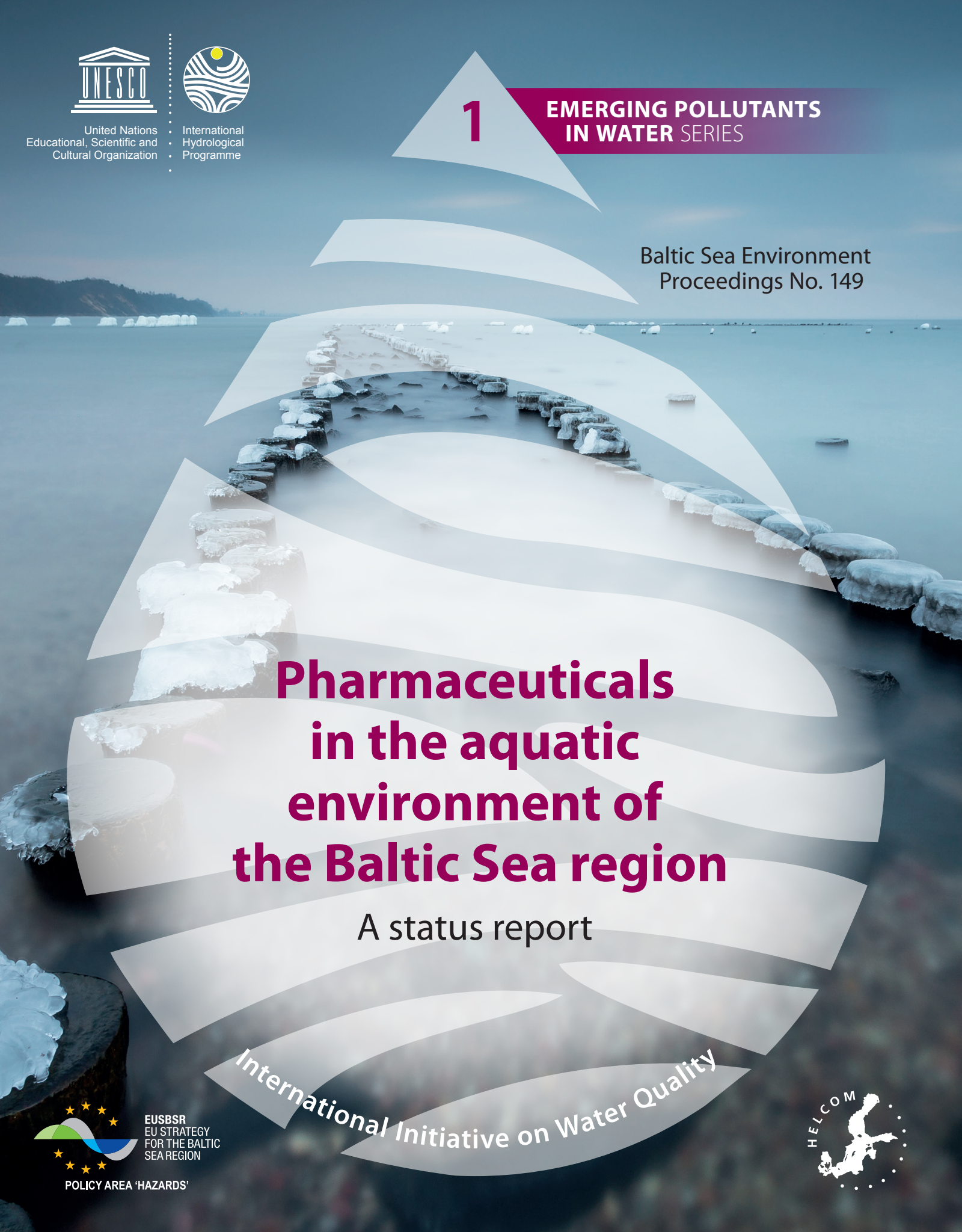


United Nations Educational, Scientific and Cultural Organization

International Hydrological Programme

1 EMERGING POLLUTANTS IN WATER SERIES

Baltic Sea Environment Proceedings No. 149

Pharmaceuticals in the aquatic environment of the Baltic Sea region

A status report

International Initiative on Water Quality

EUSBSR EU STRATEGY FOR THE BALTIC SEA REGION

POLICY AREA 'HAZARDS'

HELCOM

United Nations Educational, Scientific and Cultural Organization

International Hydrological Programme

1 EMERGING POLLUTANTS IN WATER SERIES

Baltic Sea Environment Proceedings No. 149

Pharmaceuticals in the aquatic environment of the Baltic Sea region

A status report

International Initiative on Water Quality

EUSBSR EU STRATEGY FOR THE BALTIC SEA REGION

POLICY AREA 'HAZARDS'

HELCOM

Emerging Pollutants in Water Series
Editor-in-Chief: Sarantuyaa Zandaryaa, UNESCO

Volume No.1 • Pharmaceuticals in the aquatic environment of the Baltic Sea region – A status report

Writing and editorial team
Report writing and data compilation
Niina Vieno (Law and Water Ltd.), Pär Hallgren and Petra Wallberg (Sweco Environment AB)
Editors
Minna Pyhälä (GreenWords) and Sarantuyaa Zandaryaa (UNESCO)

Contributors
Estonia
Eda Andresmaa, Margus Korsjukov and Rene Reisner, Ministry of the Environment
Denmark
Susanne Boutrup, Danish Centre for Environment and Energy, Aarhus University
National Focal Point for point sources, Danish Agency for Water and Nature Management
Finland
Päivi Fjäder, Jukka Mehtonen and Lauri Äystö, Finnish Environment Institute – SYKE
Germany
Arne Hein, Anette Küster and Ulrike Pirntke, German Environment Agency
Poland
Magdalena Kaminska, Chief Inspectorate for Environmental Protection
Aleksandra Orlita and Marta Rybka, Institute of Meteorology and Water Management, National Research Institute Gdynia
Sweden
Jenny Hedman and Maria Linderoth, Swedish Environmental Protection Agency
HELCOM Secretariat
Dmitry Frank-Kamenetsky and Ulla Li Zweifel, HELCOM Secretariat
UNESCO
Sarantuyaa Zandaryaa, Division of Water Sciences – International Hydrological Programme (IHP)

This report is a case study in the framework of UNESCO Emerging Pollutants in Water Series under UNESCO-IHP's International Initiative on Water Quality (IIWQ) Project on 'Emerging Pollutants in Wastewater Reuse in Developing Countries'. It was developed jointly by the Baltic Marine Environment Protection Commission – Helsinki Commission (HELCOM) and Policy Area (PA) Hazards of the European Union Strategy for the Baltic Sea Region (EUSBSR). The case study was funded by UNESCO, HELCOM and PA Hazard. UNESCO thanks all contributors to the publication.

Published in 2017 by

The United Nations Educational, Scientific and Cultural Organization
7, place de Fontenoy, 75352 Paris 07 SP, France

and

HELCOM

ISBN 978-92-3-100213-7

HELCOM, Baltic Sea Environment Proceedings No. 149, ISSN 0357-2994

Suggested citation: 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.

Cover photo: © Tomasz Wozniak, Shutterstock.
Graphic design: Corinne Hayworth
Printed in France by: UNESCO CLD. SC/HYD/IIWQ/2017/1 CLD 291.17

Table of contents

List of figures

List of tables

List of acronyms and abbreviations

BSAP	Baltic Sea Action Plan of HELCOM
EQS	Environmental quality standards
EU	European Union
EUSBSR	European Union Strategy for the Baltic Sea Region
GES	Good Environmental Status
HELCOM	Baltic Marine Environment Protection Commission, Helsinki Commission
IHP	International Hydrological Programme of UNESCO
IIWQ	International Initiative on Water Quality of UNESCO
LOD	Limits of detection
MSFD	Marine Strategy Framework Directive of the European Union
MWWTPs	Municipal wastewater treatment plants
PNEC	Predicted No Effect Concentration
UNESCO	United Nations Educational, Scientific and Cultural Organization
WFD	Water Framework Directive of the European Union
WWTPs	Wastewater treatment plants

Glossary

Adsorption	Adhesion of atoms, ions, or molecules from a gas, liquid, or dissolved solid to a solid or liquid surface without involving a chemical reaction
Analgesic	A drug that relieves pain
Anticoagulants	A substance that prevents blood from forming clots
Antidote	A substance that stops the harmful effects of a poison
Antihistamine	A drug that is used to treat allergic reactions and colds
Biodegradation	Decomposition of organic matter by aerobic or anaerobic microorganisms
Biota	The plant and animal life of a region
Diuretics	Drugs that increase the excretion of water from bodies
d.w.	Dry weight
Effluent	(treated) Wastewater flowing out of a treatment plant.
Emerging pollutants	Any synthetic or naturally occurring chemical or any microorganism that is not commonly monitored in the environment but has the potential to enter the environment and cause known or suspected adverse ecological and/or human health effects
HELCOM Contracting Parties	The Contracting Parties of HELCOM are Denmark, Estonia, the European Union, Finland, Germany, Latvia, Lithuania, Poland, Russia and Sweden
HELCOM sub-basin	For HELCOM assessment purposes the Baltic Sea is divided into different sub-basins as defined in Attachment 4 of the HELCOM Monitoring and Assessment Strategy (HELCOM 2013b)
Hormone	A naturally-occurring or synthetic substance with a similar effect to that of an animal or plant hormone that inhibit the function of hormones upon their specific antagonists sites
Influent	Sewage entering a wastewater treatment plant
Leaching	Process of removal of soluble and colloidal substances by water percolating downwards through soil layers
Limit of detection (LOD)	In analytical chemistry, the limit of detection is the lowest quantity of a substance that can be distinguished from the absence of that substance (a blank value) within a stated confidence limit (generally 1%)
Load	The amount of pollution entering the environment (i.e. input)
Nanofiltration	A membrane filtration-based method that uses nanometer sized cylindrical through pores
Ozonation	Ozonation (also referred to as **ozonization**) is a chemical water treatment technique based on the infusion of ozone into water

Photodegradation	The alteration of materials by light
Pollution	The result of substances/contaminants entering water bodies and thereby degrading the quality of water. Water pollution can have natural causes due to environmental causes (i.e. arsenic) or by anthropogenic activities (i.e. emerging pollutants).
Removal rates	The rate of removal of a substance through wastewater treatment
Retentate	That which is retained, for example by a filter or porous membrane
Sewage	Wastewater and excrement (blackwater) conveyed in sewers
Sludge	The residual, semi-solid material that is produced as a by-product during sewage treatment of industrial or municipal wastewater
Therapeutic group	Classification of pharmaceuticals according to their therapeutic effects
Wastewater	Water containing waste liquid or solid matter discharged after various uses
w.w.	Wet weight

Executive summary

Emerging pollutants present a new global water quality challenge with potentially-serious threats to human health and ecosystems. Pharmaceuticals represent a major group of emerging pollutants found in freshwater and coastal waters.

Pharmaceuticals are essential for human health and well-being. However, the growing use of pharmaceuticals resulting from e.g. population growth and aging has become a new environmental concern due to their potential negative effects on humans and ecosystems. Not insignificant quantities of unmetabolized and unused pharmaceuticals and their byproducts are discharged into freshwater systems with untreated wastewater and effluents from wastewater treatment plants, as well as direct discharges from use within animal husbandry and aquaculture. These pollutants reach coastal and sea waters, as ultimate sinks.

The occurrence of pharmaceutical substances in the environment is of global concern and the extent of their risks and impacts on human health and biota is largely unknown. This publication presents the first regional report with a comprehensive overview of the occurrence, concentrations and pathways of pharmaceuticals into the environment in the Baltic Sea region.

The publication provides a comprehensive compilation of available data and information on the occurrence of pharmaceuticals in the Baltic Sea freshwater and marine environment and of their main sources and pathways collected through national reporting by the Contracting Parties to the Convention on the Protection of the Marine Environment of the Baltic Sea Area (Helsinki Convention).

The report also presents estimates of sales and consumption of drugs as well as information on handling of household pharmaceutical waste in some of the Baltic Sea countries.

Compiled data include concentrations of pharmaceuticals in river water, wastewater and Baltic coastal and open seas, as well as in Baltic Sea biota and sediment. The concentrations are compared to threshold values, when such information is available. Information about the environmental effects of pharmaceuticals in the Baltic Sea is also provided.

Data were provided by Denmark, Estonia, Finland, Germany, Poland, Russia and Sweden. The data presented in the report cover the period 2003-2014 and include 47,600 data points on sources and pathways of pharmaceuticals (i.e., measurements in wastewater influents and effluents, sludge and river water) and 4,600 individual data points on concentrations of pharmaceuticals in the coastal, open sea and transitional areas of the Baltic Sea marine environment. The report includes data on 167 pharmaceutical substances measured in the marine environment and 156 pharmaceutical substances and 2 metabolites sampled in surface freshwater systems and in influents, effluents and sludge of municipal wastewater treatment plants (MWWTPs) situated in Denmark, Estonia, Finland, Germany, Russia (St. Petersburg) and Sweden.

This report is a case study in the framework of UNESCO Emerging Pollutants in Water Series under UNESCO-IHP's International Initiative on Water Quality (IIWQ) Project on 'Emerging Pollutants in Wastewater Reuse in Developing Countries'. It was developed jointly by the Baltic Marine Environment Protection Commission - Helsinki Commission (HELCOM) and Policy Area Hazards of the European Union Strategy for the Baltic Sea Region, and serves as a follow up to the commitments of the 2010 and 2013 HELCOM Ministerial Declarations to assess the pharmaceuticals contamination in the aquatic environment.

Main results

Based on the collected data, the main sources of pharmaceuticals in the freshwater and marine environment in the Baltic Sea region appear to be the excretion of active substances consumed by humans and animals through their urine and faeces. The main pathway of pharmaceuticals into the freshwater and marine environment, according to the collected data, is via the discharges of MWWTPs effluents. According to a rough estimate, MWWTPs release into the environment about 1.8 thousand tons of pharmaceuticals per year. Only nine out of 118 assessed pharmaceuticals were removed from wastewater during the treatment processes with an efficiency over 95% and nearly half of the compounds were removed only partially with an efficiency of less than 50%.

The available data indicate that the most frequently measured substances in the Baltic Sea marine environment belong to the therapeutic groups of anti-inflammatory and analgesics, cardiovascular and central nervous system agents. The most frequently detected pharmaceutical substances belong to the therapeutic groups of metabolic and gastrointestinal agents, e.g., clofibric acid (detected in 83 of 128 samples), and central nervous system agents, e.g., primidone (detected in all 51 samples) and carbamazepine (detected in 136 of 266 samples). In biota, the largest number of different pharmaceutical substances and the highest concentrations were found in blue mussels.

Data gaps

Although the reported data provide the most comprehensive overview at the regional level of the magnitude of inputs of several pharmaceutical substances to the Baltic Sea, as well as their concentrations in freshwater systems and the marine environment, there are data gaps that need to be addressed in order to carry out a more complete assessment of the extent of contamination by pharmaceuticals.

More data from the whole region are needed on:

- sales and consumption of pharmaceuticals, and pharmaceutical waste management
- concentrations of pharmaceuticals in MWWTP influents and effluents, as well as in rivers
- the occurrence and fate of metabolites in freshwater, wastewater, and sea water
- concentrations of pharmaceuticals in sewage sludge and soil
- emissions of pharmaceuticals to the environment via other pathways such as solid waste disposal and agricultural runoff
- sales and consumption of veterinary pharmaceuticals, and their sources, pathways and loading to soils, surface and groundwater systems and the aquatic environment (including aquaculture)
- analytical methods used for measuring concentrations and their sensitivity

The results on concentrations of pharmaceuticals in the freshwater and marine environment in the Baltic Sea region presented in this report might be underestimated since the analytical methods used by many laboratories were at times not sensitive enough to detect substances at the level of the environmental quality standards for 'good status'. There is, therefore, a need to improve the analytical methods used for measuring concentrations of pharmaceuticals in the environment. There is also lack of information on pharmaceuticals' concentrations in biota, as well as on their biological effects.

Recommendations

The wide variety of pharmaceuticals detected in the wastewater, freshwater and marine environment in the Baltic Sea region indicate a need to reduce emissions of pharmaceuticals into the environment. But further information on the effects and risks of pharmaceuticals in the environment is needed to support the prioritization of measures for reducing inputs of specific substances.

Based on the data compiled in the report, the following recommendations aim to reduce the emissions of pharmaceuticals into the environment.

Recommendations for improving scientific knowledge and data

Data are essential to address specific sources and pathways of pharmaceuticals' emissions into freshwater systems and the environment to help identify priority measures. Monitoring data from rivers and in effluents from MWWTPs are needed from every Baltic Sea country. In particular, research and data are needed on concentrations of pharmaceuticals in sewage sludge, soil and groundwater. Specific attention needs to be put on filling the data gap on veterinary pharmaceuticals, including their sales, consumption, sources, pathways and loading to soils, groundwater and the aquatic environment. Furthermore, research and data are needed to assess the effects and risks of pharmaceuticals and their byproducts on the ecosystem in order to provide scientific evidence for the prioritization of measures for reducing inputs of specific substances. Particularly, concentrations of pharmaceuticals in biota and their occurrence in the food chain should be more thoroughly investigated. Analytical methods of a higher resolution should be used for measuring concentrations of pharmaceuticals in the freshwater and marine environment.

Potential measures for reducing inputs of pharmaceuticals into the environment

Measures to reduce the inputs of pharmaceuticals to the environment should be taken at all stages of the product lifecycle, from manufacturing to consumption to waste management. Technical solutions can be applied in MWWTPs, mainly as tertiary advanced treatment methods. Oxidation, adsorption and filtration technologies could also be used for the pre-treatment of raw wastewater from hospital and manufacturing facilities prior to discharging it to municipal sewer. Take-back of unused medicines by pharmacies should be applied, or developed, in countries, where such systems are not yet in place or are inefficient, in order to reduce the disposal of unused pharmaceuticals via solid waste and sewers. Sustainable consumption of pharmaceuticals also need to be promoted in order to reduce their loading to sewage. Awareness on environmental impacts of pharmaceuticals need to be raised both for consumers as well as for doctors and pharmacists.

1. Introduction

Emerging pollutants present a new global water quality challenge with potentially-serious threats to human health and ecosystems. Pharmaceuticals represent a major group of emerging pollutants found in freshwater and coastal waters.

Pharmaceuticals are an important element of modern society and their beneficial effects on human and animal health are widely acknowledged. However, their undesired occurrence and potential effects in the environment are a global emerging concern. Residual and unused pharmaceuticals and their byproducts are discharged into freshwater systems with untreated wastewater and effluents from wastewater treatment plants (WWTPs). These pollutants reach coastal and open sea waters, as ultimate sinks. Residues of various types of pharmaceuticals (hormones, painkillers, antibiotics, etc.) have been detected in several environmental compartments in different regions of the world, including the Baltic Sea (Weber et al, 2014).

The occurrence of pharmaceutical substances in the environment is of global concern and the extent of their impacts on human health and biota is largely unknown. A number of regional and global projects have been carried out with the purpose of gathering data on the occurrence of medical substances in the environment as well as on harmful effects of these substances on particular species.

This publication is the first attempt to compile a regional report with a comprehensive overview of the occurrence, concentrations and environmental pressures of pharmaceuticals in the freshwater and marine environment in the Baltic Sea region, based on data available at the national level. The report also includes regional level data on sales and consumption of pharmaceuticals, identifies sources and pathways of pharmaceuticals into the freshwater and marine environment of the Baltic Sea and collects information on effects of pharmaceuticals on aquatic and marine biota.

The report is a case study of the UNESCO Project on 'Emerging Pollutants in Wastewater Reuse in Developing Countries' and part of the UNESCO's International Initiative on Water Quality (IIWQ) technical and policy case study series on emerging pollutants (UNESCO, 2016). It provides scientific data, information and knowledge on pharmaceuticals in freshwater and wastewater systems and their occurrence in the marine ecosystem. It was prepared jointly by the Baltic Marine Environment Protection Commission Helsinki Commission (HELCOM) and the Policy Area (PA) Hazards of the European Union Strategy for the Baltic Sea Region (EUSBSR). The Report was reviewed by national experts from two HELCOM Working Groups 'State and Conservation' and 'Pressure' and adopted by the meeting of Heads of HELCOM delegations.

1.1 Policy setting

In the 2010 HELCOM Ministerial Declaration, the Contracting Parties to the Helsinki Convention agreed to *'further assess the environmentally negative impacts of pharmaceuticals and other substances that are not monitored regularly, with the aim as a first step to assess in a coordinated manner their occurrence in the Baltic Sea and evaluate their impacts on the Baltic biota'* (HELCOM 2010).

The commitment was followed up by the 2013 Ministerial Declaration, in which the Contracting Parties agreed *'to collect more information and assess the state of contamination with pharmaceuticals and their degradation products of the aquatic environment'* (HELCOM 2013a).

The European Union (EU) Directive 2013/39/EU considers the contamination of water with pharmaceutical residues as an emerging environmental concern (European Commission 2013). Diclofenac, 17-beta-estradiol (E2), 17-alpha-ethinylestradiol (EE2) and estrone (E1), a breakdown product of E2, and three macrolide antibiotics erythromycin, clarithromycin and azithromycin are included on the first 'watch list' under the EU Directive 2013/39/EU, with the aim to gather monitoring data on the aquatic environment from EU Member States for the purpose of facilitating the determination of appropriate measures to address the risk posed by these substances (European Commission 2015).

The EUSBSR PA Hazards has decided to give increased attention to the topic of pharmaceuticals in the Baltic environment during the years 2015-2017. The decision was based on the general growing concern over potential environmental impacts of pharmaceutical substances and the current policy movements within the EU, HELCOM region and globally. Furthermore, a specific objective related to decreased discharges of hazardous substances (including pharmaceuticals) in the Interreg Baltic Sea Region Programme 2014-2020 opens up possibilities for financial support for new projects within this area.

Scientific evidence and information on the occurrence, fate and effects of emerging pollutants, including pharmaceuticals, in the environment is scarce, especially in developing countries. There is a need to improve scientific understanding and knowledge on pharmaceuticals in the environment. To respond to this need, UNESCO has launched a global project on 'Emerging Pollutants in Wastewater Reuse in Developing Countries' (2014-2018), which aims to support UNESCO Member States to strengthen their scientific, technical and policy capacities to manage human health and environmental risks caused by emerging pollutants in water resources and wastewater. Better scientific knowledge and information on the occurrence, fate and effects of pharmaceuticals in the environment will contribute to improved water quality and wastewater management for the protection of aquatic and marine ecosystems, and ultimately to enhanced water and food security at all levels.

At the global level, particular attention is placed on reducing the release of emerging pollutants, including pharmaceuticals, into the environment. In particular, the 2030 Agenda's Sustainable Development Goals (SDGs) emphasize the need to reduce pollution by chemicals and hazardous substances and their effects on human health and the environment:

- ***SDG 6 (clean water and sanitation)***
  Target 6.3 • Improve water quality by reducing pollution, eliminating dumping and minimizing release of hazardous chemicals and materials, halving the proportion of untreated wastewater and substantially increasing recycling and safe reuse globally
- ***SDG 3 (health)***
  Target 3.9 • Substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination
- ***SDG 12 (responsible consumption and production)***
  Target 12.4 • Achieve the environmentally sound management of chemicals and all wastes throughout their life cycle, in accordance with agreed international frameworks, and significantly reduce their release to air, water and soil in order to minimize their adverse impacts on human health and the environment
- ***SDG 14 (oceans and seas)***
  Target 14.1 • Prevent and significantly reduce marine pollution of all kinds, in particular from land-based activities, including marine debris and nutrient pollution
  Target 14.2 • Sustainably manage and protect marine and coastal ecosystems to avoid significant adverse impacts, including by strengthening their resilience, and take action for their restoration in order to achieve healthy and productive oceans.

1.2 Pharmaceuticals in the environment

Pharmaceuticals enter the environment during various stages of the product lifecycle from their production and consumption to disposal. Freshwater and marine pollution is of concern because pharmaceutical compounds and their bioactive metabolites are continually introduced to the aquatic environment via various pathways. Main pathways, in general, are discharges of untreated and treated wastewater.

In the Baltic Sea region, emissions from manufacturing facilities are generally assumed to be very low compared to inputs occurring during the consumption phase (EEA 2010). However, there might be exceptions to this rule, and in other regions of the world emissions from production may be very high. The main pathway of human consumed pharmaceuticals to the marine environment is via direct discharges of effluents from municipal wastewater treatment plants (MWWTPs) in coastal areas as well as via rivers carrying effluents from inland MWWTPs. Other sources include land application of sewage sludge, whereby pharmaceuticals may leach into surface and ground waters. Pharmaceuticals also enter the environment via agriculture, aquaculture and veterinary practices.

Awareness is growing that pharmaceuticals may have harmful effects for wildlife. Two well-documented global examples of pharmaceuticals adversely affecting wildlife are the hormone 17a-ethinylestradiol and the anti-inflammatory drug diclofenac (e.g. EEA 2010, Kidd et al 2007). The hormone 17a-ethinylestradiol has been reported to be responsible for the feminization of male fish at concentrations that can be found in surface waters downstream of sewage treatment plants and the use of diclofenac for veterinary purposes has nearly wiped-out vulture populations in Southeast Asia. Psychotherapeutic drugs such as oxazepam (Brodin et al 2013) and citalopram (Kellner et al 2015) have also been reported to alter the behavior of fish.

The Baltic Sea ecosystem is particularly sensitive to pharmaceutical pollution because of its low biodiversity, with low functional redundancy and many species experiencing an increased physiological stress due to the brackish water environment. The water exchange rate in the Baltic Sea is slow, meaning that there is a long retention time for persistent substances. This makes the Baltic Sea ecosystem more susceptible to hazardous substances in comparison with other marine areas.

2. Scope of the report

The scope of this report is to provide a comprehensive regional overview of the extent of inputs of pharmaceuticals to the freshwater and marine environment in the Baltic Sea region, as well as to estimate contamination of the marine environment. The evaluation is based on data and information compiled within the framework of HELCOM and the Policy Area Hazards of the EU Strategy for the Baltic Sea Region.

The data presented in the report comprise a regional overview of available information on the following pressures to the Baltic Sea environment:

- The use of pharmaceuticals for both human veterinary purposes in Baltic Sea countries;
- Pathways of pharmaceuticals to the freshwater and marine environment in the Baltic Sea region;
- Concentrations of pharmaceuticals in river water;
- Concentrations of pharmaceuticals in untreated and treated municipal wastewater (MWWTP influents and effluents) as well as sewage sludge;
- The handling and management of household pharmaceutical waste in Baltic Sea countries.

The estimation of the contamination of the Baltic Sea environment by pharmaceuticals is based on measured concentrations of pharmaceutical substances in Baltic coastal and offshore areas, primarily in sea water, sediment and biota. The concentrations are compared to threshold values, or Predicted No Effect Concentration (PNEC) values, where such information is available.

3. Data collection methodology and data availability

The data collection and compilation was carried out by the HELCOM Secretariat and PA Hazards as a follow up to the commitment of the 2010 and 2013 Ministerial Declarations of HELCOM Contracting Parties to assess the pharmaceuticals contamination in the aquatic environment.

Two HELCOM working groups contributed to the report: (1) the Working Group on the State of the Environment and Nature Conservation (State and Conservation) regarding concentration of pharmaceuticals in the environment and (2) the Working Group on Reduction of Pressures from the Baltic Sea Catchment Area (Pressure) regarding inputs and pathways of pharmaceuticals to the sea.

3.1 Data collection methodology

Data collection was carried out in two stages based on national reporting by HELCOM Contracting Parties through HELCOM Working Groups.

In the first stage, the HELCOM groups State and Conservation and Pressure were asked to report on the availability of data regarding occurrence of pharmaceutical substances in the marine environment as well as on their sources and pathways. Information on data availability was provided by Denmark, Finland, Germany, Poland, Russia and Sweden. All the reports, complemented by published data, were compiled into a summary of data availability.

In the second stage, a questionnaire was circulated to national contacts of the HELCOM groups State and Conservation and Pressure. The questionnaire (together with reporting guidelines) was elaborated based on the information collected during the first phase and sent out in late August 2015. Filled in templates were submitted to the HELCOM Secretariat by October 2015. In addition to the data on measured concentrations of pharmaceuticals, countries were asked to provide data on sales, prescriptions, consumption of drugs in recent years, as well as information on national systems for managing (handling) pharmaceutical waste.

The data were evaluated by experts and compiled into two background reports of which one focused on concentrations of pharmaceuticals in the environment (Hallgren and Wallberg 2015) and the other on information on sources and pathways of these substances into the environment (Vieno 2015). This publication is a compilation of these two background reports.

3.2 Reported data

The reported data were divided into two groups. One group included all measurements related to sources and pathways of pharmaceuticals into the environment, including sales and consumption of pharmaceuticals, their concentrations in freshwater and wastewater systems (river water, MWWTP influents and effluents, sludge), and household pharmaceutical waste handling.

The other group included data on concentrations of pharmaceuticals observed in compartments of the marine and coastal environment such as water, sediments and biota.

The majority of reported data on sources and pathways was on concentrations in influents and effluents of MWWTPs as well as observations in rivers. Some data on sales and consumption of drugs available through national statistics as well as information on collection and handling of unused medical substances were also reported.

The measured pharmaceuticals belong to seven therapeutic groups: anti-inflammatory and analgesics; antimicrobial (antibiotic, antifungal, antiviral, antiparasitic, disinfectant, antiseptic) and antidote; cardiovascular agents; central nervous system agents; chemotherapeutic agents and X-ray contrast media; hormones and hormone antagonists; metabolic agents and gastrointestinal agents.

An overview of the data and information reported by countries is presented in Table 1. All HELCOM Contracting Parties except Latvia and Lithuania reported at least some data.

The information received from countries included national monitoring data, screening data, and results of scientific and commissioned studies. Many data have been published in national reports (in national languages) and some are available in national databases.

In total 47,621 data points from the period 2003-2014 were included in the data set (Figure 1) on sources and pathways of pharmaceuticals (i.e. monitoring of wastewater influent and effluents, sludge and river water).

- In wastewater influents and effluents, 156 different pharmaceuticals and 2 metabolites were analysed, of which 142 pharmaceuticals and 2 metabolites were detected.
- In sewage sludge, 60 different pharmaceuticals were monitored, of which 51 were detected.
- In rivers, 111 different pharmaceuticals were monitored, of which 58 were detected.

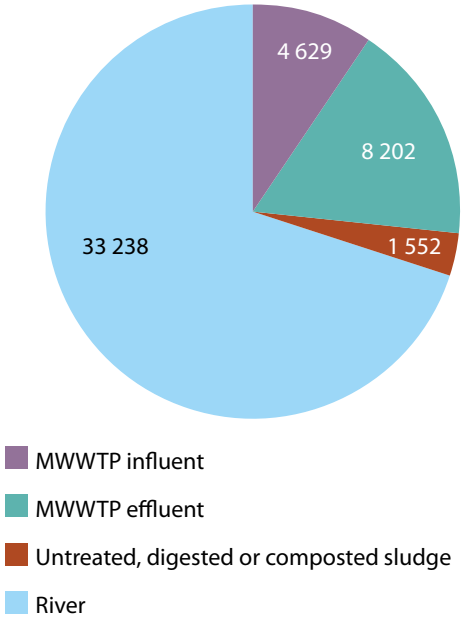
Table 1. ***An overview of data provided in response to a HELCOM questionnaire on occurrence, sources and pathways of pharmaceuticals in the Baltic Sea region.***

Source: Original data.

Country	Production & waste		Sales, Consumption		Monitoring data					
	Production	Waste management	Human	Veterinary	WWTPs	Sludge	Rivers	Sea water	Sediments	Biota
Denmark					●	●	●	●		
Estonia		●	●		●		●	●	●	
Finland	●	●	●	●	●	●	●	●	●	
Germany		●	●	●	●		●	●		
Poland								●		
Russia			●		●			●		
Sweden		●	●		●	●	●	●	●	●

Figure 1. ***Number of data points for different sample matrices***

Source: Original data.



A more detailed overview of reported data from MWWTP influents, effluents, sludge and river water is presented in Annex 1.2. The compiled results are presented in Annex 3.

Data on concentrations of pharmaceuticals in the marine environment were reported for the time period 2003-2014 and included 4,600 individual data points from coastal, open sea and transitional areas.

- 167 different pharmaceuticals were measured, of which 74 were found in at least one of the matrices (water, sediment, biota)
- 51 different pharmaceuticals were detected in water (of 148 measured)
- 9 different pharmaceuticals were detected in sediment samples (of 25 measured)
- 35 different pharmaceuticals were detected in biota samples (of 116 measured).

A more detailed overview of reported data on concentrations of pharmaceuticals in the marine environment is presented in Annex 1.2. The compiled results are presented in Annex 4.

3.3 Major data gaps

Although the report provides the most comprehensive data at the regional level of the magnitude of inputs of several pharmaceutical substances to the Baltic Sea, as well as their concentrations in freshwater systems and the marine environment, there are data gaps that need to be addressed in order to carry out a more complete assessment of the extent of contamination by pharmaceuticals.

Data were provided by the following Baltic Sea countries: Denmark, Estonia, Finland, Germany, Poland, Russia and Sweden. No data were received from Latvia and Lithuania.

The data provided by Poland did not include information on the occurrence of pharmaceuticals in freshwater and wastewater systems, for which reason it was difficult to assess in detail the loads of pharmaceuticals into the Baltic Sea since Poland has the largest portion of the Baltic Sea catchment area, as well as half of its population.

Data on pharmaceuticals sales and consumption were received only from Estonia, Finland, Germany and Sweden. The total sales and consumption of pharmaceuticals in Baltic Sea region therefore could not be assessed. Statistical reports contain information on the amount of pharmaceuticals sold, of which not all might be used.

No data were received on the occurrence of veterinary pharmaceuticals in manure or in the environment. Thus, the assessment of the contribution of veterinary pharmaceuticals to the freshwater and marine pollution is incomplete.

No data were received on the occurrence of pharmaceuticals in the sediments of inland freshwater bodies or in the soil; thus, the assessment of the role of these compartments as a source and pathway of pharmaceuticals into the Baltic Sea is incomplete.

No data were available for assessing inputs of pharmaceuticals via agriculture and aquaculture.

Information about medical and household pharmaceutical waste handling was received only from Estonia, Finland, Germany, Sweden and partially from Russia. Therefore, the estimation of the threat to the environment via disposal of unused medical substances is incomplete.

No information was collected on biological effects pharmaceuticals on aquatic and marine organisms.

More data from the whole region are needed on:

- sales and consumption of pharmaceuticals, and household pharmaceutical waste management
- concentrations of pharmaceuticals in MWWTP influents and effluents, as well as in rivers
- emissions of pharmaceuticals to the environment
- the occurrence and fate of metabolites in freshwater, wastewater, coastal and sea waters
- concentrations of pharmaceuticals in sewage sludge and soil
- sales and consumption of veterinary pharmaceuticals, and their sources, pathways and loading to soils, surface and groundwater systems and the aquatic environment (including aquaculture)
- analytical methods used for measuring concentrations and their sensitivity.

With regard to specific substances, currently there are no monitoring data on many highly consumed pharmaceuticals, especially on the following substances:

- Allopurinol
- Gabapentin
- Levetiracetam
- Mesalazin
- Valsartan

The results on concentrations of pharmaceuticals in the freshwater and marine environment in the Baltic Sea region presented in this report might be underestimated since the analytical methods used by many laboratories were at times not sensitive enough to detect substances at the level of the environmental quality standards for 'good status'. There is, therefore, a need to improve the analytical methods used for measuring concentrations of pharmaceuticals in the environment. There is also lack of information on pharmaceuticals' concentrations in biota, as well as on their biological effects.

4. Overview of existing frameworks for monitoring pharmaceuticals in the freshwater and marine environment

The HELCOM Baltic Sea Action Plan (BSAP) sets out assessment requirements for following progress towards reaching good environmental status (GES) by 2021, whereby the status is to be assessed for a set of ecological objectives. The HELCOM strategic goals and objectives are to a large extent comparable to the descriptors and criteria of the EU Marine Strategy Framework Directive (MSFD) (2008/56/EC), which stipulates that GES is to be achieved by 2020. HELCOM core indicators are used to follow up on the progress made to reach the goals of both policies within the Baltic Sea, by measuring the progress towards a BSAP objective and/or a MSFD criteria. Work has been initiated within HELCOM to develop core indicators for diclofenac and estrogenic-effects; these will be further developed using input from this assessment.

The EU Water Framework Directive (WFD) contains a 'watch list' of priority substances that present a significant risk to or via the aquatic environment. The EU Directive 2013/39/ EU requires that EU Member States monitor the 'watch list' substances across a wide range of freshwater bodies in order to ascertain the extent of presence in the environment. This is a challenge as the proposed concentration levels at which these substances should be monitored are low (Table 2) and many laboratories cannot meet these requirements.

Under the WFD, each EU Member State can select substances of national or local concern (river basin specific pollutants) in addition to the substances of EU-wide concern (the priority substances).

Table 2. ***'Watch list' of pharmaceuticals for EU-wide monitoring***

Source: European Commission Implementing Decision (EU) 2015/495.

Name of the substance	CAS number	EU number	Maximum acceptable detection limit (ng/l)
Diclofenac	15307-86-5	239-348-5	10
17-alpha-ethinylestradiol (EE2)	57-63-6	200-342-2	0.035
17-Beta-estradiol (E2), Estrone (E1)	50-28-2 53-16-7	200-023-8	0.4
Macrolide antibiotics (erythromycin, clarithromycin, azithromycin)	114-07-8 81103-11-9 83905-01-5	204-040-1 617-500-5	90

Table 3. ***Swedish assessment criteria for specific pollutants in coastal waters and transitional waters***

Source: HVMFS 2013.

Name of the substance	Good status Annual Average (ng/l)
Diclofenac	10
17-alpha-ethinylestradiol (EE2)	0.007
17-beta-estradiol (E2)	0.08

In Sweden, for example, three pharmaceuticals are listed as specific pollutants (Table 3).

In September 2015, a Swedish national working group, coordinated by the Swedish Medical Products Agency and consisting of a large number of national agencies within the health and medical sector and a representative from the industry, presented a list of substances that was suggested should be monitored in the environment on a regular basis (MPA 2015). In addition to the substances included on the WFD 'watch list', 17 pharmaceuticals were suggested (Table 4).

Table 4. ***17 pharmaceuticals suggested for monitoring by a Swedish stakeholder working group in addition to the substances on the WFD 'watch list'***

Source: MPA 2015.

Name	Justification by Swedish MPA (2015)
Ciprofloxacin	Persistent and demonstrated resistance development in the environment.
Citalopram	Has been detected in fish and drinking water. PBTproperties. Relatively large usage.
Fluconazol	Has been detected in drinking water, surface water and sludge.
Ibuprofen	Large usage and has been detected in surface water.
Carbamazepin	Has been detected in drinking water and surface water.
Cetoconazol	Has been detected in sludge.
Levonorgestrel	PBTwproperties.
Losartan	Large usage.
Metoprolol	Large usage and has been detected in drinking water, surface water and sludge.
Metotrexat	Unknown environmental effects and presence. A chemotherapy that is used by the households.
Naproxen	Has been detected in drinking water and surface water. Increased usage as it is often used as a replacer for diclofenac.
Oxazepam	Has been detected in fish, surface water and drinking water. Toxic at environmental relevant concentration.
Sertralin	Has been detected in surface water, fish and sludge.
Sulfametoxazol	Has been detected in surface water, fish and sludge.
Tramadol	Has been detected in surface water and drinking water.
Trimetroprim	Large usage. Has been detected in drinking water, surface water and sludge.
Zolpidem	Has been detected in drinking water, surface water and sludge.

5. Production, consumption and handling of pharmaceutical wastes

5.1 Pharmaceutical production

Data about pharmaceutical production were received only from Finland. The Finnish Medicines Agency, Fimea, grants licenses for facilities producing medicinal products. Currently, pharmaceuticals are produced by at least eight companies in at least twelve manufacturing plants in Finland.

Although the contribution of manufacturing facilities to emissions of medicinal products and/or their residues is generally considered to be negligible in the EU, there is no comprehensive information about pharmaceutical production facilities and their potential emissions of pharmaceutical substances in the region. Information on pharmaceutical production in other countries in the region would be useful for mapping potential hot spots for releases of pharmaceuticals.

5.2 Consumption of pharmaceuticals

The consumption phase is considered to be the biggest contributor to the emissions of pharmaceuticals into the environment, mainly through excretions and incorrect disposal of unused medicines into sinks and toilets. Between 30 to 90% of the orally administered dose is generally excreted as active substance in the urine of humans and animals, with the nature and amount of medicinal residues mainly dependent on the volumes and nature of the administered substances, the mode of administration and metabolization rates (BIO Intelligence Service 2013).

Human consumption

Four countries (Estonia, Germany, Finland and Sweden, some data also from Russia) provided information on human consumption of pharmaceuticals, mainly based on data on sold amounts. The magnitude of consumption was calculated for the most frequently prescribed pharmaceuticals as well as for those that were often found in the environment (e.g., metoprolol, carbamazepine, diclofenac). Consumption data were available for 76 pharmaceuticals in total, but data from all four countries were available for only 16 pharmaceutical substances.

About 21 million people live in the area from where data were available (compared to the 85 million residing in the entire Baltic Sea catchment), therefore, the presented figures are not representative of the total consumption of pharmaceuticals in the Baltic Sea region.

Figure 2 shows the annual consumption of the top 20 most sold pharmaceuticals. According to the available data, anti-inflammatory drug paracetamol was the most consumed pharmaceutical with a total annual sales volume of more than 520,000 kg.

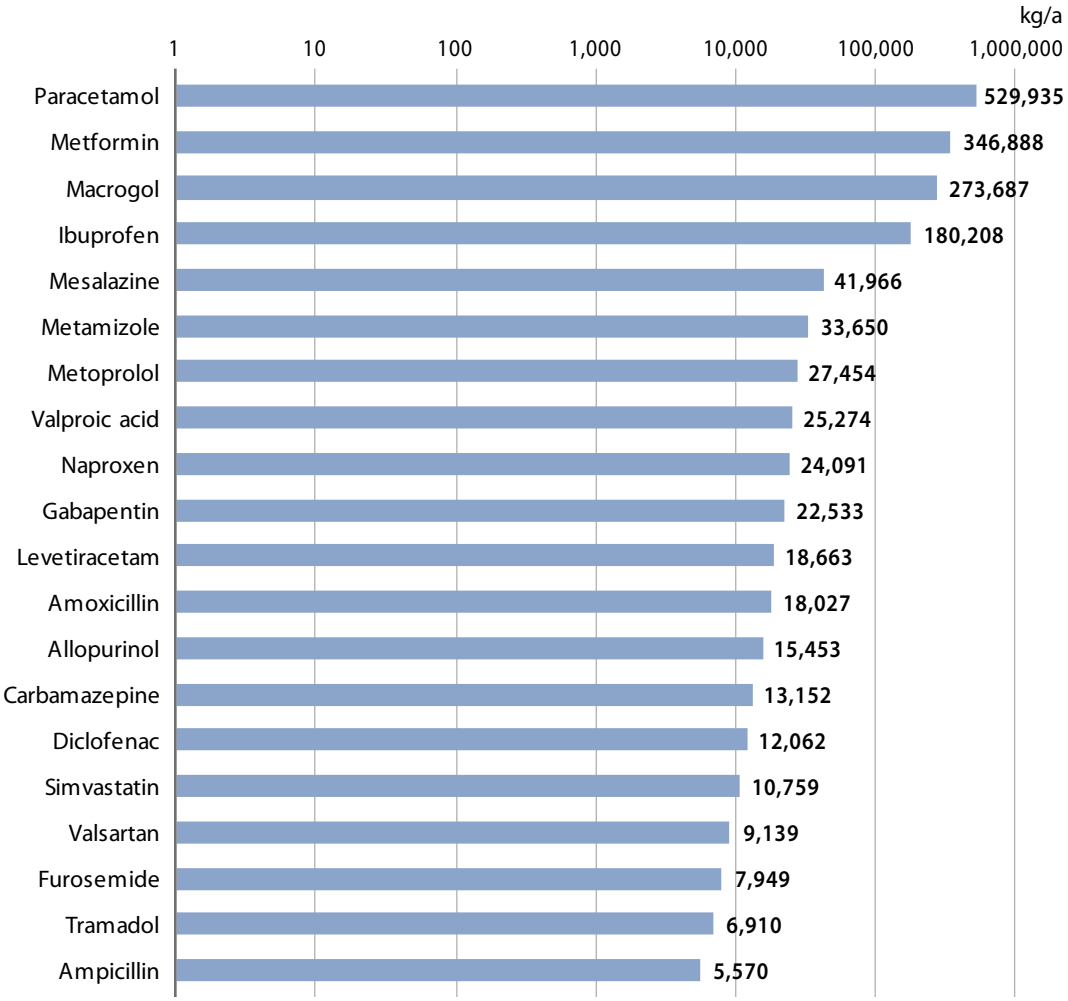
The annual sales of antidiabetic drug metformin, constipation drug macrogol and anti-inflammatory drug ibuprofen all exceeded 100,000 kg. In 2014, about 1,600 tons of the top 20 pharmaceuticals were sold in the four countries from which data were available. Per inhabitant, this amounts to about 80 g per person per year. If the consumption patterns are similar throughout the region (for the entire Baltic Sea catchment), then the volume of the top 20 most sold pharmaceuticals would be about 6,800 tons per year. More data on sales of pharmaceuticals are presented in Annex 2.

Veterinary consumption

Due to very limited data reported on veterinary consumption of pharmaceuticals, it is difficult to estimate the total amount of veterinary pharmaceuticals used in the Baltic Sea catchment area. A very rough estimation, by extrapolating from the available data from Finland and Germany, would result in annual sales and consumption of about 900 tons. This figure only includes antimicrobial drugs, since no data were reported on the sales and consumption of pharmaceuticals in other therapeutic groups. More data on the use of pharmaceuticals in veterinary are presented in Annex 2.

Figure 2. ***The top 20 most sold pharmaceuticals***

Source: Data were received from Estonia, Finland, Germany (only Mecklenburg-Vorpommern and Schleswig-Holstein – which are within the catchment area of the Baltic Sea) and Sweden. For diclofenac, also Russian (St. Petersburg) data are included. Metamizole was only prescribed in Germany. For ampicillin, furosemide, tramadol and naproxen, data were available from Estonia, Finland and Sweden.



5.3 Handling of household pharmaceutical wastes

The improvement of take-back schemes for unused medical products represents one of the simplest ways for reducing inputs of pharmaceutical products into the environment. EU medicinal legislation has required take-back schemes for unused and expired human medicinal products since 2004 (Directive 2004/27/EC) to 'ensure that appropriate collection systems are in place for human medicinal products that are unused or have expired' (European Commission 2004).

Only Estonia, Finland and Sweden provided information on the amounts of pharmaceutical waste collected (Table 5) and on procedures for handling pharmaceutical waste.

In Estonia, all pharmaceuticals are classified as hazardous waste and should therefore be collected.

In Finland, all pharmaceuticals are classified as hazardous waste and should therefore be collected. The collection of pharmaceutical waste is most commonly arranged through cooperation with local pharmacies. Pharmacies accept medicines and mercury thermometers returned by customers at no cost. The municipality provides the pharmacy with collection containers and transports the waste to a toxic waste disposal plant for proper disposal.

Table 5. ***Amounts of pharmaceutical waste collected in Estonia, Finland and Sweden***

Source: Original data.

Estonia (in 2014)	Finland (in 2006)	Sweden (in 2011)
89,190 kg All waste pharmaceuticals collected	185,000 kg Pharmaceuticals returned to the pharmacies	1,500,000 kg Estimate of the total amount involved in take-back schemes
	33,000 kg Incorrectly disposed via solid waste	800,000 kg Pharmaceuticals returned to the pharmacies
	28,000 kg Incorrectly disposed via sewers	250,000 kg Ending up in the mixed waste from households
		10,000 kg From the public to municipalities recycling centers
		50,000 kg Discarded by the internal operations of the pharmacies
		250,000 kg Discarded by the internal operations of the wholesale trades
		100,000 kg Discarded in hospital healthcare

According to surveys carried out by the Finnish University Pharmacy in 2009, the proportion of people returning medical waste properly has grown in recent years. A survey carried out in 2009 showed that about one in ten Finns admitted having thrown medicines into mixed waste or to have flushed them into the sewers. In a similar survey in 2006, the same figure was three in every ten Finns. The most common reported reason for improper disposal of medical waste was that people did not know how to treat them. Other reasons mentioned in the survey were indifference, hurry, long distances and that the amount of the medicine was small or that it was thought harmless.

In Sweden, producers are required to ensure free take-back collection systems for pharmaceutical waste from households. This is managed via the pharmacies. Pharmaceuticals classified as hazardous waste (cytostatic and cytotoxic pharmaceuticals) are, however, not formally covered by the producer responsibility, which means that municipalities are responsible for collection, transport and destruction of those wastes from household. In practice, however, the take-back systems of many pharmacies include all types of pharmaceutical waste, since distinguishing different fractions of hazardous and non-hazardous pharmaceuticals is not always straightforward. Moreover, the amounts of cytostatic and cytotoxic pharmaceuticals handled by households are considered to be very small since these types of drugs are mainly used within hospital healthcare. Medical waste from other activities, e.g., from hospitals or veterinary practices, are not covered by the producer responsibility and these practices are responsible for their own correct waste handling.

In Sweden, pharmaceutical waste is collected by pharmacies, by municipalities' collecting systems recycling centers and via other healthcare/hospital management. The County Councils' healthcare activities have also well-established routines for handling pharmaceutical waste. Currently there are some 20 facilities in Sweden which are licensed to destroy medical wastes.

Experts from the Russian Federation have indicated that there is no coherent system for handling medical wastes, especially for outdated pharmaceuticals in households. Therefore, in most cases such pharmaceuticals end up at landfills or in municipal sewage systems. A number of federal legal acts identify dumping of medical wastes at the specific sites and incineration as the most preferable way for handing medical wastes.

In Germany there is no specific national regulation on waste management of pharmaceuticals and no official take back system for pharmaceuticals is in place. The management of pharmaceutical waste is regulated at the local level, hence different ways of disposal have been established, with the most important disposal options being:

- bins for residual waste (Hausmüll, Restmülltonne),
- local recycling centers responsible for mobile services to collect hazardous waste (Recyclinghof resp. Schadstoffmobil), and
- take back by pharmacies (on a voluntary basis).

The German Federal Ministry of Education and Research has launched a project to establish a map-based website (*http://www.arzneimittelentsorgung.de*) which informs consumers about the options for environmentally sound disposal of unused pharmaceuticals in their hometowns.

6. Inputs of pharmaceuticals into the Baltic Sea

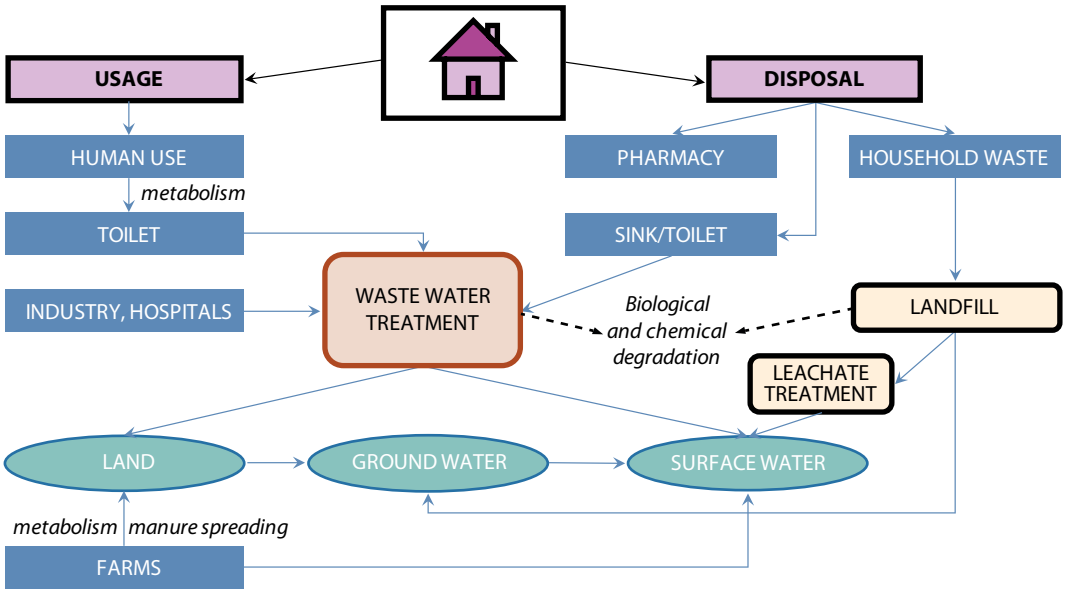
6.1 Sources and pathways

Pharmaceuticals are released into the environment during various stages of the product lifecycle (manufacturing, consumption and waste disposal). In the Baltic Sea region, the main sources of pharmaceuticals are the excretion of active substances consumed by humans and animals (via urine and faeces) as well as the incorrect disposal of unused medical products into toilets and sinks. Figure 3 illustrates the main sources and pathways of pharmaceuticals into the environment.

Since the majority of the population in the Baltic Sea region is connected to municipal wastewater treatment plants, MWWTPs are considered a major pathway of pharmaceuticals into the environment. Pharmaceuticals are directly released into the Baltic Sea via the effluents of coastal MWWTPs and indirectly by the rivers which carry effluents from inland MWWTPs. In some areas, the pharmaceutical industry and hospitals may be important sources of pharmaceuticals that end up in the sewage system.

Other pathways of pharmaceuticals to the Baltic Sea include emissions from scattered dwellings not connected to centralized sewage systems, runoff/leaching from land where manure or sewage sludge has been applied and landfill leachate, if medical waste is incorrectly disposed of via solid waste. It is not possible to assess the significance of these other pathways with the presently available data.

Figure 3. ***Main sources and pathways of pharmaceuticals to the environment***



6.2 Concentrations of pharmaceuticals in wastewater, sludge and river water

Analytical data were available for 156 pharmaceuticals and 2 metabolites sampled in wastewater and sludge from MWWTPs situated in Denmark, Estonia, Finland, Germany, Russia (St. Petersburg) and Sweden.

Figure 4 presents the top 20 pharmaceuticals present at the highest concentrations in MWWTP influents. The highest average concentration of 83 µg/l was measured for anti-inflammatory drug paracetamol. The highest concentration of 1,300 µg/l was measured for diuretic drug furosemide (in Denmark).

Figure 5 shows the top 20 pharmaceuticals with highest concentrations in MWWTP effluent (i.e., treated wastewater). The highest average concentration of 22.3 µg/l was measured for diuretic drug furosemide and the highest measured concentration of 360 µg/l was for anti-inflammatory drug paracetamol (in Denmark). In general, those compounds that were present in the influents at highest concentrations and which were the least removed during the treatment were detected in the effluents at the highest concentrations.

Removal rates in MWWTPs were calculated for 118 pharmaceuticals by comparing the reported influent and effluent concentrations (Figure 6). It should be noted, that the removal rates consider only the removal of pharmaceuticals from the aqueous phase. Removal rates were not calculated for pharmaceuticals that were not detected in influent waters.

Only nine out of 118 pharmaceuticals were efficiently (> 95%) removed during the wastewater treatment process. Nearly half of the compounds were removed with efficiencies lower than 50%. For 16 pharmaceuticals, higher concentrations were reported in effluents than in influents, which may be due to analytical errors or the release of parent compounds from β-glucuronated pharmaceuticals that were excreted by the human body.

Figure 4. ***The top 20 pharmaceuticals measured in highest concentrations in MWWTP influents***

indicates the average concentration of the measurements and *indicates the maximum measured concentration.*

Source: Original data.

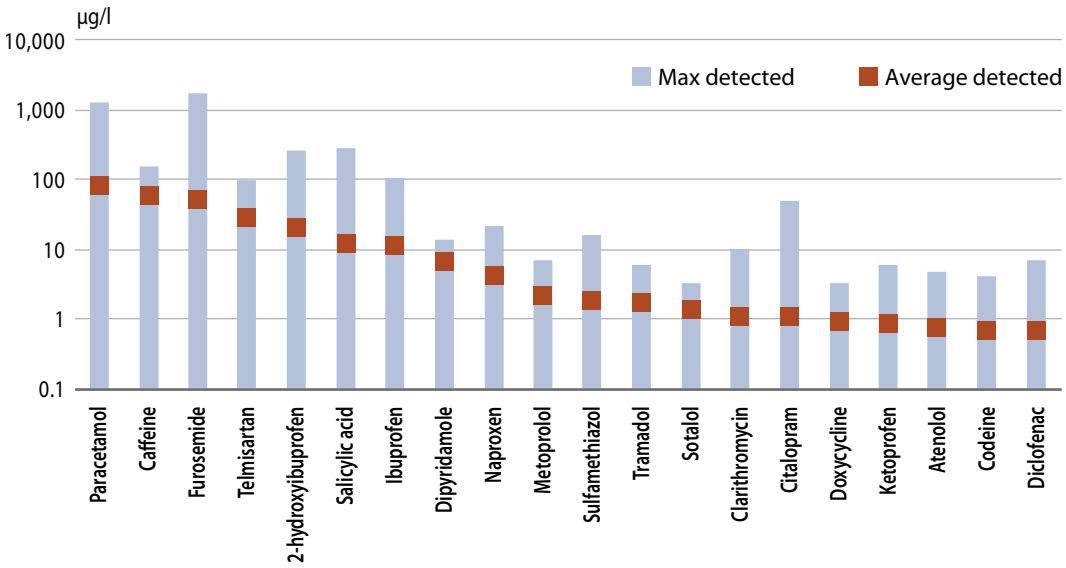
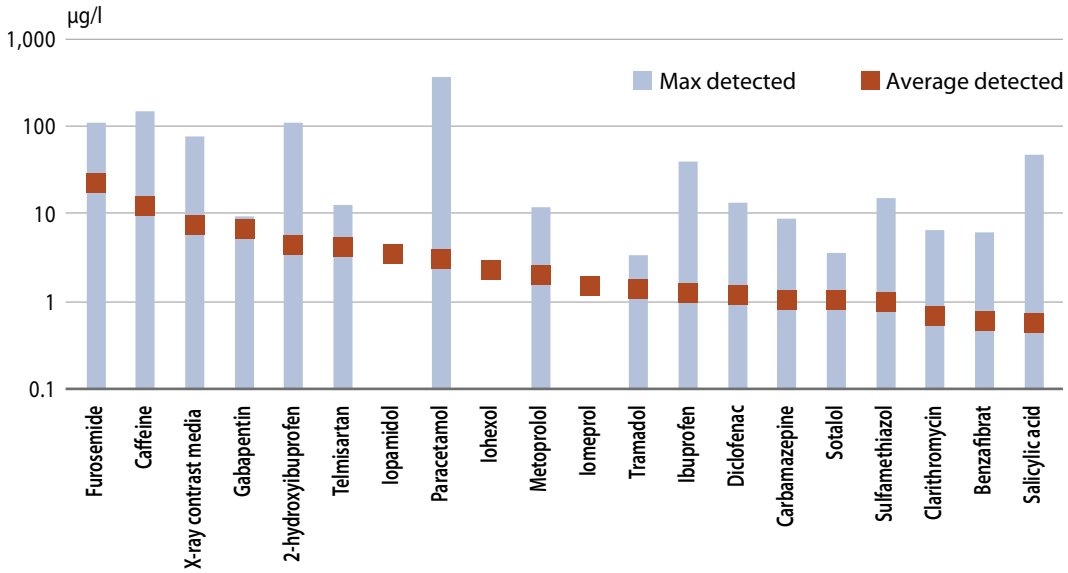


Figure 5. ***The top 20 pharmaceuticals measured in highest concentrations in treated wastewater (MWWTP effluents)***

indicates the average concentration of the measurements and indicates the maximum measured concentration. Maximum detected concentrations for iopamidol, iohexol and iomeprol are not included since only mean concentrations were reported.

Source: Original data.



Furthermore, in activated sludge, E. coli secrete β-glucuronidase enzyme, which is capable of deconjugating glucuronated metabolites and can result in releases of the active pharmaceutical into the wastewater. Additionally, two of the compounds that were identified in higher concentrations in the effluent than the influent were metabolites of ibuprofen that are formed during the biological degradation of the parent compound.

Significantly fewer data were reported for sludge samples than for influent and effluent samples, and only from Finland and Sweden. Data for composted sludge were only received from Finland. More data should be gathered on the presence of pharmaceuticals in sewage sludge as well as the fate of the compounds during sludge treatment. The top 20 pharmaceuticals (highest concentrations) in untreated sludge are presented in Figure 7. The highest average concentration of 3.3 mg/kg d.w. was measured for the antibiotic ciprofloxacin. Also the highest measured concentration was for ciprofloxacin at 8.8 mg/kg d.w. (in Finland).

Figure 6. ***Number of pharmaceuticals removed in MWWTPs at different removal rates***

Removal rates were estimated by comparing concentrations in influents and effluents.

Source: Original data.

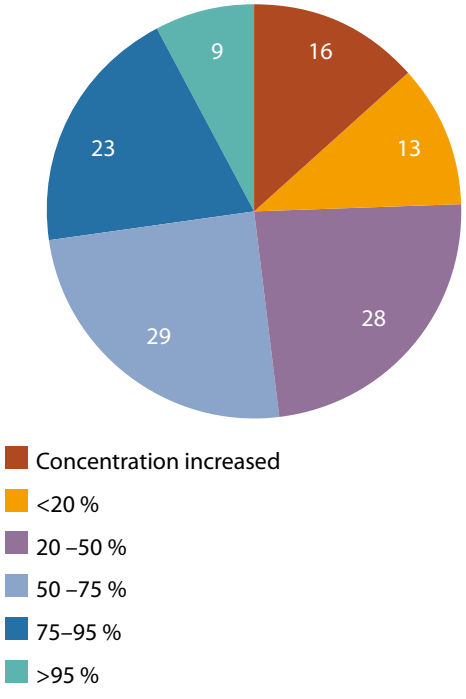


Figure 7. ***The top 20 pharmaceuticals measured in highest concentrations in untreated sewage sludge***

indicates the average concentration of the measurements and *indicates the maximum measured concentration.*

Source: Original data.

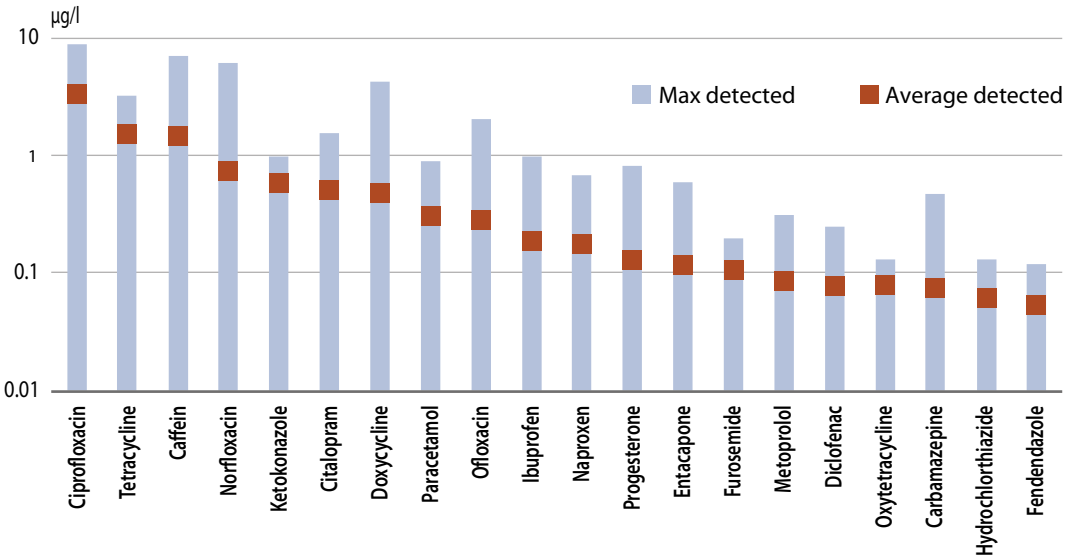
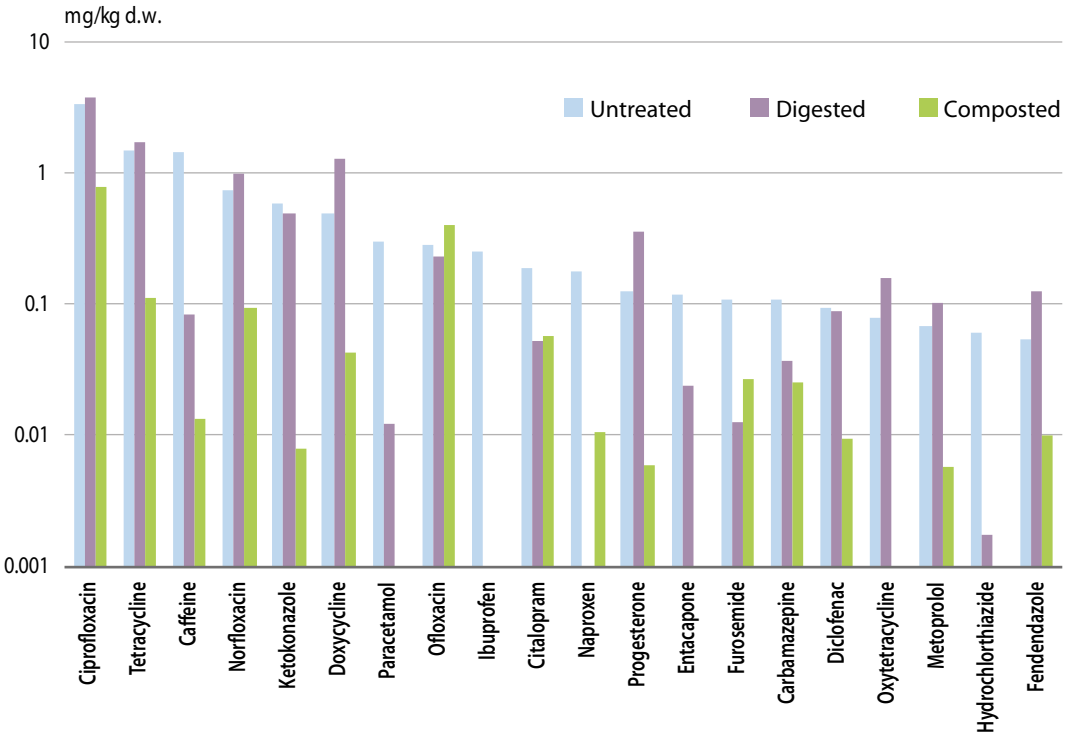


Figure 8. ***Average concentrations of pharmaceuticals in untreated, digested and composted sludge***

Source: Original data.



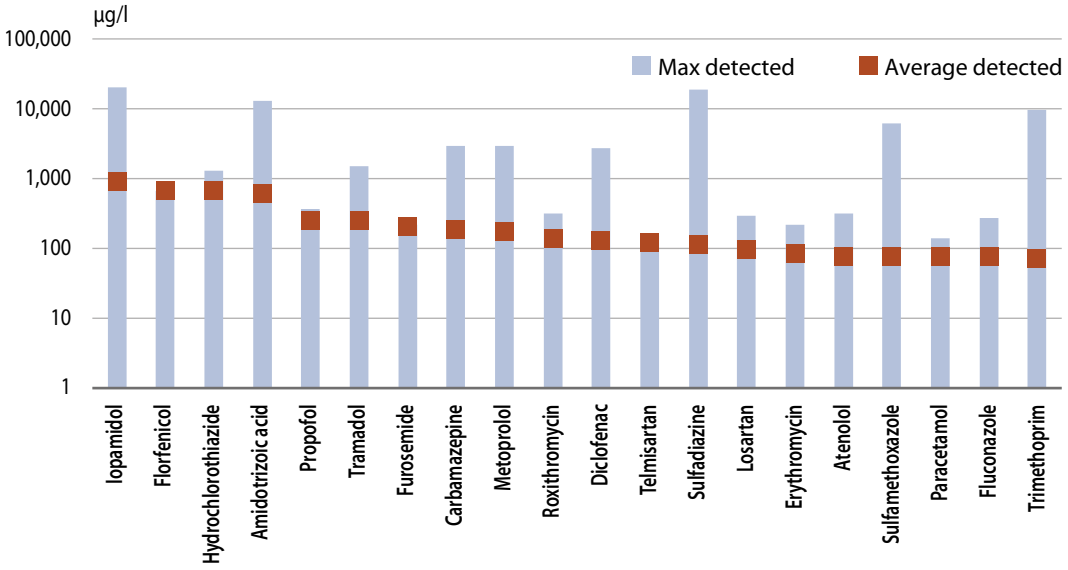
Average concentrations of pharmaceuticals in untreated, digested and composted sludge are presented in Figure 8. Concentrations of some pharmaceuticals are reduced through digestion and/or composting, however, certain compounds, such as antibiotics, seem to be fairly resistant to degradation during sludge treatment. More research is needed on the fate of pharmaceuticals in sludge treatment.

Data were reported for 111 pharmaceuticals in river water samples. Figure 9 presents the top 20 pharmaceuticals occurring at highest concentrations in sampled river water. The highest average concentration of 0.92 µg/l was measured for X-ray contrast media iopamidol. Iopamidol was also the pharmaceutical measured at the highest concentration of 20.8 µg/l (Pampower Graben, Germany). In general, the average concentrations were lower than 0.1 µg/l, however, for twelve compounds the highest concentrations exceeded 1 µg/l.

Figure 9. ***The top 20 pharmaceuticals measured in highest concentrations in river water samples***

indicates the average concentration of the measurements and *indicates the maximum measured concentration.*

Source: Original data.



7. Concentrations and effects of pharmaceuticals in the marine environment

Six Contracting Parties reported data on the concentrations of pharmaceuticals in the Baltic Sea environment for the period from 2003 to 2014. In total, 4,600 observations in water, sediments and biota were reported. Presence of pharmaceuticals was detected in 640 of these samples. One hundred and sixty-seven different pharmaceuticals were measured and 74 of these were found in at least one of the matrices (water, sediment or biota).

The presented overview of concentrations of pharmaceuticals in the environment is based on data reported by the Contracting Parties, i.e. it does not contain information on all compounds that have been detected in the Baltic Sea environment. No data on biological effects were received from the Contracting Parties, however, data from scientific studies on the effects of pharmaceuticals on Baltic biota have been included. Additional information on methods, collected samples and concentrations of the individual pharmaceuticals are presented in Annex 4. An overview of all data submitted by the Contracting Parties, including references, is presented in Annex 1.2.

Maps and figures give an overview of sampling sites, sampling matrices and the number of samples above the detection limit. The geographical distribution of all water, sediment and biota samples are presented in Figures 10 to Figure 12, respectively. For regional monitoring and assessment purposes within HELCOM, the Baltic Sea is divided into subbasins (referred to as Level 3 in the map legend) and coastal areas (see HELCOM 2013b).

Figure 10. ***Overview of all 3,647 water samples in the compiled data set***

Source: Data submitted by Denmark, Estonia, Finland, Germany, Poland, and Sweden.

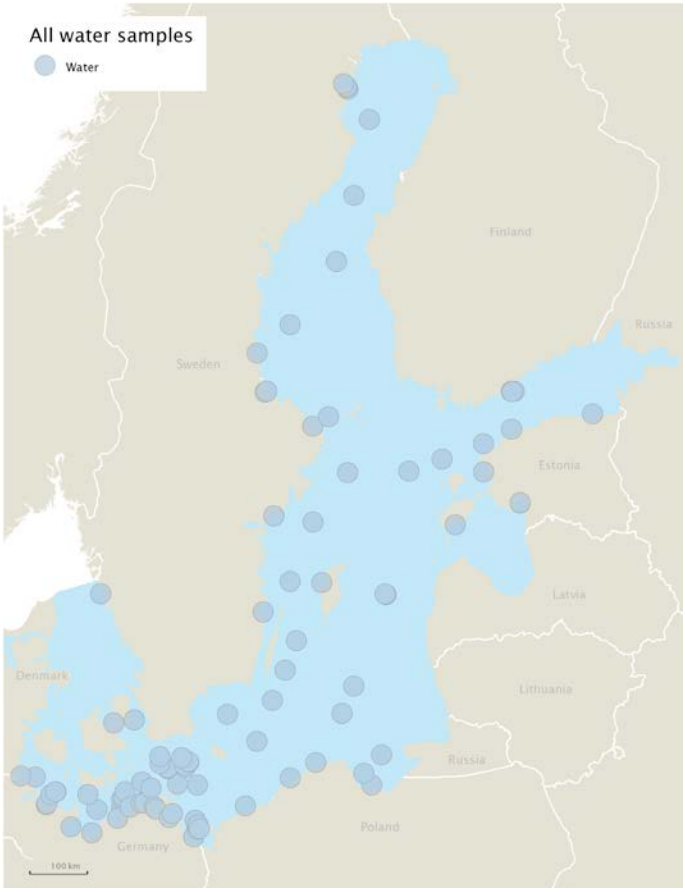
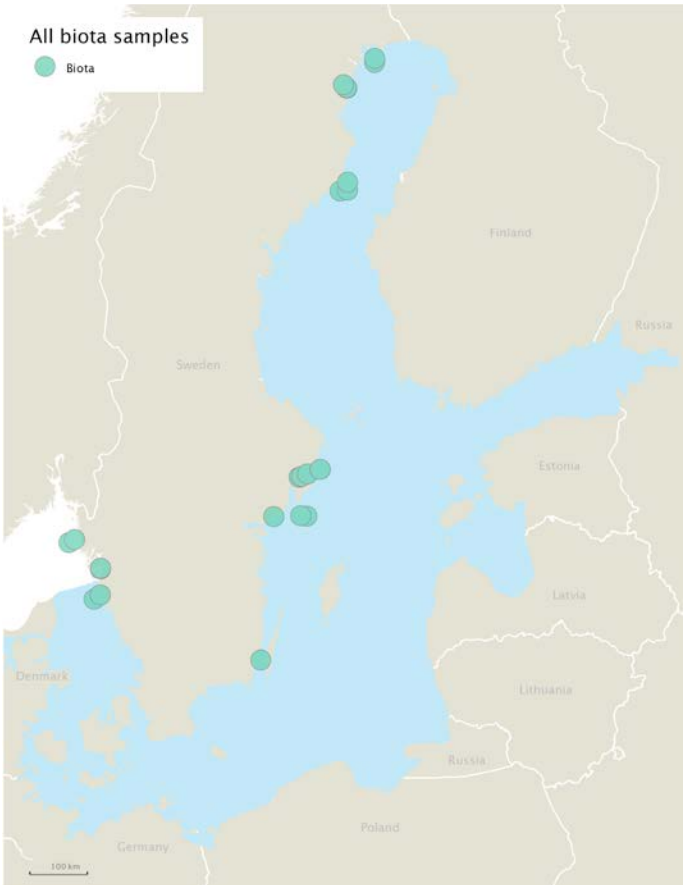


Figure 11. ***Overview of all 114 sediment samples in the compiled data set***

Source: Data submitted Estonia, Finland, and Sweden.

Figure 12. ***Overview of all 839 biota samples in the compiled data set***

Source: Data submitted by Sweden only.



7.1 Concentrations of pharmaceuticals in the marine environment

The main results are presented by grouping pharmaceuticals according to their general clinical use (therapeutic group). Maps and figures present information about selected substances belonging to each therapeutic group. More detailed information is presented in Annex 4.

The figures, presenting concentrations of individual pharmaceuticals, intend to visualize the variability in the sensitivity of the analytical methods used; referred to as LOD (limit of detection) in the figures. The highest reported limit of detection (High-LOD) in the data set represents the least sensitive analytical method used, while the Low-LOD represents the most sensitive method used. However, LOD was not reported in all data sets. Therefore, in some cases the lowest reported measured concentration is presented as a proxy for the Low-LOD, representing a worst case scenario. The LOD indicator is missing when no sufficient data on LOD were reported. The LODs presented in the figures are thus indicative.

Anti-inflammatory and analgesics

Of all monitored pharmaceuticals in the category anti-inflammatory and analgesics, 11 out of 26 (42%) substances were detected in environmental samples (water, sediment or biota). The most frequently detected substances were diclofenac (79 out of 322 samples; 25%) (Figure 13) and ibuprofen (38 out of 260 samples; 15%) (Figure 14).

Paracetamol was detected in all eight reported samples of water and sediments in which the substance was analyzed. Phenazone was observed in only five out of 137 water samples (4%) (Figure 15). Tramadol was detected in two out of four and trihexyphenidyl in three out of four biota samples (Table A4.7). The maximum concentrations measured in water samples were 54 ng/l for diclofenac, 159 ng/l for ibuprofen, 360 ng/l for paracetamol and 504 ng/l for phenazone (Figure 16).

Figure 13. ***Sample locations for the compiled data on diclofenac***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.

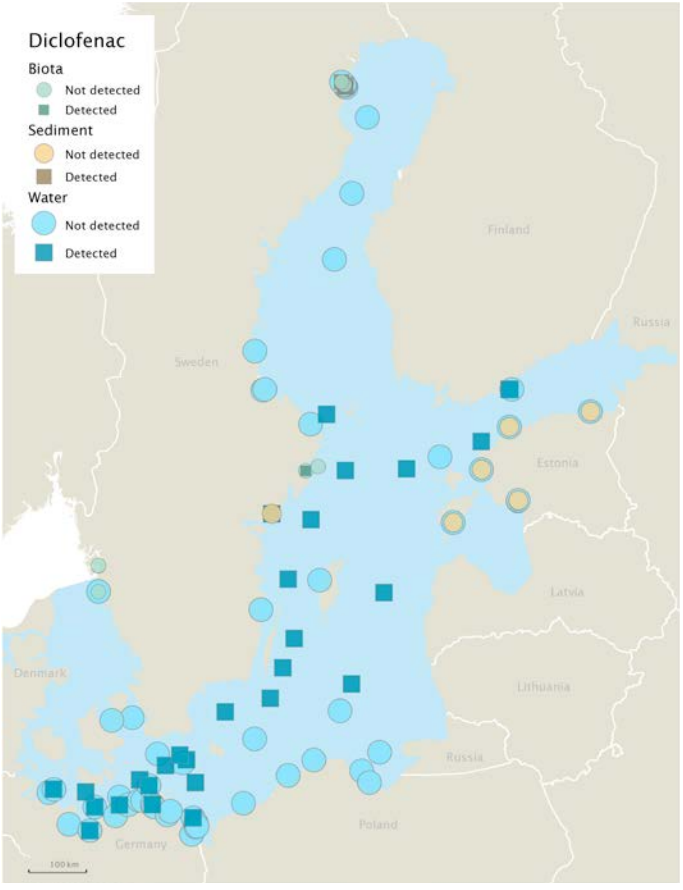


Figure 14. ***Sample locations for the compiled data on ibuprofen (including ibuprofen-OH and ibuprofen-COOH)***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.

Figure 15. ***Sample locations for the compiled data on phenazone***

Each presented data point might conceal several measurements conducted at the exact same location.

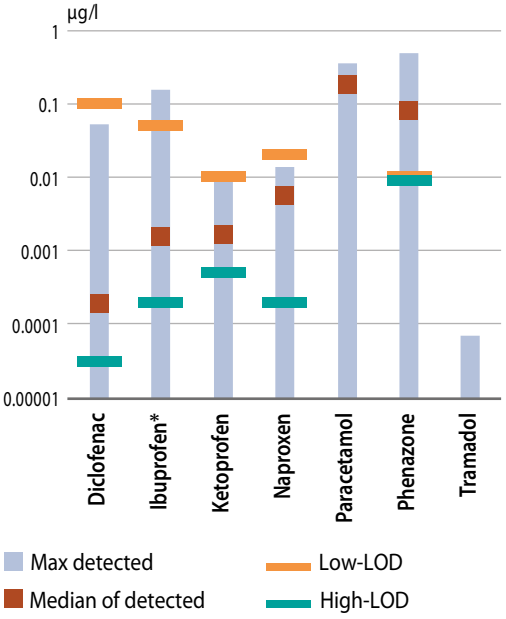
Source: Original data.

Diclofenac is on the Directive 2013/39/EU (WFD) 'watch list' of pharmaceuticals to be monitored EU-wide, and has a proposed annual average environmental quality standard (proposed AA-EQS) of 10 ng/l. This value was exceeded in six out of 257 (2.3%) samples. For 187 samples, the result was <LOD for diclofenac. In 30% of these samples (56 out of 187) the reported LOD was 20 ng/l or higher, indicating that diclofenac might be more frequently detected if more sensitive analytical methods were applied.

Figure 16. ***Anti-inflammatory and analgesics. Concentrations in Baltic Sea water***

Ibuprofen includes ibuprofen-OH and ibuprofen-COOH.*

Source: Original data.



Antimicrobials and antidotes

Of all monitored pharmaceuticals in the category of antimicrobial agents (antibiotic, antifungal, antiviral, antiparasitic, disinfectant, antiseptic) and antidote, 11 out of 30 (37%) substances were detected in environmental samples (water, sediment or biota). Concentrations of antimicrobial agents in seawater are indicated in Figure 17. Claritromycin was detected in two out of 126 water samples and on one occasion in biota. However, the reported analytical limits of detection (LODs) for some substances are above the highest value reported in other studies.

Sulfamethoxazole was detected in all matrices. In water, this compound was detected in 12 out of 140 (9%) samples; in sediments in four out of eight (50%); and on one occasion out of four this compound was detected in biota samples (Figure 18). The highest measured concentration of this compound in water was 33 ng/l, with a median concentration of about 16 ng/l.

Figure 17. ***Antimicrobial (antibiotic, antifungal, antiviral, antiparasitic, disinfectant, antiseptic) and antidote. Concentrations in Baltic Sea water***

Source: Original data.

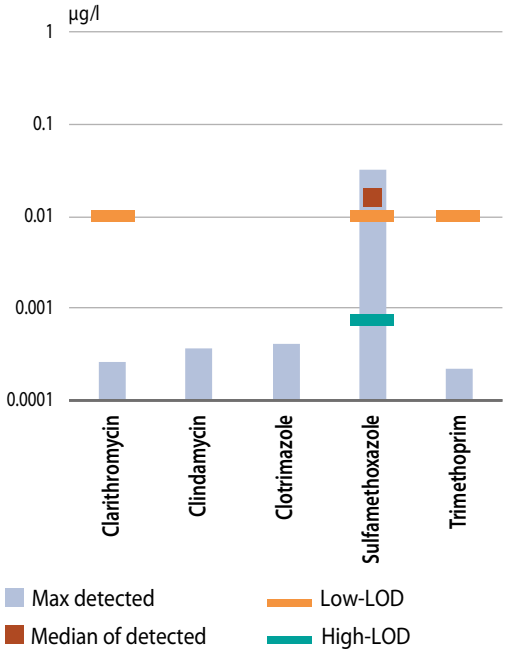


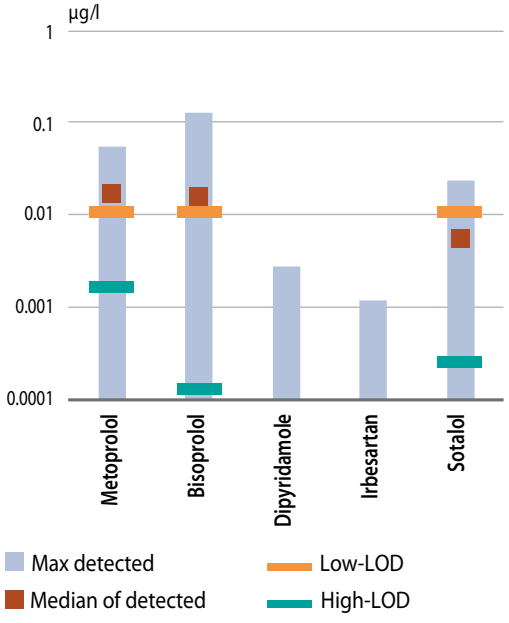
Figure 18. ***Sample locations for the compiled data on sulfamethoxazole***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.

Figure 19. ***Cardiovascular agents (blood pressure, diuretics, anticoagulants, anti-histamine). Concentrations in Baltic Sea water***

Source: Original data.



Cardiovascular agents

Fourteen out of 25 (56%) cardiovascular agents were detected in water (concentrations in sea water are indicated in Figure 19). Only bisoprolol was also detected in a biota sample. Metaprolol was detected in 23 out of 144 (16%) water samples (Figure 20) with the highest measured concentration of 55 ng/l; bisoprolol was found in 33 out of 144 (23%) water samples (Figure 21) with the highest measured concentration of 128 ng/l; and sotanol was detected in five out of 139 (4%) water samples (Figure 22) with the highest measured concentration of 24 ng/l.

Figure 20. ***Sample locations for the compiled data on metoprolol***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.

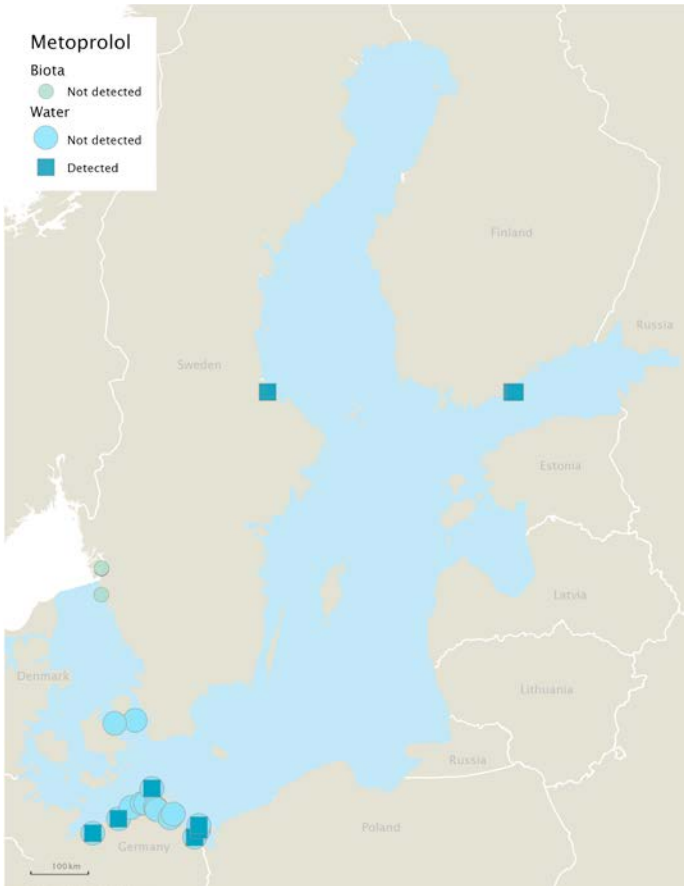
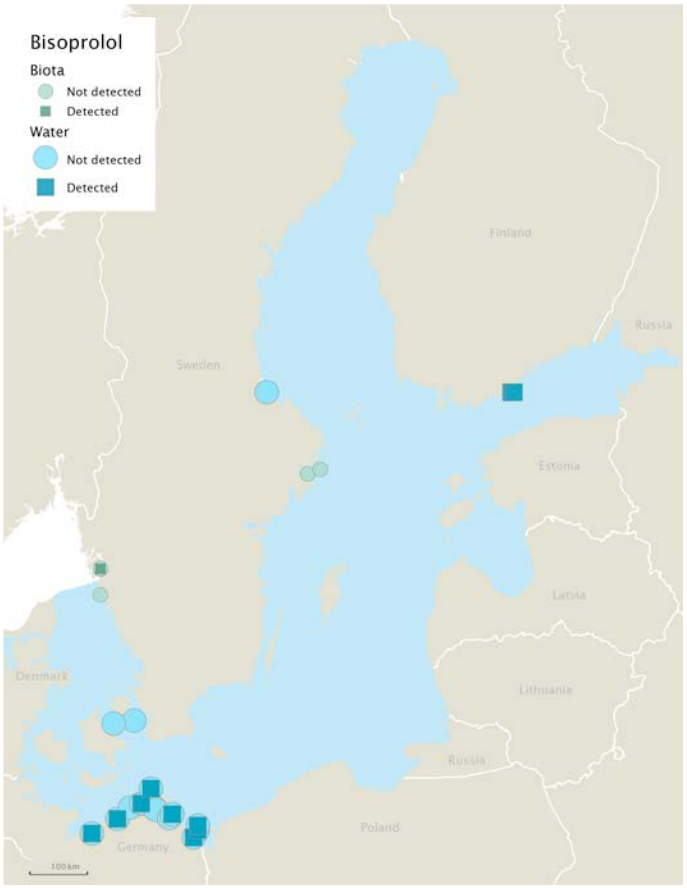


Figure 21. ***Sample locations for the compiled data on bisoprolol***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.



Central nervous system agents

Twenty-one out of 44 (48%) monitored central nervous system agents were detected in water and biota (concentrations in sea water are indicated in Figure 23). The compounds carbamazepine (Figure 24) and primidone (Figure 25) were detected on several occasions (Annex tables A4.16 and A4.18). Oxazepam (Figure 26) was detected in several cases, but its median concentration only slightly exceeded the lowest LOD, which indicates that the compound might be detected more frequently if more sensitive analytical methods were applied.

Carbamazepine was detected in more than 60% of reported water samples (135 out of 218), almost all around the Baltic Sea. This compound was detected in biota on one occasion. The highest measured concentration reached 73 ng/l. Since the median concentration of carbamazepine falls in the interval between the highest and lowest LOD, it indicates that the compound possibly occurs more frequently. Primidone was detected in all 51 reported water samples taken in almost all sub-basins of the Baltic Sea. The highest measured concentration was 58 ng/l.

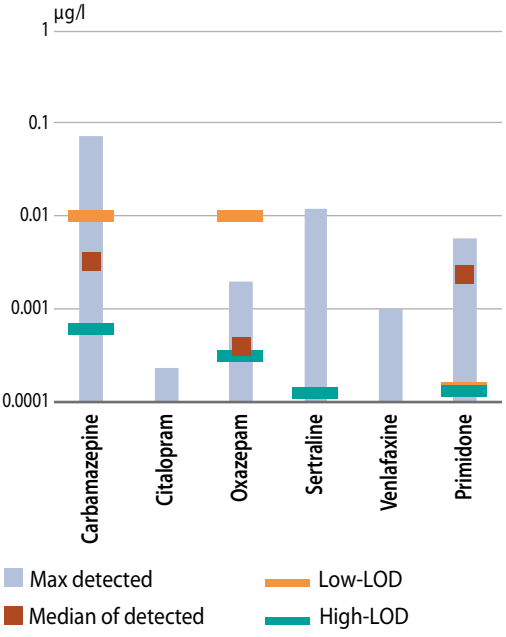
Figure 22. ***Sample locations for the compiled data on sotalol***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.

Figure 23. ***Central nervous system agents (psychotherapeutic, antiepileptic, antiparkinson, muscle relaxant). Concentrations in Baltic Sea water***

Source: Original data.



Chemotherapeutic agents and X-ray contrast media

Three different pharmaceuticals of the therapeutic group chemotherapeutic agents and X-ray contrast media were measured in water. Amidotrizoic acid was detected in 16 out of 137 (12%) water samples from Germany. The highest recorded concentration of amidotrizoic acid was 0.125 µg/l and the median among the detected samples was 0.047 µg/l. Iopamidol was detected in two out of 137 (2%) samples from Germany, with the highest concentration being 0.09 µg/l. Capecitabine was measured, but not detected, in two water samples from Denmark.

Dermatological agents

Data on salicylic acid were available for water and sediment samples from Sweden, where the substance was detected in four out of eight (50%) water samples and in all four sediment samples. None of six biota samples indicated presence of this compound. The highest reported concentration was 14 ng/l, with a median of 12 ng/l.

Figure 24. ***Sample locations for the compiled data on carbamazepine***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.

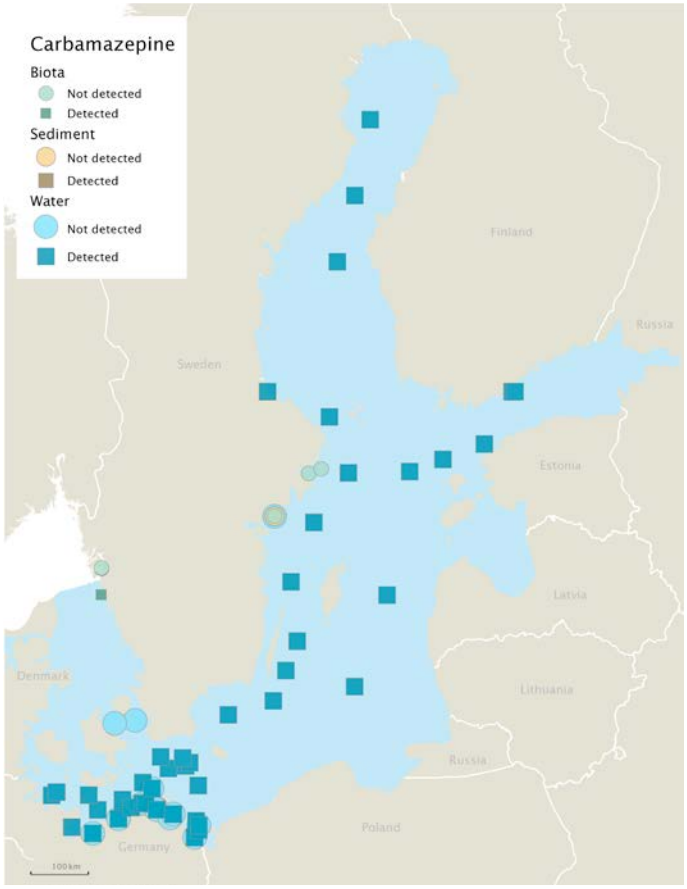
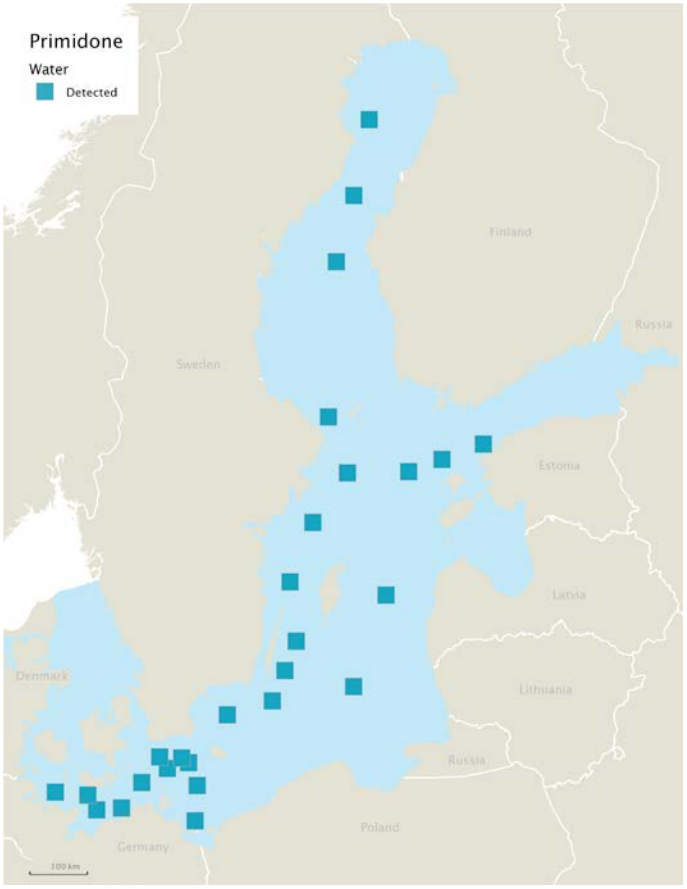


Figure 25. ***Sample locations for the compiled data on primidone***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.



Hormones and hormone antagonists

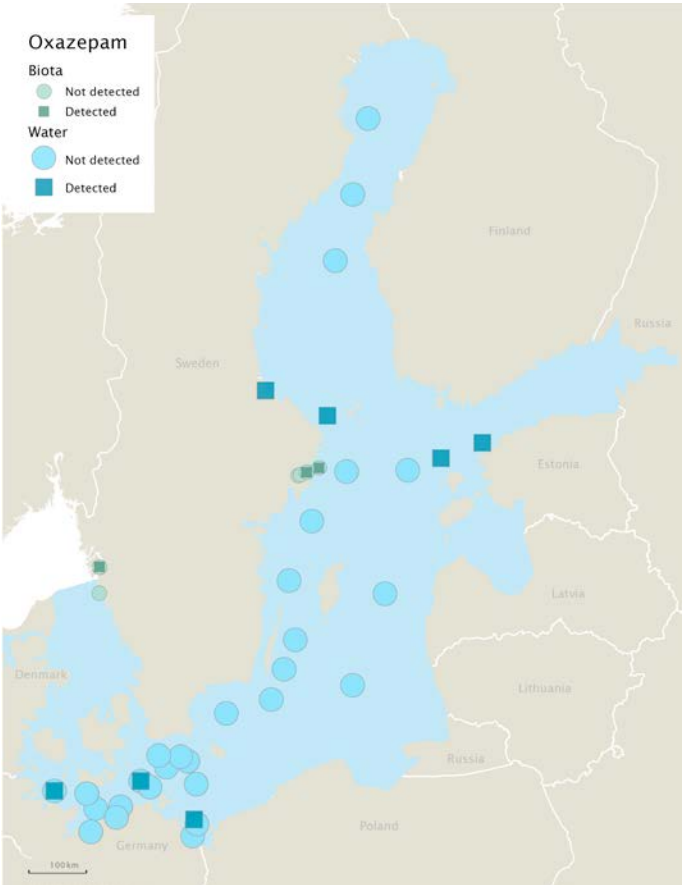
Of all monitored hormones and hormone antagonists, five out of 15 (33%) substances were detected in environmental samples (water, sediment or biota). Estradiol and 17a-ethinylestradiol were detected in only three water samples out of 228 reported samples taken from water, sediments and biota. The highest concentration detected for estradiol was 1.1 ng/l. For the synthetic estrogen 17a-ethinylestradiol, the minimum acceptable detection limit, as well as the proposed EQS, according to the EU 'watch list' (Table 2) is 0.035 ng/l.

For 105 out of 107 water samples the result was reported as being <LOD. In 90% of these cases (95 of 105) the reported LOD was 0.1 ng/l or higher, indicating that monitoring of these substances is problematic since in general the analytical methods are not sensitive enough.

Figure 26. ***Sample locations for the compiled data on oxazepam***

Each presented data point might conceal several measurements conducted at the exact same location.

Source: Original data.



Metabolic and gastrointestinal agents

Of the metabolic agents and gastrointestinal agents six out of 14 (43%) substances were detected in environmental samples. Clofibric acid concentrations were very low. Nonetheless, the compound was detected in 83 out of 128 (65%) open sea water samples all around the Baltic Sea. The maximum detected concentration was 0.4 ng/l. The fact that the median concentration is lower than the highest LOD means that the compound might be more frequently present in water bodies than can be concluded from detected samples.

7.2 Pharmaceuticals detected in marine biota

All reported biota samples were collected in Sweden and of a total of 839 measurements, 77 (9%) had concentrations of pharmaceutical substances that were above the detection limit. All results on detected pharmaceuticals in biota (grouped by species) are presented in Figure 27 to Figure 31. It should be noted that information on type of tissue sampled (e.g., fish muscle or bile) was sometimes missing in the reported data.

The results indicate that the largest number of different pharmaceutical substances and the highest concentrations are found in blue mussels (Figure 28).

Figure 27. ***Ciprofloxacin in Atlantic cod (Gadus morhua)***

Location a) Kalmar, Western Gotland Basin (HELCOM sub-basin 10).
Location b) Gothenburg, Kattegat (HELCOM sub-basin 1) – 2 samples.

Source: Original data.

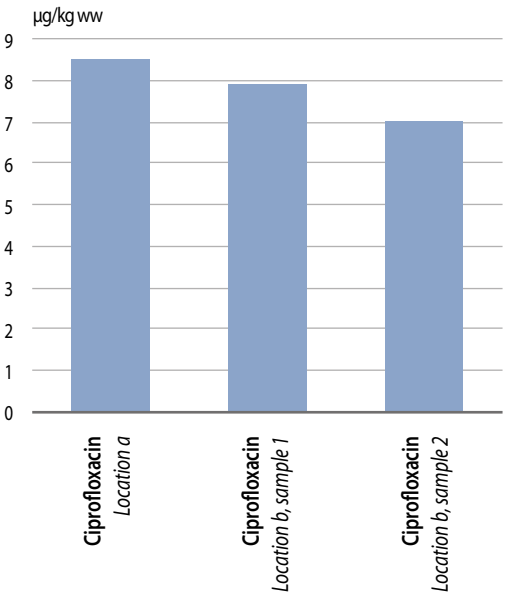


Figure 28. ***Detected pharmaceuticals in blue mussel (Mytilus edulis trossulus)***

Location a) Askeröfjorden, north of Gothenburg, Kattegat (north of HELCOM sub-basin 1).
Location b) Älvsborgsfjorden, Gothenburg, Kattegat (HELCOM sub-basin 1).

Source: Original data.

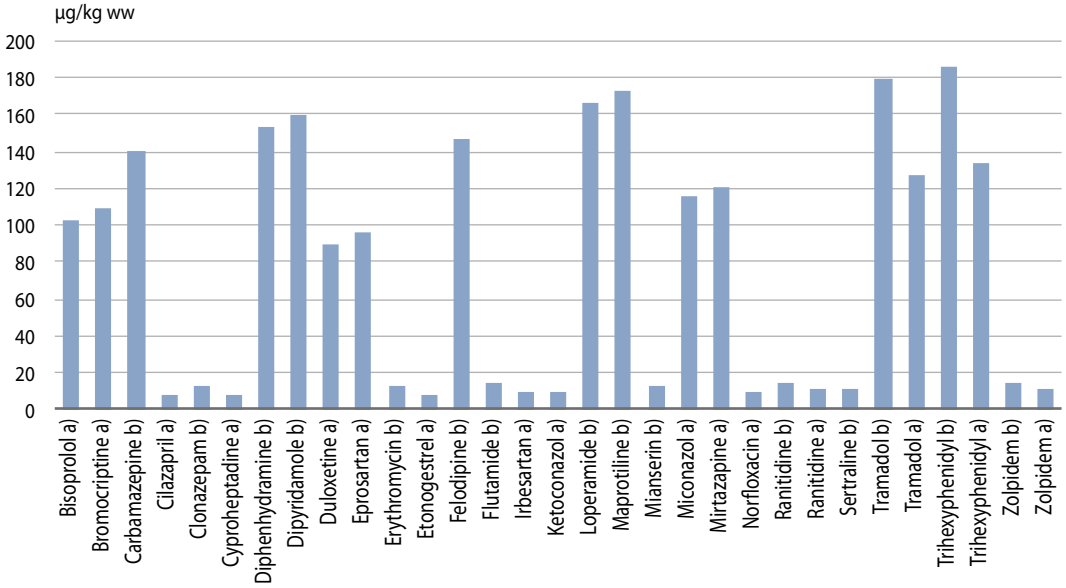


Figure 29. ***Detected pharmaceuticals in bile from European perch (Perca fluviatilis)***

Individual samples. Location a) Käppala (MWWTP), Stockholm, Northern Baltic Proper (HELCOM sub-basin 12).
Location b) Gällnö (archipelago), Stockholm, Northern Baltic Proper (HELCOM sub-basin 12).

Source: Original data.

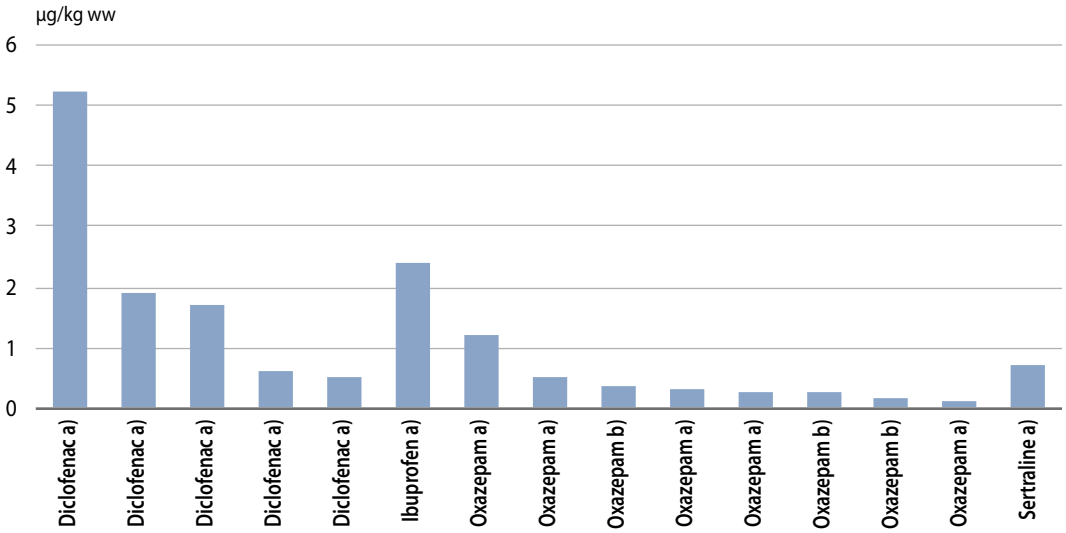


Figure 30. ***Detected pharmaceuticals in flounder (Platichthys flesus)***

All samples are from the location Askeröfjorden, north of Gothenburg, Kattegat (north of HELCOM sub-basin 1).

Source: Original data.

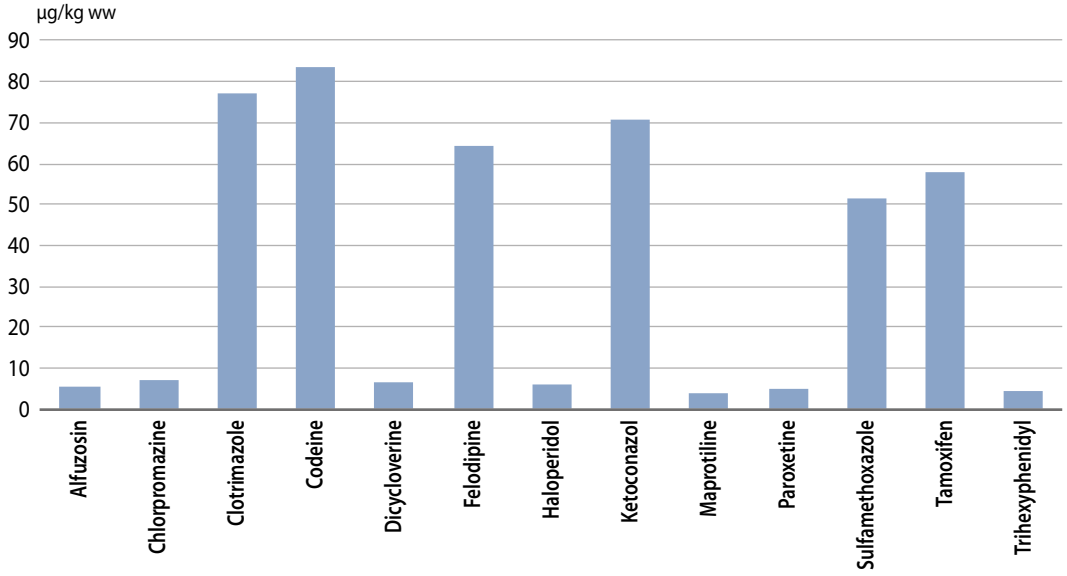
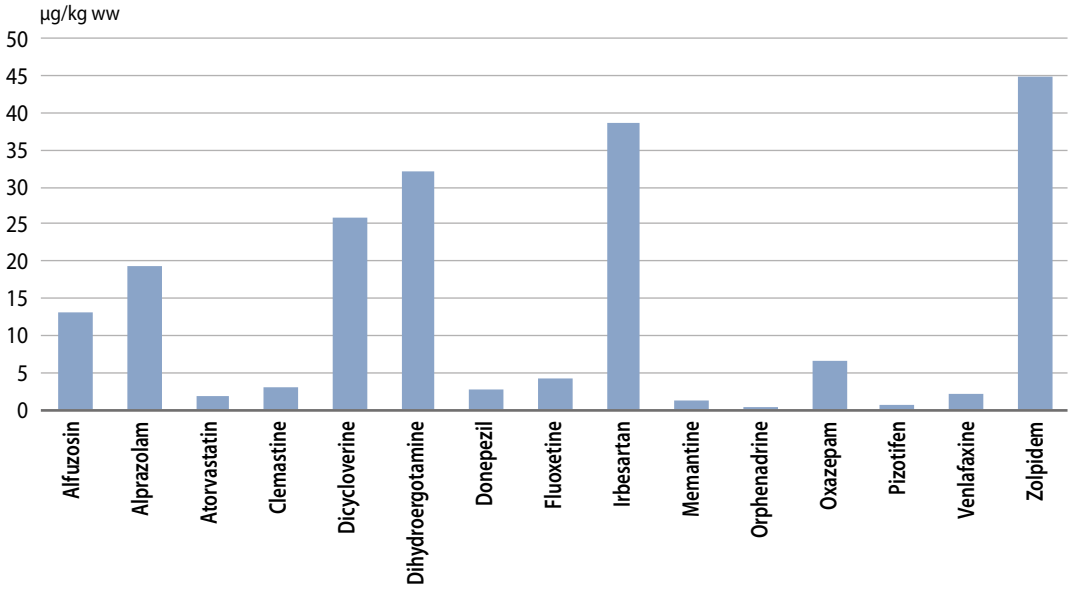


Figure 31. ***Detected pharmaceuticals in eel (Anguilla anguilla)***

All samples are from the location Askeröfjorden, north of Gothenburg, Kattegat (north of HELCOM sub-basin 1).

Source: Original data.



7.3 Effects of pharmaceuticals in the Baltic Sea marine environment

An overview of the results of different studies concerning the effects of pharmaceutical substances on Baltic Sea species is presented in Annex 5. Studies where the combined effects of pharmaceuticals and other contaminants were studied have been excluded (e.g., Turja et al 2015) since it was not within the scope of this report to assess such results.

In summary, several publications reported on effects of the β-blocker propranolol as well as the anti-inflammatory drugs diclofenac and ibuprofen on the littoral organisms blue mussel (*Mytilus edulis trossulus*), *macroalgae* (*Fucus vesiculosus* or *Ceramium tenuicorne*) and *amphipod crustacean* (*Gammarus* spp) (Ericson et al. 2010, Eriksson Wiklund et al 2011, Oskarsson et al 2012, Oskarsson et al 2014, Kumblad et al 2015). One study reported effects of the antidepressant drug citalopram on fish behavior (*Gasterosteus aculeatus*) (Kellner et al 2015). Propranolol showed effects on all the tested littoral organisms, of which the macroalgae *Fucus vesiculosus* was the most sensitive species (Kumblad et al 2015). Ibuprofen and diclofenac only showed effects on blue mussels. In a microcosm study the blue mussel was the most sensitive species.

8. Conclusions and recommendations

8.1 Overview of main results and data compilation

Pharmaceuticals are released into the environment during various stages of the product lifecycle (manufacturing, consumption and waste disposal).

In the Baltic Sea region, the main sources of pharmaceuticals in the freshwater and marine environment are believed to be the excretion of bioactive substances consumed by humans and animals (via urine and faeces) as well as the incorrect disposal of unused medical products. The main pathway of pharmaceuticals into the aquatic environment, according to the collected data, is via discharges of wastewater from MWWTPs.

The top 20 pharmaceuticals found in highest concentrations in MWWTP influents, effluents, sewage sludge and river water belong to various therapeutic groups (see Chapter 6.2). For example, the diuretic furosemide had the highest average concentration measured in MWWTP effluents at 22.3 µg/l, and the highest single concentration measurement was for the anti-inflammatory drug paracetamol at 360 µg/l (measured in Denmark). No measurements were reported of furosemide in the Baltic Sea environment.

The overall removal rate of pharmaceuticals in MWWTPs was low for most of the compounds. Only nine out of 118 assessed pharmaceuticals were efficiently removed (> 95%) from wastewater during wastewater treatment processes. Nearly half of the compounds were removed with an efficiency lower than 50% in MWWTPs.

According to the reported data on concentrations of pharmaceuticals in the Baltic Sea environment, the substances of greatest concern belong to the therapeutic groups of anti-inflammatory and analgesics, cardiovascular and central nervous system agents and antimicrobials. This conclusion is based on the detection frequency and does not take into account potential impacts of the substances on the ecosystem (see Chapter 8.2). The most frequently detected anti-inflammatory and analgesics pharmaceuticals were diclofenac, ibuprofen and paracetamol, which were detected in almost all compartments of the Baltic Sea environment. Sulfamethoxazole was the most frequently detected antimicrobial substance and was detected in all matrices. Cardiovascular agents were detected mainly in seawater samples. The most confident data were obtained for metoprolol, bisoprolol and sotalol. Bisoprolol was also detected in a biota sample. The central nervous system agents carbamazepine and primidone were frequently detected in seawater, where the latter was detected in all samples where it was measured. Carbamazepine was detected also in biota. Pharmaceuticals, which belong to the other therapeutic groups such as silicic and clofibric acids, were also detected in many samples. Hormones were only found in a few samples, possibly explained by the use of analytical methods with high detection limits.

The data on concentrations of pharmaceutically active compounds in marine biota indicate that the largest number of different substances and the highest concentrations are found in blue mussels.

The report provides the most comprehensive compilation of existing data on pharmaceuticals in the freshwater and marine environment at the national and regional levels in the Baltic Sea region. However, there are data gaps (see Chapter 3.3) that need to be addressed in order to carry out a more complete assessment of the extent of contamination by pharmaceuticals.

More data from the whole region are needed on:

- sales and consumption of pharmaceuticals, and household pharmaceutical wastes management
- concentrations of pharmaceuticals in wastewater, notably in MWWTP influents and effluents, and in sewage sludge
- concentrations of pharmaceuticals in freshwater such as surface waters (river water) and groundwater
- the occurrence and fate of metabolites in freshwater, wastewater, and sea water
- sales and consumption of veterinary pharmaceuticals, and their sources, pathways and loading to soils, surface and groundwater systems and the aquatic environment (including agriculture and aquaculture)
- emissions of pharmaceuticals to the environment via other pathways such as solid waste disposal
- analytical methods used for measuring concentrations and their sensitivity

The results of monitoring of pharmaceuticals' concentrations in the Baltic Sea marine environment likely underestimate occurrence and impacts since the analytical methods used in some cases are not sensitive enough and in some cases exceed the levels at which harmful biological effects take place.

8.2 Recommendations for improving scientific knowledge and data

Although the reported data provide an overview of the magnitude of inputs of several pharmaceutical substances to the Baltic Sea, as well as their concentrations in the freshwater systems and marine environment, there is a need to improve scientific knowledge and data in order to get a more complete and accurate assessment of the extent of contamination by pharmaceuticals.

Data are essential to address specific sources and pathways of pharmaceuticals' emissions into freshwater systems and the environment to help identify priority measures.

More monitoring data on pharmaceuticals in river water and wastewater (e.g., MWWTPs influents and effluents) are needed from every Baltic Sea country. Especially data from Poland are needed since it has the largest portion of the catchment area and population of the Baltic Sea region.

There is a need for data for many highly-consumed pharmaceuticals, on which monitoring data are missing currently, and especially for the following substances:

- Allopurinol
- Gabapentin
- Levetiracetam
- Mesalazin
- Valsartan

Research and data are needed on concentrations of pharmaceuticals in sewage sludge and soil. The fate of pharmaceuticals in sewage sludge needs further research in order to assess the risk of emerging of pharmaceuticals in soils and their possible runoff to surface waters and infiltration to groundwater.

Monitoring data and research are needed on the occurrence and fate of metabolites in freshwater systems and marine environment.

It was noted in this study that the metabolites of ibuprofen often occurred at higher concentrations than the parent compound. The role of metabolites should be studied in more detail, especially for easily biodegradable compounds.

Data on sales and consumption pharmaceuticals are needed from all Baltic Sea countries. At present, data are missing from Latvia, Lithuania, Poland and Russia. Detailed sales and consumption data are needed in order to fully estimate the priority pharmaceuticals in the region as well as to target monitoring efforts.

Specific attention needs to be put on filling the data gap on veterinary pharmaceuticals, including data on their sales, consumption, sources, pathways and loading to soils, groundwater and the aquatic environment. The very scarce data on sales and consumption of pharmaceutical substances in veterinary use indicate that the annual turnover is comparable to the amount used in human medicine. Taking into account that manure is applied on the agricultural lands as fertilizer, agriculture could be a significant pathway of medical compounds to the environment.

Analytical methods of a higher resolution should be used for measuring concentrations of pharmaceuticals in the freshwater and marine environment. The analytical methods currently used by many laboratories are at times not sensitive enough to detect substances at the level of the proposed environmental quality standards or the threshold values (see Chapter 7 and Annex 4). More sensitive analytical methods should therefore be used to measure substances at lower concentrations.

More studies on the impacts of pharmaceuticals on the freshwater and marine ecosystems should be carried out. There is limited knowledge of the effects of pharmaceuticals in the environment, especially considering that aquatic organisms are continually exposed to many different pharmaceutical substances, and of their potential combined effects. For many pharmaceutical substances, there is a lack of scientific evidence and information concerning their toxicity (i.e., base data to derive reliable threshold, or PNEC values), persistence and bioaccumulation in the environment, making it difficult to assess the potential impacts and consequences of these substances in the environment. Application of a concept of using known human therapeutic doses to assess effect on biota could be considered.

Concentrations of pharmaceuticals in freshwater and marine biota and their occurrence in the food chain should be studied through more interdisciplinary research. In a recent non-target screening conducted in Norway, a relatively large number of pharmaceuticals were found in sea birds (Miljødirektoratet, 2013). This suggests that pharmaceuticals may be transferred in aquatic food chains up to seabirds. These results, together with the results presented on pharmaceuticals in blue mussels in the Baltic Sea (see Chapter 7), suggest that it should be of interest to include sea birds, such as *Common Eider*, that primarily feed on blue mussels, in future monitoring studies for pharmaceuticals.

8.3 Potential measures for further consideration to reduce inputs of pharmaceuticals into the environment

With pharmaceuticals being emerging pollutants that need to be addressed, it is necessary to take measures to reduce the inputs of these substances to the environment. Also, further information on the effects and risks of pharmaceuticals in the environment is needed to support the prioritization of measures for reducing inputs of specific substances.

Measures to reduce the inputs of pharmaceuticals should address all stages of the product lifecycle from manufacturing to consumption to waste management. Measures can include both technical and policy solutions, as well as educational and awareness raising initiatives.

Technical solutions to remove pharmaceuticals from wastewater can be applied in MWWTPs, mainly as tertiary treatment of wastewater. At present, there are a few MWWTPs in the Baltic Sea catchment area that apply advanced techniques to enhance the removal of pharmaceuticals from wastewater. Two MWWTPs in Sweden are planning to apply ozonation to enhance wastewater treatment. Other tertiary treatment methods that could be used to enhance the removal of pharmaceuticals include oxidative processes (e.g., advanced oxidation, photocatalysis, Fenton-based and pulsed corona discharge), adsorptive methods (e.g., activated carbon) and membrane filtration (e.g., nanofiltration, reverse osmosis, etc.). It should be stressed that oxidative treatment methods produce byproducts, especially of those pharmaceuticals that are not easily oxidized; thus, removal of these byproducts is necessary before discharging the treated wastewater to the environment. Adsorptive methods transfer the pharmaceuticals from water to the solid phase (e.g., sludge), therefore the sewage sludge also needs to be treated and properly disposed. The improved tertiary treatment of wastewater does not affect the quality of sludge. In membrane filtration, pharmaceuticals remain in the retentate (or the concentrate), which needs to be further treated or properly disposed.

Oxidation, adsorption and filtration methods could also be used for the pre-treatment of raw wastewater from hospital and manufacturing facilities prior to discharging it to the sewer. However, the quality of water from these facilities differs from the municipal wastewater, therefore pre-treatment of these waters is most probably needed before applying further treatment methods. Oxidative treatments may be suitable since the byproducts that are formed during these processes may be effectively removed during the biological treatment process at MWWTPs.

Policy and educational solutions for reducing inputs of pharmaceuticals to wastewater and further to the environment need to include awareness raising of doctors and consumers concerning possible harmful effects of pharmaceuticals in the environment.

Take-back of unused medicines by pharmacies should be applied or developed in countries where such systems are not yet in place or are inefficient, in order to reduce the disposal of unused medicines via solid waste or sewers. Awareness raising and educational campaigns on human health and environmental impacts of pharmaceuticals in the environment and on the correct disposal of household pharmaceutical wastes should be carried out for the public, as well as for doctors and pharmacists.

A certification system, indicating degree of potential environmental impacts of pharmaceuticals, can help doctors, pharmacists and consumers to consider environmental aspects when choosing a medication. In Sweden, for example, the FASS database (*www.fass.se*) includes environmental data about pharmaceuticals, and information booklets are distributed to doctors to encourage the consideration of environmental aspects when prescribing medication. This system could be applied also in other Baltic Sea countries.

Promotion of sustainable consumption of pharmaceuticals also reduces inputs of unused medicine to wastewater. Measures to reduce the disposal of unused medicines to the environment could include educating the public on proper use of medicines and promoting medication packaging and dispensing systems suitable to prescribed quantities. Furthermore, when doctors prescribe a new medication, a small-sized trial package could be used to reduce household pharmaceutical waste generation if the medication is not suitable for the patient.

9. References

Agra-Europe. 2014. Antibiotikaabgabenmengenerfassung 2013. Agra-Europe 40/14, 29 September 2014. (In German).

Andersson, H., Magnér, J. and Wallberg, P. 2013. Self-declarations of environmental classification in *www.fass.se*. IVL report, B2124.

BIO Intelligence Service. 2013. Study on the environmental risks of medicinal products. Final Report prepared for Executive Agency for Health and Consumers. Available at: *http://ec.europa.eu/health/files/environment/study _environment.pdf*.

Brodin, T., Fick, J., Jonsson, M. and Klaminder, J. 2013. Dilute concentrations of a psychiatric drug alter behaviour of fish from natural populations. Science, Vol. 339, pp. 814-815.

BVL. 2014. Dritte Datenerhebung zur Antibioticaabgabe in der Tiermedizin. Bundesamt für Verbraucherschutz und Lebensmittelsicherheit. Available at: *www.bvl.bund. de.* (In German).

EEA. 2010. Pharmaceuticals in the environment. European Environmental Agency EEA Technical report 1/2010. Available at: *http://www.eea.europa.eu/publications/ pharmaceuticals-in-the-environment-result-of-an-eea-workshop*.

Ericson, H., Thorsén, G. and Kumblad, L. 2010. Physiological effects of diclofenac, ibuprofen and propranolol on Baltic Sea blue mussels. Aquatic Toxicology, Vol. 99, pp. 223-231.

Eriksson Wiklund, A.-K., Oskarsson, H., Thorsén, G. and Kumblad, L. 2011. Behavioural and physiological responses to pharmaceutical exposure in macroalgae and grazers from a Baltic Sea littoral community. Aquatic Biology, Vol. 14, pp. 29-39.

European Commission. 2004. 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. OJ L Vol. 136, pp. 34-57.

European Commission. 2008. Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/ EEC, 83/513/ EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council. OJ L, Vol. 348, pp. 84-97.

European Commission. 2008. 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). OJ L, Vol. 164, pp. 19–40.

European Commission. 2013. 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. OJ L, Vol. 226, pp. 1–17.

European Commission. 2015. Commission Implementing Decision (EU) 2015/495 of 20 March 2015 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council. *OJ L*, Vol. 78, pp. 40–42.

Hallgren, P. and Wallberg, P. 2015. Background report on pharmaceutical concentrations and effects in the Baltic Sea. Policy Area Hazards of the EU Strategy for the Baltic Sea Region.

HVMFS. 2013. Havsoch vattenmyndighetens föreskrifter om klassificering och miljökvalitetsnormer avseende ytvatten. [Swedish Agency for Marine and Water Management regulations on classification and quality standards regarding surface water]. *HVMFS* 2013: 19. (In Swedish).

HELCOM. 2007. HELCOM Baltic Sea Action Plan. Adopted 15 November 2007 in Krakow, Poland.

HELCOM. 2010. Moscow Ministerial Declaration on the implementation of the HELCOM Baltic Sea Action Plan. Adopted 20 May 2010 in Moscow, Russia.

HELCOM. 2013a. HELCOM Copenhagen Ministerial Declaration: Taking Further Action to Implement the Baltic Sea Action Plan Reaching Good Environmental Status for a healthy Baltic Sea. Adopted on 3 October 2013 in Copenhagen, Denmark.

HELCOM. 2013b. HELCOM monitoring and assessment strategy. Available at: *http://www.helcom.fi/action-areas/monitoring-and-assessment/monitoring-and-assessmentstrategy*.

Kellner, M., Porseryd, T., Porsch-Hallström, I. and Hansen, S. 2015. Environmentally relevant concentrations of citalopram partially inhibit feeding in the three-spine stickleback *(Gasterosteus aculeatus). Aquatic Toxicology*, Vol. 158, pp. 165-170.

Kidd, K. A., Blanchfield, P. J., Mills, K. H., Palace, V. P., Evand, R. E., Lazorchak, J. M. and Flick, R.W. 2007. Collapse of a fish population after exposure to a synthetic estrogen. *PNAS*, Vol. 104, pp. 8897-8901.

Kumblad, L., Oskarsson, H., Palmer, C. and Eriksson Wiklund, A.-K. 2015. Response and recovery of Baltic Sea blue mussels from exposure to pharmaceuticals. *Marin. Ecol. Prog. Ser.*, Vol. 526, pp. 89–100.

Miljødirektoratet. 2013. *Non-target screening – A powerful tool for selecting environmental pollutants*. Rapport M-27.

MPA. 2015. Miljöindikatorer inom ramen för nationella läkemedelsstrategin (NLS). [Environmental indicators under the national drugs strategy (NLS)] Report of CBL's Office, *Läkemedelsverket [MPA]* 2015-09-07. (In Swedish).

Oskarsson, H., Eriksson Wiklund, A.-K., Lindh, K. and Kumblad, L. 2012. Effect studies of human pharmaceuticals on *Fucus vesiculosus* and *Gammarus spp. Marine Environmental Research*, Vol. 74, pp. 1-8.

Oskarsson, H., Eriksson Wiklund, A.-K., Thorsén, G., Danielsson, G. and Kumblad, L. 2014. Community Interactions Modify the Effects of Pharmaceutical Exposure: A Microcosm Study on Responses to Propranolol in Baltic Sea Coastal Organisms. *PLoS ONE*, Vol. 9, No. 4, e93774. *doi:10.1371/journal.pone.0093774*.

Ravimiamet. 2015. Statistics on veterinary medicines in Estonia 11.03.2015. State Agency of medicines. Available at: *http://www.ravimiamet.ee/en/statistics-veterinary- medicines*.

Tema Nord. 2012. PPCP monitoring in the Nordic Countries – Status report. *doi:10.6027/09086692*.

Turja, R., Lehtonen, K. K., Meierjohann, A., Brozinski, J. M., Vahtera, E., Soirinsuo, A., Sokolov, A., Snoeijs, P., Budzinski, H., Devier, M. H,, Peluhet, L., Pääkkönen, J.P., Viitasalo, M. and Kronberg, L. 2015. The mussel caging approach in assessing biological effects of wastewater treatment plant discharges in the Gulf of Finland (Baltic Sea). *Mar. Pollut. Bull.*, Vol. 97, pp.135-49. doi: 10.1016/j.marpolbul.2015.06.024.

UNESCO. 2016. Emerging Pollutants in Water and Wastewater. UNESCO Project on "Emerging Pollutants in Wastewater Reuse in Developing Countries", UNESCO-IHP International Initiative on Water Quality (IIWQ). *http://en.unesco.org/emergingpollutants*.

Vieno, N. 2015. Status report on pharmaceuticals in the Baltic Sea background information on consumption, sources and pathways of pharmaceutical substances into the Baltic Sea.

Weber, F.-A., aus der Beek, T., Bergmann, A., Carius, A., Grüttner, G., Hickmann, S., Ebert, I., Hein, A., Küster, A., Rose, J., Koch-Jugl, J., and Stolzenberg, H.-C. 2014. Pharmaceuticals in the environment – the global perspective Occurrence, effects, and potential cooperative action under SAICM. German Federal Environmental Agency (UBA). Available at: *https://www.umweltbundesamt.de/en/database-pharmaceuticals-in-the-environment-0*.

Annex 1. Description of data collection and analytical methods

Annex 1.1. Data collection

Data collection was carried out using a stepwise approach and coordinated via relevant HELCOM working groups.

First phase – A review of availability and sources of data was carried out. The aim was to also identify sources of relevant data with restricted access (e.g. commercial data, data which require anonymizing etc.). No data collection was carried out during this phase. An overview of the following information was gathered via the HELCOM Working Group on the State of the Environment and Nature Conservation (State and Conservation) and the Working Group on Reduction of Pressures from the Baltic Sea Catchment Area (Pressure):

- National sources of data on concentrations of pharmaceutical substances in all compartments of the environment (e.g. programme, project, reference to data source, etc.):
  - state and local environmental monitoring and screening programmes
  - regulated monitoring, e.g. sewage treatment plants, industry
  - projects/screening studies
  - scientific studies
  - commissioned studies
- National sources of data on sales and consumption/use of pharmaceuticals by user group (e.g. human use, agriculture, veterinary):
  - authorities (environmental, health care, veterinary, agricultural etc.)
  - professional associations
  - projects/studies
- National sources of data on pathways of pharmaceuticals into the environment, such as concentrations in wastewater, sludge, manure, etc.:
  - authorities
  - professional associations
  - projects/studies
- Information on accessibility to existing data, e.g.:
  - open access data (e.g. database)
  - reports
  - restricted data and information
  - Contact persons [likely a number of contact persons in different authorities/ institutions]

Second phase – A template for data collection (a questionnaire), together with reporting guidelines, was prepared based on the results from the first phase. Available data were collected according to the following categories:

1. Environmental concentrations of pharma ceuticals in the coastal and open water areas of the Baltic Sea (e.g. water, biota, sediment)
2. Effects of pharmaceuticals on Baltic Sea biota
3. Sources and pathways of pharmaceuticals to the environment (concentration of these substances in wastewater, sludge, manure, etc.), as well as information on production, sales, consumption and waste management of pharmaceuticals.

Further, appropriate metadata were collected, such as geographical coordinates for sampling points, analytical methods, detection limits, data quality, etc.

The data submitted via national reporting through the HELCOM working groups were compiled and analyzed by experts (Vieno 2015, Hallgren and Wallberg 2015; listed in the main report reference list).

Annex 1.2. Overview of reported data

Measurements in MWWTP influents, effluents, sludge and river water

Table A1.1 ***Total number of data on pharmaceuticals detection in wastewater, sludge and river water in the Baltic Sea region from 2003 to 2014***

Note: Due to differences in limits of detection (LOD) and the nature of reported data (which integrates both individual measurements and averaged values), differences in detection frequencies between countries cannot always be interpreted as clear indicators of the level of pharmaceutical contamination.

Source: Original data.

		Number of detections/number of reported samples				
	References	Total	MWWTP influent	MWWTP effluent	Sludge*	River water
Denmark	[23] – [25]	2,907/5,698 (51%)	1,297/1,861	1,382/2,901	124/240	104/696
Estonia	[26]	173/540 (32%)	58/135	52/135		63/270
Finland	[1] – [9]	1,031/1,613 (64%)	275/301	247/306	377/804	132/202
Germany	[21, 22]	579/1,199 (48%)		972/1,253		6,126/31,943
Russia	[10]	3,030/5,656 (54%)	374/603	205/596		
Sweden	[11] – [20]	14,818/47,819 (31%)	882/1,729	1,795/3,266	307/534	46/127
Total		**7,098/33,196 (21%)**	**2,886/4,629**	**4,653/8,457**	**808/1,575**	**6,471/33,158**

*raw, digested and composted sludge

References

[1] Lindholm-Lehto, P., Knuutinen, J., Herve, S. and Ahkola, H. 2015. Lääkeaineet jäteveden puhdistamolla ja vesistössä. Ympäristö ja terveys 3/2015: 38 - 43.

[2] Munne, P. and Äystö, L. 2015. Eräiden lääkeaineiden ja triklosaanin esiintyminen puhdistamolietteissä sekä käyttäytyminen suomalaisilla maatalousmailla. Ympäristö ja terveys 4/2015: 34 - 39.

[3] Äystö, L., Mehtonen, J., and Mannio, J. 2015. Lääkeaineet Etelä-Suomen pintavesissä ja puhdistetussa jätevedessä. Ympäristö ja terveys 4/2015: 40 - 46.

[4] Vieno N. 2007. Occurrence of Pharmaceuticals in Finnish Sewage Treatment Plants, Surface Waters, and Their Elimination in Drinking Water Treatment Processes. Tampere University of Technology, Publication 666.

[5] Vieno N. 2014. Hazardous substances at wastewater treatment plants - project report. Vesilaitosyhdistyksen monistesarja nro 34.

[6] Vieno N. 2015. Haitta-aineet puhdistamoja hajalietteissä. Vantaanjoen ja Helsingin seudun vesiensuojeluyhdistys ry, julkaisu 73/2015.

[7] Vieno N. M., Tuhkanen, T., and Kronberg, L. 2006. Analysis of neutral and basic pharmaceuticals in sewage treatment plants and in recipient rivers using solid phase extraction and liquid chromatography-tandem mass spectrometry detection. Journal of Chromatography A, 1134 (2006): 101 - 111.

[8] Vieno, N.M., Härkki, H., Tuhkanen, T., and Kronberg, L. 2007. Occurence of Pharmaceuticals in River Water and Their Elimination in a Pilot-scale Drinking Water Treatment Plant. Environmental Science & Technology 41(14): 5077 - 5084.

[9] Perkola, N., Juntunen, J., Tuominen, S., Nysten, T., Rosendahl, K., Huttula, T., Pitkänen, T., Kauppinen, A., Kusnetsov, J., Hokajärvi, A.-M., Meriläinen, P., Miettinen, I. T., and Happonen, M. 2015. Kuluttajakemikaalit ja mikrobit Kokemäenjoen vesistössä. Ympäristö ja terveys 3/2015: 50 - 55.

[10] HELCOM. 2014. BASE project 2012-2014: Pilot activity to identify sources and flow patterns of pharmaceuticals in St. Petersburg to the Baltic Sea.

[11] Haglund, P. and Olofsson, U. 2007. Miljöövervakning av slam. Redovisning av resultat från 2004, 2005 och 2006 års provtagningar. Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket.

[12] Haglund, P. and Olofsson, U. 2008. Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket. Miljöövervakning av slam. Redovisning av resultat från 2007 års provtagning.

[13] Haglund, P. and Olofsson, U. 2010. Miljöövervakning av slam. Redovisning av resultat från 2008 års provtagning (inklusive en sammanfattning av åren 2004-2008). Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket.

[14] Haglund, P. and Olofsson, U. 2011a. Miljöövervakning av slam. Redovisning av resultat från 2009 års provtagning (inklusive en sammanfattning av åren 2004-2009). Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket.

[15] Haglund, P. and Olofsson, U. 2011b. Miljöövervakning av utgående vatten & slam från svenska avloppsreningsverk. Resultat från år 2010 och en sammanfattning av slamresultaten för åren 2004-2010. Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket.

[16] Haglund, P. and Olofsson, U. 2013. Miljöövervakning av utgående vatten & slam från svenska avloppsreningsverk. Resultat från år 2011 och en sammanfattning av slamresultaten för åren 2004-2011. Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket.

[17] Haglund, P. and Olofsson, U. 2014. Miljöövervakning av utgående vatten & slam från svenska avloppsreningsverk. Resultat från år 2012 och 2013 och en sammanfattning av slamresultaten för åren 2004-2013. Kemiska institutionen vid Umeå universitet på uppdrag av Naturvårdsverket.

[18] Johansson, M., Lindberg, R., Wennberg, P. and Tysklind, M. 2003. Redovisning från nationell miljöövervakning 2003. Screening av antibiotika i avloppsvatten, slam och fisk under 2002/2003. Miljökemi, Umeå Universitet, på uppdrag av Naturvårdsverket.

[19] Löfgren, H. and Gottby, L. 2012. Miljögifter i Gävleborg, resultat från verifieringar 2009 – 2011. Rapport 2012:4, Länsstyrelsen Gävleborg.

[20] IVL. 2015. Miljöövervakningsdata. Screening av miljögifter. Naturvårdsverket. Database in screening of environmental pollutants. Available at: http://dvss.ivl.se/ DataSelect.aspx.

[21] Data provided by the State Agency of Environment, Nature Protection and Geology Mecklenburg-Vorpommern.

[22] Data provided by the State Agency of Agriculture, Environment and Rural Areas Schleswig-Holstein.

[23] Naturstyrelsen. 2015. Punktkilder 2014. Miljøog Fødevareministeriet, Naturstyrelsen.

[24] Naturstyrelsen. 2015. NOVANA-screeningsundersøgelse for humane lægemidler i vandmiljøet. Miljøministeriet, Naturstyrelsen.

[25] Mogensen, B., Bossi, R., Kjær, J., Juhler, R. & Boutrup, S. 2007. Lægemidler og triclosan i punktkilder og vandmiljøet. Faglig rapport fra DMU nr. 638, 2007.

[26] Pharmaceuticals screening (2014-2015), Ministry of the Environment, Estonia.

Table A1.2 *Number of pharmaceuticals detections in MWWTP influent samples*

Source: Original data.

	Number of detections/Total number of samples						
Therapeutic group	**Denmark**	**Estonia**	**Finland**	**Germany**	**Russia**	**Sweden**	**Total**
Anti-inflammatory and analgesics	520/602	18/27	81/82	0/0	66/77	218/364	903/1,152
Antimicrobial	325/489	20/39	53/63	0/0	167/309	136/233	701/1,133
Cardiovascular agents	197/223	17/30	84/84	0/0	57/62	126/169	481/568
Central nervous system agents	33/36	3/12	34/35	0/0	31/31	292/698	393/812
Chemotherapeutic agents and X-ray contrast media	9/18						
Hormones and hormone antagonists	183/378	0/27	10/24		28/31	54/176	275/636
Metabolic agents and gastrointestinal agents	30/115		13/13		25/93	56/89	124/310
Total	**1,297/1,861**	**58/135**	**275/301**	**0/0**	**374/603**	**882/1,729**	**2,886/4,629**

Table A1.3 *Number of pharmaceuticals detections in MWWTP effluent samples*

Source: Original data.

	Number of detections/Total number of samples						
Therapeutic group	**Denmark**	**Estonia**	**Finland**	**Germany**	**Russia**	**Sweden**	**Total**
Anti-inflammatory and analgesics	477/876	14/27	72/84	234/290	48/77	667/962	1,512/2,316
Antimicrobial	442/693	19/39	43/63	108/132	93/309	156/364	861/1,600
Cardiovascular agents	250/291	16/30	84/84	166/290	30/62	183/278	729/1,035
Central nervous system agents		3/12	35/36	195/213	6/31	459/1,045	698/1,337
Chemotherapeutic agents and X-ray contrast media				269/328			269/328
Hormones and hormone antagonists	155/585	0/27	1/26	3/24	158/469	317/1,131	275/636
Metabolic agents and gastrointestinal agents	58/183	12/13	25/93	82/148	177/437	56/89	124/310
Total	**1,382/2,901**	**52/135**	**247/306**	**972/1,253**	**205/596**	**1,795/3,266**	**4,653/8,457**

Table A1.4 *Number of pharmaceuticals detections in untreated sludge samples*

Source: Original data.

	Number of detections/Total number of samples			
Therapeutic group	**Denmark**	**Finland**	**Sweden**	**Total**
Anti-inflammatory and analgesics	25/80	29/30	43/44	97/154
Antimicrobial	34/64	132/210	95/212	261/486
Cardiovascular agents	32/48	46/78		78/126
Central nervous system agents	32/32	31/36		63/68
Chemotherapeutic agents and X-ray contrast media	1/16	0/30		1/46
Hormones and hormone antagonists		1/12	11/53	12/65
Other		0/6		0/6
Total	**124/240**	**239/402**	**149/309**	**512/921**

Table A1.5 *Number of pharmaceuticals detections in digested sludge samples*

Source: Original data.

Number of detections/Total number of samples			
Therapeutic group	**Finland**	**Sweden**	**Total**
Anti-inflammatory and analgesics	7/20		7/20
Antimicrobial	36/56	158/225	194/281
Cardiovascular agents	16/52		16/52
Central nervous system agents	19/24		19/24
Chemotherapeutic agents and X-ray contrast media	0/20		0/20
Hormones and hormone antagonists	6/40		6/40
Other	0/16		0/16
Total	**84/232**	**158/225**	**242/457**

Table A1.6 *Number of pharmaceuticals detections in composted sludge samples*

Source: Original data.

Number of detections/Total number of samples	
Therapeutic group	**Finland/Total**
Anti-inflammatory and analgesics	6/15
Antimicrobial	19/42
Cardiovascular agents	7/39
Central nervous system agents	14/18
Chemotherapeutic agents and X-ray contrast media	0/15
Hormones and hormone antagonists	8/30
Other	0/12
Total	**54/171**

Table A1.7 *Number of pharmaceuticals detections in river water samples*

Source: Original data.

Number of detections/Total number of samples						
Therapeutic group	**Denmark**	**Estonia**	**Finland**	**Germany**	**Sweden**	**Total**
Anti-inflammatory and analgesics	40/104	17/60	55/75	992/6,875	9/19	1,113/7,133
Antimicrobial	26/364	26/78	7/41	413/7,948	9/17	481/8,448
Cardiovascular agents	26/108	16/66	57/67	2,262/10,352	11/29	2,372/10,622
Central nervous system agents	12/16	4/24	12/15	1,303/2,254	8/34	1,339/2,343
Chemotherapeutic agents and X-ray contrast media	0/8			1,156/3,306		1,156/3,314
Hormones and hormone antagonists	0/16	0/42	1/2	0/1,208	7/15	8/1,283
Metabolic agents and gastrointestinal agents					2/13	2/13
Other			0/2		0/0	0/2
Total	**1,382/2,901**	**52/135**	**247/306**	**972/1,253**	**1,795/3,266**	**4,653/8,457**

Measurements in the marine environment

Table A1.8 ***Total number of data on pharmaceuticals detection in the marine environment of the Baltic Sea from 2003 to 2014***

The number of data posts with detected values is presented together with the total number of data posts.

Source: Original data.

	Number of detections/number of reported samples				
	References	**Total**	**Water**	**Sediment**	**Biota**
Denmark	[13][23][24]	0/54 (0%)	0/54		
Estonia	[14]	2/75 (3%)	0/40	2/35	
Finland	[11] [12]	30/51 (59%)	19/27	11/24	
Germany	[9][25]	435/3,148 (14%)	435/3,148		
Poland	[1] [2] [3] [4] [5] [6] [7] [8]	0/18 (0%)	0/18		
Sweden	[10] [15] [16] [17] [18] [19] [20]	173/1,254 (14%) [21] [22]	78/360	18/55	77/839
Total		**640/4,600 (14%)**	**532/3,647**	**31/114**	**77/839**

References

[1] Migowska, Caban, Stepnowski, and Kumirska. 2012. Sci. Total Environ. 441, pp. 77–88.

[2] Caban, Czerwicka, Lukaszewicz, Migowska, Stepnowski, Kwiatkowski, et al. 2013. J.Chromatogr. A. 1301, pp. 215–24.

[3] Borecka, Bialk-Bielinska, Siedlewicz, Kornowska, Kumirska, Stepnowski, et al. 2013. J. Chromatogr. A. 1304, pp. 138–146.

[4] Kumirska, Migowska, Caban, Plenis, and Stepnowski. 2011. J. Chemom. 25, pp. 636–643.

[5] Nödler, Voutsa, and Licha. 2014. Mar. Pollut. Bull. 85 (1), pp. 50–9.

[6] Beck, Bruhn, Gandrass, and Ruck. 2005. J. Chromatogr. A. 1090, pp. 98–106.

[7] McEneff, G., Barron, L., Kelleher, B., Paull, B., and Quinn, B. 2014. Sci. Total Environ. 476-477, pp. 317–26.

[8] Stachel, U. Ehrhorn, O.-P. Heemken, P. Lepom, H. Reincke, G. Sawal, et al. 2003. Environ. Pollut. 124, pp. 497–507.

[9 BSH Bundesamt für Seeschifffahrt und Hydrographie.

[10] Karlsson, M. and Viktor, T. 2014. Miljöstörande ämnen i fisk från Stockholmsregionen 2013. Report B2214 from the Swedish Environmental Research Institute IVL.

[11] Muziasari, W. I., Managaki, S., Pärnänen, K., Karkman, A., Lyra, C., Tamminen, M., Suzuki, S., and Virta, M. 2014. Sulphonamide and Trimethoprim Resistance Genes Persist in Sediments at Baltic Sea Aquaculture Farms but Are Not Detected in the Surrounding Environment.

[12] Turja R., Lehtonen, K.K., Meierjohann, A., Brozinski, J.-M., Vahtera, E., Soirinsuo, A., Sokolov, A., Snoeijs, P., Budzinski, H., Devier, M.-H., Peluhe,t L., Pääkkönen, J.-P., Viitasalo, M., and Kronberg L. 2015. Marine Pollution Bulletin 97(1-2), pp. 135-49.

[13] Miljøministeriet, Naturstyrelsen. 2015. NOVANA-Screeningsundersøgelse for humane lægemidler i vandmiljøet.

[14] Estonian Environmental Research Centre. 2012. Euroopa Liidu prioriteetsete ainete nimekirja potentsiaalsete uute ainete esinemise uuring Eesti pinnaveekogudes II.

[15] Fick, J., Lindberg, R.H., Kaj, L. and Brorström-Lundén, E. 2011. Results from the Swedish national screening programme 2010. Sub-report 3: Pharmaceuticals. Report B2014 from the Swedish Environmental Research Institute IVL.

[16] Löfgren, H. and Gottby, L. 2012. Miljögifter i Gävleborg, resultat från verifieringar 2009 – 2011. Rapport 2012:4, Länsstyrelsen Gävleborg.

[17] Johansson, M., Lindberg, R., Wennberg, P. and Tysklind, M. 2003. Redovisning från nationell miljöövervakning 2003. Screening av antibiotika i avloppsvatten, slam och fisk under 2002/2003. Miljökemi, Umeå Universitet, på uppdrag av Naturvårdsverket.

[18] Törneman, N., Hallgren, P. and Bjarke M. 2014. Screening Report 2013. Occurrence of additional WFD priority substances in Sweden. Sweco Environment AB, on assignment from the Swedish Environmental Protection Agency.

[19] Andersson, J., Woldegiorgis, A., Remberger, M., Kaj, L., Ekheden, Y., Dusan, B., Svenson, A., Brorström-Lundén, E., Dye, C. and Schlabach, M. 2006. Results from the Swedish national screening programme 2005. Subreport 1: Antibiotics, anti-inflammatory.

[20] Remberger, M., Wiklund, P., Woldegiorgis, A., Viktor, T., Kaj, L. and Brorström-Lundén, E. 2009. Anti-inflammatory and analgesic drugs in WWTP influent and effluent streams and the occurrence in the aquatic environment. Report B1810 from the Swedish Environmental Research Institute IVL.

[21] Woldegiorgis, A., Green, J., Remberger, M., Kaj, L., Brorström-Lundén, E., Dye, C. and Schlabach, M. 2007. Results from the Swedish screening 2006. Sub-report 4: Pharmaceuticals. Report B1751 from the Swedish Environmental Research Institute IVL.

[22] Johansson, M., Lindberg, R., Wennberg, P. and Tysklind, M. 2003. Redovisning från nationell miljöövervakning 2003. Screening av antibiotika i avloppsvatten, slam och fisk under 2002/2003. Miljökemi, Umeå Universitet.

[23] Naturstyrelsen. 2015. Punktkilder 2014. Miljøog Fødevareministeriet, Natursty-relsen.

[24] Mogensen, B., Bossi, R., Kjær, J., Juhler, R. and Boutrup, S. 2007. Lægemidler og triclosan i punktkilder og vandmiljøet. Faglig rapport fra DMU nr. 638, 2007.

[25] State Agency of Environment, Nature Protection and Geology of Mecklenburg-Vorpommern.

Annex 2. The use of pharmaceuticals

Human consumption

The evaluation of consumption of pharmaceuticals is mainly based on data on sold amounts. Data on sales of human pharmaceuticals were received from Finland, Sweden, Estonia, Germany and Russia (only for diclofenac in St. Petersburg area). From Germany, data were received only for those pharmaceuticals that were prescribed at the highest amounts in Mecklenburg-Vorpommern and Schleswig-Holstein (the states within the Baltic Sea catchment area) in 2013 and 2014. German data were provided by GKV-Arzneimittelindex im Wissenschaftlichen Institut der AOK (WIdO) as tons per year. From Estonia, Finland and Sweden, data on pharmaceutical sales were received from the following sources in the form of statistics on the most frequently prescribed pharmaceuticals:

- Sweden: Swedish National Board of Health and Welfare, Statistikdatabas för läkemedel (2014) (www.socialstyrelsen.se/statistik/statistikdatabas/lakemedel)
- Finland: Fimea, Finnish Statistics on Medicines 2014 (http://www.fimea.fi/web/en/about_us/publications)
- Estonia: State Agency of medicines, Statistical Yearbook of the State Agency of Medicines 2015.
- Denmark: (http://www.medstat.dk/da)

The available national statistics report sold amounts of pharmaceuticals as DDD/1,000 inhabitants/day where DDD (defined daily dose) is based on the ATC/DDD (anatomical therapeutic chemical/defined daily dose) classification system developed by the World Health Organization Collaborating Centre for Drug Statistics Methodology. The reported figures indicate how many persons per 1,000 inhabitants may in theory have received the standard daily dose of a pharmaceutical. From the reported values, the annual consumption of a pharmaceutical can be calculated using the following formula:

$$\text{Consumption}_{(\text{kg/a})} = \frac{\text{DDD (g)} \times \text{DDD/1,000 inh/day} \times \text{Population} \times 365}{1{,}000{,}000}$$

It was beyond the scope of this report to calculate the consumption of all the pharmaceuticals reported in the statistics. Therefore, consumption was calculated only for the most frequently prescribed pharmaceuticals as well as for those that were most often found in the monitoring studies.

Data on the use of pharmaceuticals by therapeutic group are given in Table A2.1 to Table A2.6. If a pharmaceutical was not sold in a country, it is indicated in the tables as "0". If no data were received or calculated for a pharmaceutical, it is indicated in the tables as an empty cell. All the volumes are given in kilograms per year. The most recent available data (for the year 2014) are given. If 2014 data are not available, then data for the previous year are used.

Table A2.1 *Use of anti-inflammatory and analgesics in Baltic Sea countries (2014, kg/year)*

Source: Original data.

Compound	Finland	Estonia	Germany (Mecklenburg-Vorpommern)	Germany (Schleswig-Holstein)	Russia	Sweden
Acetylsalicylic acid			2,110	2,780		
Allopurinol	2,770	700	3,750	4,080		4,160
Buprenorphine	3.4	0.006				3
Codeine	1,800	155				60
Diclofenac	1,050	593		940	700	8,800
Fentanyl	1.2	0.02				2.1
Ibuprofen	119,000	15,100	11,900	20,000		14,400
Irbesartan	0	0	850	880		1,095
Ketoprofen	470	100				1,511
Naproxen	6,200	210				17,690
Paracetamol	173,582	16,950	618	778		338,007
Tramadol	1,756	321				4,833

Table A2.2 *Use of antimicrobial pharmaceuticals in Baltic Sea countries (2014, kg/year)*

Source: Original data.

Compound	Finland	Estonia	Germany (Mecklenburg-Vorpommern)	Germany (Schleswig-Holstein)	Sweden
Amoxicillin	9,300	2,250	570	3,270	2,630
Ampicillin	80	225			5,300
Azithromycin	300	80			95
Cefadroxil	0	245			840
Cefuroxime	615	290	560	775	0
Ciprofloxacin	1,200	370			
Clarithromycin	240	445			110
Clindamycin	16	4			420
Doxycycline	640	75			390
Erythromycin	120	0			125
Fluconazole	140	15			
Metronidazol	1,800	80			
Miconazol		40			
Norfloxacin	95	100			30
Ofloxacin	25	6			
Phenoxymethylpenicillin				970	
Roxithromycin	125				10
Sulfamethoxazole		470			1,700
Sulfasalazine			730	990	
Tetracycline	1,700	25			350
Trimethoprim	850	100			210

Table A2.3 *Use of cardiovascular agents in Baltic Sea countries (2014, kg/year)*

Source: Original data.

Compound	Finland	Estonia	Germany (Mecklenburg-Vorpommern)	Germany (Schleswig-Holstein)	Sweden
Acebutolol	0	0			0
Alfuzosin	75	6			245
Amlodipine	485	80			810
Atenolol	445	35			2,860
Atorvastatin	1,330	135			2,450
Bisoprolol	740	5			310
Cilazapril					
Colestyramine				1,200	
Diltiazem	570	11			680
Dipyridamole				660*	
Enalapril	530	135			1,830
Enalaprilat					
Eprosartan	600	6			105
Felodipine	90	13			470
Furosemide	3,000	95			4,880
Hydrochlorothiazide	330	475	955	1,475	445
Metformin	125,500	18,800	30,300	37,400	135,000
Metoprolol	4,550	1,670	2,120	5,340	13,800
Nebivolol	13	45			0
Propranolol	645	38			890
Ramipril	345	74			245
Rosuvastatin	260	120			190
Simvastatin	3,080	100	1,280	1,430	4,870
Sotalol	200	130			520
Telmisartan	590	400			53
Torasemide	0	77			3.7
Trimetazidine	0	200			0
Valsartan	1,760	215	3,500	3,000	665
Warfarin	235	30			300
Verapamil	370	410			870

*data from 2013 (no data from 2014)

Table A2.4 *Use of central nervous system agents in Baltic Sea countries (2014, kg/year)*

Source: Original data.

Compound	Finland	Estonia	Germany (Mecklenburg-Vorpommern)	Germany (Schleswig-Holstein)	Sweden
Carbamazepine	3,530	1,090	1,350	1,331	5,860
Clonazepam	14	3			6
Fluoxetine	170	29			370
Gabapentin	5,860	575	2,420	2,690	11,000
Levetiracetam	5,600	185	2,780	3,840	6,300
Levodopa			1,060	1,510	
Metamizole		0	11,800	21,850	0
Paroxetine	105	21			205
Piracetam			900		
Pregabalin			710	800	
Quetiapine	720				
Sertraline	690	68			4,160
Tilidine	640				
Valproic acid	11,200	1,050	1,880	2,550	8,600
Zopiclone	275	57			605

Table A2.5 *Use of metabolic agents and gastrointestinal agents in Baltic Sea countries (2014, kg/year)*

Source: Original data.

Compound	Finland	Estonia	Germany (Mecklenburg-Vorpommern)	Germany (Schleswig-Holstein)	Sweden
Bezafibrate	95				335
Drotaverin		215			
Macrogol	154,500	980	22,300	41,500	54,400
Mesalazine	18,000	685	2,530	3,840	17,100
Omeprazole	565	240	3,420		
Pantoprazole			1,440	1,770	
Ranitidine	740	450			830
Sitagliptin	670*				

* data from 2013 (no data from 2014)

Table A2.6 *Use of other pharmaceuticals in Baltic Sea countries (2014, kg/year)*

Source: Original data.

Compound	Finland	Estonia	Germany (Mecklenburg-Vorpommern)	Germany (Schleswig-Holstein)	Russia	Sweden
Hormones and hormone antagonists						
Finasteride	66					120
Levothyroxine sodium	0	1.1				13
Tamoxifen	42	6				105
Respiratory system						
Acetylcysteine			540*	790*		
Terbutaline	6					
Xylomeazoline	6 864 0					
Theophylline			780	780*		
Musculoskeletal system						
Methocarbamol			650*	1,020		

*year 2013 (no data from 2014)

Sales of veterinary pharmaceuticals

Data on the use of veterinary pharmaceuticals were received from Finland and Germany. Data on the use of veterinary pharmaceutical in Estonia are based on reports from wholesalers and presented only as turnovers (Ravimiamet 2015).

Finland provided data on the sales of veterinary pharmaceuticals for years 2001–2013 (Figure A2.1). The total use of veterinary pharmaceuticals varied between 12,600 and 17,000 kg/year. In 2013 it was around 13,600 kg/year. The most used antimicrobial drug was a betalactam antibiotic penicillin G, and its consumption in 2013 was 6,200 kg. Antimicrobials are the main pharmaceuticals used for treatment of animals in Finland. No data were reported on the use of other types of pharmaceuticals.

Similarly to Finland, Germany also reported the sales of antimicrobial veterinary pharmaceuticals (BVL 2014; Agra-Europe 2014). No data were available for pharmaceuticals of other therapeutic groups. Data for the years 2011–2013 are presented in Figure A2.2. As in Finland, tetracycline and penicillin were the most sold veterinary pharmaceuticals in Germany. However, the total sale of veterinary pharmaceuticals in Germany was significantly higher than in Finland. The total sale of veterinary pharmaceuticals in Germany in 2013 was 1,450,000 kg, and there was significant geographical variation in their consumption. The total sale of veterinary pharmaceuticals in those areas that are relevant for the Baltic Sea (i.e. Mecklenburg-Vorpommern and Schleswig-Holstein) was 86,000 kg in 2013.

Figure A2.1 ***Sales of veterinary pharmaceuticals in Finland***

Source: Original data.

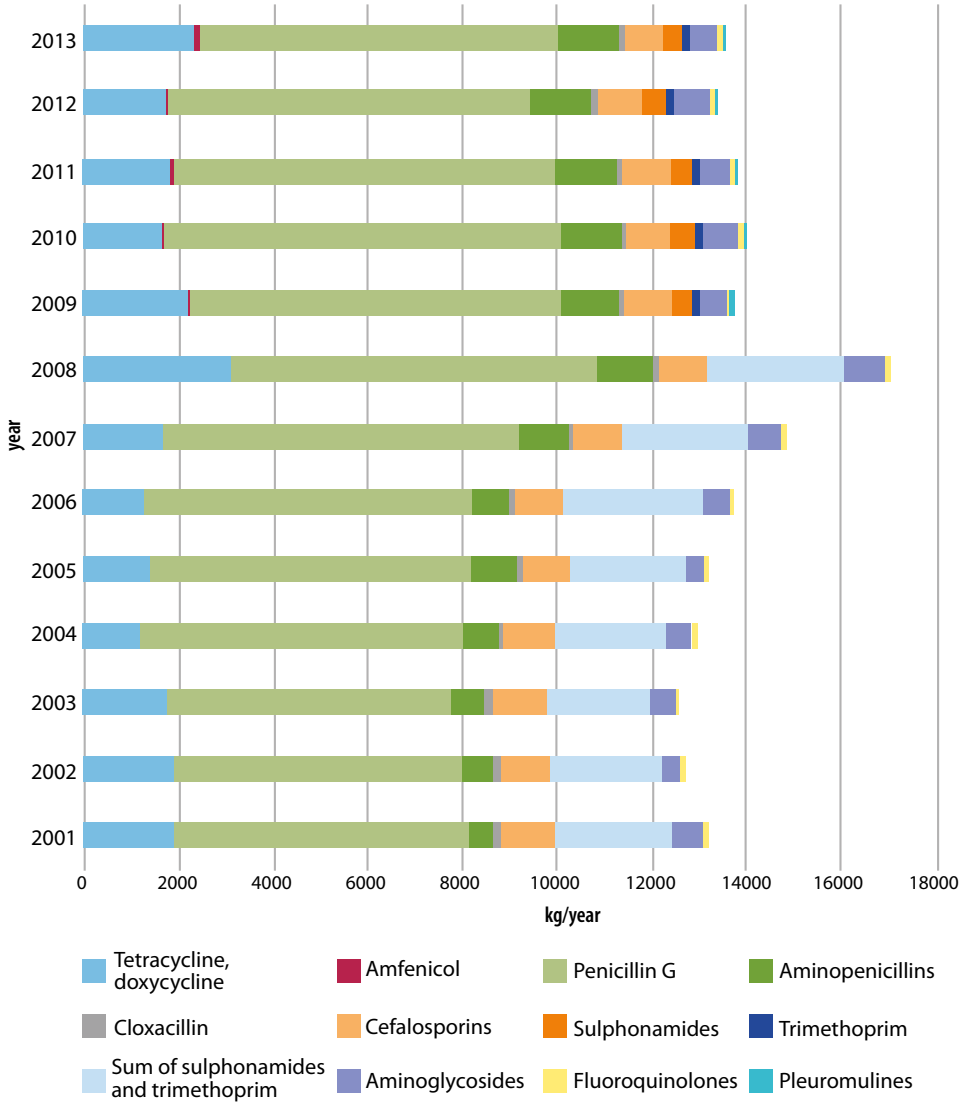
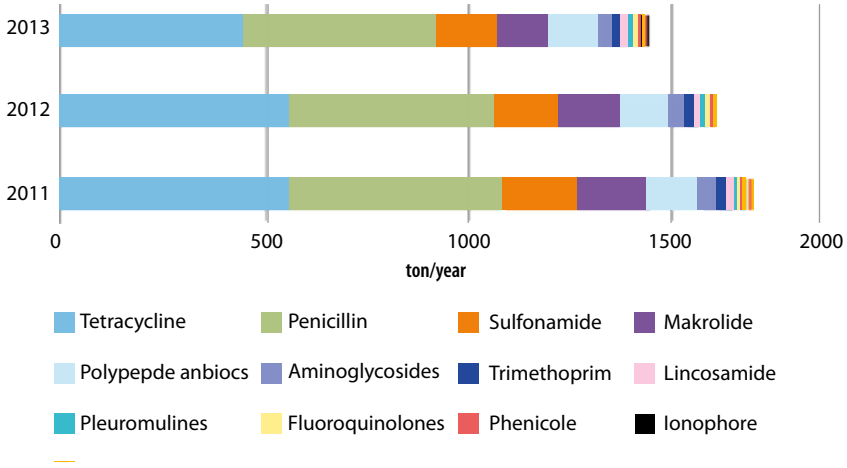


Figure A2.2 ***Sales of veterinary pharmaceuticals in Germany***

Source: Original data.



Annex 3. Data on samples from MWWTPs influent, effluent, sludge and river water by therapeutic groups

Methodology for statistical and visual presentation of data

When pharmaceuticals have been detected in MWWTP influent, effluent, sludge or river water, the average and maximum measured concentrations are presented in figures together with the sensitivity of the analytical methods.

Removal rates are presented in tables. Removal rates were calculated for the pharmaceuticals which were detected both in MWWTP influent and effluent. This rough estimation is based on the average of the concentrations of pharmaceutical substances in influents and effluents. It does not take into account technical parameters of particular wastewater treatment facilities, nor reflects variations of the removal rates between different MWWTP. The numbers of detected pharmaceuticals used in averaging are given in Table A3.1, Table A3.3, Table A3.5, Table A3.7, Table A3.9, Table A3.10 and Table A3.12. Only removal from the aqueous phase is considered. Negative values indicate a higher average concentration of a pharmaceutical substance in effluent than in influent, which might be interpreted as an increase in the concentration during the wastewater treatment. This could be e.g. a result of liberation of the substance during decomposing of other pharmaceuticals in the treatment process. The results are presented by grouping pharmaceuticals according to their therapeutic groups.

Anti-inflammatory and analgesics

An overview of reported data on pharmaceuticals belonging to the therapeutic group anti-inflammatory and analgesics is presented in Table A3.1.

Table A3.1 ***Anti-inflammatory and analgesics detected in MWWTP influents, effluents, sludge and river water in Baltic Sea countries***

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	**Influent**	**Effluent**	**Sludge**	**River**	**Pharmaceutical**	**Influent**	**Effluent**	**Sludge**	**River**
Azelastine	8/2	13/4		1/0	Beclomethasone	17	31		1
Buprenorphine	11/8	16/13		8/2	Budenoside				2
Codeine	60/50	65/37		15/14	Dextropropoxyphene	23	32		
Diclofenac	96/95	387/365	33/20	1,696/690	Norfentanyl	23	32		
Dihydroergotamine	8/1	13/0		2/0	Norpropoxyphene	23	32		
Fentanyl	52/8	66/12		14/0	Orphenadrine				1
Ibuprofen	193/193	397/268	33/9	1,716/127					
2-hydroxyibuprofen	119/119	194/182							
Ibuprofen-COOH	4/4	11/9							
Indometacin		20/4		16/0					
Ketoprofen	99/93	234/194	33/16	50/11					
Naproxen	68/68	203/182	33/17	236/37					
Paracetamol	128/97	201/55	6/6	9/6					
Phenazone		20/17		1,661/204					
Propyphenazone				1,645/4					
Pizotifen	8/7	13/10		0/0					
Salicylic acid	121/86	205/38		20/0					
Tramadol	29/29	34/34	16/10	16/10					
Trihexyphenidyl	8/7	13/13		0/0					

In total 27 pharmaceuticals in this category were monitored, out of which 21 (78%) were detected in MWWTP influent, MWWTP effluent, sludge or river water samples. The average and maximum measured concentrations measured in MWWTP influents and effluents are presented in Figure A3.1 and Figure A3.2, respectively. Removal rates of pharmaceuticals in MWWTPs are presented in Table A3.2.

Sludge monitoring results are presented in Figure A3.3 and Figure A3.4 and river water results in Figure A3.5. For the majority of pharmaceuticals, the reported analytical LOD in MWWTP influent and effluent samples were low enough to detect these substances in wastewater samples. For salicylic acid, the highest reported LOD was higher than the values reported in other studies and thus more frequent detection could be anticipated for this pharmaceutical when more sensitive methods are used.

In MWWTP influents, the highest average (83 mg/l) and maximum (1,300 mg/l) concentrations were measured for paracetamol. Additionally, 2-hydroxyibuprofen (metabolite of ibuprofen), ibuprofen and salicylic acid were detected in influents at average concentrations of >10 mg/l. Similar to the influents, paracetamol was measured at the highest concentration (360 mg/l) in effluents. The highest average concentration (4.4 mg/l) in effluents was measured for the metabolite 2-hydroxyibuprofen. Additionally, ibuprofen and tramadol were detected in effluents at average concentrations of >1 mg/l.

Removal rates of >70% were calculated for eight out of 17 compounds (i.e. buprenorphine, codeine, dihydroergotamine, ibuprofen, ketoprofen, naproxen, paracetamol and salicylic acid). Removal rates of <20% (or even increase in concentrations during the treatment) were observed for seven compounds (i.e. azelastine, diclofenac, fentanyl, 2-hydroxyibuprofen, ibuprofen-COOH, propofol and tramadol). These compounds can be considered as being of concern from an environmental point of view due to low biodegradation potential in conventional MWWTPs. Two of these compounds were metabolites of ibuprofen, which is a very biodegradable pharmaceutical. In the future, the occurrence and fate of not only the parent compounds but also their metabolites should be more thoroughly investigated.

In untreated sludge samples, highest concentrations were reported for ibuprofen and paracetamol. However, in digested sludge diclofenac had the highest average concentration and in composted sludge diclofenac and naproxen had the highest average concentrations. Ibuprofen and paracetamol were not detected in composted sludge samples.

In river water, samples the highest average concentration was measured for tramadol (256 ng/l) and the highest maximum concentration (2,71 ng/l) for diclofenac. Additionally, ibuprofen, diclofenac and phenanzone were detected in river water samples at average concentrations of >50 ng/l.

It should be noted that no data on phenazone were reported from MWWTPs. Due to its presence in river water, this compound might be of interest to monitor in the future.

Figure A3.1 ***The average and maximum concentrations of anti-inflammatory and analgesics in MWWTP influents***

Source: Original data.

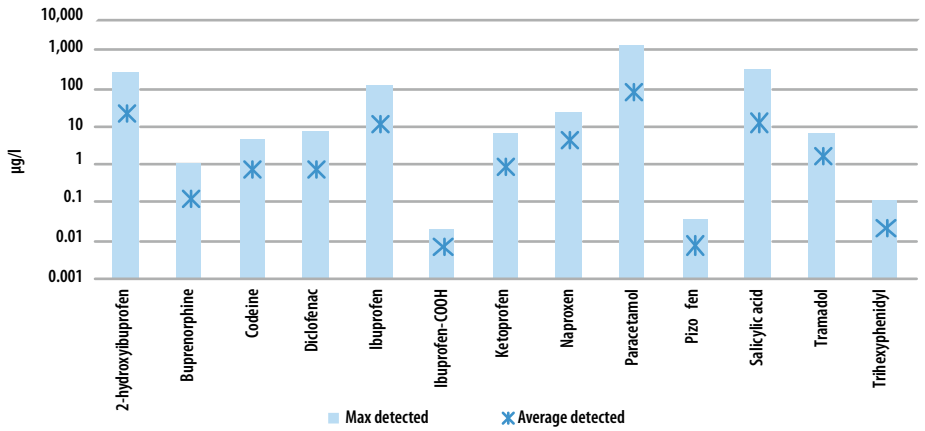


Figure A3.2 *The average and maximum concentrations of anti-inflammatory and analgesics in MWWTP effluent*

Source: Original data.

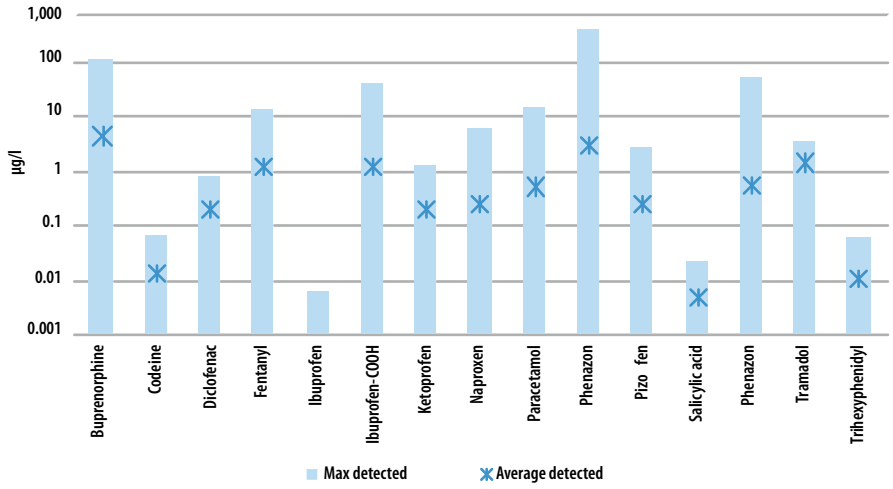


Table A3.2 *Removal rates of anti-inflammatory and analgesics in MWWTPs*

Source: Original data.

Compound	Average removal (%)
Azelastine	14%
Buprenorphine	89%
Codeine	80%
Diclofenac	1%
Dihydroergotamine	>90%*
Fentanyl	-30%
Ibuprofen	86%
2-hydroxyibuprofen	-1,000%**
Ibuprofen-COOH	-2,800%**
Ketoprofen	68%
Naproxen	83%
Paracetamol	97%
Pizotifen	32%
Propofol	4%
Salicylic acid	95%
Tramadol	3%
Trihexyphenidyl	41%

* average effluent concentration <LOD

** forms when ibuprofen biodegrades in the biological treatment process

Figure A3.3 *The average and maximum concentrations of anti-inflammatory and analgesics in untreated sludge*

Source: Original data.

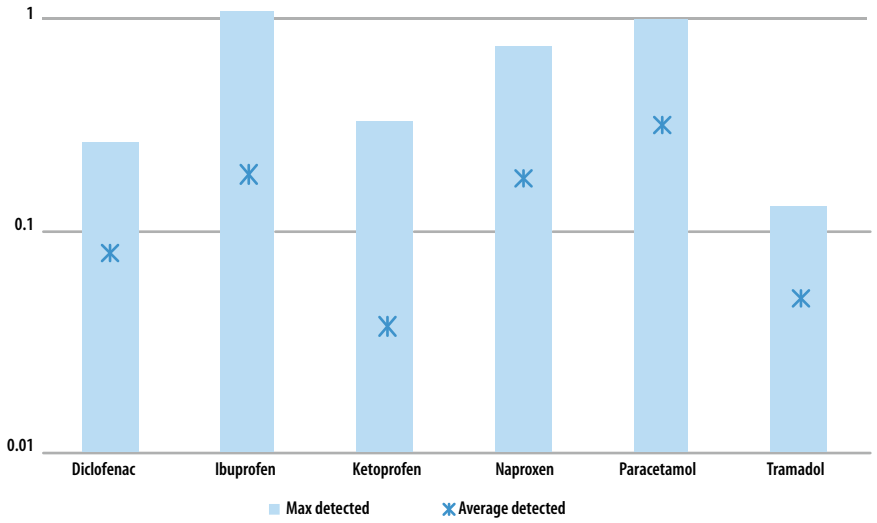


Figure A3.4 *The average concentrations of anti-inflammatory and analgesics in untreated, digested and composted sludge*

Source: Original data.

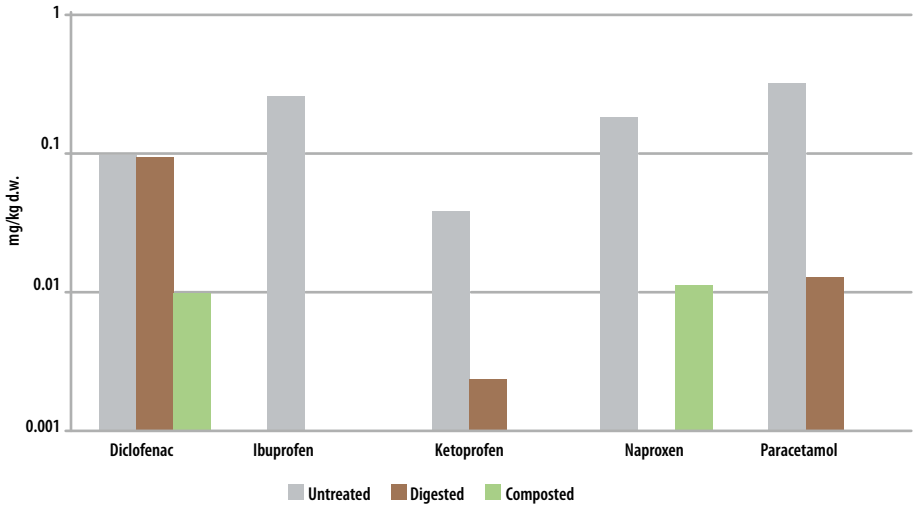
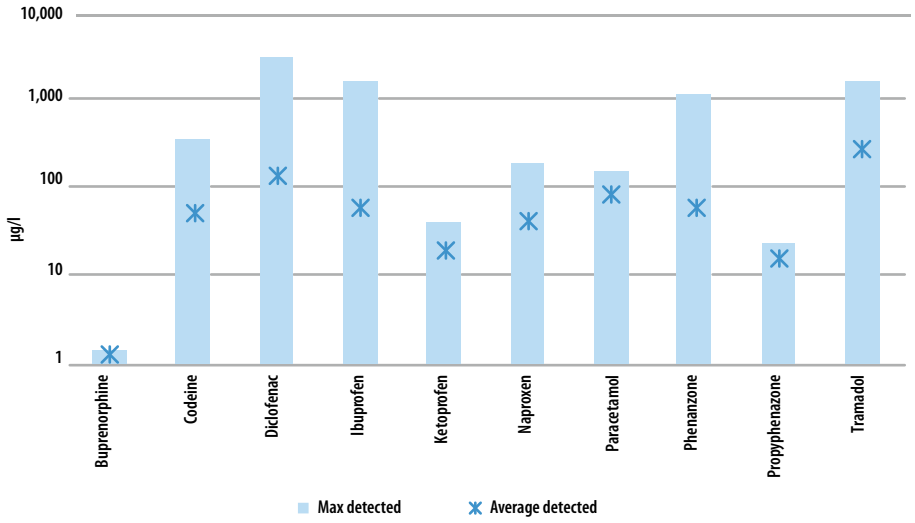


Figure A3.5 *The average and maximum concentrations of anti-inflammatory and analgesics in river water samples*

Source: Original data.



Antimicrobial (antibiotic, antifungal, antiviral, antiparasitic, disinfectant, antiseptic) and antidote

An overview of reported data on pharmaceuticals belonging to the therapeutic group of antimicrobial agents and antidotes is presented in Table A3.3.

Table A3.3 ***Antimicrobial and antidote detected in MWWTP influents, effluents, sludge and rivers in Baltic Sea countries***

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	**Influent**	**Effluent**	**Sludge**	**River**	**Pharmaceutical**	**Influent**	**Effluent**	**Sludge**	**River**
Amoxicillin	61/5	61/0	12/0	8/0	Penicillin V	12	12		
Ampicillin	43/4	43/2	12/0	20/0	Demeclocycline			11	548
Azithromycin	58/52	62/44	16/7	9/5	Chlortetracycline				20
Benzyl penicillin				20/0	Enrofloxacin				20
Cefadroxil	12/6	12/4	12/0		Sulfatroxazole				20
Cefuroxime	12/4	12/0	12/0		Tiamulin				20
Ciprofloxacin	84/79	90/53	74/74	27/11	Tylosin				
Clarithromycin	26/17	31/15	16/8	943/43					
Clindamycin	11/9	16/16		8/3					
Clotrimazol	8/2	13/9							
Dibazol	31/2	31/3							
Doxycycline	12/12	12/7	29/17	528/0					
Erythromycin	69/58	94/59	28/9	231/8					
Fenbendazole			6/6						
Flofenicol				1/1					
Flubendazole			6/5						
Fluconazole	29/29	34/34		15/8					
Ketokonazole	20/8	34/3	6/6	8/0					
Meclozine	8/2	13/6							
Metronidazol	12/6	12/2	6/1						
Miconazole	29/8	34/5		14/0					
Norfloxacin	67/48	91/15	74/47	17/2					
Ofloxacin	36/22	60/28	74/46	19/4					
Oxytetracycline	3/0	3/0	6/6	20/0					
Roxithromycin	29/24	34/22	16/10	16/4					
Sulfadiazine				947/17					
Sulfadimidine				947/7					
Sulfamethiazol	115/102	183/173		20/0					
Sulfamethoxazole	118/57	313/192	6/1	1,696/345					
Tetracycline	34/7	34/3	17/12	556/6					
Trimethoprim	161/109	244/139	18/5	208/12					

In total 38 pharmaceuticals in this category were monitored, out of which 31 (82%) were detected in MWWTP influent, MWWTP effluent, sludge or river water samples. The average and maximum concentrations measured in MWWTP influents and effluents are presented in Figure A3.6 and Figure A3.7, respectively. Removal rates of pharmaceuticals in MWWTPs are presented in Table A3.4. Sludge monitoring results are presented in Figure A3.8 and Figure A3.9 and river water results in Figure A3.10. For the majority of pharmaceuticals, the reported analytical LOD in MWWTP influent and effluent samples were low enough to detect these pharmaceuticals in wastewater samples. In the influents, the highest reported LOD was higher than the values reported in other studies for tetracycline and in effluents, for erythromycin, ketoconazole, norfloxacin and sulfamethoxazole. Thus, more frequent detection could be anticipated for these pharmaceuticals when more sensitive methods are used.

In MWWTP influents, the highest average concentration (1.85 mg/l) was measured for sulfamethiazol and the highest maximum concentration (29 mg/l) for sulfamethoxazole. Additionally, clarithromycin was detected in influents at average concentrations of >1 mg/l. Similar to the influents, sulfamethiazol was measured at the highest average concentration of 1 mg/l in effluents. The highest concentration (15 mg/l) was also measured for sulfamethiazol in effluents. Additionally, azithromycin, clarithromycin, doxycycline, erythromycin, fluconazole, metronizadole, norfloxacin, ofloxacin, roxithromycin and trimethoprim were detected in effluents at average concentrations of >0.1 mg/l.

Removal rates of >70% were observed for 12 out of 23 compounds. Increases in concentrations during the treatment were noted for three compounds (clindamycin, fluconazole and meclozine). These compounds can be considered as being of concern from the environmental point of view due to low removal potential in existing MWWTPs. For many antibiotics, adsorption to sludge seems to be an important fate in MWWTPs. Thus, the concentrations in sludge samples were relatively high. In untreated sludge samples, five out of 10 compounds were detected at concentrations higher than 1 mg/kg d.w. The highest average concentration of 3.3 mg/kg d.w. was also reported for ciprofloxacin. The highest observed concentration of 8.8 mg/kg d.w. was reported for ciprofloxacin. Many antibiotics were present at similar concentrations in untreated and digested sludge. Only trimethoprim was not detected in digested sludge samples. In composted sludge samples, the concentrations were lower but still detectable for all other compounds except flubendazole, oxytetracycline and trimethoprim. In the future, the fate of antimicrobials and antidotes should be more thoroughly studied, especially in sludge treatment and land application of sludge.

In river water samples, the highest average concentration (147 ng/l) was measured for roxithromycin and the highest maximum concentration (19,000 ng/l) for sulfadiazine. Ad-ditionally, erythromycin, fluconazole, sulfadimidine, sulfamethoxazole and trimethoprim were detected in river water samples at average concentrations of >50 ng/l.

Figure A3.6 *The average and maximum concentrations of antimicrobial and antidote in MWWTP influents*

Source: Original data.

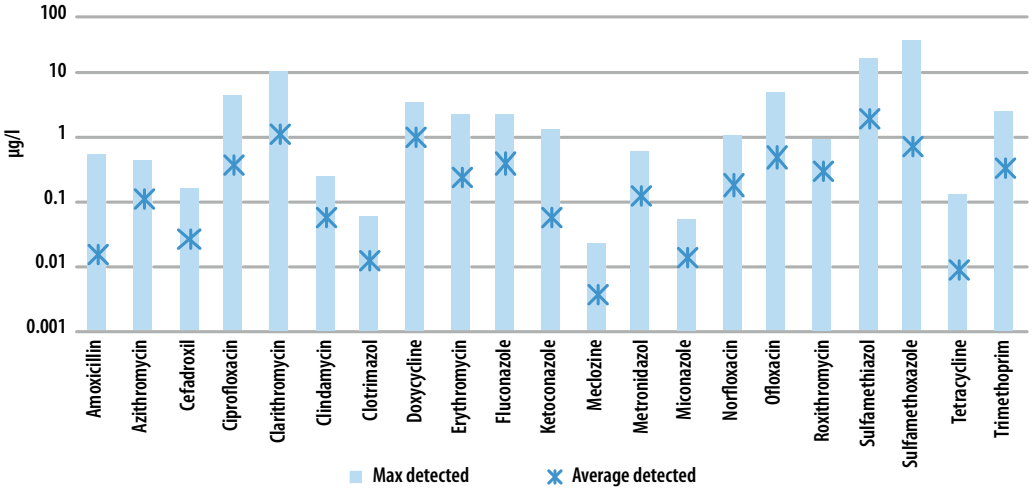


Figure A3.7 *The average and maximum concentrations of antimicrobial and antidote in MWWTP effluents*

Source: Original data.

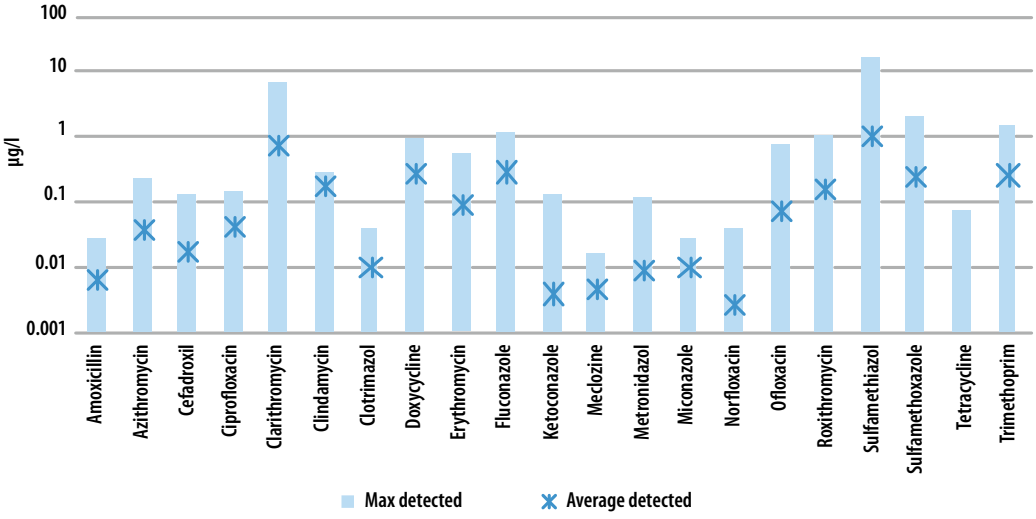


Table A3.4 *Removal rates of antimicrobial and antidote in MWWTPs*

Source: Original data.

Compound	Average removal (%)
Amoxicillin	>90%*
Ampicillin	62%
Azithromycin	73%
Cefadroxil	31%
Cefuroxime	>90%*
Ciprofloxacin	89%
Clarithromycin	34%
Clindamycin	-470%
Clotrimazol	19%
Doxycycline	74%
Erythromycin	91%
Fluconazole	-39%
Ketokonazole	93%
Meclozine	-24%
Metronidazol	93%
Miconazole	43%
Norfloxacin	99%
Ofloxacin	87%
Roxithromycin	47%
Sulfamethiazol	46%
Sulfamethoxazole	79%
Tetracycline	>90%*
Trimethoprim	45%

* average effluent concentration <LOD

Figure A3.8 *The average and maximum concentrations of antimicrobial and antidote in untreated sludge*

Source: Original data.

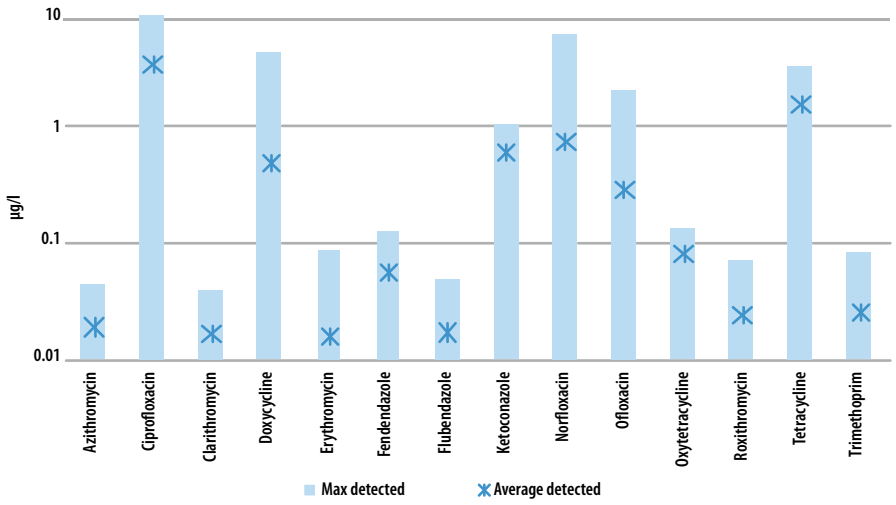


Figure A3.9 *The average concentrations of antimicrobial and antidote in untreated, digested and composted sludge*

Source: Original data.

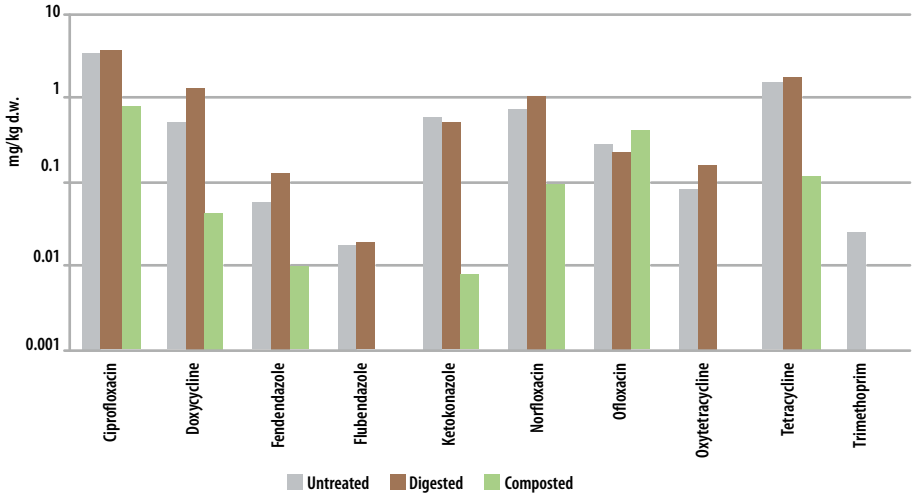
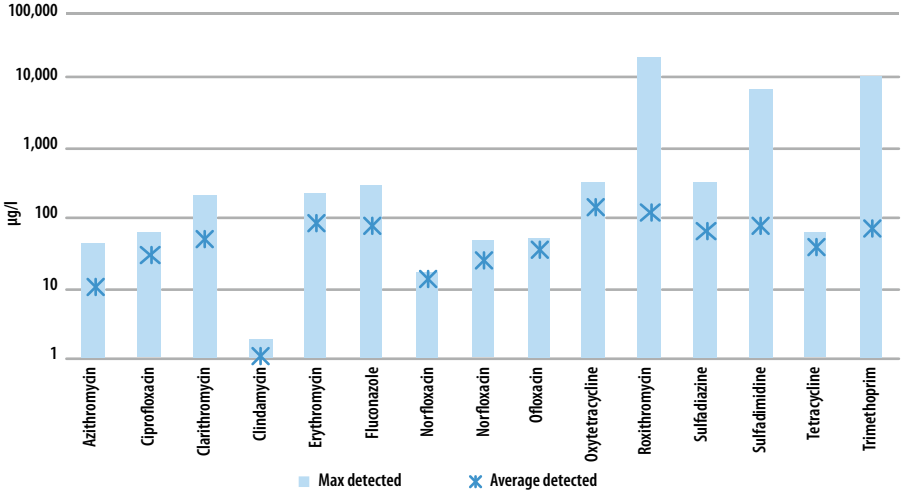


Figure A3.10 *The average and maximum concentrations of antimicrobial and antidote in river water samples*

Source: Original data.



Cardiovascular agents (blood pressure, diuretics, anticoagulants, antihistamine)

An overview of reported data on pharmaceuticals belonging to the therapeutic group of cardiovascular agents is presented in Table A3.5.

Table A3.5 ***Cardiovascular agents detected in MWWTP influents, effluents, sludge and river water in Baltic Sea countries***

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	**Influent**	**Effluent**	**Sludge**	**River**	**Pharmaceutical**	**Influent**	**Effluent**	**Sludge**	**River**
Acebutelol	21/21	21/21		11/10	Amiodarone	8	13		
Amiloride	18/18	18/3		8/0	Amlodipine			11	20
Alfuzosin	11/8	16/13		8/0	Bendroflumethiazid				20
Atenolol	50/47	74/68	6/2	1,690/112	Felodipine Primidone	17	31		
Benzafibrat		19/13		12/0	Sulfatroxazole				12
Bisoprolol	26/8	50/32	22/5	1,675/552					
Cilazapril	11/7	16/6		8/0					
Clemastine	8/2	13/6		2/0					
Cyproheptadine	8/2	13/6							
Desloratidin	8/8	13/13		2/0					
Diltiazem	11/8	16/13		8/0					
Diphenhydramine	8/8	13/13		2/0					
Dipyridamole	8/8	13/0		2/0					
Enalapril	31/30	31/10	6/5	20/0					
Enalaprilat	31/27	31/20							
Eprosartan	11/11	16/15		8/4					
Fexofenadine	8/8	13/13		2/2					
Flecainide	8/8	13/13							
Furosemide	115/113	183/181	6/6	3/3					
Gemfibrozil		20/1		203/0					
Hydrochlorthiazide			6/6	2/2					
Irbesartan	8/8	13/13		8/2					
Losartan		18/18		12/3					
Metoprolol	50/50	228/228	22/22	1,687/962					
Promethazine	8/6	13/5							
Propranolol	18/15	38/32	22/22	1,664/96					
Simvastatatin			6/1						
Sotalol	24/24	44/41	6/2	1,680/477					
Telmisartan	11/8	16/12		7/4					
Verapamil	11/10	16/11		8/0					
Warfarin			6/15	208/12					

Of all the monitored pharmaceuticals in this category, 31 out of 36 (86%) were detected in MWWTP influent, MWWTP effluent, sludge or river water samples. The average and maximum concentrations measured in MWWTP influents and effluents are presented in Figure A3.11 and Figure A3.12, respectively. Removal rates of pharmaceuticals in MWWTPs are presented in Table A3.6. Sludge monitoring results are presented in Figure A3.13 and Figure A3.14 and river water results in Figure A3.15. For all

the pharmaceuticals, the reported analytical LOD in influent and effluent samples were low enough to detect these pharmaceuticals in wastewater samples.

In MWWTP influents, the highest average and maximum concentrations (52 mg/l and 1,800 mg/l, respectively) were measured for furosemide. Additionally, telmisartan was detected in influents at average concentrations of >10 mg/l and dipyridamole, metoprolol and sotalol at >1 mg/l. Similar to the influents, furosemide was measured at the highest average and maximum concentrations of 22mg/l and 110 mg/l, respectively, in effluents. Additionally, metoprolol, sotalol and telmisartan were detected in effluents at an average concentration of >1 mg/l and acebutolol, atenolol, benzafibrat, bisoprolol, eprosartan, fexofenadine, flecainide, irbesartan and losartan at concentrations of >0.1 mg/l.

Removal rates of >70% were calculated for only three out of 23 compounds. For two compounds (alfuzosin and atenolol) the removal rates were <20% and for one compound (clemastine) an increase in concentrations during the treatment was observed. Generally, due to relatively poor removal in MWWTPs, many compounds in this therapeutic group can be considered relevant from the point of view of the aquatic environment.

Concentrations in sludge samples were available for only six substances. Out of these six compounds, the highest maximum concentration (0.315 mg/kg d.w.) was reported for metoprolol. The highest average concentration (0.11 mg/kg d.w.) was reported for furosemide. Felodipine was not detected in digested sludge. Furosemide and propranolol were detected in the composted sludge samples at the highest concentrations.

In river water samples, the highest average concentration (670 ng/l) was measured for hydrochlorotiazide and the highest maximum concentration (3,810 ng/l) for bisoprolol. The maximum concentration of metoprolol and sotalol exceeded 1,000 ng/l and furosemide and telmisartan were detected in rivers at average concentrations of >100 ng/l.

Figure A3.11 ***The average and maximum concentrations of cardiovascular agents in MWWTP influents***

Source: Original data.

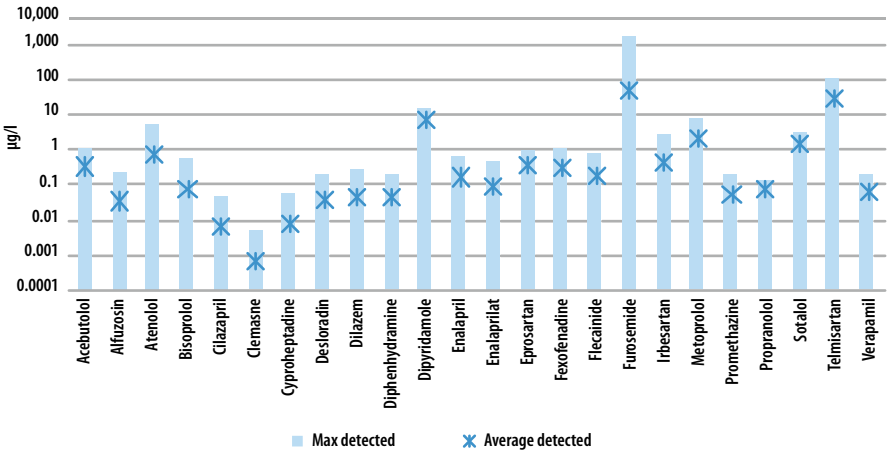


Figure A3.12 *The average and maximum concentrations of cardiovascular agents in MWWTP effluents*

Source: Original data.

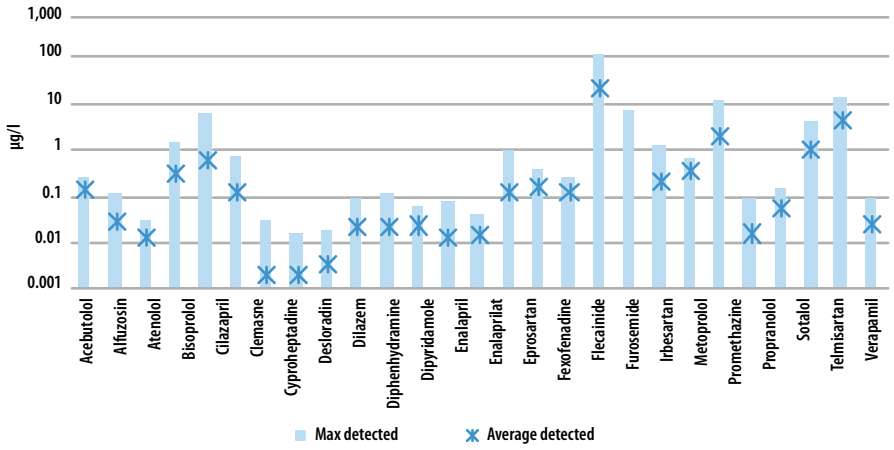


Table A3.6 *Removal rates of cardiovascular agents in MWWTPs*

Source: Original data.

Compound	Average removal (%)
Acebutolol	59%
Alfuzosin	18%
Atenolol	29%
Bisoprolol	51%
Cilazapril	66%
Clemastine	-214%
Cyproheptadine	50%
Desloratidin	38%
Diltiazem	50%
Diphenhydramine	46%
Dipyridamole	>90%
Enalapril	92%
Enalaprilat	85%
Eprosartan	65%
Fexofenadine	49%
Flecainide	32%
Furosemide	57%
Irbesartan	49%
Losartan	82%
Metoprolol	26%
Promethazine	68%
Propofol	54%
Propranolol	8%
Sotalol	36%
Telmisartan	80%
Verapamil	62%

Figure A3.13 *The average and maximum concentrations of cardiovascular agents in untreated sludge*

Source: Original data.

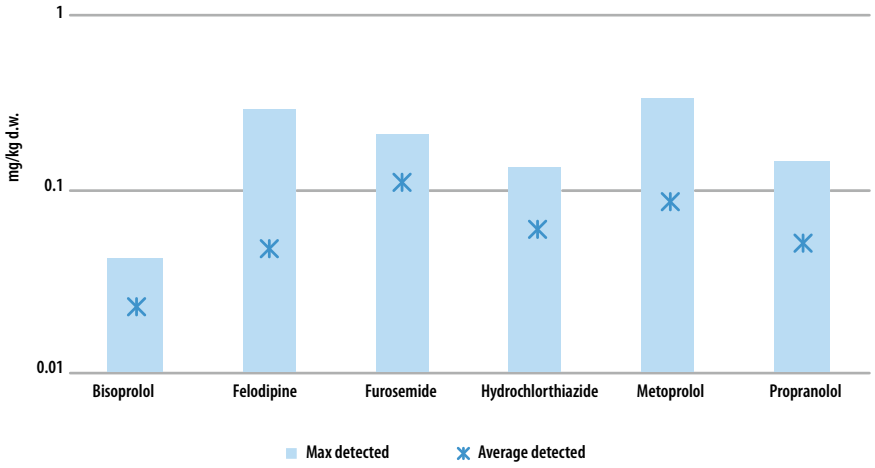


Figure A3.14 *The average concentrations of cardiovascular agents in untreated, digested and composted sludge*

Source: Original data.

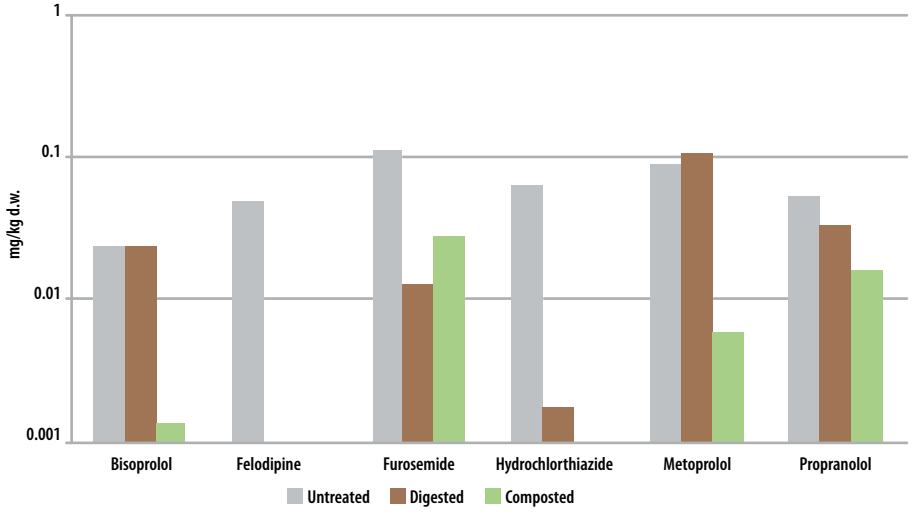
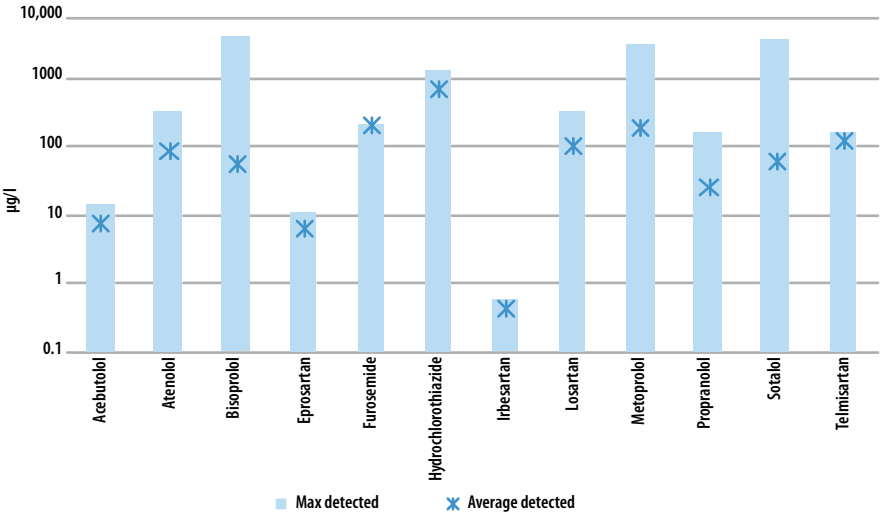


Figure A3.15 ***The average and maximum concentrations of cardiovascular agents in river water samples***

Source: Original data.



Central nervous system agents (psychotherapeutic, antiepileptic, antiparkinson, muscle relaxant)

An overview of reported data on pharmaceuticals belonging to the therapeutic group of central nervous system agents is presented in Table A3.7.

In total 46 pharmaceuticals in this category were monitored, out of which 40 (87%) were detected in MWWTP influent, MWWTP effluent, sludge or river water samples. The average and maximum concentrations measured in MWWTP influents and effluents are presented in Figure A3.16 and Figure A3.17, respectively. Removal rates of pharmaceuticals in MWWTPs are presented in Table A3.8. Sludge monitoring results are presented in Figure A3.18 and Figure A3.19 and river water monitoring results in Figure A3.20.

In MWWTP influents, the highest average and maximum concentrations (62 and 150 mg/l, respectively) were measured for caffeine. Additionally, citalopram was detected in influents at average concentrations of >1 mg/l and carbamazepine, mirtazapine, oxazepam, propofol and venlafaxine at >0.1 mg/l. Similar to the influents, caffeine was measured at the highest average and maximum concentrations of 12 and 150 mg/l, respectively, in effluents. Additionally, carbamazepine and gabapentin were detected in effluents at average concentrations of >1 mg/l and citalopram, mirtazapine, oxazepam, primidone and venlafaxine at >0.1 mg/l.

Removal rates of >70% were calculated for only nine out of 35 compounds. For 11 compounds the removal rates were <20% or the concentrations were noted to increase during the treatment. Generally, due to relatively poor removal in MWWTPs, many compounds in this therapeutic group can be considered relevant from the point of view of the aquatic environment.

Data on concentrations in sludge were submitted for only six compounds. Out of these six, the highest average and maximum concentrations (1.46 and 7 mg/kg d.w., respectively) were reported for caffeine. All the six compounds were also detected in digested sludge samples and all, except entacapone, also in composted sludge samples.

Twenty central nervous systems agents were measured in river water, out of which eight were detected. The highest average and maximum concentrations (138 and 2,950 ng/l) were measured for carbamazepine. The average and maximum concentrations of other pharmaceuticals were <100 ng/l. More environmental monitoring data should be gathered for the pharmaceuticals that are present in the highest concentrations and are poorly removed in the MWWTP, such as oxazepam and mirtazapine.

Table A3.7 *Central nervous systems agents detected in MWWTP influents, effluents, sludge and river water in Baltic Sea countries*

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	Influent	Effluent	Sludge	River	Pharmaceutical	Influent	Effluent	Sludge	River
7-aminofluni-trazepam	22/1	32/1			Clozapine	23	32		
Alprazolam	8/7	13/6		2/0	Diazepam	23	32	11	187
Amitryptiline	8/6	13/6			Levopromazine	8	13		1
Atracurium	8/8	13/13			N-demethyl-flunitrazepam	23	32		
Biperiden	8/5	13/13		2/0	Thioridazine	23	32		12
Bromocriptine	31/3	45/1		2/0	Zopiclone	23	32		
Bupropion	8/8	13/13							
Caffeine	23/21	32/26	6/6						
Carbamazepine	107/103	277/248	22/22	1,674/1,321					
Chlorpromazine	8/4	13/1		2/0					
Citalopram	49/36	63/62	22/22	10/8					
Clomipramine	8/8	13/13							
Clonazepam	11/0	16/1		7/0					
Donepezil	8/8	13/12		2/0					
Duloxetine	8/3	13/7		2/0					
Entacapone			6/1						
Flunitrazepam	31/1	45/0							
Fluoxetine	34/9	48/20	6/6	6/0					
Flupentixol	8/2	13/10							
Fluphenazine	8/2	13/2							
Gabapentin		15/15		12/6					
Haloperidol	8/8	13/13							
Hydroxyzine	8/8	13/13							
Maprotiline	8/5	13/6							
Memantine	8/8	13/13							
Mianserin	8/8	13/13		2/0					
Mirtazapin	8/8	13/13							
Nefazodone	8/6	13/11							
Nordiazepam	23/3	32/12							
Orphenadrine	8/8	13/13							
Oxazepam	31/29	45/45		189/3					
Paroxetine	31/10	45/14	6/6	2/1					
Perphenazine	8/1	13/3							
Primidone		15/15							
Propofol	51/36	66/50		16/12					
Risperidone	31/12	45/16		2/0					
Sertraline	43/14	66/17		8/0					
Temazepam				187/2					
Venlafaxine	8/8	13/13		2/2					
Zolpidem	31/11	45/19		2/0					
Zopiclone	23/1	32/1							
N-oxide									
Zuclopenthixol				2/0					

Figure A3.16 *The average and maximum concentrations of central nervous system agents in MWWTP influents*

Source: Original data.

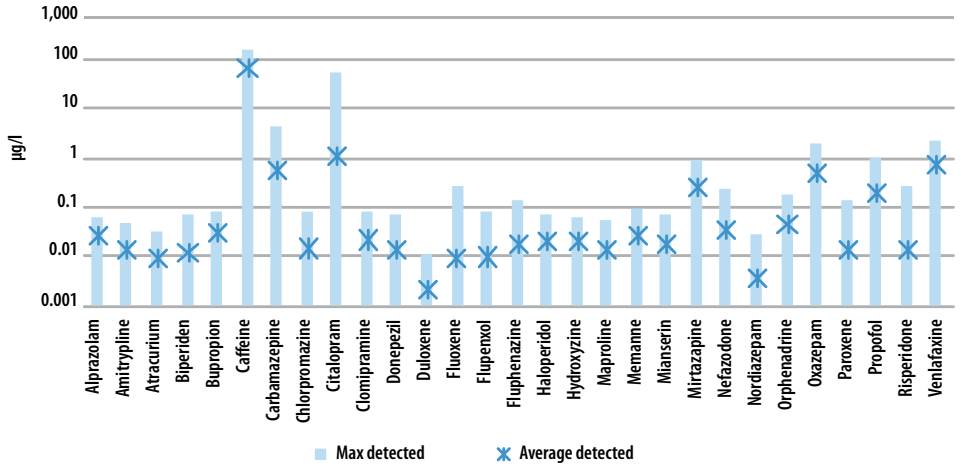


Figure A3.17 *The average and maximum concentrations of central nervous system agents in MWWTP effluents*

Source: Original data.

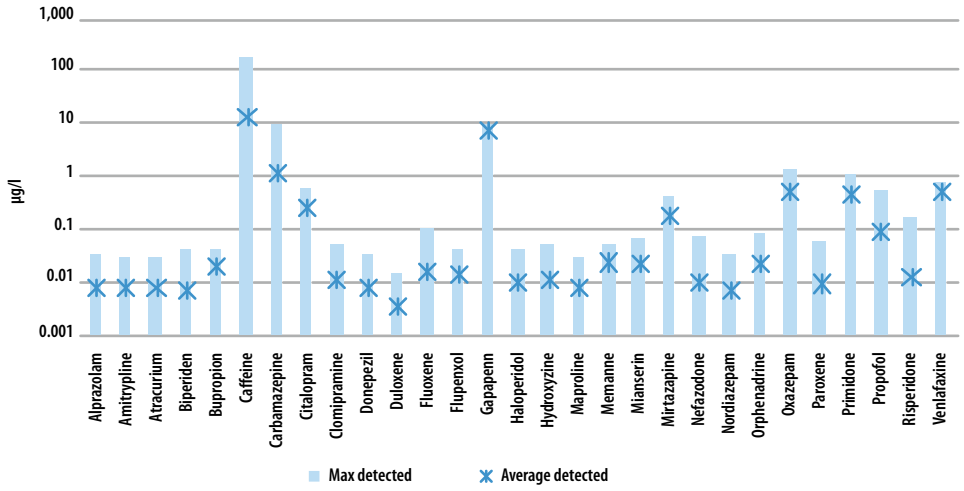


Table A3.8 ***Removal rates of central nervous system agents in MWWTPs***

Source: Original data.

Compound	Average removal (%)
7-aminoflunitrazepam	77%
Alprazolam	68%
Amitryptiline	44%
Atracurium	15%
Biperiden	40%
Bromocriptine	93%
Bupropion	37%
Caffeine	81%
Carbamazepine	-86%
Chlorpromazine	81%
Citalopram	78%
Clomipramine	50%
Donepezil	43%
Duloxetine	-72%
Flunitrazepam	>90%*
Fluoxetine	-77%
Flupentixol	-39%
Fluphenazine	89%
Haloperidol	53%
Hydroxyzine	45%
Maprotiline	44%
Memantine	14%
Mianserin	-17%
Mirtazapine	31%
Nefazodone	70%
Nordiazepam	-111%
Orphenadrine	50%
Oxazepam	-9%
Paroxetine	35%
Perphenazine	71%
Propofol	51%
Risperidone	7%
Sertraline	67%
Venlafaxine	34%
Zolpidem	10%
Zopiclone N-oxide	72%

* average effluent concentration <LOD

Figure A3.18 *The average and maximum concentrations of central nervous systems agents in untreated sludge*

Source: Original data.

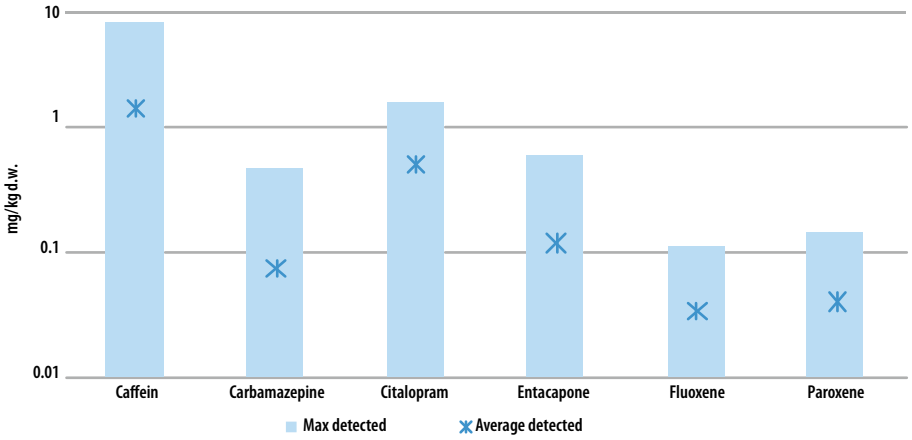


Figure A3.19 *The average concentrations of central nervous system agents in untreated, digested and composted sludge*

Source: Original data.

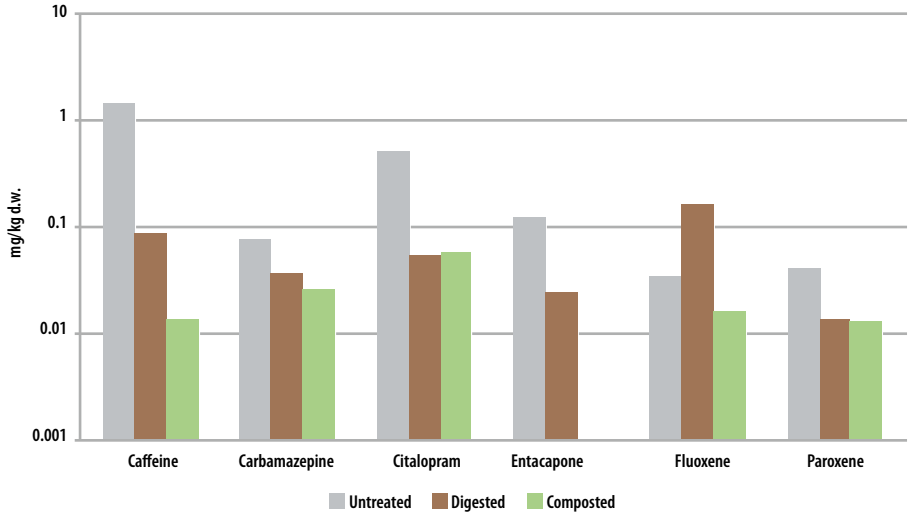
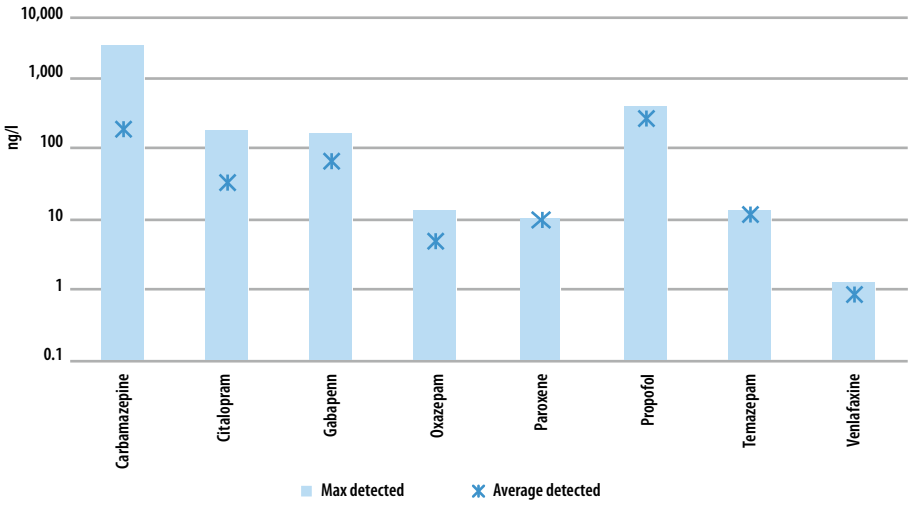


Figure A3.20 *The average and maximum concentrations of central nervous system agents in river water samples*

Source: Original data.



Chemotherapeutic agents and X-ray contrast media

An overview of reported data on pharmaceuticals belonging to the therapeutic group of chemotherapeutic agents and X-ray contrast media is presented in Table A3.9.

Table A3.9 *Chemotherapeutic agents and X-ray contrast media detected in MWWTP influents, effluents, sludge and river water in Baltic Sea countries*

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	Influent	Effluent	Sludge	River	Pharmaceutical	Influent	Effluent	Sludge	River
Amidotrizoic				1,645/806	Cyclofosfamide			6	
Capecitabin	18/15	18/0	16/1	8/0	Ifosfamide			6	
Iohexol				4/0	Methotrexate			6	
Iomeprol		5/5		4/0					
Iopamidol		5/5	6/0	1,649/350					
Iopromide		5/5	6/0	4/0					
X-ray contrast media		308/249							

Data on X-ray contrast media were submitted only by Germany. In influent samples, only the chemotherapeutic agent capecitabin was analyzed and detected at average and maximum concentrations of 0.05 and 0.11 mg/l. The average removal rate for capecitabin was 49%. In MWWTP effluent samples, concentrations of X-ray contrast media compounds were partly reported as concentrations of individual compounds or as a total concentration of a therapeutic group. In the MWWTP effluents, X-ray contrast media compounds were detected at the average concentration of 7.4 mg/l and at the highest concentration of 78 mg/l.

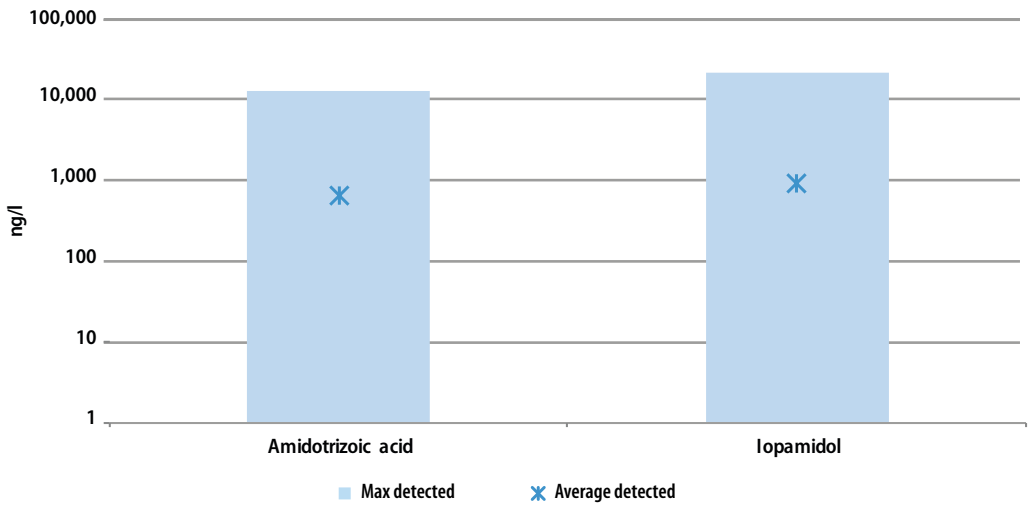
Mean concentrations of iohexol, iomeprol, iopamidol and iopromide were reported as 2.31, 1.54, 3.44 and 0.09 mg/l, respectively.

Nearly all data on concentrations in sludge for X-ray contrast media or chemotherapeutic agents were under the detection limits. Only capecitabin was detected in sludge at a maximum concentration of 0.012 mg/kg d.w. In the river water samples submitted by Germany, the X-ray contrast media agents amidotrizoic acid, iomeprol and iopamidol were detected at average concentrations of 630, 36 and 920 ng/l, respectively (Figure A3.21).

Figure A3.21 ***The average and maximum concentrations of X-ray contrast media agents in river water samples***

For iomeprol, only the mean concentration was reported.

Source: Original data.



Hormones and hormone antagonists

An overview of reported data on pharmaceuticals belonging to the therapeutic group of hormones and hormone antagonists is presented in Table A3.10.

Table A3.10 ***Hormones and hormone antagonists detected in MWWTP influents, effluents, sludge and river water in Baltic Sea countries***

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	**Influent**	**Effluent**	**Sludge**	**River**	**Pharmaceutical**	**Influent**	**Effluent**	**Sludge**	**River**
17a-ethinylestradiol	160/4	273/5	11/1	612/1	Medroxyprogesterone		13		1
17b-estradiol	157/89	270/34	11/0	405/1	Hydrocortisone			6	
Estriol	26/4	64/10	11/1	1/1					
Estrone	148/133	210/127		3/1					
Etonogestrel	11/0	16/11		6/0					
Finasterinde	11/4	16/5		7/0					
Flutamide	11/4	16/2		7/0					
Levonorgestrel	20/0	53/19		8/2					
Megestrol		13/12		1/0					
Mestranol				201/0					
Methylprednisolone			6/1						
Norethindrone	22/15	58/17	2/11						
Norethisteron	18/3	18/0		8/0					
Progesterone	23/18	77/66	7/9	7/0					
Tamoxifen	29/3	34/9	6/0	8/0					
Testosterone			3/6	208/12					

Eighteen pharmaceuticals in this category were monitored, out of which 16 (89%) were detected in MWWTP influent, MWWTP effluent, sludge or river water samples. The average and maximum concentrations measured in MWWTP influents and effluents are presented in Figure A3.22 and Figure A3.23, respectively. Removal rates of pharmaceuticals in MWWTPs are presented in Table A3.11. Sludge monitoring results are presented in Figure A3.24 and Figure A3.25 and river water results in Figure A3.26. For 17a-ethinylestradiol, 17b-estradiol and estrone, the highest reported LOD were higher than the values reported in other studies and thus more frequent detection could be anticipated for these pharmaceuticals if more sensitive methods were used.

In MWWTP influents, the highest average concentration (0.06 mg/l) was measured for estrone. The highest maximum concentration (1.3 mg/l) was measured for 17b-estradiol.

Additionally, the highest maximum concentration of estrone exceeded 1 mg/l. In the effluents, estrone and etonogestrel were measured at the highest concentration (0.61 mg/l). The highest average concentration of 0.08 mg/l was measured for etonogestrel.

The maximum concentrations of levonogestrel, progesterone and tamoxifen also exceeded 0.1 mg/l.

Removal rates of >70% were estimated for three out of nine compounds. The concentration of progesterone was noted to increase during the treatment. It should be taken into account that 17b-estradiol can break down to estriol in aerobic conditions and thus removal rates of estriol may not be correctly estimated.

Similarly to MWWTP influent and effluent samples, the LOD values in sludge samples were often so high that the concentrations of hormones and hormone antagonists were below these values.

The highest concentrations in sludge samples were measured for progesterone (0.83 mg/kg d.w.), 17a-ethinylestradiol (0.69 mg/kg d.w.) and norethindrone (0.57 mg/ kg d.w.). It should be noted that for all substances of this group, except progesterone and testosterone in sludge, only a single reported concentration exceeded LOD. Generally, all hormones and hormone antagonists except progesterone and testosterone were sporadically detected in sludge samples. Estrone and progesterone were detected also in digested and composted sludge samples.

In river water, hormones and hormone antagonists were only detected sporadically. This is most probably due to higher detection limits than the occurrence of the compounds in the environmental waters. Estrone was measured at the highest concentration of 20 ng/l.

Figure A3.22 ***The average and maximum concentrations of hormones and hormone antagonists in MWWTP influents***

Source: Original data.

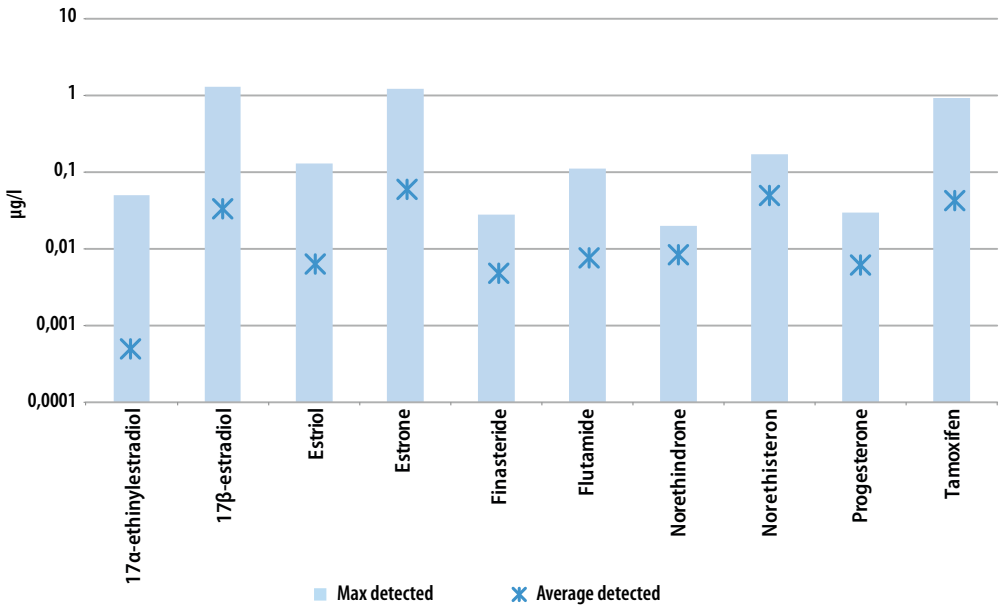


Figure A3.23 *The average and maximum concentrations of hormones and hormone antagonists in MWWTP effluents*

Source: Original data.

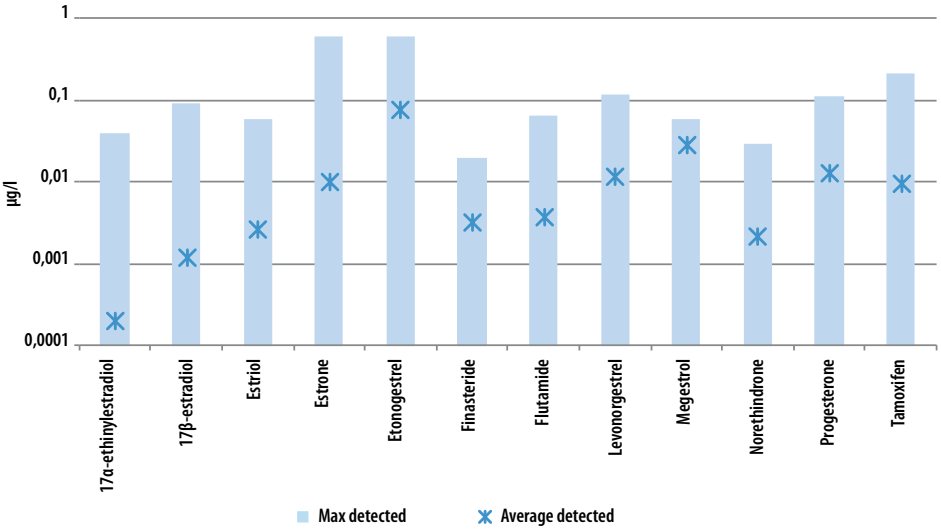


Table A3.11 *Removal rates of hormones and hormone antagonists in MWWTPs*

Source: Original data.

Compound	Average removal (%)
17α-ethinylestradiol	59%
17β-estradiol	62%
Estriol	58%
Estrone	88%
Finasteride	33%
Flutamide	51%
Norethindrone	73%
Progesterone	-60%
Tamoxifen	65%

Figure A3.24 ***The average and maximum concentrations of hormones and hormone antagonists in untreated sludge***

For estriol, ethinylestradiol, hydrocortisone, methylprednisolone and norethindrone, only one reported concentration exceeded LOD and thus only the maximum value is displayed.

Source: Original data.

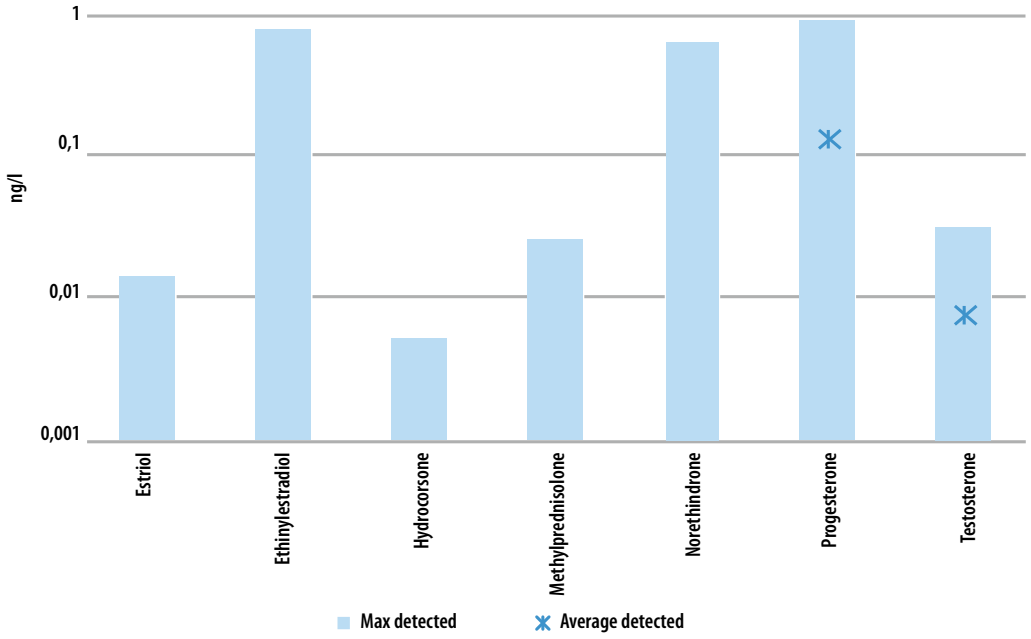


Figure A3.25 ***The average concentrations of hormones and hormone antagonists in untreated, digested and composted sludge***

Source: Original data.

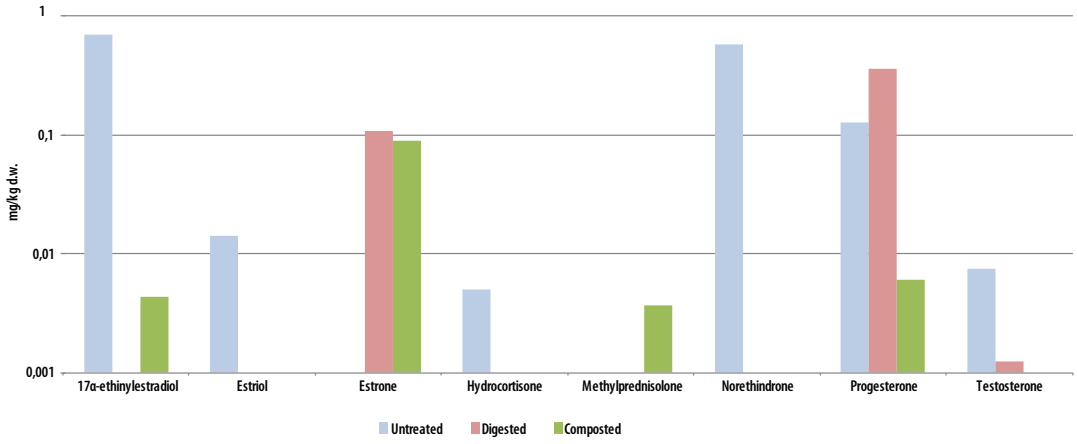
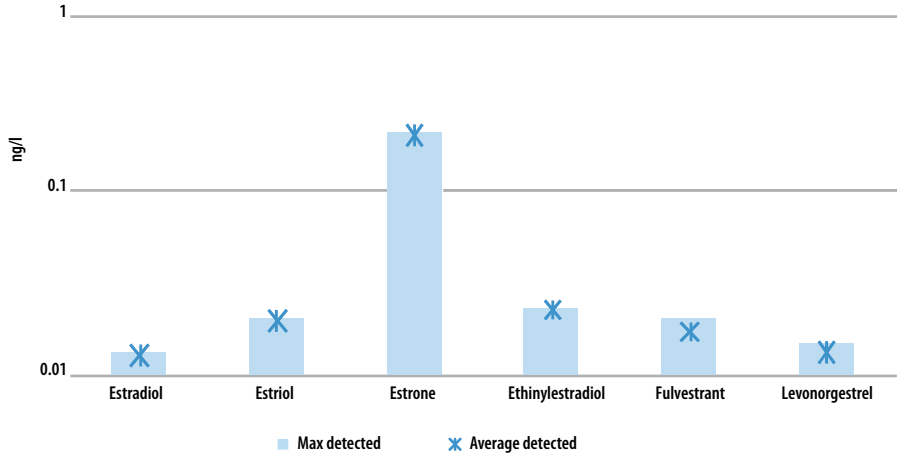


Figure A3.26 ***The maximum concentrations of hormones and hormone antagonists in river water samples***

Source: Original data.



Metabolic agents and gastrointestinal agents

An overview of data reported on pharmaceuticals belonging to the therapeutic group of metabolic agents and gastrointestinal agents is presented in Table A3.12.

Table A3.12 ***Metabolic agents and gastrointestinal agents detected in MWWTP influents, effluents, sludge and river water in Baltic Sea countries***

Source: Original data.

Sampled/detected					Not detected, number of samples				
Pharmaceutical	Influent	Effluent	Sludge	River	Pharmaceutical	Influent	Effluent	Sludge	River
Atorvastatin	8/3	13/2							
Bezafibrate	44/14	44/13	6/0	135/1,661					
Cimetidin	115/30	183/58							
Dicycloverin	8/1	13/2		2/0					
Drotaverin	31/20	31/23							
Ezetimibe	8/1	13/0		2/0					
Glimepiride	8/1	13/8		1/0					
Loperamide	8/8	13/13							
Metformin	17/11	31/15							
Ranitidine	39/12	44/12		2/0					
Repaglinide	8/8	13/13		2/0					
Rosuvastatin	8/8	13/8		2/2					

Twelve pharmaceuticals in this category were monitored and all 12 (100%) were detected in MWWTP influent, MWWTP effluent, sludge or river water samples. The average and maximum concentrations measured in MWWTP influents and effluents are presented in Figure A3.27 and Figure A3.28, respectively. Removal rates of pharmaceuticals in MWWTPs are presented in Table A3.13. River water monitoring results are presented in Figure A3.29. Sludge monitoring data were submitted only for bezafibrate and all the values were lower than the detection limits for the used methods. For the majority of pharmaceuticals, the reported analytical LOD in MWWTP influent and effluent samples were low enough to detect these pharmaceuticals in wastewater samples.

In MWWTP influents, the highest average and maximum concentrations (0.5 mg/l and 3.2 mg/l, respectively) were measured for bezafibrate. The highest maximum concentration of metformin also exceeded 1 mg/l and the average concentrations of ranitidine and rosuvastatin exceeded 0.1 mg/l. In effluents, the highest average and maximum concentrations were measured for metformin (0.16 mg/l and 0.92 mg/l, respectively). The average concentration of bezafibrate exceeded 0.1 mg/l. Generally, the average concentrations of the compounds in effluents were <0.02 mg/l.

Removal rates of >70% were estimated for five out of 12 compounds. For cimetidine, the removal rate was <20% and for dicycloverin, glimepiride and loperamide, the concentrations were noted to increase during treatment. In river water samples, only data for bezafibrate were submitted. The maximum detected concentration of bezafibrate was 290 ng/l and the average concentration was 53 ng/l.

Figure A3.27 *The average and maximum concentrations of metabolic agents and gastrointestinal agents in MWWTP influents*

Source: Original data.

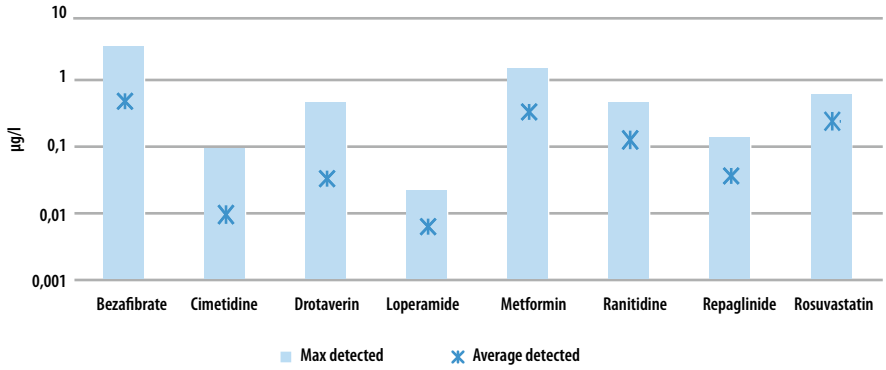


Figure A3.28 *The average and maximum concentrations of metabolic agents and gastrointestinal agents in MWWTP effluents*

Source: Original data.

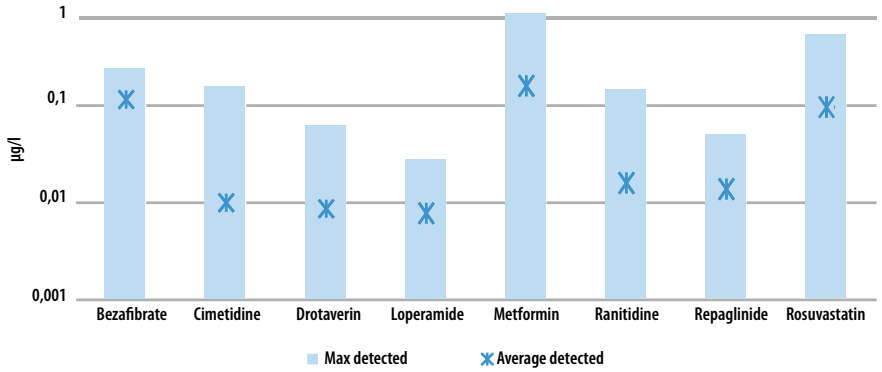


Table A3.13 *Removal rates of metabolic agents and gastrointestinal agents in MWWTPs*

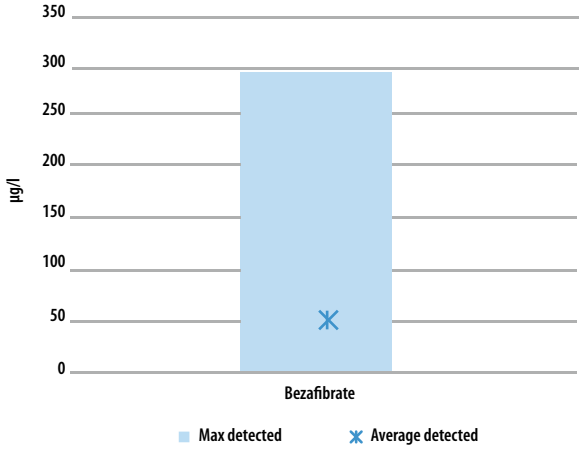
Source: Original data.

Compound	Average removal (%)
Atorvastatin	77%
Bezafibrate	75%
Cimetidin	0%
Dicycloverin	-37%
Drotaverin	74%
Ezetimibe	> 90%*
Glimepiride	-678%
Loperamide	-24%
Metformin	51%
Ranitidine	93%
Repaglinide	62%
Rosuvastatin	60%

* average effluent concentration <LOD

Figure A3.29 ***The average and maximum concentrations of metabolic agents and gastrointestinal agents in river water samples***

Source: Original data.



Annex 4. Data on samples from the marine environment

Methodology for statistical and visual presentation of data

For pharmaceuticals detected in the Baltic Sea water, the median and maximum concentrations are presented in graphs together with the sensitivity of the analytical methods used. For pharmaceuticals with a WFD assessment criterion detected in water, the assessment criterion has been included in the graphic presentation. Concentration data from Baltic Sea sediment and biota samples are not presented in graphs as these data are less suitable for comparison due to few data points and monitoring results being highly affected by choice of sampling method, analytical method, sampled species, age of species, sampled tissue etc.

Figures and maps have been elaborated for pharmaceuticals that are:

- on the EU WFD 'watch list' (Table 2 in main report) and have been detected
- of relevance for monitoring according to the Swedish Medical Products Agency (Table 4 in main report) and have been detected in >5 measurements
- none of the above but have been detected in >5 measurements

The presented maps give an overview of sampling sites, sampling matrices and samples above the detection limit.

An overview of all data submitted by the countries, including references, is presented in Annex 1.2.

For more information, see the Background report on pharmaceutical concentrations and effects in the Baltic Sea by Hallgren and Wallberg (2015).

Anti-inflammatory and analgesics

An overview of data on pharmaceuticals belonging to the therapeutic group of anti-inflammatory and analgesics is presented in Table A4.1. In total 26 pharmaceuticals in this category were monitored, out of which 11 (42%) were detected in water, sediment or biota samples.

Table A4.1 ***Summary of anti-inflammatory and analgesic pharmaceuticals monitored in the Baltic Sea***

Pharmaceuticals detected in any sample of water, sediment or biota, are listed in the left column. Pharmaceuticals not detected in any media are listed to the right along with further information on number of samples analyzed for each media.

Source: Original data.

Detected, details in tables and figures below				Not detected, number of samples			
Pharmaceutical	**Detected, map (*in main report)**	**Concentration, graph (*in main report)**	**Detected, statistics**	**Pharmaceutical**	**Water**	**Sediment**	**Biota**
Codein			Table A4.6	Acetylsalicylic acid	8	4	6
Diclofenac	Figure 13*	Figure 16*	Table A4.2	Azelastine	2	1	4
Dihydroergotamine			Table A4.6	Beclomethasone	3		5
Ibuprofen	Figure 14*	Figure 16*	Table A4.3	Biperiden	2		4
Ketoprofen		Figure 16*	Table A4.6	Bromocriptine	2		2
Naproxen	Figure A4.1	Figure 16*	Table A4.4	Budesonide	1		6
Paracetamol		Figure 16*	Table A4.6	Buprenorphine	2		2
Phenazone	Figure 15*	Figure 16*	Table A4.5	Dextropropoxyphene	1		2
Pizotifen			Table A4.7	Fenoprofen	4		
Tramadol		Figure 16*	Table A4.7	Fentanyl	1		
Trihexyphenidyl			Table A4.7	Indomethacin	2		
				Norpropoxyphene	137		
				Propofol	1		
				Propyphenazone			
				Tolfenamic acid			

* in main report

Table A4.2 ***Overview of data on measurements of diclofenac in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected. The WFD assessment criterion for diclofenac in coastal waters and transitional waters is 0.01 µg/l.

Source: Original data.

Diclofenac	**Total**	**Denmark**	**Estonia**	**Finland**	**Germany**	**Poland**	**Sweden**
Water							
Detected/sampled	70/257	0/2	0/10	2/3	67/212	0/9	1/21
Max (µg/l)	**0.054**			*	**0.054**		**0.002**
MD (µg/l)	0.002						
Sediment							
Detected/sampled	4/15		0/10				4/5
Max (µg/kg d.w.)	**3.5**						**3.5**
Biota							
Detected/sampled	5/50	5/50					
Max (µg/kg w.w.)							**5.2**

*33 ng/passive sampler (POCIS), not translatable to a concentration per litre

Table A4.3 ***Overview of data on measurements of ibuprofen in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Ibuprofen**	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	31/180	0/2	0/10	1/3	6/137		24/28
Max (µg/l)				*	**0.158**		**0.011**
MD (µg/l)	0.0016						
Sediment							
Detected/sampled	6/18		2/5				4/13
Max (µg/kg d.w.)			**45**				**6**
Biota							
Detected/sampled	1/62						1/62
Max (µg/kg w.w.)							**2.4**

12 ng/passive sampler (POCIS), not translatable to a concentration per litre
**including Ibuprofen-OH and Ibuprofen-COOH

Figure A4.1 ***Sample locations for the compiled data of naproxen***

Each presented data point might conceal several measurements conducted on the exact same location.

Source: Original data.

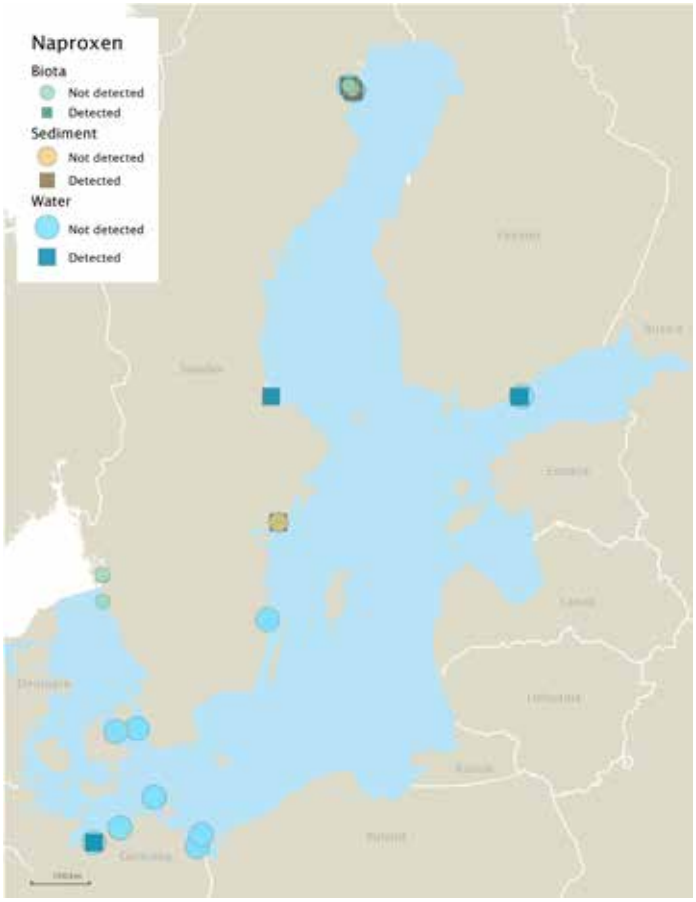


Table A4.4 ***Overview of data on measurements of naproxen in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Naproxen	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	10/33	0/2		2/3	1/16		7/12
Max (µg/l)				*	**0.014**		
MD (µg/l)	0.0056						
Sediment							
Detected/sampled	2/5						2/5
Max (µg/kg d.w.)							**0.31**
Biota							
Detected/sampled	0/10						0/10
Max (µg/kg w.w.)							

*39 ng/passive sampler (POCIS), not translatable to a concentration per litre

Table A4.5 ***Overview of data on measurements of phenazone in water***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Phenazone	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	5/137				5/137		
Max (µg/l)					**0.504**		
MD (µg/l)	0.034						

Table A4.6 ***Overview of data on measurements of codein, dihydroergotamine, ketoprofen and paracetamol in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Codein	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	0/4	0/2					0/2
Max (µg/l)							
MD (µg/l)							
Biota							
Detected/sampled	1/4						1/4
Max (µg/kg d.w.)	**83**						**83**
Dihydro-ergotamine	**Total**	**Denmark**	**Estonia**	**Finland**	**Germany**	**Poland**	**Sweden**
Water							
Detected/sampled	0/2						0/2
Max (µg/l)							
MD (µg/l)							
Biota							
Detected/sampled	1/4						1/4
Max (µg/kg d.w.)	**32**						**32**
Ketoprofen	**Total**	**Denmark**	**Estonia**	**Finland**	**Germany**	**Poland**	**Sweden**
Water							
Detected/sampled	6/17	0/2		1/3			5/12
Max (µg/l)				*			
MD (µg/l)	0.0017						
Sediment							
Detected/sampled	0/5						0/5
Max (µg/kg d.w.)							
Biota							
Detected/sampled	0/10						0/10
Max (µg/kg w.w.)							
Paracetamol	**Total**	**Denmark**	**Estonia**	**Finland**	**Germany**	**Poland**	**Sweden**
Water							
Detected/sampled	4/4						4/4
Max (µg/l)							**0.36**
MD (µg/l)							
Sediment							
Detected/sampled	4/4						4/4
Max (µg/kg d.w.)							**69**
Biota							
Detected/sampled	0/10						0/10
Max (µg/kg w.w.)							

*20 ng/passive sampler (POCIS), not translatable to a concentration per litre

Table A4.7 ***Overview of data on measurements of pizotifen, tramadol and trehexyphenidyl in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Pizotifen	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	0/2						0/2
Max (µg/l)							
MD (µg/l)							
Biota							
Detected/sampled	1/4						1/4
Max (µg/kg w.w.)							**0.7**
Tramadol	**Total**	**Denmark**	**Estonia**	**Finland**	**Germany**	**Poland**	**Sweden**
Water							
Detected/sampled	3/4	1/2					2/2
Max (µg/l)		**0.0016**					**0.00069**
MD (µg/l)							
Biota							
Detected/sampled	2/4						2/4
Max (µg/kg w.w.)							**179**
Trihexy-phenidyl	**Total**	**Denmark**	**Estonia**	**Finland**	**Germany**	**Poland**	**Sweden**
Water							
Detected/sampled	0/2						0/2
Max (µg/l)							
MD (µg/l)							
Biota							
Detected/sampled	3/4						3/4
Max (µg/kg w.w.)							**185**

Antimicrobial (antibiotic, antifungal, antiviral, antiparasitic, disinfectant, antiseptic) and antidote

An overview of data reported on pharmaceuticals belonging to the therapeutic group of antimicrobial agents and antidotes is presented in Table A4.8 below.

Table A4.8 ***Summary of antimicrobial and antidote pharmaceuticals monitored in the Baltic Sea***

Pharmaceuticals detected in any sample of water, sediment or biota, are listed in the left column. Pharmaceuticals not detected in any media are listed to the right along with further information on number of samples analysed for each media.

Source: Original data.

Detected, details in tables and figures below				Not detected, number of samples			
Pharmaceutical	**Detected, map (*in main report)**	**Concentration, graph (*in main report)**	**Detected, statistics**	**Pharmaceutical**	**Water**	**Sediment**	**Biota**
Ciprofloxacin				9,10-Anthraquinone	9		
Clarithromycin	Figure A4.2	Figure 17*	Table A4.9	Amoxicillin	2		
Clindamycin		Figure 17*		Azithromycin	4		4
Clotrimazole		Figure 17*		Chloramphenicol	1		
Erythromycin	Figure A4.2		Table A4.9	Chlortetracyline	51	1	
Ketoconazol				Cloxacilline	1		
Miconazol				Demeclocycline	1	1	1
Norfloxacin				Dicloxacilline	1		
Sulfadiazine				Doxycycline	51	1	
Sulfamethoxazole	Figure 18*	Figure 17*	Table A4.10	Fluconazole	4	3	4
Trimethoprim		Figure 17*		Lufenuron	9		
				Nafcilline	1		
				Naloxone	2		
				Ofloxacin	2		4
				Oxacillin	1		
				Oxytetracycline	51	1	
				Phoxim	101		
				Roxithromycin	4		4
				Tetracy	51	1	4

* in main report

Note: Some data on triclosan were made available as well but this substance was not included into this report.

Figure A4.2 ***Sample locations for the compiled data of erythromycin, clarithromycin and azithromycin***

Each presented data point might conceal several measurements conducted on the exact same location.

Source: Original data.

Table A4.9 ***Overview of data on measurements of erythromycin, clarithromycin and azithromycin in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Erythromycin, Clarithomycin, Azithromycin	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	2/126	0/6			0/116		2/4
Max (µg/l)	**0.00027**						**0.00027**
MD (µg/l)							
Biota							
Detected/sampled	1/8						1/8
Max (µg/kg d.w.)							**12.7**
MD (µg/l)							

Table A4.10 ***Overview of data on measurements of sulfamethoxazole in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Sulfamethoxazole	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	12/140				12/137		0/3
Max (µg/l)	**0.033**			*	**0.033**		
MD (µg/l)	0.0016						
Sediment							
Detected/sampled	4/8			4/8			
Max (µg/kg d.w.)				**101**			
Biota							
Detected/sampled	1/4						1/4
Max (µg/kg w.w.)							**51**

Cardiovascular agents (blood pressure, diuretics, anticoagulants, antihistamine)

An overview of data reported on pharmaceuticals belonging to the therapeutic group of cardiovascular agents is presented in Table A4.11.

Table A4.11 ***Summary of cardiovascular agent pharmaceuticals monitored in the Baltic Sea***

Pharmaceuticals detected in any sample of water, sediment or biota, are listed in the left column. Pharmaceuticals not detected in any media are listed to the right along with further information on number of samples analyzed for each media.

Source: Original data.

Detected, details in tables and figures below				Not detected, number of samples			
Pharmaceutical	**Detected, map (*in main report)**	**Concentration, graph (*in main report)**	**Detected, statistics**	**Pharmaceutical**	**Water**	**Sediment**	**Biota**
Acebutolol				Amiloride	2		
Alfuzosin				Amiodarone	2		2
Atenolol				Desloratadine	2		4
Bisoprolol	Figure 21*	Figure 19	Table A4.13	Diltiazem	2		4
Cilazapril				Fexofenadine	2		4
Clemastine				Flecainide			4
Cyproheptadine				Isradipine	1		
Diphenhydramine				Losartan	2		
Dipyridamole		Figure 19		Meclozine	2		4
Eprosartan				Promethazine	2		4
Felodipine				Propranolol	139		40
Irbesartan		Figure 19					
Metoprolol	Figure 20*	Figure 19	Table A4.12				
Sotalol	Figure 22*	Figure 19	Table A4.14				

* in main report

Table A4.12 ***Overview of data on measurements of metoprolol in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Metoprolol	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	23/144	0/2		3/3	18/137		2/2
Max (µg/l)	**0.00027**			*	**0.055**		**0.0016**
MD (µg/l)							
Biota							
Detected/sampled	0/4						0/4
Max (µg/kg d.w.)							
MD (µg/l)							

*40 ng/passive sampler (POCIS), not translatable to a concentration per liter

Table A4.13 ***Overview of submitted data on measurements of bisoprolol in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Bisoprolol	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	33/142			3/3	30/137		0/2
Max (µg/l)				*	**0.128**		
MD (µg/l)							
Biota							
Detected/sampled	1/44						1/44
Max (µg/kg d.w.)							**102**
MD (µg/l)							

*39 ng/passive sampler (POCIS), not translatable to a concentration per liter

Table A4.14 ***Overview of data on measurements of sotalol in water***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Sotalol	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	5/139				3/137		2/2
Max (µg/l)					**0.024**		**0.00024**
MD (µg/l)							

Central nervous system agents (psychotherapeutic, antiepileptic, antiparkinson, muscle relaxant)

Table A4.15 ***Summary of central nervous system agents monitored in the Baltic Sea***

Pharmaceuticals detected in any sample of water, sediment or biota, are listed in the left column. Pharmaceuticals not detected in any media are listed to the right along with further information on number of samples analyzed for each media.

Source: Original data.

Detected, details in tables and figures below				Not detected, number of samples			
Pharmaceutical	**Detected, map (*in main report)**	**Concentration, graph (*in main report)**	**Detected, statistics**	**Pharmaceutical**	**Water**	**Sediment**	**Biota**
Alprazolam				7-aminoflunitrazepam			2
Bromocriptine				Amitryptiline	2		4
Carbamazepine	Figure 24*	Figure 23*	Table A4.16	Atracurium besylate	2		4
Chlorpromazine				Biperiden			4
Citalopram	Figure 23*			Bupropion	2		4
Clonazepam				Caffeine			2
Donepezil				Clomipramine	2		4
Duloxetine				Clozapine			2
Fluoxetine				Diazepam	16		4
Haloperidol				Flunitrazepam			6
Maprotiline				Flupentixol	2		4
Memantine				Fluphenazine	2		4
Mianserin				Hydroxyzine	2		4
Mirtazapine				Levomepromazine	2		4
Orphenadrine				N-demethylflunitrazepam			2
Oxazepam	Figure 26*	Figure 23*	Table A4.17	Nefazodone	2		4
Paroxetine				Perphenazine	2		4
Primidone	Figure 25*	Figure 23*	Table A4.18	Risperidone	2		6
Sertraline		Figure 23*		Temazepam	16		
Venlafaxine		Figure 23*		Thioridazine			2
Zolpidem				Zopiclone			2
				Zopiclone N-oxide			2
				Zuclopenthixol	1		

* in main report

Table A4.16 ***Overview of data on measurements of carbamazepine in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Carbamazepine	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	135/220	0/2		3/3	130/212		2/3
Max (µg/l)	**0.033**			*	**0.073**		**0.0031**
MD (µg/l)	0.0016						
Sediment							
Detected/sampled	0/1						0/1
Max (µg/kg d.w.)							
Biota							
Detected/sampled	1/45						1/45
Max (µg/kg w.w.)							**141**

*232 ng/passive sampler (POCIS), not directly translatable to a concentration per liter

Table A4.17 ***Overview of data on measurements of oxazepam in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Oxazepam	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	11/69				9/67		2/2
Max (µg/l)					**0.0019**		**0.00085**
MD (µg/l)							
Biota							
Detected/sampled	9/46						9/46
Max (µg/kg d.w.)							**6.7**

Table A4.18 ***Overview of data on measurements of primidone in sea water***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Primidone	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	51/51						51/51
Max (µg/l)					**0.0058**		
MD (µg/l)							

Chemotherapeutic agents and X-ray contrast media

Figure A4.3 ***Sample locations for the compiled data of amidotrizoic acid***

Each presented data point might conceal several measurements conducted on the exact same location.

Source: Original data.

Dermatological agents

Table A4.19 ***Overview of data on measurements of salicylic acid in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Salicylic acid	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	4/8						4/8
Max (µg/l)	**0.014**						**0.014**
MD (µg/l)	0.012						0.012
Sediment							
Detected/sampled	4/4						4/4
Max (µg/kg d.w.)	**3.9**						**3.9**
Biota							
Detected/sampled	1/45						1/45
Max (µg/kg w.w.)							**141**

Hormones and hormone antagonists

Table A4.20 ***Summary of hormones and hormone antagonists monitored in the Baltic Sea***

Pharmaceuticals detected in any sample of water, sediment or biota, are listed in the left column. Pharmaceuticals not detected in any media are listed to the right along with further information on number of samples analyzed for each media.

Source: Original data.

Detected, details in tables and figures below				Not detected, number of samples			
Pharmaceutical	**Detected, map (*in main report)**	**Concentration, graph (*in main report)**	**Detected, statistics**	**Pharmaceutical**	**Water**	**Sediment**	**Biota**
17b-estradiol	Figure A4.4		A4.21	Estriol	3	1	
17a-ethinylestradiol	Figure A4.4		A4.21	Estrone	1		
Etonogestrel				Finasteride	2		4
Flutamide				Fulvestrant	1		
Tamoxifen				Levonorgestrel	3	1	5
				Medroxyprogesterone	2		
				Mestranol	43	1	
				Norethindrone			
				Norethisteron	2		
				Progesterone	2		

Figure A4.4 ***Sample locations for the compiled data of 17a-ethinylestradiol, 17b-estradiol and estrone***

Each presented data point might conceal several measurements conducted on the exact same location.

Source: Original data.

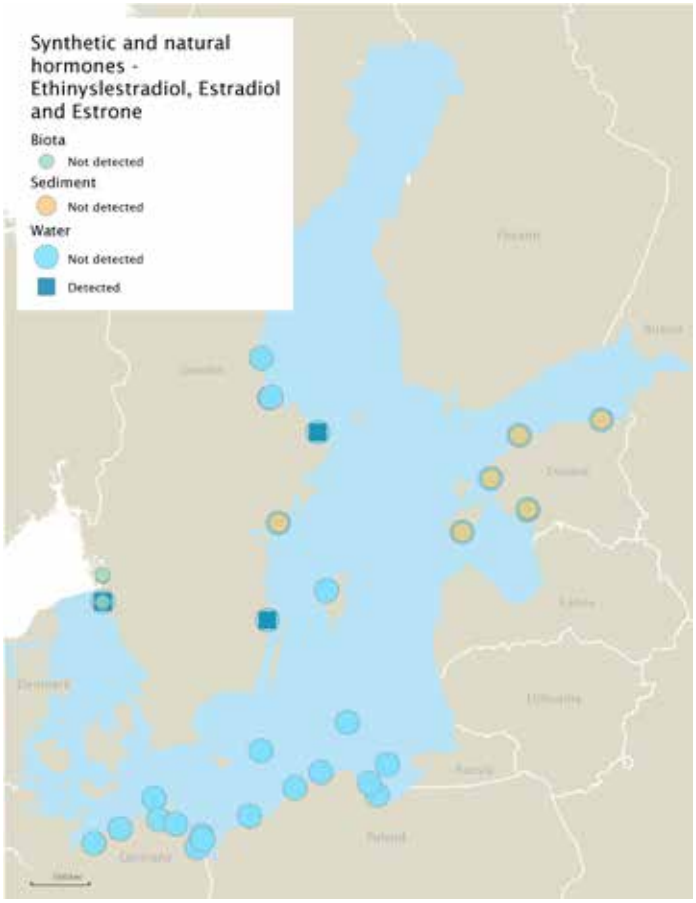


Table A4.21 ***Overview of data on measurements of 17a-ethinylestradiol, 17b-estradiol and estrone in different marine matrices***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

17a-ethinylestradiol, 17b-estradiol, Estrone	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	3/198		0/20		0/154		3/24
Max (µg/l)							**0.0011***
MD (µg/l)							
Sediment							
Detected/sampled	0/22		0/20				0/2
Max (µg/kg d.w.)							
Biota							
Detected/sampled	0/8						0/8
Max (µg/kg w.w.)							

*maximum detected concentration is for 17b-estradiol

Metabolic agents and gastrointestinal agents

Table A4.22 ***Summary of metabolic and gastrointestinal agents monitored in the Baltic Sea***

Pharmaceuticals detected in any sample of water, sediment or biota, are listed in the left column. Pharmaceuticals not detected in any media are listed to the right along with further information on number of samples analyzed for each media.

Source: Original data.

Detected, details in tables and figures below				Not detected, number of samples			
Pharmaceutical	**Detected, map (*in main report)**	**Concentration, graph (*in main report)**	**Detected, statistics**	**Pharmaceutical**	**Water**	**Sediment**	**Biota**
Atorvastatin				Bezafibrate	139		
Clofibric acid (metabolite of Clofibrate)		Figure A4.5	Table A4.23	Ezetimibe	2		4
Dicycloverine				Fenofibrate	1		
Loperamide				Gemfibrozil	17		
Ranitidine				Glibenclamide			4
Rosuvastatin				Glimepiride	2		4
				Metformin	1		5
				Repaglinide	2		4

Figure A4.5 ***Sample locations for the compiled data of clofibric acid***

Each presented data point might conceal several measurements conducted on the exact same location.

Source: Original data.

Table A4.23 ***Overview of data on measurements of clofibric acid in water***

Number of detected values is presented together with the total number of measurements. Max= maximum value, MD= median among detected.

Source: Original data.

Clofibric acid	Total	Denmark	Estonia	Finland	Germany	Poland	Sweden
Water							
Detected/sampled	83/128				83/127		0/1
Max (µg/l)	**0.0004**				**0.0004**		
MD (µg/l)	0.0001						

Annex 5. Overview of studies carried out on effects of pharmaceuticals on Baltic biota

The tables below provide an overview of the results of different studies concerning the effects of pharmaceutical substances on Baltic Sea species.

The results are summarized according to species, test conditions (concentration and duration) and the essential outcome of the studies.

Table A5.1 ***Effects of propranolol on Baltic Sea species***

LOEC= lowest observable effect concentration.

Source: Original data.

Species	Test conditions	LOEC (µg/l)	Endpoints	Reference
Mytilus edulis trossulus	1, 100, 1,000, 5,000 and 10,000 µg/l (1-3 weeks)	1,000	Physiology: Lower byssus strength and lower byssus thread abundance at 10,000 µg/l. Lower SFG* after 2 weeks at 1,000 µg/l. Mortality 16% > 1,000 µg/l (2% in control treatments)	Ericson (2010)
Gammarus spp.	10, 100, and 1,000 µg/l (4 weeks)	100	Behavioral: Swimming activity decreased and time to find habitat increased with increased concentration. Feeding rates were more than 2 times higher than the control.	Ericson (2011)
Fucus vesiculosus	10, 100, and1,000 µg/l (4 weeks)	5,000	Physiology: Significant dose-response relationship and the significantly lower GP/R**	Ericson (2011)
Fucus vesiculosus	10 – 1,000 µg/l 10 (8 weeks)	10	Physiology: Lower GP/R** at 10 µg/l after 4 weeks. Effects increased with increasing concentration and with exposure time. Lower chlorophyll fluorescence after 4 weeks at 1,000 µg/l Negative effect on the photosynthesis.	Oskarsson (2012)
Gammarus spp.	10 -1,000 µg/l (8 weeks)	100	Physiology: Reduced respiration (4 weeks). Inconsistent results at different concentrations over time.	Oskarsson (2012)
Microcosm study Ceramium tenuicorne, Mytilus edulis trossulus, Gammarus spp., water and sediment	1,000 µg/l 100 µg/l (6 weeks)	1,000	Algae: Higher carbon content at 1,000 µg/l. At 1,000 µg/l: Mussels: increased mortality Amphipods: Increased reproduction Algae: Higher carbon content Ecosystem structural change: The effect on the mussel led to a feeding shift from alga to mussel by the amphipods. Better food quality increased reproduction. Less amphipod grazing, and increased nutrient levels in the water was favorable for the alga.	Oskarsson (2012)

*(SFG) Scope for growth: the energy available for normal metabolism

**(GP/R): primary production (GP) to respiration (R) ratio

Table A5.2 ***Effects of diclofenac on Baltic Sea species***

LOEC= lowest observable effect concentration.

Source: Original data.

Species	Test conditions	LOEC (µg/l)	Endpoints	Reference
Mytilus edulis trossulus	1, 100, 1,000, 5,000 and 10,000 µg/l (1-3 weeks)	100	Physiology: Lower byssus strength and lower byssus thread abundance at 10,000 µg/l. Lower SFG* after 2 weeks at 1,000 µg/l. Mortality 14% > 1,000 µg/l (2% in control treatments)	Ericson (2010)
Fucus vesiculosus	10, 100, and 1,000 µg/l (4 weeks)	>1,000	No significant effects	Oskarsson (2012)
Gammarus spp	10, 100, and1,000 µg/l (4 weeks)	>1,000	No significant effects	Oskarsson (2012)

*(SFG) Scope for growth: the energy available for normal metabolism

Table A5.3 ***Effects of a mixture of diclofenac (D) and propanolol (P) on blue mussels in the Baltic Sea***

LOEC= lowest observable effect concentration.

Source: Original data.

Species	Test conditions	LOEC (µg/l)	Endpoints	Reference
Mytilus edulis trossulus	Mixture exposure (2 weeks)	P: 250 D: 750 Total: 1,000	Physiology: lower SFG*	Ericson (2010)
Mytilus edulistrossulus	50/50 mixture of iclofenac and propranolol. Total exposure concentration: 20, 200 and 2,000 µg/l. Sampled with increasing distance to a MWWTP outlet, exposed to the mixture for 3 weeks, and then tested for their physiological response and subsequent recovery from the exposure.	P: 100 D: 100 Total: 200	Physiology: increased effect on SFG (and its components) Mussels collected further from outlet were more affected by the exposure and did not recover to the same extent as mussels closer to the outlet. The authors suggest that the mussels sampled closer to the MWWTP, have a higher food availability (= improved health status) and/or pre-exposure to natural disturbances, and the test substances, via the MWWTP effluent.	Kumblad (2015)
Gammarus spp	10, 100, and1,000 µg/l (4 weeks)	>1,000	No significant effects	Oskarsson (2012)

*(SFG) Scope for growth: the energy available for normal metabolism

Table A5.4 ***Effects of ibuprofen on Baltic Sea species***

LOEC= lowest observable effect concentration.

Source: Original data.

Species	Test conditions	LOEC (µg/l)	Endpoints	Reference
Mytilus edulis trossulus	1, 100, 1,000, 5,000 and 10,000 µg/l (1-3 weeks)	1,000	Physiology: lower SFG* after 2 weeks at 1,000 µg/l Byssus strength = Control treatment Mortality = Control treatments	Ericson (2010)
Gammarus spp.	1, 1,000, and 10,000 µg/l (1 weeks)	> 10,000	No significant effects	Ericson (2011)
Fucus vesiculosus	1, 1,000 and 10,000 µg/l (1 week)	> 10,000	No significant effects	Ericson (2011)
Fucus vesiculosus	10, 100, and 1,000 µg/l (4 weeks)	> 1,000	No significant effects	Oskarsson (2012)
Gammarus spp.	110, 100, and 1,000 µg/l (4 weeks)	> 1,000	No significant effects.	Oskarsson (2012)

*(SFG) Scope for growth: the energy available for normal metabolism

Table A5.5 ***Effects of citalopram on three-spined stickleback in the Baltic Sea***

LOEC= lowest observable effect concentration.

Source: Original data.

Species	Test conditions	LOEC (µg/l)	Endpoints	Reference
Gasterosteus aculeatus	0.15 and 1.5 µg/l (3 weeks)	< 0.15 (based on mode of action)	Behavioral: Decreased food intake within less than 1 week.	Kellner (2015)

International Initiative on Water Quality – IIWQ

The International Initiative on Water Quality (IIWQ) was established by the official endorsement by the Intergovernmental Council of the International Hydrological Programme (IHP) of UNESCO at its 20th session in 2012 (Resolution XX-4), following recommendations of IHP Regional Consultation Meetings on Water Quality.

The IIWQ supports Member States in protecting, enhancing and sustainably managing the quality of the world's freshwater resources by mobilizing, generating and disseminating scientific knowledge, providing policy advice and advocacy, promoting international scientific cooperation and raising awareness on water quality. It implements activities and projects focusing on specific water quality issues in both developing and developed countries to respond to global water quality challenges in a holistic interdisciplinary, participatory and cooperative way towards ensuring water security for sustainable development.

For more information:
http://en.unesco.org/waterquality-iiwq
http://en.unesco.org/emergingpollutants

This publication is published in the framework of UNESCO Project on *Emerging Pollutants in Wastewater Reuse in Developing Countries*, funded by the Government of Sweden.

SWEDEN

Sida

United Nations Educational, Scientific and Cultural Organization

International Hydrological Programme

International Initiative on Water Quality

HELCOM

9 789231 002137