.01
Koc [L/kg]	KOCWIN, v2.00
Photodegradation half-life [d]	AOPWIN, v1.92

This section describes the justification for the models and approaches used, while the estimated physico-chemical properties are presented at the end of this Annex.

Vapour pressure (25 °C) [Pa]

The MPBPWIN model as implemented in EpiSuite™ calculates the vapour pressure by three different methods: (1) Antoine method, (2) modified Grain method and (3) Mackay method. All methods rely on the boiling point of the substance and the melting point is required for solids as well. The MPBPWIN estimates the vapour pressure with all three methods and automatically selects a final value.

Log Kow

The KOWWIN model is based on the type and number of chemical fragments (atoms or larger functional groups) present in the molecule. For example, the five methyl groups in tertiary octyl moiety of octylphenols ethoxylates are counted as five methyl groups attached to an aliphatic carbon, while the terminal hydroxyl group of the polyethoxylate is counted as one OH group attached to an aliphatic carbon. In 4tOP, this latter group is counted as one OH group attached to an aromatic ring.

Water solubility (25 °C) [mg/L]

Two different models are available within the EpiSuite™ to estimate the water solubility: (a) WSKOWWIN estimates water solubility from the (estimated) log Kow and the molecular weight and (b) WATERNT estimates water solubility based on chemical fragments using the method as described for log Kow above. Values from both models are presented below. It is obvious that the values estimated by the two methods differ substantially and the difference increases with the number of EO units. Based on the limited experimental data available, the WATERNT estimates appear to be more reliable (see Figure A1-1 below).

Koc

As discussed in detail in Annex 1-1 above, Koc was estimated using the MCI-based model implemented in the EpiSuite™, since this is considered to be more adequate than the one based on the log Kow.

Photodegradation half-life [d]

The AOPWIN model calculates the half-life (T1/2) for the reaction of photochemically generated hydroxyl radicals with organic molecules. The values shown here are based a 12-h daylight cycle and a hydroxyl radical concentration of 1.5 x 10^6 radicals/cm^3 as recommended in the help file of the software.

4-t-OP and lower ethoxylated OPnEOs

Parameter	**4-t-OP**	**OP1EO**	**OP2EO**	**OP3EO**
Molecular Formula	$C_{14}H_{22}O_1$	$C_{16}H_{26}O_2$	$C_{18}H_{30}O_3$	$C_{20}H_{34}O_4$
Molecular weight [g/mol]	206.33	250.38	294.44	338.49
Conversion factor	1	0.824	0.701	0.610
Vapour pressure [Pa]	0.0691	0.00193	0.0000187	1.03E-06
Log Kow	5.28	4.86	4.59	4.31
Water solubility (from log Kow) [mg/L]	4.821	5.356	5.162	4.864
Water solubility (from fragments)	31.633	10.787	20.13	36.725
KOC [L/kg]	9979.30	795.24	646.85	526.26
Photogradation half-life [d]	0.252	0.273	0.201	0.159

Higher ethoxylated OPnEOs

Parameter	**OP4EO**	**OP5EO**	**OP6EO**	**OP7EO**	**OP8EO**	**OP9EO**	**OP10EO**	**OP11EO**
Molecular Formula	$C_{22}H_{38}O_5$	$C_{24}H_{42}O_6$	$C_{26}H_{46}O_7$	$C_{28}H_{50}O_8$	$C_{30}H_{54}O_9$	$C_{32}H_{58}O_{10}$	$C_{34}H_{62}O_{11}$	$C_{36}H_{66}O_{12}$
Molecular weight [g/mol]	382.55	426.6	470.65	514.71	558.76	602.81	646.87	690.92
Conversion factor	0.539	0.484	0.438	0.401	0.369	0.342	0.319	0.299
Vapour pressure [Pa]	5.38E-08	2.39E-09	1.01E-10	5.16E-12	2.58E-13	1.25E-14	5.9E-16	2.7E-17
Log Kow	4.04	3.77	3.49	3.22	2.94	2.67	2.39	2.12
Water solubility (from log Kow) [mg/L]	4.506	4.118	3.724	3.338	2.970	2.627	2.31	2.023
Water solubility (from fragments)	65.864	116.56	204.07	354.16	610.13	1044.6	1778.8	3015
KOC [L/kg]	428.06	348.27	283.28	230.47	187.46	152.52	124.06	100.93
Photogradation half-life [d]	0.132	0.112	0.098	0.087	0.078	0.071	0.065	0.060

Relevant carboxylic acid degradation products (OPnECs)

Parameter		**OP1EC**	**OP2EC**	**OP3EC**
Molecular Formula		$C_{16}H_{24}O_3$	$C_{18}H_{28}O_4$	$C_{20}H_{32}O_5$
Molecular weight [g/mol]		264.37	308.42	352.48
Conversion factor		0.780	0.669	0.585
Vapour pressure [Pa]		0.000816	0.000071	0.00000502
Log Kow		5.09	4.82	4.54
Water solubility (from log Kow) [mg/L]		2.192	2.096	1.964
Water solubility (from fragments)		6.1904	11.461	20.785
KOC [L/kg]		601.20	489.10	397.80
Photogradation half-life [d]		0.326	0.228	0.176

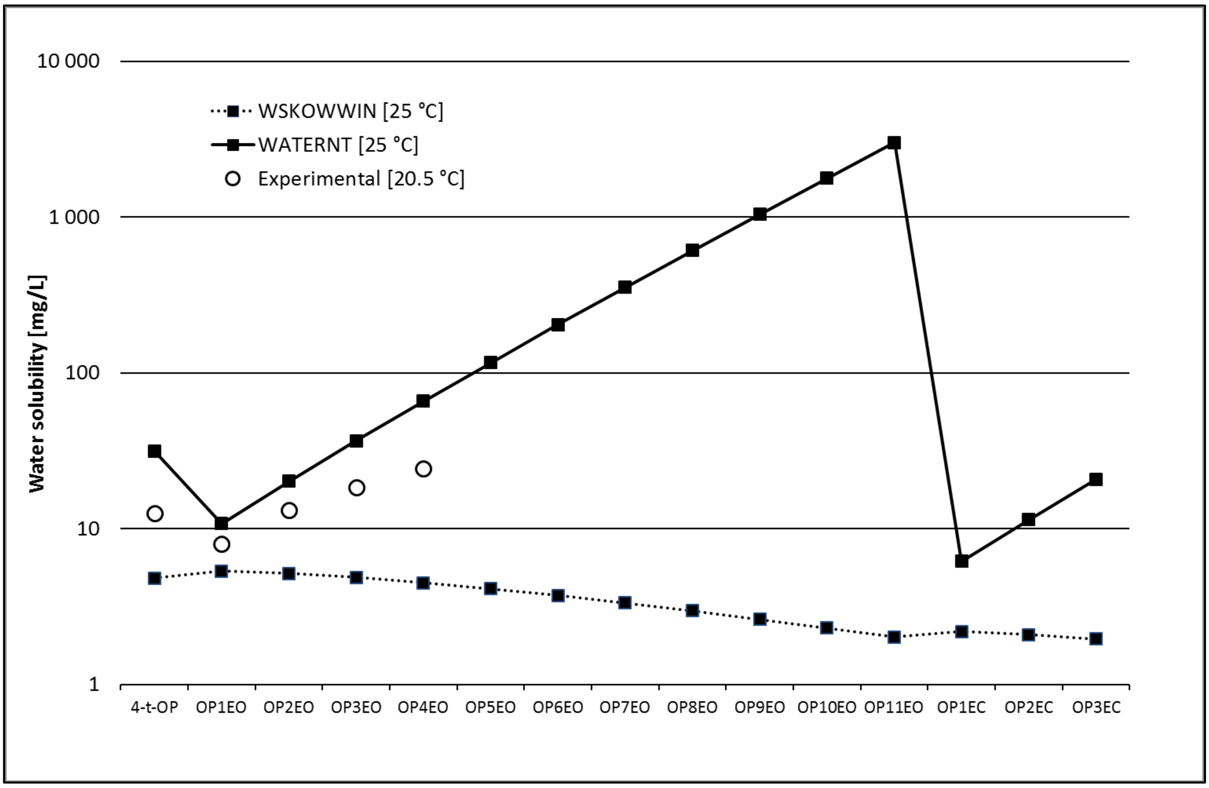

Figure A1- 1 Water solubility of 4tOP, OPnEOs and OPnECs estimated by two models and comparison with experimental data (Ahel and Giger, 1993)

Annex 2 PNEC derivation

This section presents relevant Environmental Quality Standards (EQSs) and Predicted No-Effect Concentrations (PNECs). These values are used in section 5.7.1.1.7 to calculate Risk Characterisation Ratios (RCRs). However, RCRs were only used to demonstrate low exposures against an existing benchmark, but this approach is not intended to imply adequate control of all risks.

Table 24 summarises the PNEC values used in section 5.7.1.1.7 for the risk characterisation ratio calculation.

Table 24 Hazard assessment conclusion for the environment.

Protection target	Description of value	Hazard conclusion
Freshwater	EQS – AA-QS inland surface waters*	0.1 µg/L
Sediment (freshwater)	PNEC sediment (EPM based on EQS), freshwater (Koc 9979 L/kg)	100 µg/kg sediment dw**
Sewage treatment plant	PNEC STP	100 µg/L
Air	No hazard identified	--
Agricultural soil	PNEC Soil	2.3 mg/kg soil dw
Predator	PNEC secondary poisoning oral (predators)	2.36 mg/kg food

* see DIRECTIVE 2008/105/EC - value rounded to one significant figure compared to EQS background document (EC, 2005) – value: 0.122 µg/L.

** Based on rounded EQS-value of 0.1 µg/L – the corresponding value (not used for the risk assessment) based on 0.122 µg/L is 122 µg/kg sed. dw

Hazard Assessment for Freshwater

The EQS (AA-QS) for inland surface waters (EC, 2005) was based on a "traditional" ecotoxicity base set with an assessment factor of 50 applied to the NOEC value of 6.1 µg/L for growth in a chronic study with fish. An AF of 50 was chosen because a) of the uncertainty associated with data for aquatic algae (but algae are not considered the most sensitive trophic level) and more importantly b) the freshwater invertebrate *Gammarus pulex* was more sensitive than any other tested organism in the acute dataset (EC50 96 h: 13.3 µg/L), but there was not a chronic study available for this species. The data with *G. pulex* suggested that certain aquatic invertebrates could be more sensitive than fish in chronic exposures.

Given the endocrine activity of 4tOP, relevant data indicating effects of an endocrine mode of action was also considered (EC 2005). Comparing available data in fish involving endocrine effects potentially caused by an endocrine mode of action, the lowest valid NOEC (21 d) for fish of 1.6 µg/L 4tOP was based on induction of vitellogenin in adult male Rainbow trout (*Oncorhynchus mykiss*). Other available data in fish (including life cycle studies) reported endocrine mode of action endpoints with NOECs between 2 and ca. 7 µg/L and adverse effects around 20 µg/L (*e.g.* 50% reduction of eggs from non-exposed female medaka (*Oryzias latipes*) mated with males exposed at 20 µg/L OP for 3 weeks). In EC 2005, it was concluded that the NOEC from *Oncorhynchus mykiss* (60 d; flow-through; growth) of 6.1 µg OP/L could be due to an endocrine mode of action and is well within the range of concentrations specifying NOEC-LOEC transition of endocrine-related adverse effects.

To consider endocrine related effects in organisms other than standard test species, the derived EQS for inland surface waters of 0.12 µg/L was compared with (no)effect concentrations reported for a copepod, Amphibia and Mollusca (EC, 2005). These data were mostly judged to be of a "use with care" status, based on lacking validated testing guidelines and/or missing analytical verification of exposure concentrations. Overall, in agreement with the risk assessment report by Brooke et al. (2005), EC (2005) concludes that the EQS of 0.12 µg/L provided "*…a sufficient margin of safety against potential ED-mediated effects of 4-tert-octylphenol*".

Hazard Assessment for Freshwater Sediment

The EQS derived for freshwater sediment is based on the aquatic EQS for inland surface waters using the equilibrium partitioning (EPM) approach (EC, 2005). A Koc of 2740 L/kg was chosen for the calculation, albeit the range for Koc was high (up to 19950 L/kg), leading to a corresponding uncertainty. The derived PNEC amounts to 34 µg OP/kg sediment dry weight.

In contrast, in the registration dossier for p-tert-octylphenol (ECHA Dissemination, 2022)the PNEC for freshwater sediment was based on the experimental data set for nonylphenol (read-across) comprising two chronic long-term tests involving different relevant sediment-dwelling organisms. According to ECHA guidance document R.10 (ECHA, 2008), this justifies an AF of 50. Using the NOEC from *C. riparius* results in a PNEC of 4.62 mg NP/kg sediment dw. Because the value is derived from chronic studies on relevant sediment dwelling organisms it is deemed to be reliable. Read-across to nonylphenol is justified based on the work of Brooke et al. (2005), demonstrating similar aquatic toxicity compared to p-tert-octylphenol, with nonylphenol generally being of somewhat higher toxicity (within a factor of 3). Further, no correction for molecular weight was performed based on the fact that nonylphenol is not a pure substance but a mixture containing typically around 5% of p-tert-octylphenol as well as other octylphenol isomers. Compared to the value derived from the EPM approach, the resulting PNEC based on the experimental data with nonylphenol is higher by a factor of about 135. This suggests an overestimation of toxicity using EPM.

In this AfA, as a conservative approach for sediment environmental risk assessment has been chosen by using an EPM-derived PNEC. However, as outlined in detail in section Annex 1-1, a higher and more reliable Koc value of 9979 L/kg is used for exposure assessment. The value of the Koc determines the fraction partitioning to the sediment, *i.e.* it determines the concentration of p-tert-octylphenol calculated for the sediment. For a valid risk assessment it is mandatory to use the same Koc value for both exposure and hazard assessment (*i.e.* calculation of $PNEC_{sediment}$ by EPM). Therefore, the same procedure for derivation of $PNEC_{sediment}$ by EPM as described in the EQS background document (EC, 2005) and Brooke et al. (2005) was followed, but using a) the AA EQS for inland surface waters of 0.1 µg/L and b) the same Koc as used for environmental exposure assessment, *i.e.* 9979 L/kg. The **$PNEC_{sediment}$ (EPM) is recalculated to be 100 µg 4tOP/kg sediment dry weight and is used for the calculation of risk quotients in this AfA**. Considering the $PNEC_{sediment}$ of 4.62 mg/kg sediment dw derived from long-term sediment data for nonylphenol, this EPM derived value is regarded as conservative (factor of 46 lower).

Recently, a sediment quality criterion (SQC, = EQS_{sed}) was derived for Switzerland (Kroll and Casado-Martinez, 2020). Based on a Koc of nearly the same size as used in this assessment (9736.61), the equilibrium partitioning method was applied to estimate the SQC based on the aquatic EQS for inland surface waters of 0.122 µg/L. Considering the low organic carbon content of Swiss sediments the resulting value was reported based on an OC content of 1% as SQC (1% OC) = 12.1 µg/kg sediment dry weight. A further value for SQC based on an OC content of 5% was also given (59.6 µg/kg sed. dw). In the EU, local risk assessment for sediment is performed under the assumption of a carbon content of 10% (same as for suspended matter), and PNECs are given with respect to this OC content. Scaling the most recently derived Swiss SQC to an OC content of 10%, the value for SQC (10% OC) becomes 120 µg/kg. This is higher (less conservative) than the $\text{PNEC}_{\text{sediment}}$ derived in this CSR (100 µg/kg sed. dw) based on the rounded aquatic EQS of 0.1 µg/L as outlined in the preceding paragraph. Interestingly, a parallel assessment based on reliable (RL 1 to 2) long-term experimental toxicity data on 4tOP for three sediment organisms (*Chironomus riparius*, Insecta; *Hyalella azteca*, Crustacea; *Lumbriculus variegatus*, Annelida) was performed. 10% effect concentrations normalized to 1% OC for all three species were in a narrow range between 3.92 (*Lumbriculus*) and 7.6 (Chironomus) mg/kg sed. dw. Based on a standard assessment factor of 10 for three long-term results on species representing different living and feeding conditions, a $\text{QS}_{\text{sediment}}$ of 392 µg/kg sed. dw (1% OC) and 1960 µg/kg sed. dw (5% OC) was derived. The Swiss assessment proposes however the values based on EPM for the definitive SQC "*… assuming that this value should be also protective for preventing the occurrence of endocrine effects from contaminated sediments*."

Hazard Assessment for Sewage Treatment Plant (STP) microorganisms

A relevant activated sludge respiration inhibition test equivalent to OECD 209 is available from the IUCLID dossier under REACH (ECHA Dissemination, 2022) with the following result:

EC50 (3h; respiration inhibition): >10 mg/L

Since STP microorganisms are not in focus for endocrine disruption, no further details on this study are provided here.
The PNEC_{STP} was derived using an assessment factor of 100, yielding a value of 100 µg/L.

Hazard Assessment for Soil

The terrestrial compartment is not considered relevant in this assessment, as there is no exposure of soil to OPnEO. Further, if a PNEC for agricultural soil is derived via equilibrium partitioning from the aquatic EQS, depending on the Koc used (2740 L/kg according to EQS data sheet or 9979 L/kg according to the discussion presented in Annex 1-1) the corresponding PNEC for agricultural soil spans a range from 5.5 µg/kg soil dw to 20 µg/kg soil dw. Because the aquatic freshwater EQS of 0.1 µg/L used for these calculations covers effects possibly related to an endocrine mode of action, EPM-based terrestrial PNECs implicitly cover endocrine mode of actions. In comparison, for the read-across substance nonylphenol a broad database on long-term soil studies covering reproduction are available, covering three invertebrate species, *i.e.* earth worm (*Eisenia andreii*), enchytraeids (*Encyhtraeus crypticus*) as well as spring tails (*Folsomia sp.*). In addition, subchronic data on plants as well as data on soil microorganism toxicity are available. These data justify an assessment factor of 10, resulting in a robust terrestrial PNEC of 2.3 mg/kg soil dw. Comparing this to the EPM-derived values, the PNEC based on soil experimental data is higher by a factor of 115 to 418. This is an indication that effects based on an endocrine-related mode of action may at least be not pronounced for terrestrial annelids and arthropods. Thus, the assumption of equal toxicity for aquatic and terrestrial species on which EPM is founded would not be applicable in this case, therefore disqualifying the EPM approach. In support of this, Brooke et al. (2005) noted: 'Based on the similarity of the PNECs for surface water for the two substances [*i.e.* 4tOP and nonylphenol], the low terrestrial PNEC [by EPM] for 4-tert-octylphenol needs careful consideration.'

In conclusion, **the PNEC for agricultural soil of 2.3 mg/kg soil dw derived in the disseminated dossier based on the read-across substance nonylphenol is regarded to be appropriate for deriving risk quotients for agricultural soil in this report.**

Hazard Assessment for Secondary Poisoning

With regard to secondary poisoning, the Annex XV dossier for OPnEO states that secondary poisoning is not relevant for the substance (ECHA, 2012). The SVHC support document states that 4tOP 'has some but low estrogenic potential in mammals' (ECHA, 2011b)

It is not clear how the PNEC for secondary poisoning given in the disseminated dossier for 4tOP (ECHA Dissemination, 2022) was exactly derived. However, starting from different data and following the methodology outlined in ECHA guidance document R.10 (ECHA, 2008), similar values are derived:

Based on the results from the OECD 206 study (Avian Reproduction Test; NOEL ≥20.63 mg OP/kg bw/d) as mentioned in the table above, a PNEC_oral is derived the following way:

NOEC_bird = NOAEL_bird *CONV_bird = 20.63 mg/kg bw/d * 8 = 165.04 mg/kg food, with AF 90 for subchronic studies: PNEC_oral (birds) = 1.834 mg/kg food.

Based on the available subchronic study in rats (OECD 408; NOAEL 300 ppm), a PNEC_oral value of 3.33 mg/kg food is calculated (300 ppm equiv. to 300 mg/kg food; AF 90 for subchronic study).

The PNEC_oral given in the disseminated dossier of 2.36 mg/kg food is somewhat lower compared to the arithmetic mean of the values derived from the OECD 206 and OECD 408 studies (2.58 mg/kg food). It therefore **is appropriate for deriving risk quotients for secondary poisoning in this report.**

Annex 3 Wastewater Monitoring Values

This annex summarises the results of the Triton X-100 monitoring campaigns performed by CSL (see also section 5.3.2.1). All values presented in this annex are results from 24-h autosampler collection samples. Whereas in the first monitoring campaign in November 2021 autosampler samples were only available for the sampling points 2 and 3, a complete dataset for all four sampling points indicated in the figure below was obtained in April 2022. Two additional samples for sampling point 1 are also available from June 2022.

All values presented in this annex are concentrations of the different OPnEOs as received from the laboratory. For mass balance calculations and EUSES modelling these values were transformed into 4tOP EQV.

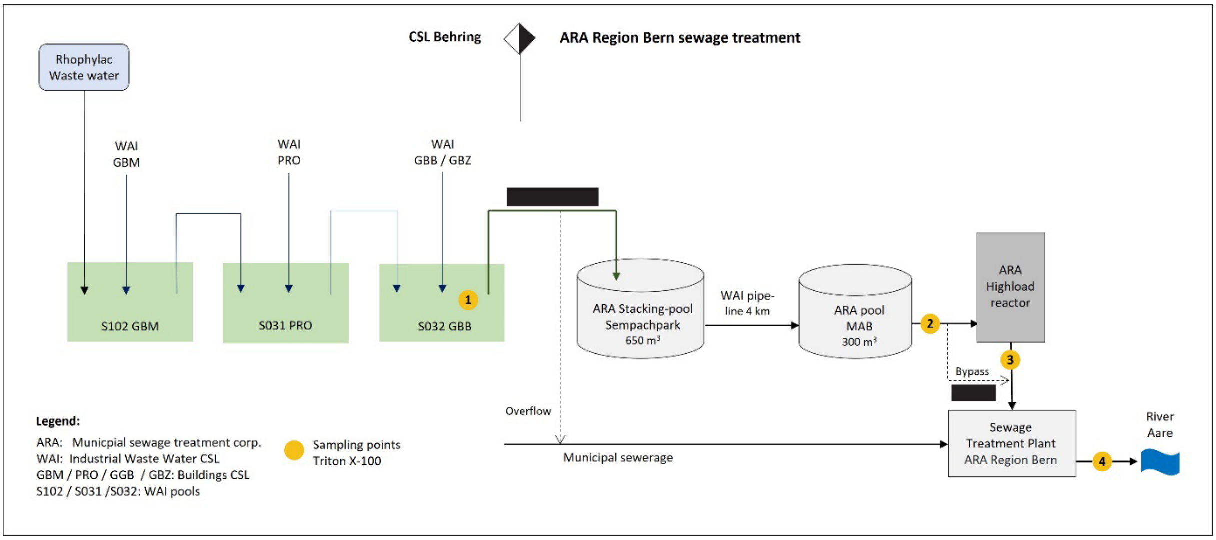

Figure 6. Triton X-100 wastewater streams and sampling points for wastewater monitoring

Table 25 Wastewater monitoring values 2022 (part 1)

	CSL-GBB (sampling point 1)(*)								**ARA basin MAB (sampling point 2)**					
Date	04.04.22	05.04.22	06.04.22	07.04.22	08.04.22	09.04.22	20.06.22	21.06.22	04.04.22	05.04.22	06.04.22	07.04.22	08.04.22	09.04.22
Parameter	**Result [µg/L]**													
4tOP	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP1EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP2EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP3EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP4EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP5EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP6EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP7EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP8EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP9EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP10EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP11EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP12EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP13EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP14EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP15EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP16EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP17EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
flow rate (m^3/24h)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Concentration 0.0 means that the concentration was below the limit of quantification (<LoQ)

(*) Sampling point 1 analytical values from 04.04.22 to 09.04.22 are invalid probably due to a systematic error of the used autosampler.

Table 26 Wastewater monitoring values 2022 (part 2)

	ARA exit high-load reactor (sampling point 3)						**ARA discharge point (sampling point 4)**					
Date	04.04.22	05.04.22	06.04.22	07.04.22	08.04.22	09.04.22	04.04.22	05.04.22	06.04.22	07.04.22	08.04.22	09.04.22
Parameter	**Result [µg/L]**											
4tOP	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP1EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP2EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP3EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP4EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP5EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP6EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP7EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP8EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP9EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP10EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP11EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP12EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP13EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP14EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP15EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP16EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP17EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
flow rate (m^3/24h)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Concentration 0.0 means that the concentration was below the limit of quantification (<LoQ)

Table 27 Wastewater monitoring values 2021

	ARA basin MAB (sampling point 2)						ARA exit high-load reactor (sampling point 3)					
Date	15.11.21	16.11.21	17.11.21	18.11.21	19.11.21	22.11.21	15.11.21	16.11.21	17.11.21	18.11.21	19.11.21	22.11.21
Parameter	**Result [µg/L]**											
4tOP	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP2EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP3EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP4EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP5EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP6EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP7EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP8EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP9EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP10EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP11EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP12EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP13EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP14EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP15EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP16EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP17EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
flow rate (m^3/24 h)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Concentration 0.0 means that the concentration was below the limit of quantification (<LoQ)

Table 28 Limits of Quantification (LoQ) for the individual measurement campaigns

Parameter	LoQ [µg/L] Nov 21	LoQ [µg/L] April 22	LoQ [µg/L] June 22
4tOP	10.0	10.3	9.7
OP1EO	-*	380.1	194.0
OP2EO	0.6	1.1	1.1
OP3EO	0.2	0.2	0.2
OP4EO	0.4	0.4	0.4
OP5EO	0.7	0.7	0.7
OP6EO	0.9	0.9	1.0
OP7EO	1.1	1.2	1.2
OP8EO	1.3	1.3	1.4
OP9EO	1.3	1.3	1.4
OP10EO	1.2	1.2	1.3
OP11EO	1.0	1.0	1.0
OP12EO	0.7	0.8	0.8
OP13EO	0.5	0.5	0.6
OP14EO	0.3	0.4	0.4
OP15EO	0.2	0.2	0.2
OP16EO	0.1	0.1	0.1
OP17EO	0.1	0.1	0.1

* not analysed during first monitoring campaign

Table 29 Comparison of the OPnEO concentrations at the inlet (sampling point 2) and the outlet (sampling point 3) of the high-load reactor

	SP 2	SP 3	SP 2	SP 3	SP 2	SP 3	SP 2	SP 3	SP 2	SP 3	SP 2	SP 3
Parameter	**Result [µg/L]**											
Date	04.04.22	04.04.22	05.04.22	05.04.22	06.04.22	06.04.22	07.04.22	07.04.22	08.04.22	08.04.22	09.04.22	09.04.22
4tOP	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP1EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP2EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP3EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP4EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP5EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP6EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP7EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP8EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP9EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP10EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP11EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP12EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP13EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP14EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP15EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP16EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OP17EO	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Sum (µg 4tOP EQV/L)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Concentration 0.0 means that the concentration was below the limit of quantification (<LoQ); Values below the detection limit were taken into account with LoQ/2 for the total value except for OP1EO: instead of LoQ/2, the LoQ of OP2EO was used.

Annex 4 Sludge Disposal

Disposal routes for sludge from wastewater

The main components of the waste sludge are inorganic diatomaceous earth containing filter aids with adsorbed proteins and other plasma components accumulates at the bottom of CSL's GBM, PRO and GBB wastewater collection tanks on site.

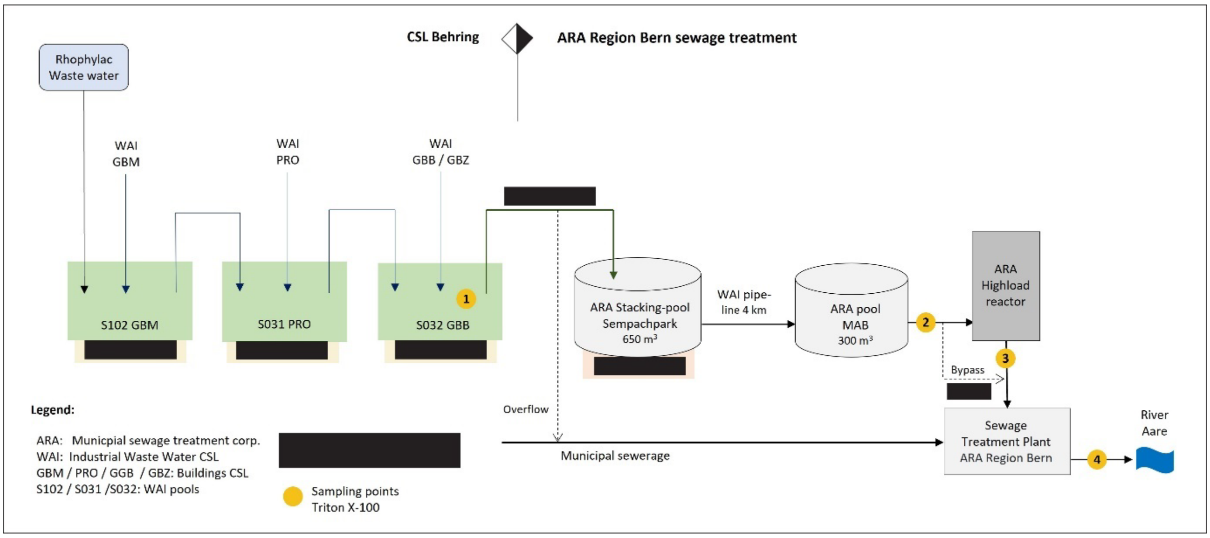

Figure 7: Overview of the wastewater flows from Rhophylac® production and the sludge from the CSL collection basins

This sludge is pumped at regular intervals and dispatched for disposal. Thereby, [redacted] of sludge per year from the CSL owned basins are forwarded to an external company ([redacted]). This amount results from [redacted] of sludge from the GBM and PRO basins, which is emptied once a year, and [redacted] originating from the GBB basin, which is emptied on four days a year. The additional [redacted] of sludge from the ARA basin at Sempachpark as presented in Figure 7 as well as the sewage sludge from ARA Region Bern are forwarded to the waste incineration plant (KVA, Kehrrichtverbrennungsanlage) where they are completely incinerated and therefore do not need to be considered further in this section.

CSL sludge is treated by the disposal procedures R5 and R9[10] In the R5 disposal process, mainly inorganic sludge components (> ~ 95% of the solids) and small amounts of organic components (< ~ 5%) are separated from the aqueous phase.

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[10] https://www.bafu.admin.ch/dam/bafu/de/dokumente/abfall/fachinfo-daten/hinweise_fuer_diezuordnungderentsorgungsverfahren.pdf.download.pdf/hinweise_fuer_diezuordnungderentsorgungsverfahren.pdf

- About 66% of the sludge from process R5 is gravel and sand and is used for trenches as crusher or filling material, or for lean concrete formation, and
- about 33% of the sludge is fine sludge and organic material used in cement industry as raw material or fuel substitute.

The aqueous phase from process R5 with residual solid material is subsequently processed in procedure R9 together with other organic sludges. The proportion of the liquid phase R5 in the process R9 is unknown to CSL. Unknown and varying subsets of solid sludge components being e.g. incinerated, used as fossil fuel replacement or opportunities from waste oil manufacture. Aqueous phase from R process is diverted to ARA[redacted].

There are no data available or measurements available on Triton X-100 distribution or flow in the various fractions in the processes R5 and R9.

Triton X-100 contained in the gravel and sand can, in principle, be released into the environment in the long term. The thermal treatments of the fine sludge and organic materials is expected to completely destroy Triton X-100.

For practical reasons (time for sucking off sludge at CSL and transport it to the external company) not more than 2 transports with a total of [redacted] of sludge can take place per day. The [redacted] of CSL sludge contribute to <10% of sludge processed at the external company daily. However the various solid fractions from a varying number of days, not known to CSL, are mixed at the external company before forwarding to subsequent treatment or use. This leads to a further decrease in the concentration in the sludge

The above mentioned [redacted] of sludge from CSL contribute with <1% to the total amount of sludge processed yearly by the external company.

Semi-quantitative assessment of Triton X-100 content in sludge

As shown above. a total of [redacted] of CSL sludge is processed externally. Based on current disposal practice. a maximum of [redacted] is removed during one disposal cycle. As described above and based on wastewater monitoring data it can reasonably be assumed that the total amount of Triton X-100 from the Rhophylac® production that enters the wastewater also enters the environment with the wastewater via ARA Region Bern. However, since no Triton X-100 measurements are available in the sludge and a theoretical estimation taking into account physico-chemical properties is not reasonably possible given the diversity of the individual OPnEOs, two worst-case scenarios considering the amount of Triton X-100 in the sludge that can enter the environment via gravel and sand are presented:

- Worst-case scenario 1: Assumption of 100% adsorption of Triton X-100 to the sludge, *i.e.* all Triton X-100 in the wastewater is discharged via the sludge
- Worst-case scenario 2: Assumption of 10% adsorption of Trition X-100 to the sludge, *i.e.* 10% of Triton X-100 in the wastewater is discharged via the sludge

Worst-case scenario 1:

It is assumed in this scenario that the total amount of Triton X-100 in the wastewater (*i.e.* [redacted] [redacted] 4tOP EQV) of the maximum amount of Triton X-100 used per year ([redacted] kg of Triton X-100; corresponding to [redacted] kg 4tOP EQV) will adsorb to the sludge. Note that this worst-case scenario is a purely theoretical scenario as shown by monitoring data in Section 5.3.2.1.

The maximal daily amount of sludge transported to the external company is [redacted] based on the available experience. This corresponds to a proportion of [redacted] 4tOP EQV per [redacted] of sludge (see equation 1), equivalent to 280 mg 4tOP EQV per kg CSL sludge (see equation 2) With CSL sludge share of <10% this would be reduced further, resulting in a concentration of < 28 mg 4tOP EQV per kg. This is equal to 0.0028% and a factor of about 35 lower than the concentration of 0.1% w/w below which no consideration of an endocrine disruptor in a mixture has to be considered in an application for authorisation (see Regulation (EC) No 1907/2006, Article 56, paragraph 6a). In other words, even considering this unrealistic worst-case scenario would end up in an exposure estimate which needs no consideration in an application for authorisation.

$$(1)\ \frac{\text{[redacted]}\ \text{4tOP EQV}}{\text{[redacted]}\ sludge} = \frac{x}{\text{[redacted]}\ sludge} \quad => \quad x = \text{[redacted]}\ \text{4tOP EQV}$$

$$(2)\ \frac{\text{[redacted]}}{\text{[redacted]}} = \frac{x}{1\ kg\ sludge} \quad => \quad x = 280\ mg\ 4tOP\ EQV \text{ per kg sludge}$$

Worst-case scenario 2:

In the second, more realistic worst-case scenario, 10% of 4tOP EQV are assumed to be absorbed to the sludge. This would equal to 2.8 mg 4tOP EQV/kg sludge and a concentration of 0.00028% (about 350-times lower than the concentration limit for consideration of an endocrine disruptor in an AfA). As described above, the sludge from the external company is distributed in proportions of approx. 66% and 33%. In this scenario, an amount of 1.86 or 0.93 mg 4tOP EQV/kg sludge would enter the respective paths, indicating that the theoretical amount of Triton X-100, which can be released to the environment via gravel, sand or lean concrete is rather negligible.

Annex 5 On-Site Wastewater treatment

CSL performed a feasibility study assessing various Triton X-100 degradation options and possible treatment plants which could be installed on the limited space on the site premises to reduce the amount of Triton X-100 discharged with the wastewater. After investigating different strategies that would be efficient for Triton X-100 reduction in the site-specific wastewater CSL decided to conduct treatability trials to identify the most appropriate method.

The following treatment options tested were

a. [redacted]
b. [redacted]
c. [redacted]
d. [redacted]
e. [redacted].

As outlined in section 5.3.2, a total of [redacted]/lot of wastewater results from the CM1 operation of the Rhophylac®-production, whereof the first [redacted] of the total amount of Triton X-100 washed out of CM1. This is due to the relatively high release of Triton X-100 from the columns during the first washes. To optimise the ratio of effort and costs versus benefits, CSL decided to only consider those [redacted] for wastewater treatment, because the additional effort to treat the remaining [redacted] is disproportionally high for only about [redacted] of Triton X-100 remaining in this volume.

Three suppliers ([redacted]) were engaged to perform treatability trials on laboratory scale as summarized in the table below (Table 30). Apart from successfully reducing the amount of Triton X-100 in the wastewater, the most important criteria for CSL for the on-site feasibility of the new technology are the following:

1) The available space for the new equipment on site is restricted, as building a new construction is out of scope and not possible due to space constraints. Therefore, only a room [redacted].
2) The manual operations around the new treatment system must be reduced to a minimum.
3) The new treatment system should consume as little energy as possible.
4) If possible, it should use the existing utilities already installed on site (*e.g.*. compressed air, water, chemical products).

Up to now results of the feasibility trials are available for [redacted]. Both treatments would result in a total mineralization of the degraded Triton X-100. Laboratory trials for [redacted] have proved to be the most promising option, so far. Most importantly, under laboratory conditions this system [redacted] eliminated Triton X-100 within [redacted]. Assuming a reduction [redacted] wastewater from column CM1 would lead to a reduction of about 88% of the total Triton X-100 discharged with the wastewater. Furthermore, no octylphenol or octylphenol-ethoxylates are formed during this process. Then, no manual operations are needed (or at least are reduced to a minimum) and a customized treatment plant can be fit into the restricted space available on site. In addition to that, already existing utilities like compressed air and electricity can be used with few chemicals ([redacted]) to be acquired.

[redacted].

[redacted]

[redacted].

Table 30 Summary of treatability trials

	[redacted]	[redacted]	[redacted]	[redacted]
Technologies	[redacted]	[redacted]	[redacted]	[redacted]
Treatability Trials	[redacted]	[redacted]	[redacted]	[redacted]
Comments	[redacted]	[redacted]	[redacted]	[redacted]

At the moment, not all the results of the laboratory tests are available and no pilot plant tests have been carried out, so it is not yet possible to decide which type of wastewater treatment will ultimately be the most efficient and feasible. However, in the interest of sustainable exposure minimisation, CSL decided to implement an on-site wastewater treatment system. Without a final decision being made as to which system should be implemented, the following example calculation, taking into account the laboratory [redacted] - the most promising method according to the results currently available - is intended to show how efficiently such wastewater treatment would minimise Triton X-100 emissions.

The following figure (Figure 8) shows the expected Triton X-100 release with the technology [redacted] and its development in course of the stepwise implementation of the alternative detergent. It is expected that the use of Triton X-100 will decrease in a stepwise manner by 90% over the five years period due to an increasing number of approvals for the substitution of Triton X-100. The blue bars indicate the amount of Triton X-100 used in kg/y. [redacted] of this amount would be discharged via the wastewater into the ARA Region Bern without additional on-site wastewater treatment (orange bars). However, only approximately 1.5% of the total amount of Triton X-100 would be discharged via wastewater into the ARA Region Bern after treatment with the new technology (grey bars; assuming a reduction efficiency of 90% under large-scale conditions). This would indicate a reduction of the Triton X-release of 88% in comparison to the current situation. The electrochemical oxidation would lead to a relevant minimisation of the Triton X-100 release into the environment. By treating the wastewater directly after the Rhophylac®-production, this technology would lead to a relief of the wastewater treatment plant. The [redacted] process thereby shows to be a promising asset for the aim of reducing the release of Triton X-100 into the wastewater on Bern site.

[redacted]

Figure 8: Reduction of Triton X-100 in WW due to stepwise substitution of Triton X-100 [redacted] (assuming ca. 88% reduction of total Triton X-100 in WW) (confidential information)

Based on current planning, commissioning of the wastewater treatment technology before the sunset date is envisaged. This best-case scenario as displayed in Figure 9 would foresee three months for pilot plant testing and one year for design, procurement, and construction of the new plant, so that the new technology can be applied already about three months before sunset date. Depending on the success of pilot plant tests and construction (*e.g.* availability of materials, pandemic situation) a possible delay in this timeline cannot be excluded, though.

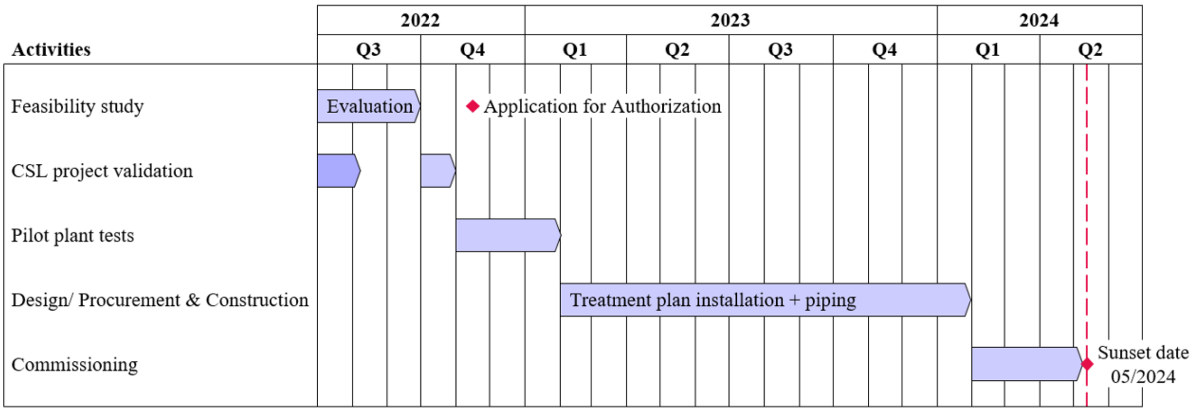

Figure 9: Planning proposal - time line of implementation of on-site WW-treatment