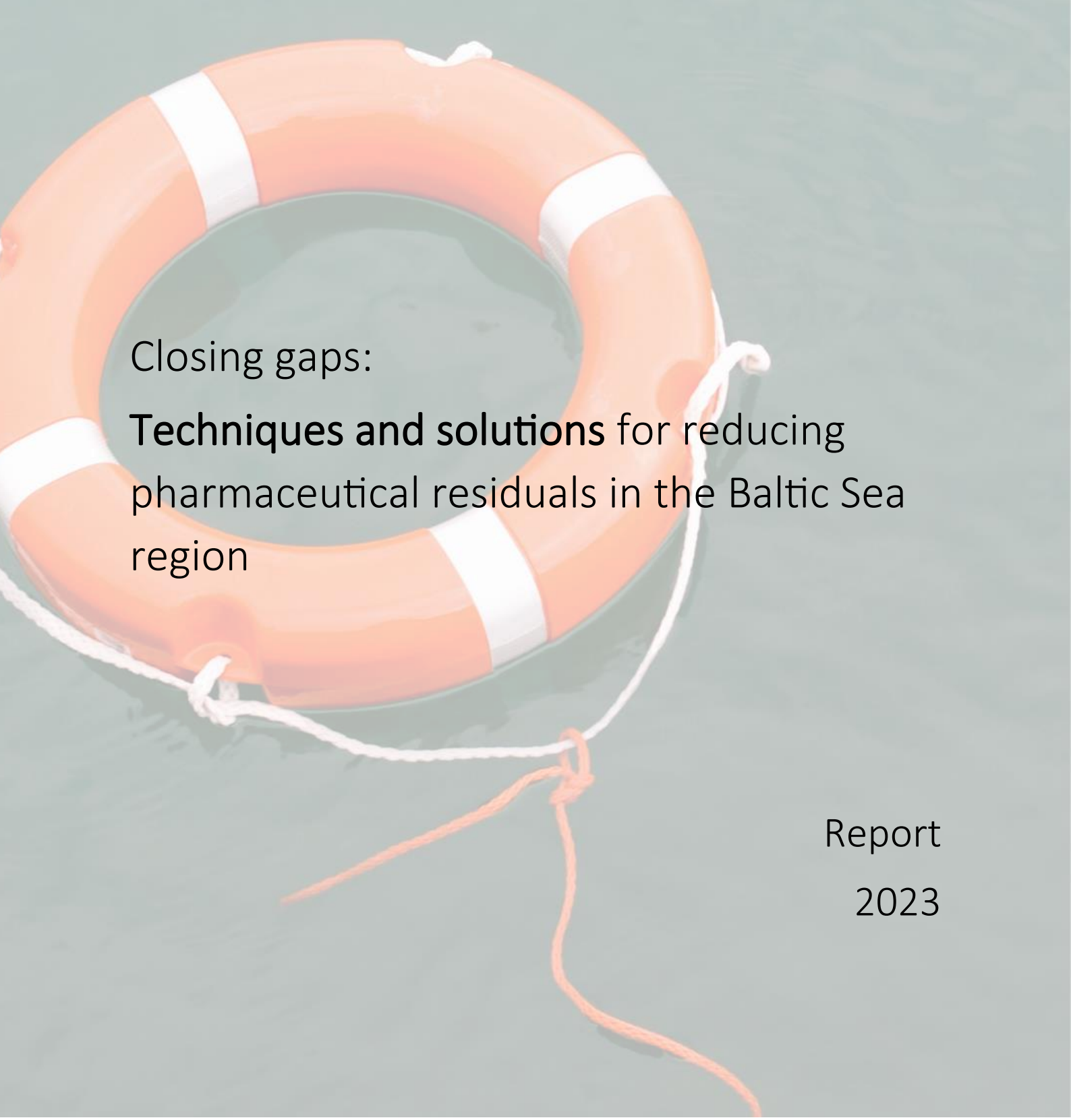

Closing gaps:

Techniques and solutions for reducing pharmaceutical residuals in the Baltic Sea region

Report

2023

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The Swedish Institute is a public agency that builds interest and trust in Sweden around the world. We work with Sweden's promotion, cooperation in the Baltic Sea region and global development.

Contents

Summary

"*Closing gaps: Techniques and solutions for reducing pharmaceutical residuals in the Baltic Sea region*" (Closing Gaps) is a project to identify, share and compare techniques, and best practices to reduce pharmaceutical residuals in the Baltic Sea.

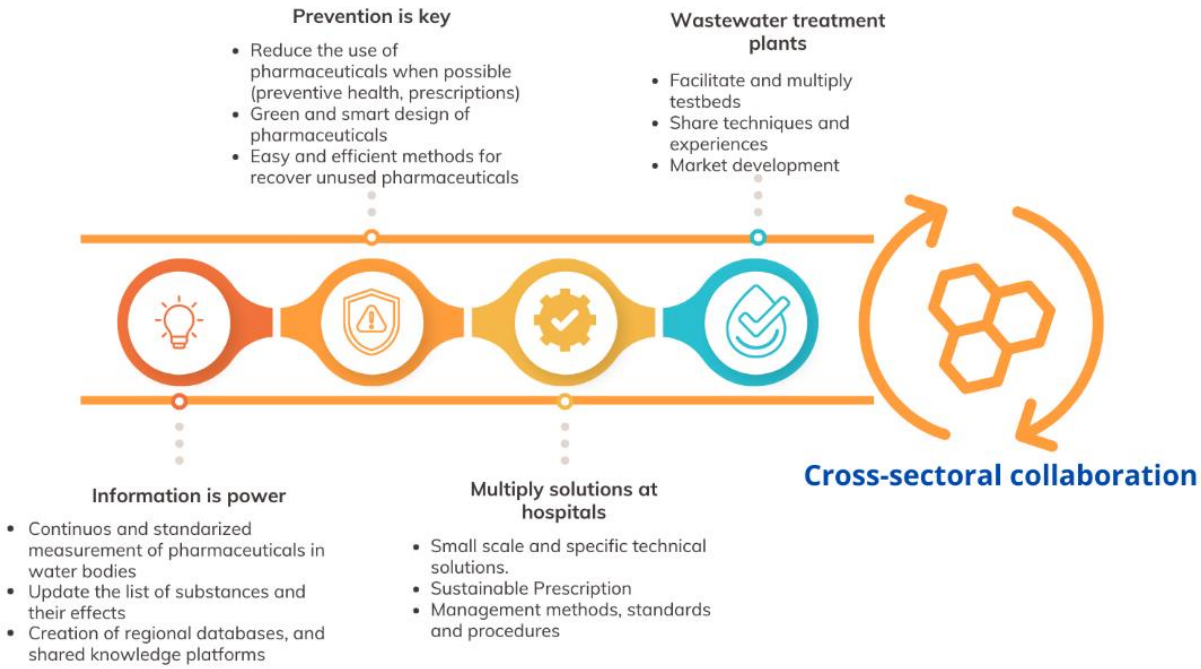
The project was implemented in three countries (Sweden, Estonia, and Lithuania), by a consortium led by the Nordic Center for Sustainable Healthcare (NCSH), and including Scanbalt, Association LithuaniaBIO, and Business Region Gothenburg, in a common effort funded by the Swedish Institute.

The project uses the cornerstone of sustainability, working upstream of the value chain, and taking care of the hazard as close to the pollution source as possible. Much of available research of pharmaceutical residuals focuses on the measurement of the substances or on the end pipe solutions. The idea with Closing Gaps is to look at the whole value chain. In this sense, the aim is to present solutions (practices, methods, techniques, and technologies) throughout the value chain, without claiming that any of the presented or existing solutions could be 100% effective by its own.

The project comprised the organization of three workshops, desk research, as well as the implementation of interviews with relevant stakeholders. The result is an updated overview of the current situation as well as the identification of some of the practical gaps present in this topic.

Closing Gaps suggests that effective implementation and sharing of existing practices and technical solutions can be accelerated by identifying the existing gaps among the countries and fostering collaboration with a cross-sectoral perspective. (Figure- Roadmap)

Figure 1. Roadmap
Sharing solutions for reducing pharmaceutical residuals in the Baltic Sea



Introduction

The project **"*Closing gaps: Techniques and solutions for reducing pharmaceutical residual in the Baltic Sea region*"** aims to understand and document the gaps and the existence of available techniques and solutions for managing pharmaceutical residuals and minimizing them from ending up in the Baltic Sea.

Pharmaceutical residuals in freshwaters, coastal waters and oceans have become an increasingly important topic. The negative effects on the ecosystems and the health of people are the main reasons for targeting the reduction of these substances.

The reduction of pharmaceutical residuals is a multifaceted process as the value chain is extended and complex. In a generic and simplified analysis, the value chain includes the pharmaceutical producers, the consumer, the healthcare facilities (hospitals, primary- and elderly care), pharmacies, veterinary institutions, farms, and finally the waste plants and wastewater treatment plants which take care of the residual waters. The main part of pollution stems from use in home treatment. This includes all from prescriptions to self-medication.
In the specific context of the Baltic Sea Region, the challenge of dealing with pharmaceutical residuals implies the work in a shared space between nations. This situation is reflected in various levels of regulations, incentives, and techniques, and in practical gaps between sectors and nations.

Nowadays research and collaboration regarding technical solutions and best practices along the entire value chain is a big area of opportunity as most of the available research focus on the concentration of pharmaceutical residuals in the water or on end pipe solutions. For that, we need to accelerate the adoption of new strategies that include stopping hazardous chemicals and other pollutants close to the source, so that they do not enter the cycle of water or nutrients.

With this objective, four relevant partners from different countries formed a consortium with a multi-stakeholder approach. The organizations set the common objective of influencing and accelerating the adoption and use of technologies and solutions that can reduce the quantities and impact of pharmaceutical residuals in the Baltic Sea. The partnership is integrated by **the Nordic Center for Sustainable Healthcare (NCSH), ScanBalt, Association LithuaniaBIO and Business Region Gothenburg (BRG)**.

The project focused on the revision of 1) techniques, procedures, and solutions, 2) the existing normative aspects, 3) cross-sectoral capacities for the adoption and implementation of new technologies, and 4) new business models and value chains associated with the sector. With the generated information through research, interviews and workshops, the project created a roadmap that will help to identify potential strategies to reduce the gaps between countries and sectors regarding the reduction of pharmaceutical residuals in the healthcare sector.

This report presents the results of the project. First, presents the methodology and different activities, second, introduces an overview of the challenge and the situation in the region, and third, presents the identified best practices and solutions. The last section included the developed roadmap that presents the main recommendations as the base for increasing collaboration among the actors in the region.

Methodology

The project implemented a mixed methodology that included desk review, as well as interviews and consultations with relevant stakeholders. The desk research builds on previous projects in the region and includes the revision of literature, normative (frameworks and legislations at national and European levels) related to the management of pharmaceutical residuals, and practices and models for wastewater management.

The project's practical approach was fulfilled by three workshops (Table 1), with the objective to get inputs and key learnings, as well as for fostering collaboration and improve the relationship between stakeholders at the Baltic Sea region. Each workshop focused on a different specific objective or thematic within the project and was led by a partner. The workshops were a space of exchange where different stakeholders shared their role and vision regarding ways of addressing the issue. The first one in Malmö, Sweden, the second one in Tartu, Estonia and the third one in Vilnius, Lithuania.

Table 1
Workshops

Workshops	Presenting	Participants
Workshop 1: Malmö, Sweden Topic: *Reducing pharmaceutical residuals in the Baltic Sea Region* Organized by the NCSH September 13th 2022	• Lif De forskande läkemedelsföretagen • Pharem • Pactosafe • NSVA	In total more than 150 persons, (including representatives from different ministries and local governments, universities, companies, hospitals, research institutions, from the Baltic Sea region) participated actively in the workshops. The main impact has been the establishment of collaborative basis across the different countries and including different sectors.
Workshop 2: Tartu, Estonia Topic: *Identifying potential gaps on techniques and solutions for reducing pharmaceutical residuals in the Baltic Sea Region* Organized by Scanbalt November 17th 2022	• Estonian Environmental Research center • University of Tartu • North Estonia Medical Center • Pharmafilter B.V.	
Workshop 3: Vilnius, Lithuania Topic: *Comparative analysis and assessment of collaborative possibilities according to the specific characteristics of the Baltic countries* Organized by Association LithuaniaBIO February 9th 2023	• Medicines for Europe • Astra Zeneca's Wastewater Treatment Plant • Yaquatec • Paxxo • Klaipeda University, Marine Research Institute	

The interviews were selected based on national representativity, including actors who play a role in the value chain of pharmaceutical residuals management, and included solution providers, researchers, actors with an official role within the healthcare sector, producers. These actors provided input and validation to some of the research findings. A total of 21 interviews were conducted, representing a broad spectrum of visions about the topic (Table 2).

Table 2 List of interviews		
Organization	Role in the residual pharmaceuticals	Country
Ministry of Environment of the Republic of Lithuania	Governmental sector, fields of waste management and environmental protection	Lithuania
Environmental Protection Agency under the Ministry of Environment	Governmental sector, field of environmental protection	Lithuania
Estonian Ministry of Environment	Field of environment protection, Water Department, Department of Environmental Technology	Estonia
TBD Pharmatech	Pharmaceutical producer	Estonia
Pharmaceutical Manufacturers' Association – VGA	Pharmaceutical industry	Lithuania
Skånes Universitetssjukhus	Hospital	Sweden
Tartu University Hospital	Hospital	Estonia
North Estonian Medical Centre	Hospital	Estonia
Floow2, PharmaSwap	Market place for pharmacists that reduce the possibility of early disposal of pharmaceuticals.	Netherlands
Apoteket	Company- Pharmacy- Recollection system of non-used pharmaceuticals	Sweden
Tartu City, Environmental Service	Wastewater treatment plant	Estonia
Tartu Veevärk AS	Wastewater treatment	Estonia
Lithuanian Water Suppliers' Association - LVTA	Water management, incl. wastewater treatment	Lithuania
Responsible water management association "VANDENS JĖGA"	Water management, incl. wastewater treatment	Lithuania
Company "Aukštaitijos vandenys"	Water management, incl. wastewater treatment	Lithuania
Company "Kretingos vandenys"	Water management, incl. wastewater treatment	Lithuania
Nordic Water Solutions	Wastewater treatment	Sweden
Yaquatec (Bioksa), private company	Technology sector	Lithuania
Mativesi OÜ	Technology producer	Estonia
IVL Swedish Environmental Research Institute	Research Institute	Sweden
Lif	Research institution for the pharma industry in Sweden	Sweden
Klaipėda University Marine Research Institute	Research and academic sector	Lithuania
Vytautas Magnus University Water Engineering Department	Research and academic sector	Lithuania
TEM	Multi sectorial network	Sweden

The workshops and interviews gave to the project a direct insight on the challenges along the value chain of pharmaceuticals and helped to identify a list of solutions that can be applied in different segments of the process related to the management of pharmaceutical residuals, with the final objective to reduce the quantity of these in the Baltic Sea region. This makes the analyses more contextual than legal or conceptual per se.

Quantitative indicators

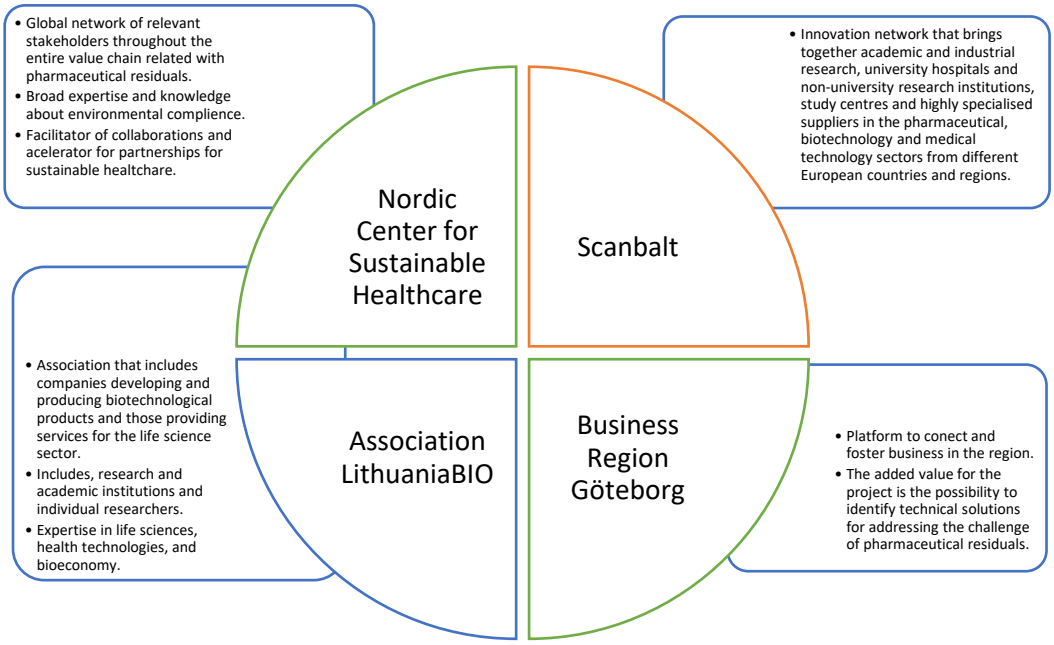
The project had as main financial support a seed fund from the Swedish Institute through the Balti Sea Neighborhood Programme[1]. The seed fund was used to complete pre-determined limited in terms of the geographical scope and outreach of the variables included in the problematic. Considering the available resources and time available there were defined quantitative indicators included in the Table 3.

Table 3 Quantitative indicators	Completed
10 Technologies and solutions identified and analyzed	✓
10 Best practices identified and analyzed	✓
20 interviews from different key stakeholders	✓
At least 100 stakeholders participating in the workshops (from at least 4 countries and representing the different sectors)	✓
Gap analysis (regulations, collaboration, implementation)	✓
Roadmap	✓

Qualitative indicators

The first qualitative indicator was the effectiveness of the consortium, as a collaborative platform between the countries represented and a mutual benefit and complementarity principle. The project used the main strengths of each partner of the consortium, as well as the complementarity of their networks and projects. This represents a multistakeholder and cross-sectorial perspective from the definition and work within the consortium (Fig.1). The main impact has been to strengthen the relations among the countries in the Baltic Sea region.

Figure 1. Complementarity and strengths of the partners within the project



Source: Prepared by the project

The second qualitative indicator was based on the possibility to represent the whole chain of stakeholders engaged in the process of the project, from production to end pipe solutions. The project was planned and implemented in a way that each activity implies cross-sectoral collaboration and discussion between the

[1] For more information about the work of the Swedish Institute check: https://si.se/

different stakeholders involved in the topic such as treatment plants, pharmaceutical companies, hospitals, and others. This can be tracked and demonstrated with the diverse participation of actors at the different events and initiatives.

Project limitations

The foremost limitation was time and available funding. Some of the inputs from the different activities indicated the need to go in-depth with some of the areas, but it was not possible considering the limitations of the seed funding.

Participating countries

One of the limitations of the project is the focus on three countries Sweden, Estonia, and Lithuania. The Baltic Sea entails many more adjacent nations. This study can be spread in the region and function as a base to go further in a larger project. The findings give us useful insights and knowledge to be used forward in new projects and implementation processes. And finally, the implemented methodology can be replicated in another countries or regions with similar challenges.

Validation of the identified techniques, procedures, and methods

The project differentiates from previous studies by including the whole value chain, instead of previous research mostly focusing on measuring concentration of pharmaceuticals and end pipe solutions. As it is seed funding, it was not possible to have the means to validate and evaluate the effectiveness of each identified solution. The project does not aim for each solution to be 100 per cent effective on its own, but rather, all solutions do some to reduce their part in the total reduction.

The other consideration is to understand that the validation for the different techniques responds also to contextual variables, so it would be different in different environments. The different methods need to be tested for real-life circumstances. When scaling up the sewage may entail all kinds of pollutants besides pharmaceuticals. This could be the base for another project focused on the development of concrete methodologies for the validation of techniques, which includes variables such as collaboration, innovation, and so on.

Veterinarian medicine and agriculture not included.

The different stages of the project confirmed that veterinarian medicine, agriculture and animal food are big generators of pharmaceutical residuals which end in the Baltic Sea. Nevertheless, this pre-study is limited in scope and does not include a detailed analysis of this segment of the pharmaceuticals value chain.

The challenge: Pharmaceutical residuals in the Baltic Sea

The Baltic Sea (BS) is a complex ecosystem, a shared space between nations that requires joint actions beyond national borders or sectoral perspectives. The presence of pharmaceutical residuals in the BS has been tracked and analyzed by different actors at the national and regional levels.[2]

The use of pharmaceuticals is very common and includes substances from a broad spectrum of therapeutics such as antibiotics, cardiovascular, antidepressants, pain killers, antibacterial, anti-inflammatory, neuroleptics, sedatives, anesthetics, hormones, blood thinners, and other substances some of them for complex treatments related to specific diseases such as cancer. The extensive use of these substances has caused long term negative impacts on the environment, and even human health. For example, some pharmaceuticals are designed to cope with the acidic pH values in the stomach and cannot be broken down in a fast and efficient way in the environment, also antibiotic resistance is classified as one of the greatest threats to world health by the World Health Organization (WHO).[3]

It exists a wide variety of pharmaceuticals, some of them without really knowing the long-term impact on the marine environment, less if we considered the potential effect of the mix of different pharmaceuticals, e.g. close to hospitals or other hot spot areas.

The effects on the environment within the BS are diverse and differentiated but, in this case, it has been documented that could affect the roles of the BS as climate regulator, biodiversity hub and resource provider[4].

According to the 2019 HELCOM study *"Pharmaceuticals in the aquatic environment of the Baltic Sea region –A status report*" the most measured pharmaceutical in the Baltic Sea was Paracetamol, followed by caffeine and Furosemide. The measurement in wastewater treatment plants was furosemide, followed by caffeine and X-ray contrast media. In the case of pharmaceuticals measured in untreated sewage sludge, the most present were ciprofloxacin, followed by tetracycline and caffeine. In the case of pharmaceuticals measured in river water samples, there was Iopamidol, followed by florfenicol and Hydrochlorothiazide[5].

Pharmaceutical residuals chain

The beginning of the chain of processes related with pharmaceutical residuals is located at the production sites. Risks of negative environmental impact include the raw material manufacturing, production of Active Pharmaceutical Ingredients (APIs) and the formulation of medicines. Some cases are related to deficient manufacturing facilities that release active ingredients into nearby waterways, creating localized hotspots of pharmaceutical pollution.

Most of the major pharmaceutical companies with base in EU have their productions sites outside EU, but according to the new EU Due Diligence directive, production companies with base in EU have responsibility to track and protect human rights conditions for its production outside EU, what includes the protection to hazardous effects of the utilized substances[6]. This adds an additional level as the techniques used in the BS to minimize pharmaceuticals can and should also be implemented in third countries (non-EU members).

After the production and transportation of pharmaceuticals, the combination of factors or routes of the pharmaceuticals reaching BS became more complex as includes healthcare sector, pharmacies, WWTP and households. As was mentioned most of the pharmaceutical residuals ended at water by the consumer and users,

[2] For example, the Global Sewage project makes surveillance over antimicrobial resistance. https://gls.genepi.dk/resistance

[3] Workshop presentation and interview- IVL. Swedish Environmental Research Institute.

[4] UNESCO and HELCOM. 2017. Pharmaceuticals in the aquatic environment of the Baltic Sea region –A status report. UNESCO Emerging Pollutants in Water Series – No. 1, UNESCO Publishing, Paris. p. 18.
For an overview of the situation and existing treatment plants available please advise the urban wastewater treatment map from European Environment Agency. Available in https://www.eea.europa.eu/themes/water/european-waters/water-use-and-environmental-pressures/uwwtd/interactive-maps/urban-waste-water-treatment-maps-3

[5] The report covers the period 2003-2014, including 47,600 data points on sources and pathways of 167 pharmaceutical substances measured in the marine environment. HELCOM, 2019. P. 31

[6] EU Due diligence directive. Available in https://eur-lex.europa.eu/resource.html?uri=cellar:bc4dcea4-9584-11ec-b4e4-01aa75ed71a1.0001.02/DOC_1&format=PDF

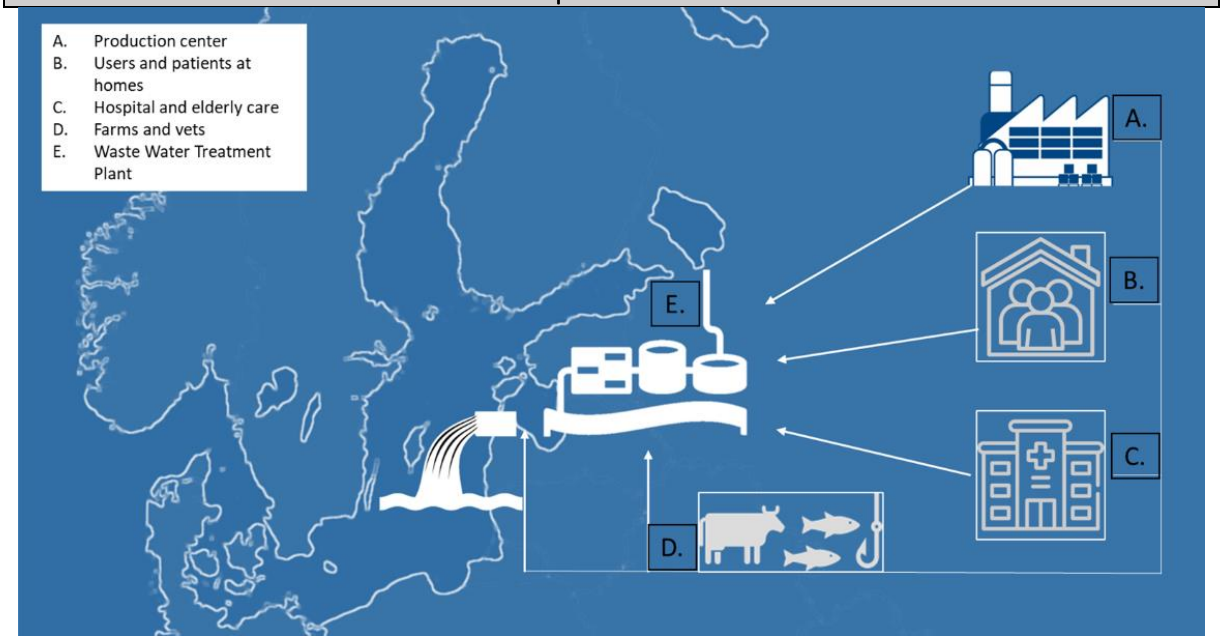
but regarding the more specialized products such as X-ray contrast agents, cytostatic drugs and others are mainly because are used in hospitals.

A comparatively smaller, localized contribution stems from manufacturing emissions or incorrect disposal of unused/expired medicines. To this situation it must be added the improper disposal of drugs i.e when people fail to complete a prescription or throw leftover drugs down the drain, drugs end up in sewage treatment plants. Poor handling of discarded medicines, pharmaceutical dumping and sewage sludge are also some sources.

Another source stems from agriculture and veterinarian use of pharmaceuticals (which are excluded from this project). The pharmaceutical residues from the animals enter the environment directly on, for example, fields and pastures.

The way these substances to the BS is long and complex, associated with the entire value chain and such as the potential solutions that can be part of a strategy to attend to it (Figure 2). From the manufacturing and production to the rest of the last processes in wastewater treatment plants, the pharmaceuticals get into the water bodies and end up in the BS with potentially disastrous consequences. The project concludes that is possible is to combine several solutions along the entire value chain, tailored to the specific and contextual characteristics of societies and manage to substantially reduce collateral environmental impacts of these.

Figure 2
Sources of the pharmaceutical residuals



Source: Prepared by the project.

The role of the healthcare sector

The use of pharmaceuticals represents a balancing act between hazardousness and the right to life. As one of the interviewees described "*Pharmaceuticals would never been allowed because of their effects if they were used for other purposes than for healthcare. Imagine if cytostatic were used in the production industry of cars, it would have not been permitted. The substance is harmful for the environment, for caregivers and people around, to some extent to the patient and it's very expensive to use and produce*".

The healthcare sector is key, even if it is not the main source of pharmaceuticals which is patients at home [7]. The reason for its relevance is its role in the whole value chain of pharmaceuticals is the processes related to prescription of pharmaceuticals and the change of healthcare system to be more of homecare treatment not necessarily with

[7] Between 30 to 90% of the active substance is excreted directly from the user. HELCOM, op. cit. 2019

the same possibility regarding standards, procedures and means to take care of medical hazardous waste, for example diapers.

Relevant policies and regulations

There are different policies and regulations that impact the management of pharmaceuticals. These exist at different levels, local, national and at EU level. Some of these are "soft law" (standards and guidelines) with no-legal binding, and some are "hard law" that can be legally enforced. At the same time exists broader European agendas and commitments, that is the case of the *European Green Deal* a policy that looks at the protection of the environment and oceans.[8] Apart of these exist the political commitments emanated within the Baltic Marine Environment Protection Commission, known as the Helsinki Commission (HELCOM), a regional platform stablished in 1974 to protect the marine environment of the Baltic Sea from all sources of pollution.[9]

At regional level, all EU members are required to implement the Directives from EU in the national legislation. In this context exists several specific regulations regarding the use of pharmaceuticals, the water treatment, and others that impact directly in the reduce of its presence in the BS.

Some of the existent normative are:

- Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy
- Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use
- Directive 2008/56/EC of the European Parliament and of the Council of 17 June 2008 establishing a framework for community action in the field of marine environmental policy (Marine Strategy Framework Directive)
- Directive 2013/39/EU Of The European Parliament and of The Council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy
- Guidelines for Separate Collection of Household Hazardous Waste. (2020/C 375/01)

The two foremost frameworks to consider that is common for the EU and the BS are the EU water Directive and Urban wastewater Directive.

The urban wastewater directive is about to be renewed and the Content of the proposal sets out six areas for action which are in line with the project outcome regarding gaps and solutions [10]:

- Raise awareness and promote responsible use of medicines
- Support the development of medicines that are less hazardous to the environment and promote greener manufacturing
- Improve environmental risk assessment and review
- Reduce waste and improve waste management
- Expand environmental monitoring
- Filling knowledge gaps

It is important to point out that EU Directives are not directly applicable and have no direct grievance mechanism connected to them and they need to be implemented in national law. The different countries have specific regulations, policies and locally implemented procedures that address the issue.

[8] More information regarding the European Green Deal can be consulted in https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/european-green-deal/delivering-european-green-deal_en

[9] For more information about the Helsinki commission check: https://helcom.fi/

[10] Sveriges Riksdagen. Meddelande om strategi för läkemedel i miljön Fakta-pm om EU-förslag 2018/19:FPM42 KOM(2019) 128 - Riksdagen. Available in https://www.riksdagen.se/sv/dokument-och-lagar/dokument/fakta-pm-om-eu-forslag/meddelande-om-strategi-for-lakemedel-i-miljon_H606FPM42/

Country situation reports presented in the project

This section is an overview of the current situation regarding the management of pharmaceutical residuals at National level with limitation to the countries represented in the consortium: Estonia, Lithuania, and Sweden.

Estonia

Pharma industry

The pharmaceutical industry is not obliged to analyze pharmaceutical residues in wastewater and are not included in monitoring programs and no emission limit values are set. There are in fact no water quality standards for the maximum pharmaceutical residue limits, for wastewater. Emission limit values for some specific parameters have been set only for discharges. The majority of pharmaceutical (still only a rather small number) plants discharge their wastewater into collective sewage systems (under separate contracts with water companies, which are not public).

There are practically no data on the on-site treatment of wastewater from the pharmaceutical industry. Usually, no obligations for on-site treatment of pharmaceutical effluents are laid down in the contracts, in that sense the need for on-site treatment needs to be assessed on a case-by-case basis.

Hospitals and nursing homes

Hospitals are generally located in the most populated areas and have less impact on wastewater treatment plants, what it is generally different to the case of nursing homes which are often located in small populations where a large proportion of the wastewater comes from and where the concentration of pharmaceutical residues in the wastewater is higher.

Estonian hospitals do not use point-of-use treatment, i.e., wastewater is discharged to the combined sewer system. Specific actions, e.g., the need for on-site treatment, need to be assessed on a case-by-case basis. Most of the unused pharmaceuticals are collected from hospitals. In this context, all bigger hospitals have in-house quality-management systems that regulate the collection of unused medicines.

The point-of-use treatment is necessary and desirable in cases where the quality of the wastewater does not meet the requirements for treatment in the collecting system, meaning. measurements of the concentration of the pharmaceutical residuals would be necessary.

The waste pharmaceuticals, i.e., medicines which are no longer fit for use and waste contaminated with pharmaceutical residues, are collected, and handed over with the appropriate environmental permit (i.e., the disposal or recovery of medicines may be carried out by a company holding a waste permit). In the case of hazardous waste, in addition to the waste permit, the company must also hold a hazardous waste management license) to be incinerated by a waste treatment operator.

It is important to highlight that only those hospitals that have a waste permit (e.g., Tartu University Hospital) must submit waste reports. These describe the facility's generation of pharmaceutical waste and the waste quantities conveyed to waste management companies. Pharmacies, small hospitals, clinics, dental practices, and other small-scale handlers do not have a reporting obligation, but the quantities of unused medicines collected in these cases are still reported by the waste-management companies.

In any case, medicines must be identified as either hazardous (cytotoxic and cytostatic medicines, antibiotics, narcotic and psychotropic medicines, other medicines containing hazardous active substances and unsorted unsuitable medicines are always hazardous waste) or non-hazardous waste (e.g., herbal preparations) before disposal, as this will determine how the medicines are disposed of.

Common techniques and methods used in Estonia

In Estonia exists systems for pharmaceuticals recovering from private individuals who can give away unused pharmaceuticals for free in the pharmacies (no obligation to accept medical devices, natural products, etc.) and the municipal hazardous waste collection points/waste collection stations. One important aspect of the current situation is that, at the normative level, the transfer of ineligible medicinal products received from consumers as hazardous waste from the operator to the waste management company is the subject of a transfer for destruction record, which indicates the total quantity of medicinal products transferred, the name of the person who transferred the medicinal products for destruction and the name of the person who received the medicinal products – however, according to the interviews, this is not actually done in practice.

Companies and institutions are required to hand over waste pharmaceuticals to a waste manager who holds an environmental permit. Waste pharmaceuticals generated during business activities, including the provision of health and veterinary services, must be handed over to a licensed waste handler authorized to handle hazardous waste, including pharmaceutical waste. Disposal of narcotic drugs and psychotropic medicinal products must take place immediately after the transfer.

In the case of wastewater treatment, the process removes various foreign bodies by mechanical treatment - debris and sand. It must be kept in mind, that not every liquid is wastewater - not all liquids from production should be discharged directly to the sewer. Concentrations should still be determined and, if necessary, collected separately and treated e.g., as hazardous waste.

The secondary treatment technologies used in Estonia are disc filters and sand filters. This allows that for example organic matter, in the biological treatment process and, in secondary treatment are extracted nutrients i.e., nitrogen and phosphorus. In the case of drinking water treatment ozonation and active carbon are used. In Estonia, there is currently no post-treatment for pharmaceutical residue used in water treatment plants.

At the same time, there are some techniques that are widely used in other countries but that have an implementation challenge in Estonia. That is the case of ozonation, which is a technology that is not applicable in many areas of Estonia because our groundwater, including wastewater, often contains bromine, which reacts with ozone to produce bromate, which can be even more dangerous for the environment. The Interreg project EMPEREST is underway and will test different post-treatment technologies in pilot plants in Estonia from 2023-2025.

Some of the challenges identified by the project were the need to accelerate the sharing of learning experiences and the combination of different techniques that could attend to the practical challenges such as the removal of particulate phosphorus, the removal of non-biodegradable organic matter, metabolites, heavy metals, among others.

Legislation

Estonia has national legislation that regulates the handling of pharmaceutical residuals such as:

- Medicinal Products Act
- Waste Act, Regulation of the Minister of Social Affairs "Procedure for the reception and disposal of medicines unsuitable for consumers in general and veterinary pharmacies".

The Medicinal Products Act (§ 35) stipulates that all medicinal products which do not meet the quality requirements or have reached the end of life, or the use of which has been prohibited in Estonia, or which for any other reason cannot be used for their intended purpose, must be withdrawn from the market.

Estonia's views on the EU strategic approach to pharmaceuticals in the environment

Estonia has not planned specific actions based on the EU Pharmaceutical Strategy. The most important has been the prevention side, i.e., ensuring that unused medicines reach hazardous waste management. On the waste side, activities to inform the relevant stakeholders and the general population are the most important, as a system is in place to enable people to (free of charge) drop off medicines at pharmacies and waste stations. Thus, the main

requirements in Estonia are currently based on preventing medicines that are not fit for use from ending up in the wrong place. The responsibility to ensure that unused pharmaceuticals are handled properly lies with local authorities.

Lithuania

As summarised in Figure 3, the activities of preventing and handling pharmaceutical residues in Lithuania are being implemented within healthcare and environmental sectors. The Ministry of Health is responsible for the legal regulation of medical waste generated in healthcare institutions, and for the procedures of accepting medicinal products from residents in pharmacies and of paying for the handling costs. Meanwhile, the Ministry of Environment oversees general requirements for waste and legal regulation of the treatment. The Environmental Protection Agency under the Ministry of Environment oversees environmental monitoring and reporting.

Figure 3. *Key stakeholders in Lithuania and some the observed trends*

<table>
<tr><th colspan="2">Healthcare sector</th><th colspan="2">Environmental sector</th></tr>
<tr><td colspan="2">Ministry of Health
✓ Legal regulation of medical waste generated in healthcare institutions
✓ Procedures for accepting medicinal products from residents in pharmacies and paying for the handling costs.</td><td colspan="2">Ministry of Environment
✓ General requirements for waste and legal regulation of the treatment
Environmental Protection Agency
✓ Environmental monitoring and reporting</td></tr>
<tr><td colspan="4">Pharmaceutical waste holders (hospitals, etc.)
Residents
Pharmacies</td></tr>
<tr><td colspan="2">Selected waste managers handling (pharmaceutical) waste
✓ Increasing amounts of such waste collected (2021-240 tons; 2022- 288 tons)</td><td colspan="2">Water management (wastewater treatment) companies
✓ No systemic monitoring and specific treatment of pharmaceutical residuals
✓ Increasing level of medicinal active substances in water</td></tr>
<tr><td colspan="4">Challenges with waste that pharmacies do not accept (e.g. syringe needles)</td></tr>
</table>

Source: Prepared by the project

Main sources of pharmaceutical residues are organisations classified as pharmaceutical waste holders, such as hospitals, and the residents. Pharmaceutical waste holders are obligated to submit medical (pharmaceutical) waste to the selected waste managers handling this waste. Residents submit unused medicines through pharmacies.

Totally, 288 tons of medical (pharmaceutical) waste were collected in 2022, compared to 240 tons in 2021. The increasing amounts of such waste collected can signify that more medical (pharmaceutical) waste is being generated. On the other hand, this can also indicate that such waste is being collected more effectively. One of the challenges observed is waste that pharmacies do not except (e.g., syringe needles). This type of waste is being found in different places, including in the water, near wastewater treatment plants.

Apart waste managers selected to handle collected medical (pharmaceutical) waste, water management (wastewater treatment) companies are part of the system dealing with pharmaceutical residues. There are project-based (ad-hoc) activities focused on the investigation of pharmaceutical residues in waters and on the testing of different treatment technologies. The most recent project is the Interreg V-A Latvia–Lithuania Programme funded project No. LLI-527 "*Pharmaceuticals in wastewaters – levels, impacts and reduction", shortly called MEDWwater*[11]. At this time, no systemic monitoring and specific treatment of pharmaceutical residuals in wastewaters is yet established, although the increasing level of medicinal active substances in water is being observed.

[11] Interreg V-A Latvia–Lithuania Programme funded project No. LLI-527 "Pharmaceuticals in wastewaters – levels, impacts and reduction": https://2014-2020.latlit.eu/pharmaceuticals-in-wastewaters-levels-impacts-and-reduction-medwwater/

Review of "*Good practices for take-back and disposal of unused pharmaceuticals in the Baltic Sea region*"[12] also drove attention to the requirements for the management of veterinary medical waste. In Lithuania, these requirements are approved by an order of the Director of the State Food and Veterinary Service and they establish procedures for sorting, packaging, labelling, initial processing, temporary storage, and accounting for veterinary medical waste.

Legislation

Legal basis for handling pharmaceutical waste is laid in the *Law of the Republic of Lithuania on Pharmacy No. X-709*[13]. According to this law:

- Pharmaceutical waste is defined as medicinal products that are subject to disposal and chemical materials either used in implementation of trials for medicinal products or that are defective or past their expiry date and were acquired for the purpose of conducting such trials.
- Pharmaceutical waste shall be collected as a separate category of waste from pharmaceutical waste holders and the residents, managed and treated in accordance with waste management regulations.
- The management of pharmaceutical waste collected from the residents shall be paid for from the State budget.

The normative description shows a differentiated panorama with the common possibility of use the European framework as a facilitator for practical dialogue. In the next section the identified solutions and best practices are presented, followed by a gap analysis. Together, including the normative description, are the basis for a roadmap to foster regional collaboration for reducing the pharmaceutical residuals in the Baltic Sea.

Sweden

There are in general a good overview and transparency regarding measurement of pharmaceutical residuals in Swedish lakes, streams, and coastlines in recent years, according to figures from the Water Information System Sweden (VISS), compiled by Swedish Water. [14]

The Swedish Agency for Marine and Water Management develops assessment criteria based on ecotoxicological data and most pharmaceutical substances approved for use before 2006 lack reliable ecotoxicological data. The Swedish Agency for Marine and Water Management can although receive signals from environmental monitoring on new substances that pose a risk. So far, all substances that show the influence or possible influence on the sea environment are prescribed substances, except Diclofenac in gel for topical use. That is, the use of drugs is currently limited based on a medical assessment and prescriptions[15].

In the case of Sweden, pharmaceutical producers are required to ensure free take-back collection systems from households. This is managed via the pharmacies, but also includes municipalities and healthcare facilities. In the case of cytostatic and cytotoxic pharmaceuticals, the amount handled by households is very small, as there are mainly used at hospitals and other healthcare facilities.

[12] Mehtonen, J., Äystö, L., Junttila, V., Perkola, N., Lehtinen, T., Bregendahl, J., ..., Kaskelainen, E. (2020). Good practices for take-back and disposal of unused pharmaceuticals in the Baltic Sea region. Clear Waters from Pharmaceuticals (CWPharma) Activity 4.1 Report. – https://helda.helsinki.fi/bitstream/handle/10138/319009/SYKEre_34_2020_CWPharma.pdf?s

[13] Law of the Republic of Lithuania on Pharmacy No. X-709 and its changes: https://www.lrs.lt/pls/inter3/dokpaieska.rezult_l?p_nr=&p_nuo=&p_iki=&p_org=&p_drus=&p_kalb_id=1&p_title=farmacijos%20%E1statymas&p_text=&p_pub=&p_met=&p_lnr=&p_denr=&p_es=0&p_tid=&p_tkid=&p_t=0&p_tr1=2&p_tr2=2&p_gal=&p_rus=1

[14] ReningsVÄRK - Läkemedelsrester i vår gemensamma vattenmiljö | Vattenbokhandeln (svensktvatten.se)

[15] Läkemedel i vattenrecipienter hur prioriterar vi framtidens rening? Länsstyrelsen Skåne Författare: Pardis Pirzadeh, Ola Svahn, Susann Milenkovski, 2021:13 p 59-61.

One of the relevant best practices is the national policy for physiotherapy at prescription[16], and the fact that in Sweden drugs are graded by their environmental effects, and doctors are required to prescribe a less damaging drug where the option exists[17]. The National Board of Health and Welfare has developed regulations on drug reviews with the aim of quality assuring patients' drug treatment, ensuring that prescribed drugs do not have the opposite effect when combined with each other, that no more drugs are used than needed. It exists national routines and legal standards regarding discarded medicines and waste handling in the healthcare system[18]: Regarding private individuals it is stated that they must deliver their pharmaceutical waste to pharmacies.

Common techniques and methods used in Sweden.

Most of the Swedish treatment plants has three steps cleansing technique and will require a fourth step to uphold the new EU Urban Wastewater Directive. The techniques are very similar but with some small alterations due to the special conditions at the specific site showing that there is no one size fits all even if the general steps are the same. Individual circumstances can be an outlet from an industry creating more chlorides in the water compared to another site. There are two wastewater treatment plants in Sweden with full scale implementation that includes treatment of pharmaceuticals (Simrishamn and Linköping). Those are using ozone as an additional step to the regular cleaning process. With the help of ozone, over 90 percent of the pharmaceutical residues that leave the body are purified. The wastewater treatment plant in Simrishamn, is the first full-scale wastewater treatment plant of its kind after the expansion of further advanced treatment steps, which include DynaDisc, DynaSand, DynaSand Carbon and ozonation. The advanced processes are designed for the removal of pharmaceutical residues and micropollutants as a first step to be able to reuse wastewater in the region that periodically struggles with drought.[19] The rest have applied for funding and many of them have techniques installed as pilots and testbeds but not permanent installations to treat pharmaceuticals.

The supervisory authorities currently primarily impose requirements according to what is stated in the environmental permit. At the same time, the new reality is that the requirements of the Water Framework Directive apply today.

Swedish treatment plants are awaiting the new Wastewater Directive and its implication into decision making about investments in the "right" technique. There is also a need for financial help with the investments. For certain groups in society, the VA (water and sewage) fee may then be higher than the UN's recommendation that the VA fee should be a maximum of five percent of disposable income.[20]

Legislation

Pharmaceutical waste treatment is regulated in The Environmental Code[21] and the Waste ordinance (2020:614). The ordinance states, among other things, the type of waste that is classified as hazardous waste, the obligations of operations and transporters and the National Board of Health and Welfare's right to issue regulations on the management of infectious waste from health care. Regarding the infectious waste from health care the National Board of Health and Welfare's regulations and general advice on the handling of infectious waste from health care regulate how the waste is to be handled, stored, labelled, and transported[22]. The regulations also apply to infectious waste generated in home care provided by staff.

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[16]Swedish National Board of Health and Welfare. National Guidelines for prevention and treatment of unhealthy lifestyles. "Nationella riktlinjer för prevention och behandling vid ohälsosamma levnadsvanor – information till patienter" Available in https://www.socialstyrelsen.se/kunskapsstod-och-regler/regler-och-riktlinjer/nationella-riktlinjer/information-till-patienter/om-publicerade-riktlinjer/levnadsvanor/

[17] Pharmaceuticals in the environment: a growing problem. The Pharmaceutical Journal, PJ, 21 February 2015, Vol 294, No 7850;294(7850):DOI:10.1211/PJ.2015.20067898

[18] SOSFS 2005:21, SFS 2020:614

[19]Information from Nordic Water available at https://www.nordicwater.com/sv/cases/simrishamn-framtidens-kommunala-reningsverk/

[20] ReningsVÄRK - Läkemedelsrester i vår gemensamma vattenmiljö | Vattenbokhandeln (svensktvatten.se)

[21] miljöbalken (1998:808)

[22] (SOSFS 2005:26), Kasserade läkemedel - Vårdhandboken (vardhandboken.se)

Regarding the pharmaceutical production you need to seek permission for the industrial process. This is legislated in the Environmental Assessment Ordenance "*Mliljöprövningsförordningen*" (kap 12, 38-41§§). Production sites that are connected to this law are also under the post processing responsibility within the County Administrative Board "Länsstyrelsen"[23]. The County Administrative Board (Länsstyrelsen) is responsible for regional environmental monitoring, has several roles in the work with the EU's water directives and is also the supervisory authority for several of the county's treatment plants. The County Administrative Board map the drug load downstream of the treatment plants and a greater understanding of the impact it has. This knowledge can also become a basis for setting requirements for self-control of drug substances through supervision and reconsideration to advanced purification through licensing[24]. However, it must be highlighted that wastewater treatment plants have no legal obligation to eliminate pharmaceutical residues during the purification process.

Regarding which pharmaceuticals that are permitted on the market it is the Swedish Medicines Agency "Läkemedelsverket" who confirms registration and market distribution of Pharmaceuticals[25].

In Sweden, it has been forbidden since 1986 to mix antibiotics in animal feed. When Sweden joined the EU, Sweden was allowed to keep the ban for four years. However, by using a safeguard clause by the government, the ban could remain in place until all use of antibiotics for so-called growth-promoting purposes was banned in 2006 throughout the EU.

Sweden's views on the EU strategic approach to pharmaceuticals in the environment

Sweden is faced with the fact that many treatment plants will need to introduce complementary treatment steps or make a total reconstruction for full-scale treatment. Sweden is committed to achieving the goals of the Water Framework Directive, to achieve good status by 2027 in waters designated as water bodies [26].

[23] Available in https://www.naturvardsverket.se/4a4386/globalassets/media/publikationer-pdf/6500/978-91-620-6501-0.pdf
[24] Läkemedel i vattenrecipienter hur prioriterar vi framtidens rening? Länsstyrelsen Skåne Författare: Pardis Pirzadeh, Ola Svahn, Susann Milenkovski, 2021:13
[25] 4 kap 11§ SFS 2021:914.
[26] Ibid.

Best practices and techniques for reducing pharmaceutical residuals

The project focus on the identification of the possibilities for practical collaboration between different sectors and stakeholders in the region, as the way to reduce the pharmaceutical residuals in the Baltic Sea. In that sense, the different stages (research, interviews, and workshops) included the identification of best practices and technological solutions implemented that could be source not only for inspiration but for collaboration, as well as a gap analysis for an effective implementation.

Mapping the solutions along the value chain of pharmaceutical residuals

Preventive solutions

The preventive aspect of pharmaceutical residuals ending in the water bodies has three main aspects from the perspective of the project. The first one is related to the change of behavior from medical personnel, hospital and consumer, in terms of avoiding the excessive use of pharmaceuticals.

The second aspect for preventive approach is related with the design of pharmaceuticals. The "*Green design*" of pharmaceuticals refers to a small-molecule-pharmaceutical substance that is non-toxic, non-bio-accumulative, and easily degradable. The design should be less toxic to human health and the environment, including aspects such as the designed to be easily and safely broken down in the environment. Besides this, it should be included in the production process to minimize the risk of accidents and the release of hazardous substances. In the pharmaceutical industry, green chemistry principles can be applied to the design, synthesis, and manufacturing of pharmaceutical products, as well as to the disposal of pharmaceutical waste. These efforts should involve the engagement with public actors such as education, as it is necessary to educate chemists and other stakeholders about green chemistry principles and their importance[27].

Text box: Pharmaceutical producers' engagement.

The pharmaceutical producers have formed the Antimicrobial Resistance Industry Alliance (AMRIA) and developed the Antibiotic manufacturing standard with tools to analyze the potential risks, to prioritize potentially harmful Active Pharmaceutical Ingredients (APIs) for further testing and to implement strategies for reducing environmental risks if necessary. For industry, the output of PiE (pharmaceuticals in the environment) helps to avoid unnecessary testing for environmental risks and to consider the mitigation of potential environmental risks at an early stage of development.[28]

Solution - Information sharing regarding production and effects of pharmaceuticals in the environment[29]

The third aspect is to avoid the pharmaceuticals arriving at the waste stream. This could involve the recovery in early stages, such as in the pharmacies, or with an active engagement from the pharmaceutical companies. For example, through regulation that made them recover the pharmaceuticals, and invest in the treatment and prevention of pharmaceuticals reaching the sewage.

Solutions at hospitals

As has been described, hospitals are not the main source of pharmaceutical residuals, but they are the main source of some specific hazardous pharmaceuticals that are present in the water and hot spots for antibiotic resistance. It

[27] Among the activities is the Industry Roadmap for Progress on Combating Antimicrobial Resistance known as the Davos Declaration in 2016, a document signed by more than 100 companies and trade associations called for collective action to create a sustainable and predictable market for antibiotics, vaccines and diagnostics.

[28] Innovative Medicines Initiative. Final Report of the project: Intelligent Assessment of Pharmaceutical in the Environment. Grant Agreement: 115735. Project Duration: 01/01/2015 - 30/06/2019 https://www.imi.europa.eu/sites/default/files/events/115735_iPiE_Publishable_Summary.pdf

[29] More information can be consulted at https://www.imi.europa.eu/projects-results/project-factsheets/ipie

must be established that this category includes other healthcare facilities such as elderly care facilities that present a much higher effect on the use and emissions on the effect of pharmaceutical residuals.

The many kinds of solutions that a hospital can implement goes from procurement policies, behavioral changes regarding prescriptions and management, the application of protocols, and other collaborations with technological developers, academy, and other sectors for develop wastewater treatment solutions on-site.

Water treatment plants

Water treatment plants are some of the most common solutions and can be applied at different dimensions. It can be a small dimension water treatment solution installed in a hospital or other healthcare facilities, or a big wastewater treatment plant providing services to communities and cities. In the case of hospitals, it is possible to find different methods such as oxidation, adsorption and filtration as a pre-treatment, prior discharging. In both cases they use a wide selection of technologies.[30].

Some of the solutions used by WWTP have indirect impacts, for example in the case of oxidative treatment methods, this produces by products that are not easily oxidized. Absorptive methods transfer residuals to a solid phase, so the sewage needs also to be treated. In the case of membranes filtration, the pharmaceutical remains in the retentate.

The treatment principles can be classified as physical, oxidative, adsorptive, biological/enzymatic, and mixed methods or combination or two of more of the mentioned ones. According to the findings the most used technologies are:

- Activated carbon

It is used mainly to remove xenobiotics such as pesticides or chlorinated solvents[31]. Carbon is in granulated or powdered form. The effectivity of this technique depends on different aspects such as the chemical characteristics and concentration of the pharmaceuticals, the amount and characteristics of the activated carbon, the time of contact between the carbon and water (at least 24 hours) and even the temperature of the water.

- Ozonation

This method is based on the use of ozone for disinfection. There are several companies and products available. This project does not research effectiveness and cost benefit analysis of every solution presented as it is a limited seed fund. Nor comparing the more environmental friendliness of the different techniques as for example, generally *ozonation are more hazardous as a treatment, on the other hand it is effective*.

- UV

The method is described in projects and testbeds and has been proven to be 90% efficient.[32] There are different projects available for UV processes. One of them are described as an advanced oxidation process, H2O2 is dosed into the wastewater flow and injected into an Advanox reactor. The UV light breaks down H2O2 into a very reactive form of oxygen, the hydroxyl radical (OH), which breaks down organic pollutants in less than a millisecond. This removes micropollutants, such as hormones, medicines, and other persistent compounds. The high UV dose helps to kill bacteria in the water, in this way it can reduce the risk to develop antibiotic resistance.[33] One important aspect to take into consideration is that independently of the process, the best examples include the combination of at least two techniques. But it is important to mention that can work differently, mostly regarding what kind of

[30]The effectiveness of the wastewater treatment plants is said to have 20-80%. However, the RecoLab project, included in this report, is said to be able to have 100% of effectiveness. In this solution, its separate waste streams in food, gray and black water making the concentrations and volumes of treating blackwater by itself less.

[31] CW Pharma. Guideline for advanced API removal. December 2020. Available in the webpage of the project CW pharma https://www.cwpharma.fi/en-US/Publications

[32] Karin Persson. New method for removing pharmaceutical residues from wastewater. RISE. Swedish Research Institute

[33] Amanda Jasi. Removing pharmaceutical pollutants from wastewater. The Chemical Engineer. Available in https://www.thechemicalengineer.com/news/removing-pharmaceutical-pollutants-from-wastewater/

substances that are present, for example, ozonation are more effective on some substances, carbon on others. Sometimes it's better to have them in combination.

Some of the technologies that are usually used in combination within WWTP are:

- Fenton reactions
- Reverse osmosis
- Membrane
- Moving Bed Biofilm Reactors (MBBR)
- Membrane Bioreactors (MBR)
- Deep bed filters

Added to this, exists other solutions such as the three-pipe out that sort and separates wastewater streams in food, gray and black water making the concentrations and volumes of treating blackwater by itself less and then more efficient to clean. In general, there is a need to adapt and contextualize the analysis to evaluate it is enough with smaller cleaning facilities closed to highly polluted areas (hospital, elderly care, production sites) or if we need to combine this with several cleaning steps also in the general wastewater treatment plant. Possible ideas forward to be validated- small wastewater treatment plants or cleaning facilities close to where there is most hazard- hospitals, elderly care facilities[34].

The next section showcases the identified solutions, including best practices (referring to management strategies or methods) as well as technologies and techniques. These solutions were shared at the three countries in multi stakeholder workshops that contributed to the general objective of the project.

Best practices

The vision of **ClosingGaps** is to contribute to the increasing and strengthening of relations between the actors in the regions through practical tools.

The list is not conclusive and do not pretend to set a standard (see section limitations of the project) but represents a methodology that facilitates and accelerate practical collaboration in the region.

Table 4
Best Practices

Practice	Description
Public awareness campaigns	Medsdisposal[35] is a campaign to raise awareness on how to dispose unused or expired medicines appropriately in Europe, bringing information on current disposal schemes in European countries to one place. The desired effect is the improvement of public awareness on medicines reverse logistics and the effects of improper disposal of unused medicines.
Environmental permit	This could be especially important for producers, as has been showed legal process used as a standard for pharmaceutical industries can even include a continuous measuring of substances in sewage water.
Physiotherapy on prescription	Physical activity on Prescription (FaR), is part of the National and regional policies for health in Sweden[36]. The FaR method is scientific, and evidence-based and has been used on a larger scale in Sweden for more than 20 years. Regular physical activity is important for our health and well-being, but it is also proven to prevent and treat different diseases, such as heart disease, stroke, diabetes and depression. In the

[34] For more information RecoLab at https://www.recolab.se/

[35] For more information about this initiative check https://medsdisposal.eu

[36] More information: https://www.folkhalsomyndigheten.se/livsvillkor-levnadsvanor/fysisk-aktivitet-och-matvanor/fysisk-aktivitet/fysisk-aktivitet-pa-recept-far/

	context of the challenge represented by the intensive use of pharmaceuticals, the FaR can represent a practice that will increase the well-being of the population and decrease the demand for medicines, and residuals in the environment [37]
Preventive support for risk patients	Standards on how to support individuals with unhealthy habits with aim to minimize the risk to develop Diabetes, heart disease, cancer etc[38] can have an important impact on the consumption of extremely hazardous substances usually related to these treatments.
Prescription when hazardous substances	For environmentally hazardous substances it is highly recommended that these require prescription. This to not make them easily accessible. For example, antibiotics, and Diclofenac are not on prescription in all countries, making overuse possible.
Prescription- choose less hazardous substances	Prescribe a less hazardous alternative pharmaceutical when is possible, without affecting the treatment of the patient. This requires engagement of the medical staff as well as updated guidelines on the different medicines and its effects.
Drug Review. "*Minimizing by responsibility*"	At primary care – go through patient medication list if more than five drugs are prescribed. This procedure to check if all are necessary and if they are well combined.[39]
Waste management routines	This can derive from legislation, but also from internal documents, such as protocols and routines from the daily operation within healthcare facilities. This can derive in the development of material tailor to users and patients that use and dispose the medicines at home.
Environmental information about the medication.	Information about what a specific medication contains not only the description of the Active Pharmaceutical Ingredient (API), but also the Instructions on how to dispose of it. In the most complete possibilities, it would include information about environmental impact. In the case of Sweden exist the platform FASS. [40]
Sustainability criteria in public procurement	The sustainable criterion in public procurement is used in countries such as Sweden and Norway, among others, to create incentives for environmental consideration in pharmaceutical manufacturing.[41]
Collection of drugs	The way to collect unused drugs differs between countries, from waste plants to healthcare facilities and pharmacies. Best practices should be compared to find the most efficient and safe way to do it. Apoteket in Sweden have a take back principle

[37] More information can be found at Fysisk aktivitet på recept (FaR) in https://www.folkhalsomyndigheten.se/livsvillkor-levnadsvanor/mat-fysisk-aktivitet-overvikt-och-fetma/fysisk-aktivitet-och-stillasittande/fysisk-aktivitet-inom-vard-och-omsorg/fysisk-aktivitet-pa-recept-far/

[38] The Swedish authority (Socialstyrelsen) has Guidelines. Available in https://www.socialstyrelsen.se/kunskapsstod-och-regler/regler-och-riktlinjer/nationella-riktlinjer/information-till-patienter/om-publicerade-riktlinjer/levnadsvanor/

[39] Social Styrelsen. HSLF-FS 2017:37 Socialstyrelsens föreskrifter och allmänna råd om ordination och hantering av läkemedel i hälso- och sjukvården - Socialstyrelsen. Chapter 11. Available in https://www.socialstyrelsen.se/kunskapsstod-och-regler/regler-och-riktlinjer/foreskrifter-och-allmanna-rad/konsoliderade-foreskrifter/201737-om-ordination-och-hantering-av-lakemedel-i-halso--och-sjukvarden/

[40] For more information access: https://www.fass.se/LIF/startpage; https://www.lif.se/contentassets/f71a626a8c5746dfbddfe3e23f17ad32/environmental-classification-of-apis-on-fass-se.pdf

[41] Lif has participated in the development of sustainability criteria for public procurement. For more information consult: https://www.lif.se/contentassets/b7cf255755504f78a906f3eba8a6ae38/environmental-classification-of-pharmaceuticals-att-wwwfassse.pdf, https://www.lif.se/contentassets/f71a626a8c5746dfbddfe3e23f17ad32/environmental-classification-of-apis-on-fass-se.pdf

	where you gain points to shop for to increase individuals to hand in the pharmaceuticals[42].
Smart Marketing	The generation of positive incentives for responsible consumption and use of the medicines[43].
Pharma Swap	Floow2[44] has develop a sharing marketplace where pharmacists can share demand and supply of subscription medication. Wholesale organization can share stock approaching the expiry date. By optimizing usage of medication, it contributes to enormous cost savings in healthcare, whilst at the same time working on a more sustainable system by preventing potentially hazardous medicines from unnecessarily entering waste streams.
Regulated Monitoring	Requirement to monitor substances to define concentrations in connection to wastewater treatment plants, hospitals and hot spot areas.
Cross-sectorial cooperation	Better coordination between the organizations of the healthcare and environmental sectors regarding the prevention and handling of pharmaceutical residues throughout the whole chain. The strengthening of the conditions for collaboration can be foster through events, dialogues or projects as has been shown by the project ClosingGaps.

Technical /technological solutions

ClosingGaps presents techniques/technologies available at the market, already in use, which address different parts of the chain related with pharmaceutical residuals (Fig.1). These were used as the main vehicle for discussion and for facilitate and contribute to regional strategies to reduce the pharmaceutical residuals in the Baltic Sea.

The identified solutions cover different stages over the chain related to the problematic, starting with the preventive measures and finalizing with wastewater treatment installations.

Table 5
Technical/ technological solutions

Name	Stage in the value chain	Description
Smart and green design of medicine	Preventive	"Green design" of pharmaceuticals is defined as a small-molecule-pharmaceutical substance that is non-toxic, non-bio-accumulative, and easily degradable.
Smart packaging	Preventive	Exists several best practices that use packaging to reduce at minimum the possibility of waste medicines. These include carts, or blister packaging instead of jars, to facilitate a proper use of the medicine.
Pcure by Pharem	Preventive	pCure is designed to work against pharmaceutical residues that have passed through the body. There are many different residues that are considered harmful for the environment and are generally found in many medicines such as antibiotics, painkillers, birth control pills, anti-depressants also. The advantage of the product is that it can be used at home, targeting the part of the value chain

[42] For more information: Apotekets kundklubb. https://www.apoteket.se/apotekets-kundklubb/
[43] An example of the use of marketing as a tool for information can be checked in https://www.apoteket.se/hallbarhet/socialt-ansvar/
[44] The details of the design of the sharing market place can be consulted in https://www.floow2.com/

		where most pollution occurs and where there are less solutions available[45].
Zymatic by Pharem	Preventive/Hospitals and healthcare facilities	The Zymatic solutions provide water treatment based on a mixture of different chemical reaction mechanisms. This feature offers advances over many older and conventional water treatment methods that have only one reaction mechanism[46].
Pactosafe by Paxxo	Preventive/Hospitals and healthcare facilities	Safety cabinets as the aerosol-tight heat sealing creates a safe interim storage and a safe disposal of hazardous waste. The waste sealing unit is well suited for toxic waste and drugs as the waste can be packed airtight[47].
Pharmafilter	Wastewater treatment plant at the hospital/healthcare facilities	Filtration process connected to hospitals. The Pharmafilter system is made up of the purification installation and grinders. The materials that have been ground up by the grinders are combined with the wastewater and then transported to the Pharmafilter installation using the hospital's internal sewage system[48].
Bioksa by Yaquatec	Wastewater treatment plant	Hybrid nanofiltration and advanced oxidation system to treat greywater effluent from smart city; Coupled Ozonation and Biological Active Carbon (BAC) to treat WWTP secondary effluent[49].
Three Pipes out by Recolab	Wastewater treatment plant / Recovery Laboratory	A recovery system in the Swedish city of Helsingborg. It pioneers an energy-efficient, circular sanitation process that source-separates blackwater, greywater and food waste through separate pipelines to recover nutrients, produce biogas and recycle greywater to drinking water quality. Also extraditing in the process Phosphorus and nitrogen that are fertilizers for agriculture when adding microbes that are otherwise expensive to mine and produce[50].
Ozonates	Wastewater treatment plant	
Nordic Water Dyna Sand Dyna Disc Dyna Cloth	Wastewater treatment plant	Nordic Pharma is a concept on how to purify pharmaceuticals, assembled into systems[51].

[45] For more information visit https://www.pharem.se/pcure/
[46] For more information visit https://www.pharem.se/zymatic/
[47] For more information visit https://paxxo.se/en/our-solutions/pactosafe-waste-sealing-unit/
[48] For more information visit https://pharmafilter.nl/en/oplossingen/pharmafilter-platform/
[49] For more information visit https://yaquatec.com/en/technologies/
[50] For more information visit https://www.recolab.se/
[51] For more information visit https://www.nordicwater.com/sv/

ClosingGaps report an alignment between the normative principles, and the availability of best practices, techniques and technologies for reducing pharmaceutical residuals. The solutions present in the project represent a sample not an exhaustive market analysis. The project represented an initiative that show the need to have a platform to facilitate the regional collaboration, exchange and mutual learning in topics as important as the reduction of pharmaceutical residues in the Baltic Sea. This will only be beneficial in the common sharing of knowledge and for the environment and humans. The project has increased the potential synergies between sectors in the region.

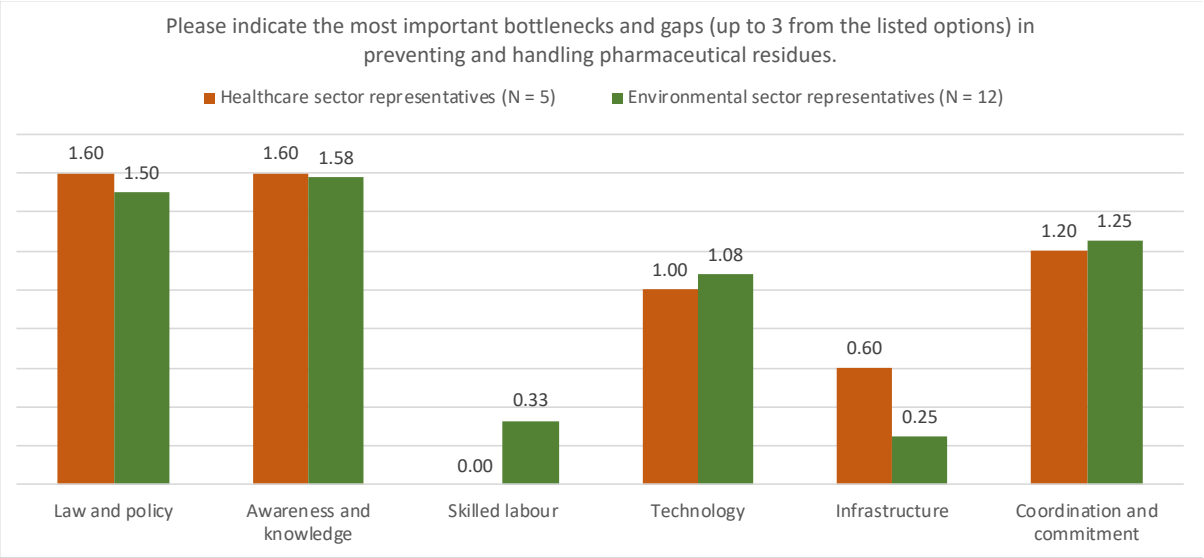
Gap analysis

The process of identification of solutions has also facilitated the identification of practical gaps for the sharing of these a long the region. This has been part of the learnings from the information generated by the desk research, but especially the information generated by the interviews and the discussions during the workshops.

In this context ClosingGaps has identified several gaps that can be turn in opportunity areas for collaboration between the different countries in the Baltic Sea region. For this project, they have been organized in four types: Knowledge Gap, Normative Gap, Technical access and market Gaps and Collaborative Gap.

This in line with the practitioners when asked to select up to three most important bottlenecks and gaps, the participants of the Workshop 3 representing both healthcare sector and environmental sector indicated that the priority should be to improve awareness and knowledge, law and policy, and that there is a need for a better coordination and increased commitment, as well as for advances in technology (Figure 4).

Figure 4. *Importance of the identified bottlenecks and gaps*



Knowledge gap

The highest raised concern common among all stakeholders are awareness. It was commonly highlighted that there is a need of knowledge sharing along the whole value chain between the countries.

The first level regarding knowledge is linked to the importance and implications of the pharmaceuticals at large. In the three countries exist some awareness of the importance and complexity of the issue. The available information and knowledge tools exist within the pharmacies and at certain extent in medical personal, but still exist a gap in terms of the outreach of the material to different and broad audiences. Countries have different levels of priority for this subject, being significant that in Sweden exist more measures implemented. The information needs to be adjusted to each stakeholder that is approached. In

example doctors are educated on diagnosis and patient treatment not necessarily on sustainability. Engineers (chemicals, technical) are educated in their segment, the public are not aware.

The second level of knowledge refers to the dissemination of techniques and technologies. In this sense, there is a challenge related with the lack of testbeds, meaning mid-size laboratories for the innovation with techniques at large scale.

Normative Gap

The normative gap includes policy, regulations, and normative standards. Regulations are important as they can play the function of a catalyst for investments and collaborations.

The main gap that has been identified is that the EU framework represent a challenge regarding the application of regulations. In practice, the EU directives have no specification of what chemicals to search for in the wastewater treatment plants, being a negative incentive to update the wastewater treatment plants with new techniques.

Another normative incentive that can be considered is the environmental requirements and permissions that different industries have in each country. This kind of regulations represent a security measure for the environment and relieves at least the cost of maintenance of the purification methods in the municipal treatment plant.

Finally, it is important to highlight the role that the global/regional frameworks and commitments on sustainability can play in the generation of efforts and political commitments from the different actors involved. In this case has been mentioned the Agenda 2030 for Sustainable Development, the European Green Deal and the Helsinki declaration over the Baltic Sea.

Market maturity gap

Related to the legal gaps are also the maturity of the market, this relation is mainly because it is usually after regulations that investments or innovations are accelerated. This has been made clear through the interviews and the statements of WWTP awaiting the new regulations before doing investments, and limit somehow the innovation process that can evolve to a more competitive market that could turn into more and more diverse collaborations.

The largest implication is that is hard to implement new techniques tried in testbeds or smaller facilities as they are not tried for full scale activities. The challenges regarding new innovations entering the scene are often related to standards and law requirements, they can't risk anything because of lawsuits against them better to choose proven techniques[52]. The maturity of the market, as it is with the rest of the gaps, it is highly connected to a cross sectoral collaboration. The technical institutions, universities, and research must be taken into combination with public policies and incentives as well as the possibility to have a broader possibility for having testbeds. This is different across the countries, but in general, points to the added value of collaboration and the need to establish platforms for sharing experiences and techniques that could generate incentives for all the actors involved to accelerate the sustainable transformation of the healthcare sector.

Effective collaborations gap

It was mentioned along all the activities that a more and deeper collaboration between the sectors and actors should be one of the main priorities to any strategy designed for reducing the pharmaceutical residuals in the Baltic Sea. A very concrete example is the healthcare and environmental sectors, just to mention two areas that require a more urgent collaboration. When asked to evaluate to what extent this cooperation is important in preventing and handling pharmaceutical residues, the participants from the Workshop 3, representing both healthcare sector and environmental sector indicated that it is important (Figure 5).

[52] Interview with Svenskt Vatten

Moreover, the participants indicated that the current level of cooperation between these two sectors could be improved (Figure 6).

Figure 5. *Importance of cooperation*

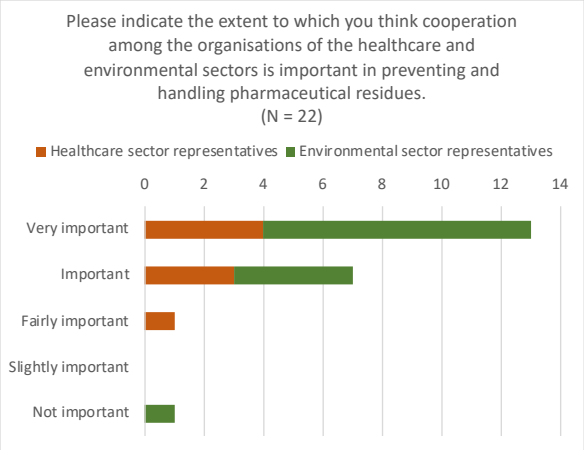
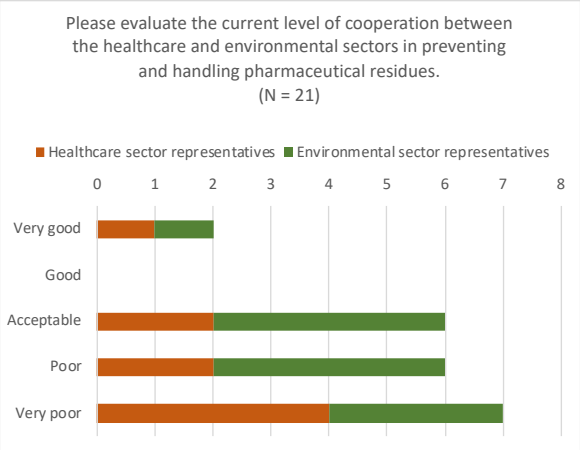


Figure 6. *Current level of cooperation*



Research and development are areas that are linked to the development of innovations and the possibility to set the conditions for the market to take risks in new products, solutions that could contribute to the solution of a specific challenge. But the collaborative efforts go beyond the healthcare and environmental areas. One of the main findings is the mention of financial institutions, companies, NGOs, academia, and development cooperation actors, showing that the challenge is perceived as a systemic threat, a complex chain that should be addressed by most of the sectors and across the countries.

The interviews shows that there are two realities from collaboration, one is the desired reality where the cross-sectoral collaborations occur, the actors recognize their complementarity and define common agendas, and projects where everyone can have a benefit and the major would be to the healthcare sector and the population beneficiaries from the provision of health services. In this desired reality exist a common language, technical instruments, and enough resources to implement the defined projects. Unfortunately, this reality is not the common scenario. The second reality shows a fragmented reality, where it is possible to find collaborations but are very punctual a not generalized.

The **ClosingGaps** project is by itself a multi stake holder collaboration that shows the importance of addressing the challenge in a collective and inclusive practical dialogue[53].

Considering the results and findings of the project, it is proposed a Roadmap that try to influence positively on the challenge from the approach of the project, this is with the focus on the **sharing and learning about best practices, techniques, and technologies**, to reduce the identified gaps and increase the practical collaboration between the different relevant actors in the Baltic Sea.

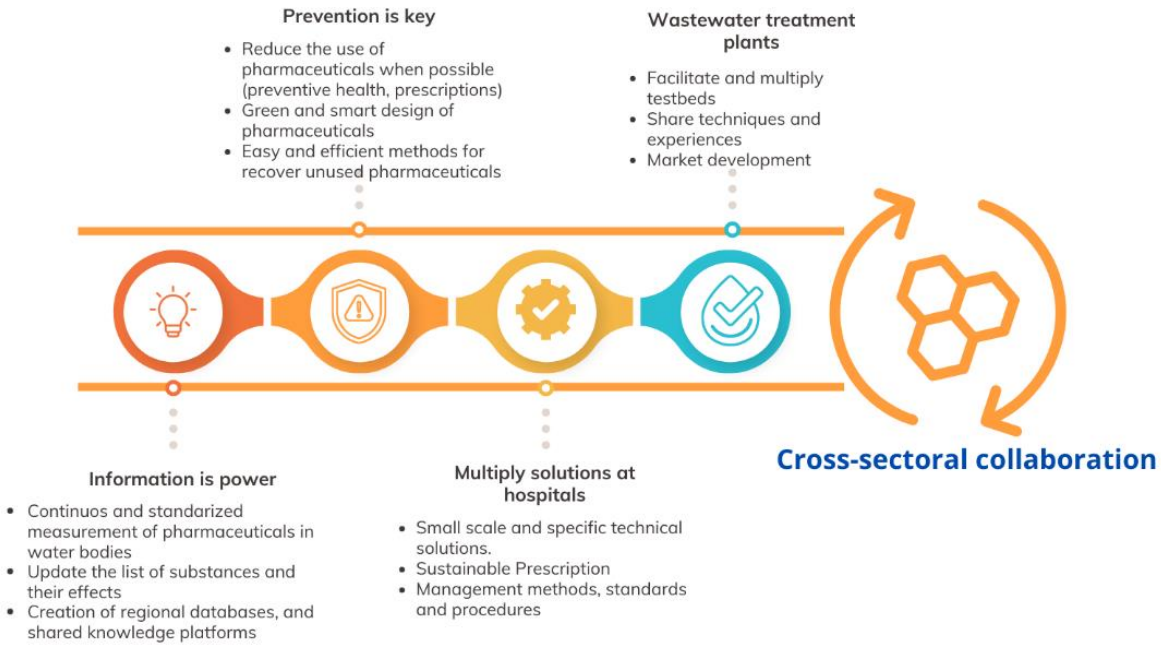
[53] Another example is the EMPEREST (interreg funded project) with plan to test different technologies in pilot settings- incl pharmaceuticals and other micro pollutants as micro plastics.

Roadmap

The project has had very relevant results which contributes to the general objective to reduce pharmaceutical residuals. The description of the normative framework and the identification of the best practices and solutions allow to identify the practical gaps for the effective implementation of strategies and the adoption of techniques and technologies for the general purpose.

Using the main findings and the information produced within the project a roadmap is presented. The roadmap reflects the opportunity areas identified in the gap analysis and so it is structured as a collaborative course of action for the relevant stakeholders, a systemic overview for change.

Figure 7: Roadmap



Information

This includes several specific activities to take into consideration: The regional context requires a continuous and standardized methods for measurement and reporting the presence of pharmaceuticals in the water, this includes not only the Baltic Sea, but also the rivers and the sewage systems, particularly those close to healthcare facilities. This can help to define a baseline, and measure improvements, and the possibility to choose the most suitable solutions according to the specific context.

A big opportunity area in terms of collaborations around information sharing is the regional and coordinated updating of the list of substances and its effects on the environment. This requires targeted and customized information, for example, information for the public, for healthcare workers, medical staff, technical solutions producers, decision—makers or wastewater plant operators.

The impact from this specific step is the increase of awareness of the pathways by which medicines enter the environment, the impacts, and the nature of their effects. This can incentivize behavioral changes of the users, but also of the producers and the medical staff. This will also contribute to other aspects of the healthcare provision agenda such as preventive health. It is important to remember that almost all the pharmaceutical residuals end in the sewage directly from the user, that will say the public. To facilitate the

flowing of information and incentivize collaboration it is important to generate regional platforms, where the shared knowledge in the whole value chain can be consulted in an easy way.

Prevention

As has been stated, the preventive dimension of this issue has different variables that we need to take into consideration. The first is to reduce the demand of pharmaceuticals, when possible; this includes the preventive health and prescription, when necessary, instead of full access, without compromising the health of the patient.

Added to this is to give special attention to the green and smart design of the pharmaceuticals. This means increasing the possibility to reduce the impact on the environment from the design of the substance and the packaging. As has been stated, this should include a wide range of collaborations that can connect the pharmaceutical producers with the environmental experts, and the engineers of packaging, just to mention a couple of actors that should be included.

Finally, as part of the preventive measures is the possibility to recover as much as possible of pharmaceuticals not used. This implies the improvement of the systems for the collection and management of unused medicinal products and waste pharmaceuticals. In terms of prevention every actor could have a level of ownership and impact to address the challenge.

Solutions at Healthcare facilities

The role of healthcare facilities in reducing pharmaceutical residuals can be multiple. Healthcare facilities are the origin of prescriptions and have a key role in handling pharmaceuticals and in the recovery of non-used substances, as well as redistribution internally at hospitals.

The Healthcare facilities can impact the number of residuals by the handling and management systems in place. This includes standards, procedures, techniques, and solutions. As major sources of pharmaceutical residuals can be considered pre-treatment of wastewater before discharging into sewage systems.

Finally, it is important to foster the use and implementation of solutions taking care of pharmaceutical residuals and other hazardous substances hinder them to reach water bodies. The collaboration of companies with hospitals would be a factor that can accelerate this process.

Wastewater treatment

The last stage of the roadmap is the work within wastewater treatment plants. At a first action it should be exchanging information about the available techniques. ClosingGaps has shown the potential of practical dialogue to identify the best solutions, but specially the great value of exchange of experiences and knowledge between the countries. As one practical example participant actors within the workshops expressed the importance to know more about what the other countries are doing, about installed techniques and the efficiency of them in different settings. One of the reasons is the language difference and then the information is not easily collected by others.

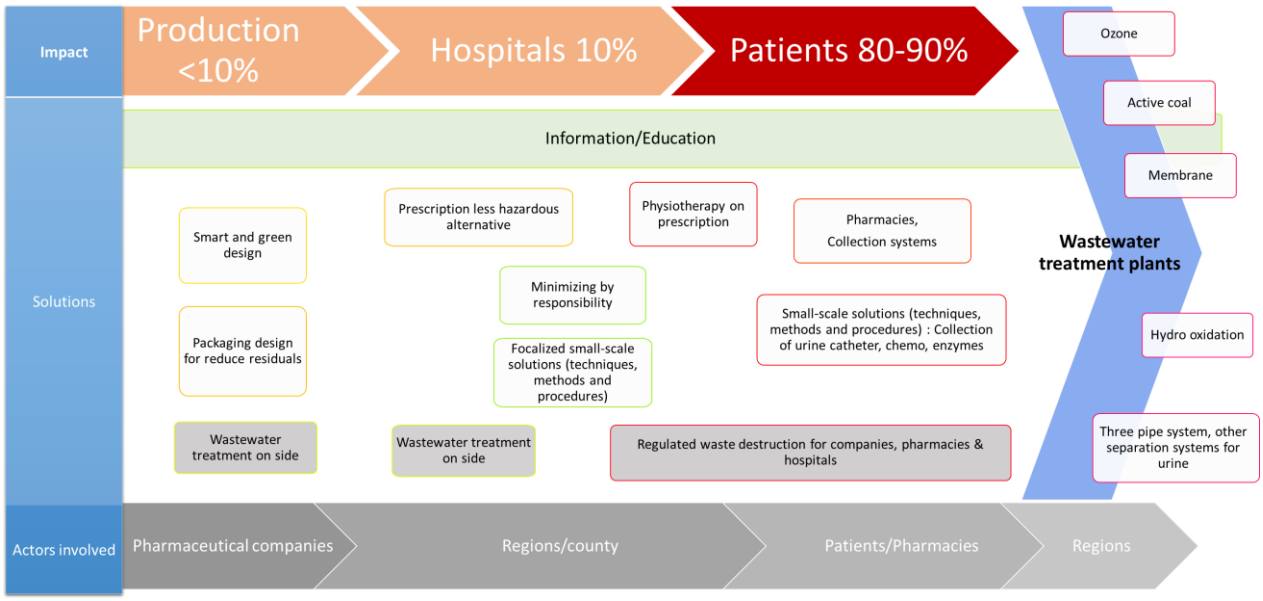
One specific example is the discussion about the normative framework and the best options for reduction of pharmaceutical residuals in the Baltic Sea. The wastewater treatment plants implementation of new techniques require economical investments and support how to meet legal and normative requirements. [54]

It is very expensive for WWTP to invest in techniques that are not proven. One specific action that can contribute is to facilitate testbeds or small-scale laboratories to test technologies or having R&D collaboration. This would contribute to the maturity of the market, one of the specific gaps identified previously to foster innovations and collaborations. An extra added value would be to have testbeds where actors from different sectors and countries could collaborate.

Conclusion

Completing the project has indicated the challenge to find effective techniques and practices that focus on the reduction of pharmaceutical residuals early in the value chain. A lot of existing techniques are implemented in the end pipe which is logical due to the circumstance that most of the pollution is through patients. Although we need to do what we can to deter pharmaceutical from ending up in the sea and freshwater as much as we can and all solutions in the value chain are important.

Figure 8: Conclusions overview



Starting in the beginning of the value chain, 10% is said to be stemming from production. The biggest polluter is the patients, being up to 90% of the source of pharmaceutical residuals. In below chart we can see the overview of the situation and conclude that is crucial that all stakeholders take responsibility and precautions for their parts in the value chain. The role of regulation can easily impact companies, and hospitals, but not as much in the patients, making public awareness important for any strategy in the matter. Such a strategy needs tailored messages and relevant information that can influence a very particular actor in the value chain. This applies to every actor, for example with medical staff educated in patient care but not very much on environmental and sustainability issues. The same applies to actors such as pharmacies, or WWTP.

In this perspective, information, education, and knowledge would be the main instrument for facilitating dialogue. The way that the different gaps are reflected among partner countries shows that it is necessary to

[54] Svensk Vatten. Wastewater Treatment Pains – Pharmaceuticals in our water environment. March 2021. Available in https://vattenbokhandeln.svensktvatten.se/produkt/waste-water-treatment-pains/

educate about the importance and relevance of the topic in the whole value chain and the actors involved. There is a need to think of preventive measures as far as it is possible without compromising patients' needs and safety.

Pharmaceutical companies have the possibility to minimize pharmaceuticals in the sewage, this includes reviewing the productive model used to assess environmental risk and to inform about it. There are several incentives from the production side to do it as safe and environmentally friendly as possible. New techniques regarding the composition of drugs are important, i.e. the creation of pharmaceuticals that are bio-degradable. It is easier and more economically effective to innovate and produce new coming drugs bio friendly than to alter old existing medicines.

Substitution with another substance requires that one is available and to give the effect that the new substance has a less environmental impact. Pharmaceutical substances are designed to be effective at very low levels and to be persistent enough to cope with our gastrointestinal tract to reach the right receptor in the body and therefore also indirectly become very potent environmentally hazardous substances [55].

The EU introduction of the Producer Responsibility, in the polluter pays principle, may finance in part the investments and the treatment of pharmaceutical residues in municipal wastewater treatment plants. With this said the Pharma industry finds that if EU wants to implement such a principle, they should do it broader as there are furthermore critical industries that also should pay for their pollution.

The collection and organized take back of leftover pharmaceuticals to the pharmacies is an important scheme to hinder pharmaceuticals from ending up in the water waste stream. Disposal of medicines and medicines is sent to incineration in specially adapted incineration plants.

According to research, it seems like the most efficient way of reducing pharmaceutical upstream is to limit their use. The economic and environmental gains also seem to be more beneficial when reducing pharmaceuticals early in the value chain.

When talking about WWTP including end pipe solutions, the most efficient way to minimize the pharmaceuticals ending up in sewage is to separate urine and faces by i.e three pipes out system or other system that minimize the concentration of volume to be treated. One potential gain by doing this is the possibility to use phosphorus and nitrates to be used in agriculture as fertilizer, and to gain excess heat and sometimes gas in the process, just to mention some possibilities.

Globally, the water and wastewater organizations need to continue to monitor developments and, in dialogue with the regulatory authorities. For among other things, investigate the need to implement advanced purification systems at the treatment plants.[56] There are parallel development of regulations in EU looking at pharmaceuticals and PFAS, it is important to have an overview that includes techniques and solutions that take care of all challenges as part of the decision for the best solutions.

According to the interviews, the most efficient techniques for treating pharmaceutical residuals today are the ozone treatment and the active coal. Those solutions have negative impacts on the environment and are not energy efficient. This creates an opportunity area to continue with the quest for better techniques through mutual learning and collaboration.

One of the main discussions was the potential of installing small-scale treatment plants near hospitals or elderly care facilities. The response from the actors interviewed shows that on one hand it could be said that is not a cost-efficient solution, as this can be considered extra costs as still is necessary to have municipal/city wastewater treatment plants. On the other hand, it was mentioned that local treatment can counteract the

[55] Läkemedel i vattenrecipienter hur prioriterar vi framtidens rening? Länsstyrelsen Skåne Författare: Pardis Pirzadeh, Ola Svahn, Susann Milenkovski, 2021:13 p 59-61, Interview with LIF, Bengt Mattson.

[56] Svensk Vatten. Wastewater Treatment Pains – Pharmaceuticals in our water environment. March 2021. Available in https://vattenbokhandeln.svensktvatten.se/produkt/waste-water-treatment-pains/

release of antibiotics in high concentrations from hospitals, which could reduce the spread of resistant bacteria. What is clear is that installing local treatment on the sub-flow from the hospitals is therefore not a sufficient solution for drug emissions in general.[57]

If we are open for new models, for example, the RecoLab's three pipe out, could be one part of the solution, for example treating greywater and/or food waste, closer to the community. This could have an economic impact by simplifying the process on a local scale and also shortening the pipelines.

In conclusion, there is no solution that is 100% efficient on its own and so we need to work with the issue along the entire value chain and do what we can in each step. The strategies and potential solutions depend on local contexts, incentives, and others. As the Roadmap indicates, it is important to make information and knowledge available, not only about the effects of the substances but also about the existence and availability of different solutions (methods, techniques and technologies).

The project has created a useful collaborative methodology that allow to envision the development of a platform to accelerate the dissemination of techniques, technologies, and solutions, thereby creating incentives for new partnerships and business models. Such an effort should include other sectors and areas such as veterinary, farming and elderly care as hot spots for pharmaceutical residuals. Society at large should also work to reduce the need for drug use by working preventively with public health such as wellness and work to prevent illness, including mental health.

There will be no possible improvement in the strategies to reduce pharmaceutical residuals if collective responsibility is not pursued as the course of action. In this sense, information sharing and coordinated action including all stakeholder along the value chain, is required to close the gaps to implement regulations, new technical solutions and efficient practices for reducing the pharmaceutical residuals in the Baltic Sea Region.

[57] Ibid.

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