Health Care Without Harm

PHARMACEUTICAL RESIDUES IN HOSPITAL WASTEWATER

FIVE CASE STUDIES FROM EUROPEAN HOSPITALS

INTRODUCTION

The healthcare sector has a unique healing mission, yet hospitals are key point sources for specialised pharmaceutical residues entering the environment, a serious source of pollution that can threaten ecosystems and the environment, as well as drive the development of antimicrobial resistance (AMR)– a serious public health threat.[1]

Up to 90% of orally administered pharmaceuticals are excreted into wastewater as active substances in the faeces and urine of patients.[2] Wastewater treatment plants widely vary in their capacity to eliminate these active substances; one study recorded removal rates ranging from 0%-97%.[3] This means that parent compounds or their metabolites can be discharged into the aquatic ecosystem through effluents and enter the water cycle.[4]

UP TO 90% OF ORALLY ADMINISTERED PHARMACEUTICALS ARE EXCRETED INTO WASTEWATER AS ACTIVE SUBSTANCES IN THE FAECES AND URINE OF PATIENTS

Pharmaceuticals are biologically active, often mobile (particularly in the case of metabolites), and not readily biodegradable in the environment.[5] As they are designed to interact with living systems at low doses, even low concentrations in the environment are a concern.[6] Whilst common medicines are often consumed in the community, more specialised pharmaceutical products such as cytostatic drugs, some antibiotics, and X-ray contrast agents are mainly administered in hospitals.[7]

This report explores how hospital wastewater contributes to the pharmaceutical load released into the environment and features five case studies illustrating how European hospitals are dealing with pharmaceutical residues in their wastewater. It also looks at resistant bacteria because of their potential link with antibiotic residues in hospital effluents.

HOW DOES HOSPITAL WASTEWATER CONTRIBUTE TO PHARMACEUTICAL POLLUTION?

HUMAN CONSUMPTION AS A KEY PATHWAY IN EUROPE

With more than 3,000 active pharmaceutical ingredients (APIs) available, the EU is the second largest market in the world for pharmaceuticals after the United States.[2] This trend is expected to increase as EU populations age and grow and new medicines enter the market every year.[8] [9]

Pharmaceutical residues can enter the environment throughout their life cycle (production, consumption, and disposal). In the EU, 596 pharmaceutical substances have been reported in the environment above detection limit i.e. the lowest concentration where they can be detected. These molecules can be found in their original forms (APIs) or as metabolites or other transformation products.[10]

IN THE EU, 596 PHARMACEUTICAL SUBSTANCES HAVE BEEN REPORTED IN THE ENVIRONMENT ABOVE DETECTION LIMIT

In OECD countries, consumption is considered the largest contributor to the environmental load of medicines in aquatic environments.[1] It is estimated that 30%-90% of orally administered pharmaceuticals are excreted into wastewater as active substances in the faeces and urine of patients; these emissions reach wastewater treatment plants through sanitary sewer systems.[2]

Wastewater treatment plants are primarily designed to eliminate biodegradable substances and nutrients and are therefore not able to completely remove pharmaceutical substances. These residues are then discharged via effluent into surface waters (e.g. lakes and rivers), entering the water cycle. They can ultimately end up in drinking water, where low concentrations of pharmaceutical residues have been detected.[7]

COMMUNITY USE IS THE MAIN POINT OF ENTRY

Whilst up to 70% of the total medicine consumption within a hospital may be excreted or washed off into wastewater, hospitals are not the main point of entry of pharmaceutical residues into the municipal sewage system. As medicines are mostly consumed in the community, pharmaceutical residues that reach wastewater treatment plants largely come from private households.[7]

Only around 20% of APIs in municipal wastewater come from healthcare facilities.[11] Nevertheless, hospital wastewater's contribution to the pharmaceutical load released into the environment can widely vary based on factors such as number of beds, services provided, and number and types of wards and units.[12]

There is also variation between countries. In the Netherlands, for example, pharmaceutical residues from hospitals and other healthcare facilities on average represent less than 5% of the total pharmaceutical load entering wastewater treatment plants, with only a few hospitals reaching approximately 10%.[13]

HOSPITALS ARE POLLUTION HOTSPOTS FOR SPECIALISED PHARMACEUTICALS

The nature and quantity of pharmaceutical residues in hospital effluents and their entry into municipal wastewater depends on pharmaceutical administration and consumption in hospitals. This may vary across countries and regions according to the hospital activity, the predominance of diseases in the area, and the on-site recommended formulary (list of medicines).[12]

Whilst the overall contribution of hospital wastewater to the municipal pharmaceutical load is relatively small in comparison with community settings, hospitals emit particularly high concentrations of pharmaceutically active compounds and administer specialised pharmaceuticals that are not commonly taken at home.[7 14]

Hospitals are considered as key point-sources for specialised pharmaceuticals, such as cytostatic drugs, some antibiotics, and X-ray contrast media, which typically hold a much higher environmental risk for aquatic ecosystems.[1 7] These hospital-specific pharmaceuticals, further assessed below, should receive priority attention. It is worth noting that analgesics/anti-inflammatories are also widely detected in hospital wastewater (particularly ibuprofen and paracetamol), but these drugs are not considered in this report as they are predominantly used in the community.[12 15]

Rural hospitals are of particular concern for pharmaceutical pollution hotspots. In the absence of large population centres, these hospitals might be located in smaller towns, but provide a wide range of treatments to a larger population.[15] Wastewater treatment plants in rural areas might also be smaller and less advanced and therefore less efficient in eliminating APIs from wastewater.[16]

CYTOSTATICS

Widely used in cancer therapy and chemotherapy, many cytostatics are known to be carcinogenic, mutagenic, and toxic for reproduction.[17] The level of degradation of cytostatics by human metabolism is highly variable, ranging from 10%-97%. Removal rate in wastewater treatment plants also widely varies from one compound to another.[18]

Patient excretion (urine, faeces, transpiration, and vomit) is the main pathway for cytostatics to enter the aquatic environment and hospital wastewater is a key emission source to surface water, but it is not the only one. Household wastewater is also an important source with the development of home treatments and patient excretion at home after being discharged from hospital.[19]

Research in the Netherlands showed that most cytostatic residues do not pose a risk to the environment, although the risk assessment of some substances could not be performed due to a lack of environmental information.[18] The CytoThreat project concluded that environmental risk could not be excluded for three out of four tested cytostatics (5-fluorouracil, cisplatin, and imatinib).[20]

ANTIBIOTICS AND RESISTANT BACTERIA

In Europe, 20%-30% of inpatients receive an antibiotic treatment during their hospital stay.[21] Antibiotic residues discharged into hospital wastewater can directly affect human health as chemical contaminants, as well as contribute to the development of antimicrobial resistance (AMR), a global health threat that is annually responsible for 33,000 deaths in the EU.[22][23] If no effective action is taken, AMR could cause 390,000 deaths per year in Europe by 2050.[24]

Hospitals are high-risk point sources of antibiotics and antibiotic resistance genes (ARGs); last-resort antibiotics such as piperacillin and vancomycin are used more frequently in hospitals than in the community, hospital wastewater can therefore have a different ARG profile and a higher risk potential than household wastewater.[25]

The proportion of resistance genes or resistant bacteria is usually higher in hospital wastewater than in household wastewater – this could be due to resistant faecal bacteria being more common in hospitals than in the community but also on-site selection, which is caused by high antibiotic concentrations in hospital effluents.[26]

Due to the selective pressure exerted by antibiotics in hospital wastewater, resistant bacteria have been included in the scope of this report. Some hospitals are investigating how to remove these bacteria in their wastewater such as Aarhus University Hospital in Denmark, which is testing peracetic acid as a tool to neutralise ciprofloxacin-resistant bacteria (page 18).

X-RAY CONTRAST AGENTS

X-ray contrast agents are used in medical imaging, often in high concentrations; they are both inert and mobile, and difficult to remove through wastewater treatment plants.[1] X-ray contrast agents have a low toxicity but are highly persistent, which means they accumulate in the environment and end up in the water cycle. [27]

They originate from a number of departments, such as cardiology and radiology, but can also be excreted by patients at home. It takes approximately 24 hours for contrast agents to be completely eliminated by the body.[28] Up to 30%-40% of X-ray contrast agents are excreted by patients in their first visit to the toilet after examination.[27] Iodinated contrast media (ICM) account for the highest load of micropollutants found in hospital effluents by order of magnitude.[29]

The German Environmental Agency (UBA) and the Dutch government are supporting the use of urine bags to prevent X-ray contrast media entering the aquatic environment.[11] [30] There are several pilot projects in hospitals and radiology practices, such as MERK'MAL in Germany (page 22) or Plaszakziekenhuis in the Netherlands.[i]

[i] *Plaszakziekenhuis. (2021) www.plaszakziekenhuis.nl*

POINT-SOURCE TREATMENT IS NOT A SILVER BULLET

There are currently no EU-wide limit values for pharmaceuticals in surface water (page 12) and regulation concerning hospital discharges varies from country to country across Europe. In some countries, hospital wastewater must meet specific characteristics before being discharged into municipal sewage, whereas other countries have not implemented such regulations.

Several hospitals have opted to install or test an on-site treatment system such as the Reinier de Graaf Hospital, the Netherlands,[ii] or the Clinique Saint-Pierre Ottignies, Belgium (page 14). Others are investigating technologies to degrade pharmaceuticals in specific wastewater streams such as Radboudumc in the Netherlands (page 25).

Decentralised wastewater treatment at a hospital level prevents the dilution of hospital wastewater with urban wastewater.[12] Only a relatively small proportion of pharmaceutical emissions originate from hospitals, however, so point-source treatment might not always have a substantial impact on pharmaceutical loads entering wastewater treatment plants.[31]

The effectiveness of point-source treatments (generally or for specific wastewater streams) should therefore be assessed on a case-by-case basis. The 2012 Pharmaceutical Input and Elimination from Local Point Sources (PILLS) project[7] developed a useful series of criteria to support decision for hospital-based wastewater treatment:

- Antibiotic-resistant bacteria/ecotoxicity
- Costs
- Efficiency
- Energy consumption
- Legal compliance
- Life-cycle analysis
- Local aspects
- Operation experiences and responsibilities

[ii] *Pharmafilter. (2012) www.pharmafilter.nl/reinier-de-graaf-gasthuis-delft-zet-pharmafilter-in*

COMPLEMENTARY OR ALTERNATIVE SOLUTIONS

There is no easy fix to the complex problem of pharmaceutical residues in hospital wastewater, but alongside or as an alternative to point-source treatment, there are many actions that hospitals can take to significantly reduce the amount of high-risk pharmaceuticals and metabolites entering aquatic ecosystems:

- Adhere to green formularies (e.g. the Wise List in Region Stockholm)
- Implement separate collection systems such as urine bags
- Follow protocols to safely dispose pharmaceutical waste
- Promote procurement practices that favour greener pharmaceuticals
- Develop stewardship activities to curb inappropriate prescribing
- Embed green social prescribing in healthcare

Hospitals, such as Caithness General Hospital in the United Kingdom (page 29), can take a leadership role in investigating the extent of pharmaceutical residues discharged into municipal wastewater and onwards into the environment. They can leverage their ethical, economic, and political influence to raise awareness and drive change in healthcare systems and medical and patient communities.

THE EU WATCH LIST

UNDER THE WATER FRAMEWORK DIRECTIVE

The EU Water Framework Directive (WFD) aims to maintain and improve the aquatic environment in the EU. It includes a Watch List of potential water pollutants that should be carefully monitored by Member States to determine the risk they pose to surface water. Over the years, this list has featured several pharmaceutical products.

2015
1ST WATCH LIST

17-Alpha-ethinylestradiol (EE2)
17-Beta-estradiol (E2)
Diclofenac

2018
2ND WATCH LIST

17-Alpha-ethinylestradiol (EE2)
17-Beta-estradiol (E2)
Macrolide antibiotics: Azithromycin, Clarithromycin, and Erythromycin
Amoxicillin
Ciprofloxacin

2020
3RD WATCH LIST

Amoxicillin
Ciprofloxacin
Sulfamethoxazole
Trimethoprim
Venlafaxine
O-Desmethylvenlafaxine (metabolite)
Azole compounds: Clotrimazole, Fluconazole, and Miconazole

Aside from compulsory monitoring, there are no EU-wide limit values for pharmaceuticals in surface water. This might, however, change as the European Commission is considering adding pharmaceutical products to the List of Priority Substances, a list of identified water pollutants for which measures must be taken to reduce pollution of surface waters.

EUROPEAN HOSPITALS

REDUCING PHARMACEUTICAL RESIDUES IN HOSPITAL WASTEWATER

This section features five case studies illustrating how some European hospitals are dealing with pharmaceutical residues and resistant bacteria in their wastewater. It aims to showcase what hospitals are doing and investigating in this field, but is not an endorsement from Health Care Without Harm Europe of specific technologies hospitals might use or entities they might partner with.

CASE STUDY

01

A PILOT WASTEWATER TREATMENT PLANT BASED ON BIOLOGICAL PROCESSES

CLINIQUE SAINT-PIERRE OTTIGNIES (CSPO)

BELGIUM

The Clinique Saint-Pierre Ottignies is a regional hospital with 425 beds located in the province of Walloon Brabant in the centre of Belgium. It provides care for more than 70,000 inpatients annually across a wide range of specialised departments.

For several years, the hospital has been working on reducing its environmental impact, for example through low-energy buildings. More recently, they have structured all sustainability-related initiatives under the project *"Hôpital en transition" (Hospital in transition)* and created seven working groups bringing together healthcare and technical staff to advance their sustainability agenda in different fields:

1. Leadership and governance
2. Procurement
3. IT management and energy
4. Mobility
5. Food chain
6. Communication and awareness-raising
7. Respect for the environment

The project aims to support a more sustainable, fairer, and socially responsible environment (in line with the UN Framework Convention on Climate Change) by delivering results-oriented sustainability projects based on scientific literature and the internal and external expertise within each working group.

This approach seeks to empower hospital staff, but also the wider local community, by engaging with farmers, patients, residents, and suppliers. It also opens the door for partnerships with the private sector and universities in the area of scientific research.

Since 2019 the Clinique Saint-Pierre Ottignies has partnered with the engineering company John Cockerill Balteau to test a pilot wastewater treatment technology. The pilot project aims to treat macro-pollution, pharmaceutical pollution, and pathogenic microorganisms and antibiotic-resistant bacteria in the hospital's wastewater.

The pilot plant is based on biological processes that are more energy efficient than oxidation methods that require a large amount of electricity to generate oxidant molecules and free radicals to degrade pharmaceutical residues. As the pilot plant does not require chemical or physical oxidation, it is also less likely to generate oxidation by-products that can be highly toxic for the environment.

The first step in the process involves promoting the development of microorganisms that can degrade micropollutants in a bioreactor divided into ecological ‘niches’. These microorganisms take the forms of flocks (suspended in the bioreactor) and colonies (fixed to synthetic materials suspended in the bioreactor by aeration) called ‘biofilms’. They evolve alternatively under aerobic (with dissolved oxygen) and anoxic (without dissolved oxygen but with nitrates) conditions.

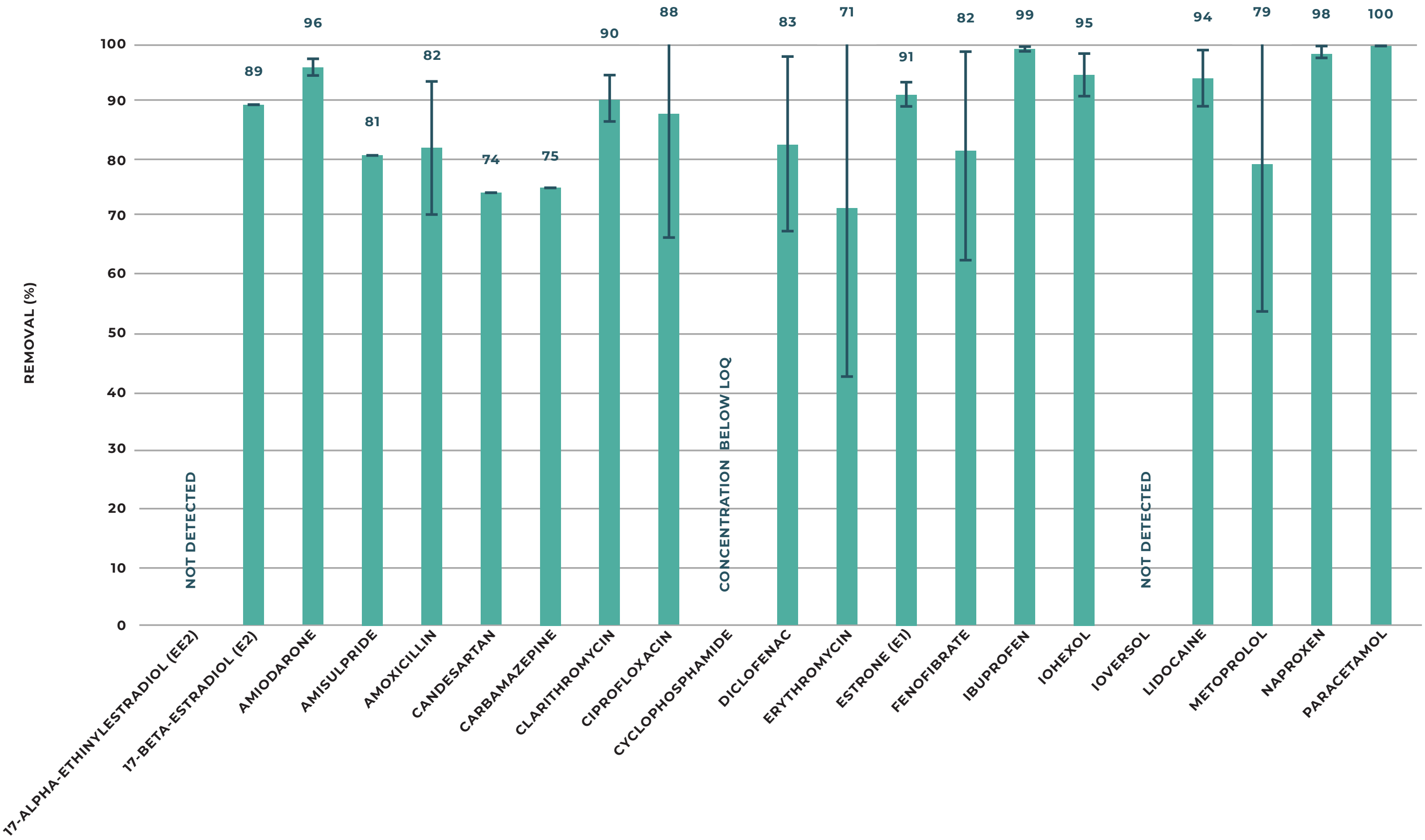
When a large part of micro-pollution is degraded, the microorganisms are separated from treated water by membrane filtration. Thanks to their low porosity, membranes capture 99.9% of pathogenic microorganisms such as bacteria and viruses. This step generates sludge waste that needs to be incinerated off-site.

The second step to the biological process involves biofiltration: water is filtered through recycled, activated carbon colonised by a new microbial population that uses pharmaceutical residues as an energy source. Activated carbon is used for its capacity to adsorb organic pollutants easily.

This pilot project is currently treating a nominal flow of $1m^3$/hour, which represents wastewater from some 70-80 hospital beds. The whole process leads to a >90% removal rate of macro-pollution and an overall >95% removal rate of pharmaceutical residues in wastewater.

The graph gives an overview of the performance rate against key pharmaceuticals. EE2 and ioversol have not been detected in the hospital wastewater and levels of cyclophosphamide were largely below the limit of quantification at the point of entry into the treatment process; it was therefore not possible to assess the performance against this medication.

REMOVAL OF PHARMACEUTICAL MICROPOLLUTANTS IN THE PILOT WASTEWATER TREATMENT PLANT AT THE CLINIQUE SAINT-PIERRE OTTIGNIES



CASE STUDY

02

PERACETIC ACID TO NEUTRALISE ANTIBIOTIC-RESISTANT BACTERIA

AARHUS UNIVERSITY HOSPITAL

DENMARK

Aarhus University Hospital is a global medical treatment, research and education hub located in the Central Denmark Region. It is the local hospital of the city of Aarhus and the island of Samsø, but it also provides specialised treatments to people living in the Central Denmark Region and all over Denmark. It treats 926,000 patients annually.

In 2019, the hospital investigated how peracetic acid could reduce the level of antibiotic-resistant bacteria in its untreated wastewater before central treatment at the local wastewater treatment plant. The research focused on ciprofloxacin-resistant bacteria as model organisms because ciprofloxacin, a broad-spectrum antibiotic, is commonly used in hospitals and in primary care.

It was known that ciprofloxacin consumed at Aarhus University Hospital had a significant impact on the environment when discharged with wastewater. It was therefore expected that the concentration of ciprofloxacin-resistant bacteria in hospital wastewater would be high and that the concentration of peracetic acid needed to neutralise them would also be sufficient to reduce other antibiotic-resistant bacteria with lower concentration levels.

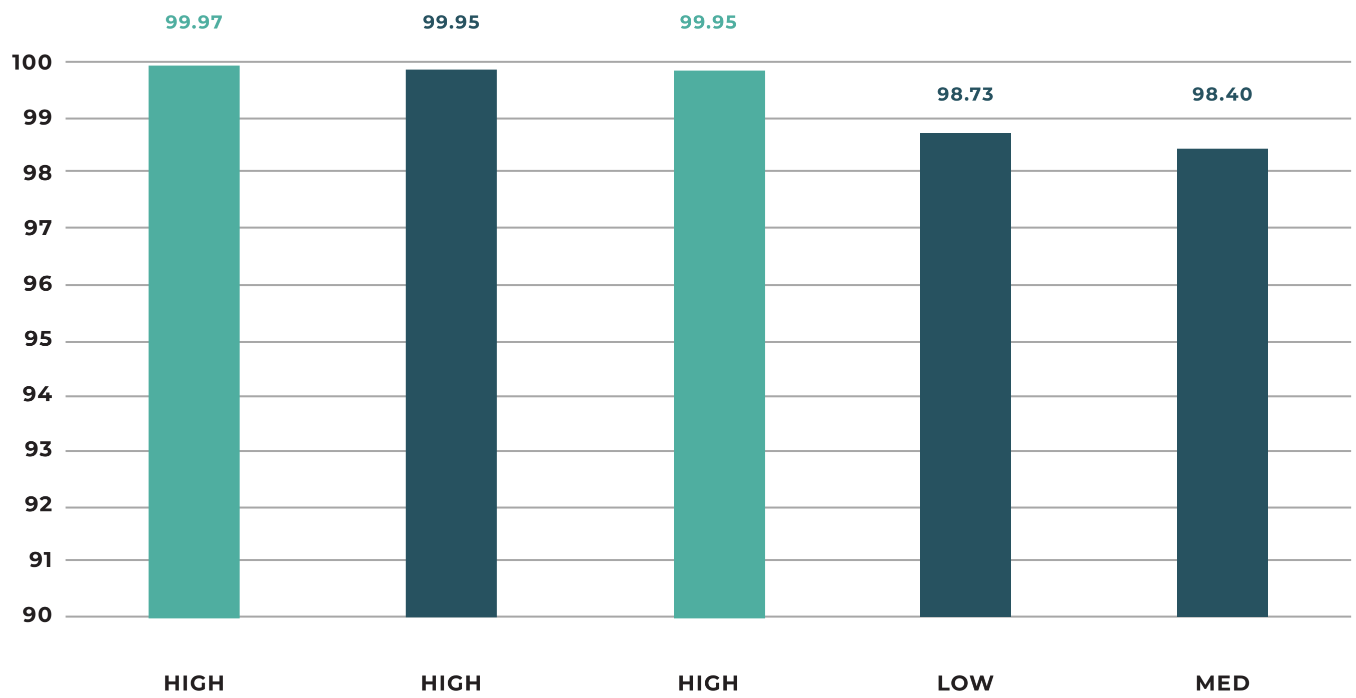
In the absence of specific regulation in Denmark, it was decided in dialogue with the waterworks Aarhus Vand and the Aarhus municipality that the level of ciprofloxacin-resistant bacteria in the hospital wastewater should reach the same level as in household wastewater. The average level of six samples of ciprofloxacin-resistant bacteria from the Viby municipal wastewater treatment plant in Aarhus, which is not influenced by hospital wastewater, was used as a benchmark.

Laboratory testing has measured the effect of peracetic acid on ciprofloxacin-resistant bacteria when injected directly into the hospital's untreated wastewater. The challenge was that the desired level of concentration had to be reached in a relatively short time frame before the wastewater leaves the hospital premises.

Testing was carried out with different concentrations of peracetic acid and corresponding reaction times to identify the optimal concentration and time.
It was demonstrated that peracetic acid at different concentrations could reach a reduction rate of between 98%-99.9% of ciprofloxacin-resistant bacteria after a reaction time of ten minutes.

REDUCTION OF CIPROFLOXACIN-RESISTANT BACTERIA (%) AT DIFFERENT DOSES OF PERACETIC ACID AFTER 10 MIN REACTION TIME

(THE COLOURS REFLECT DIFFERENT SAMPLING DAYS)

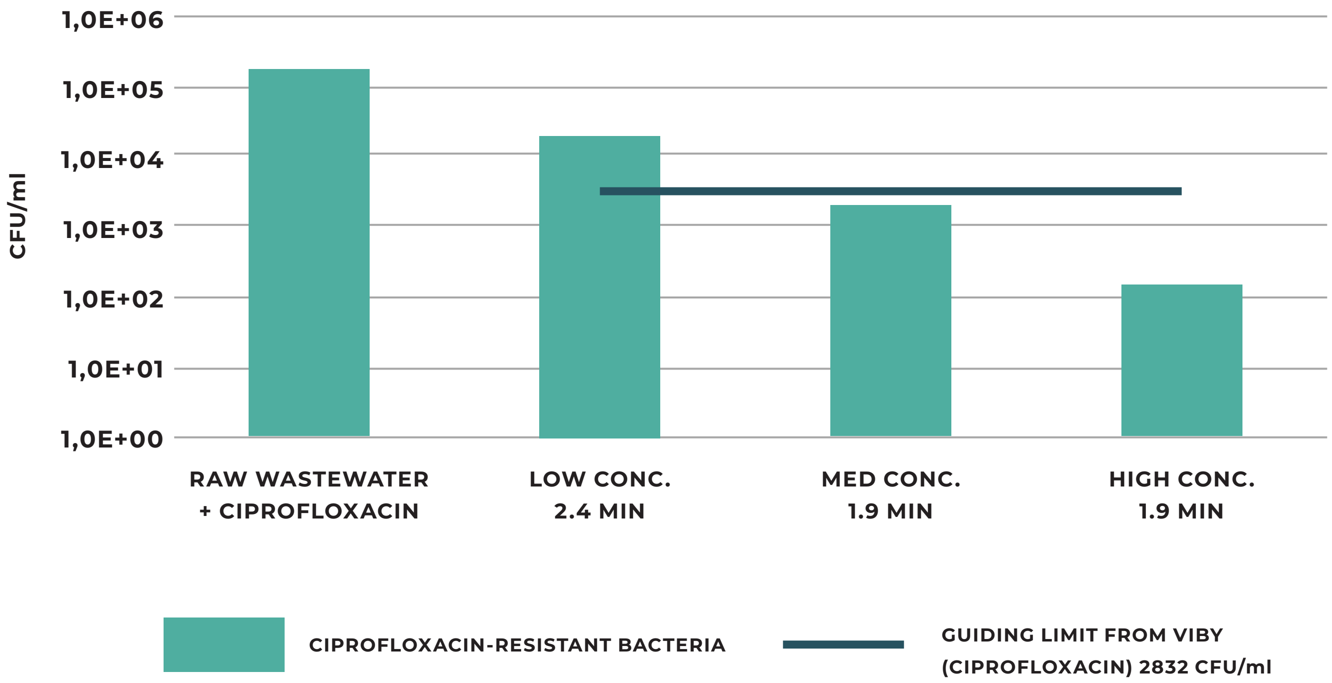


Additional experiments, with increased dosage of peracetic acid, reduced reaction times to two, three, and five minutes.

A pilot plant was installed on-site with untreated wastewater pumped directly from the sewer and directed to a closed-circuit where the peracetic acid treatment was carried out. Sampling in the plant was possible at different locations to evaluate the treatment level; the treated wastewater was then discharged to the sewage system.

Relatively high concentrations of peracetic acid were required in the pilot scale test to reach the desired threshold level with a short reaction time of approximately two minutes. Peracetic acid residues are very low after reaction – they easily react with wastewater before the biological treatment in the wastewater treatment plant, and therefore do not affect bacteria in the biological process.

NEUTRALISATION OF CIPROFLOXACIN-RESISTANT BACTERIA WITH PERACETIC ACID TREATMENT AT DIFFERENT CONCENTRATION LEVELS AFTER AROUND 2 MIN REACTION TIME



A follow-up project, *Disinfection of resistant bacteria in hospital wastewater (REBAHS)*, investigated the average amount of ciprofloxacin-resistant bacteria in household wastewater using a much larger data set from different wastewater treatment plants across Denmark.

The concentrations needed for different hospitals have been identified. A long, separate wastewater pipe from the hospital to the wastewater treatment plant acts as a reaction tank, allowing long reaction times. In the case of a shared sewer system, the disinfection must be completed before mixing with household wastewater, resulting in short reaction times. The results are currently awaiting publication.

CASE STUDY

03

URINE BAGS TO KEEP IODINATED CONTRAST MEDIA OUT OF THE WATER CYCLE

MERK'MAL PROJECT (MERKMAL-RUHR.DE)

GERMANY

Iodinated contrast media (ICM) are contrast agents containing iodine used for X-ray medical imaging examinations such as computed tomography (CT). They help medical doctors make a diagnosis by improving the visibility of blood vessels, organs, or tissues in radiology.

Due to their high biological stability, ICM are generally excreted unmetabolised into sewage systems via human urine within 24 hours after consumption. As they cannot be completely removed by wastewater treatment plants (without expensive tertiary treatment), these substances reach surface water and enter the water cycle where they accumulate over time.

ICM are not currently considered toxicologically harmful, however, adverse risks to human, animal, and environmental health cannot be completely excluded; measures to reduce water pollution from ICM align with the precautionary principle. This is particularly relevant for the production of drinking water, as the chlorination of water with a high concentration of the contrast agent iopamidol can lead to the formation of toxic by-products.

In 2016, the German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU) consulted stakeholders to develop a strategy for dealing with anthropogenic micropollutants, such as ICM, in Germany's water system. Recommendations included developing specific technical and organisational measures, such as collection/containment systems at home or in institutions.[32]

In 2017, the IWW Water Centre coordinated and launched the MERK'MAL project, funded by the German Federal Environmental Foundation (DBU), to explore whether urine bags would be a cost-effective measure to reduce ICM in water bodies. The pilot tested urine collection of patients who had taken ICM before a radiological examination in the city of Mülheim, Germany. This city was chosen because of its close location to the Ruhr river, which is used as a source of drinking water.

The project focused on an area around two hospitals and two radiology practices where ICM are used regularly: St. Marien-Hospital Mülheim an der Ruhr, Evangelisches Krankenhaus Mülheim, Radiologische Gemeinschaftspraxis Mülheim, and Medizinisches Versorgungszentrum Mülheim an der Ruhr.

Over a period of four months, 2,000 patients (both ambulant and stationary) received a pack of four urine bags together with instructions for use and feedback materials. Staff in the four participating medical facilities received training, information, and communication materials to facilitate their use. The drip-free urine bags contain substances to absorb urine and neutralise odours; they can also be disposed of in domestic waste.

The project led to significant reduction of ICM concentrations in the effluent of the local wastewater treatment plant, between 20%-34% for the mean values and 7%-33% for the median values. The individual reductions for the median values were 64% for amidotrizoic acid, 7% for iobitridol, 33% for iohexol, 31% for iomeprol, and 37% for iopromide. It was estimated that urine collection could prevent the discharge of 270kg of ICM into surface water in the city of Mülheim annually.

The urine bags are provided in packs of four and cost approximately €5.40 in radiological practices and €6.10 in hospitals per examination with ICM, which represents less than 10% of the overall treatment cost. This price estimation includes production, labour, delivery, storage, and disposal costs. This option was considered more cost-efficient than additional wastewater treatment.

The MERK'MAL project concluded that the use of urine bags in reducing ICM can complement organisational and technical efforts to reduce organic micropollutants in the water cycle. The project also helped increase awareness and interest among patients in preventive water protection measures. The ambition is now to extend the project to the entire Ruhr catchment area, which includes 29 hospitals and 58 radiological practices.

CASE STUDY

04

THERMAL PLASMA TO DEGRADE PHARMACEUTICAL RESIDUES

RADBOUD UNIVERSITY MEDICAL CENTER (RADBOUDUMC)

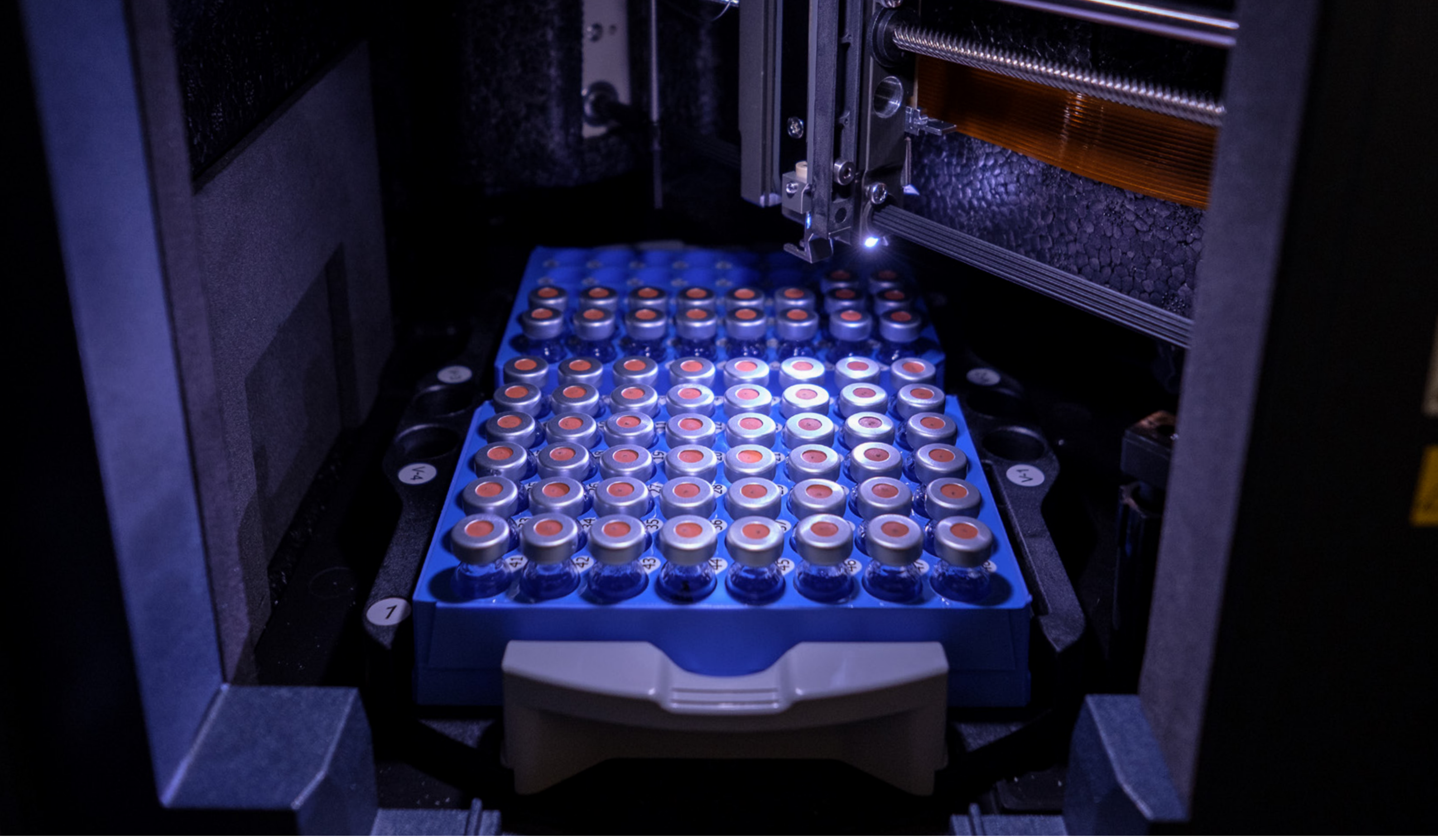
THE NETHERLANDS

Radboudumc is a university medical centre with 596 beds located in Nijmegen, the Netherlands. It specialises in patient care, scientific research, and training and education. In 2019, the hospital registered approximately 25,600 admissions and over 400,000 consultations.

The hospital's Department for Health Evidence brings together scientists to carry out cross-disciplinary research for improving healthcare and public health with a focus on research methodology and data analysis. The department includes a research group on risk assessment and molecular epidemiology that investigates environmental factors that affect public health.

In 2014, Radboudumc joined the MEDUWA-Vecht(e) project,[iii] financially supported by the INTERREG Deutschland-Nederland programme. MEDUWA-Vecht(e) aimed to find solutions to reduce or prevent the contamination of food, soil, and water by pharmaceuticals and multi-resistant microorganisms in the Dutch-German cross-border catchment area of the Vechte river.

[iii] *MEDUWA. (2021) www.meduwa.uni-osnabrueck.de/en*

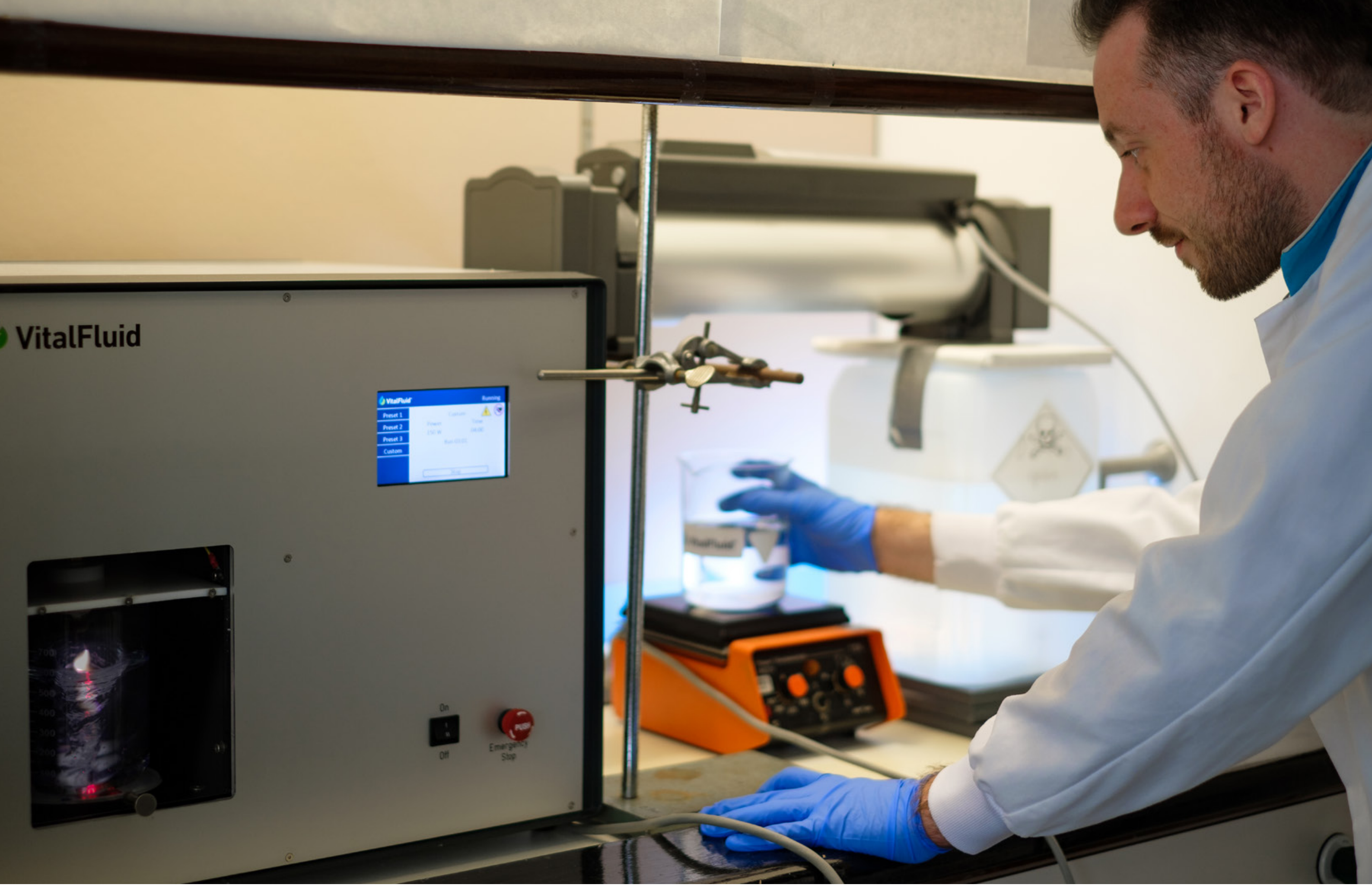


The MEDUWA consortium brought together 27 Dutch and German companies, hospitals, universities, and governmental and non-governmental organisations who developed 12 innovative solutions to communicate, measure, model, and reduce emissions of medicines and multi-resistant microorganisms in the environment.

In the framework of this project, Radboudumc's research group on risk assessment and molecular epidemiology partnered with Dutch company VitalFluid to investigate whether plasma-driven water activation could be used to degrade pharmaceutical residues from hospital wastewater before it is discharged into the sewage system.

Plasma-driven water activation is a new, advanced oxidation process that uses a hot arc (thermal plasma) in air over water to increase both reactive oxygen and nitrogen species (RONS) that dissolve in the water and break down contaminants.

In a controlled laboratory setting, researchers at Radboudumc compared the efficiency of thermal plasma with the more conventional UV/H_2O_2 treatment technique in degrading pharmaceuticals in five different matrices: Milli-Q water (purified and highly deionised water), tap water, synthetic urine, diluted urine, and synthetic sewage.[33]



The 14 pharmaceutical compounds tested were selected based on their presence in the Vechte river, wide use in hospitals, and properties:

- Carbamazepine - antiepileptic
- Ciprofloxacin - antibiotic
- Cyclophosphamide - anticancer
- Diatrizoic acid - contrast agent
- Diclofenac - nonsteroidal anti-inflammatory drug
- Doxycycline - antibiotic
- Fluoxetine - antidepressant
- Iomeprol - contrast agent
- Iopamidol - contrast agent
- Metformin - antidiabetic
- Metoprolol - beta blocker
- Paracetamol - analgesic
- Phenazone - analgesic and nonsteroidal anti-inflammatory drug
- Terbutaline - bronchodilator

The lab study demonstrated that, in water with these pharmaceuticals at a concentration of 5µg/L, all compounds were reduced or completely decomposed by both 150W thermal plasma and UV/H_2O_2 treatment.

Researchers also tested thermal plasma and UV/H_2O_2 treatment on wastewater from Radboudumc where 10 pharmaceutical residues from the above list (all but iopamidol, doxycycline, phenazone, and terbutaline) were determined at concentrations ranging from 0.08-2400μg/L by liquid chromatography-mass spectrometry.

The overall pharmaceutical degradation in hospital wastewater was nearly the same as in synthetic sewage water. The degree of degradation, however, decreased with increasing matrix complexity such as hospital wastewater where pharmaceuticals and metabolites mix with other ingredients such as detergents, hormones, and soap.

Thermal plasma was proven effective to treat most identified pharmaceuticals in hospital wastewater. The process continuously produces RONS that are used for the degradation of pharmaceutical residues and therefore was considered more advantageous than UV/H_2O_2 treatment. It is important to note that the remaining level of toxicity is the subject of further research.

A lower degradation efficiency was observed for diatrizoic acid and iomeprol due to high concentrations, but it is expected that a higher plasma power would lead to a better and faster degradation of these compounds. This work is in progress – the researchers would like to start using a much more powerful laboratory unit of 700W compared to the 150W unit they are currently using.

This study is a useful first step in the experimental validation of thermal plasma as a potential hospital-level treatment technique to complement conventional wastewater treatment in wastewater treatment plants. As a next step, Radboudumc is considering testing thermal plasma to treat wastewater streams from specific departments (e.g. cardiology, radiology) before being flushed into the sewage system.

CASE STUDY

05

A TEST BED FOR BEST PRACTICES TO REDUCE PHARMACEUTICAL POLLUTION

CAITHNESS GENERAL HOSPITAL (CGH)

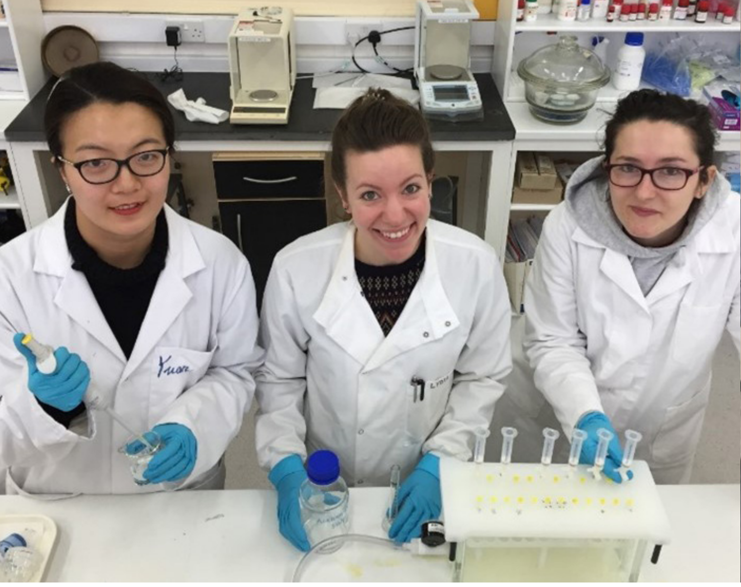
UNITED KINGDOM

In 2017, a meeting about emerging contaminants, organised by Health Care Without Harm Europe, the Highlands and Islands Enterprise (HIE), and NHS Highland in Inverness, Scotland, led to the development of the One Health Breakthrough Partnership (OHBP), a collaboration among four public agencies and two local and world-leading environmental research institutes aiming for a non-toxic environment in the Scottish Highlands.

The partners were NHS Highland, Scottish Water, the Scottish Environment Protection Agency (SEPA), HIE, the James Hutton Institute, and the Environmental Research Institute of the University of the Highlands and Islands.

The multi-stakeholder platform adopted a ‘One Health’ approach recognising that the health of humans, animals, and ecosystems are closely interconnected and interdependent. As water is a central feature of the ‘One Health’ concept and has a disproportionate importance to the rural economy in the Highlands of Scotland, it was agreed that the initial focus would be on the impact of pharmaceuticals in the water environment.

The OHBP engaged in collaborative, cross-sectorial efforts to raise visibility of the issue of pharmaceutical pollution and reduce its impact in the Scottish Highlands through an upstream public health approach. The aim was to demonstrate that it is possible to reduce the accumulation, load, persistence, and toxicity of pharmaceuticals in the environment.



Rural hospitals are a particularly concerning key point-source of pharmaceuticals entering municipal waterways because wastewater treatment plants may be less efficient than in urban areas due to their smaller size and less advanced technology.

The OHBP identified Caithness General Hospital (CGH) as a good case study to determine the impact of a rural hospital on pharmaceutical levels in municipal wastewater in the Scottish Highlands, where there is a limited understanding of pharmaceutical presence in the local environment.

CGH is an acute general hospital with 68 beds in the north of Scotland operated by NHS Highland. It provides a broad range of healthcare services to a population of 34,000 people in the local town of Wick and the surrounding district. Its water supply comes from Loch Calder, a lowland freshwater lake located approximately 30 kilometres away.

OHBP partners conducted research in CGH to determine the level of pharmaceuticals in the hospital wastewater compared to the municipal wastewater, and assess the efficiency of the local wastewater treatment plant in removing pharmaceutical residues.[16]

Eight pharmaceutical compounds were selected based on their classes, properties, usage, and regular detection in surface waters:

- Diclofenac, ibuprofen, and paracetamol - analgesics/anti-inflammatories
- Clarithromycin and trimethoprim - antibiotics
- Carbamazepine and fluoxetine - psychiatric drugs
- 17-Alpha-ethinylestradiol - hormone

All compounds, except 17-Alpha-ethinylestradiol (which was not observed above the limit of quantification), were detected in the hospital wastewater and in the influent and effluent of the local wastewater treatment plant in Wick.

The study revealed that diclofenac, clarithromycin, paracetamol, and trimethoprim were detected at maximum concentrations in the hospital wastewater and that the wastewater treatment plant had a varying capacity to treat pharmaceutical contaminants before release into receiving water. Whilst paracetamol was removed at 87%, carbamazepine and clarithromycin demonstrated <0% removal.

This work provided an initial insight into the extent of pharmaceutical residues discharged by the hospital into the municipal wastewater cycle and onwards into the environment, and encouraged NHS Highland to develop an action plan to reduce pharmaceutical pollution that includes:

- Conducting a medicine waste ‘amnesty’ scheme to prevent unused pharmaceuticals from being flushed down the toilet or sink
- Developing educational tools and public messaging to raise awareness
- Greening the formulary (list of medicines) i.e. substituting the most environmentally harmful medicines for less toxic ones
- Testing an innovative wastewater treatment filter to remove pharmaceuticals

CGH is acting as a test bed for all other hospitals managed by NHS Highland. Thanks to its pioneering work to reduce the impact of pharmaceuticals on the environment, in 2020, this hospital became the first in the world to gain the Alliance of Water Stewardship Standard, a global benchmark for environmentally and socially responsible water stewardship.

RECOMMENDATIONS

MOVING FORWARD

This report aims to shed light on how hospitals contribute to the total pharmaceutical load discharged into the environment and highlight actions that can be taken.

Pharmaceuticals play a key role in modern medicine – they are necessary tools to diagnose, cure, treat, and prevent diseases in humans. They can, however, also pose an environmental risk as pharmaceutical residues can enter the environment across their life cycle causing adverse effects on human, animal, and environmental health.

As 20% of medicines are distributed in hospitals, these institutions have a responsibility to take the lead in mitigating pharmaceutical emissions to aquatic ecosystems.

Hospitals are only responsible for a limited part of the pharmaceutical pollution in comparison with private households. Actions at the hospital level are therefore only part of the solution and will not be sufficient individually. There is a need for a multi-stakeholder approach with actions across the life cycle of pharmaceuticals to reduce pharmaceutical pollution.

However, this report highlights how many hospitals have already developed initiatives to address this issue. Drawing from the case studies featured in this report, HCWH Europe proposes five courses of action for hospitals to develop strategies to deal with pharmaceutical residues in their wastewater:

01 INVESTIGATE

Develop a better understanding of your hospital's contribution to pharmaceutical pollution in your specific area and identify priority pollutants to be addressed.

02 EDUCATE

Inform staff, particularly healthcare professionals, about the environmental effects of pharmaceuticals and teach simple practices that can help reduce unnecessary pharmaceutical emissions in the environment.

03 DEVELOP PARTNERSHIPS

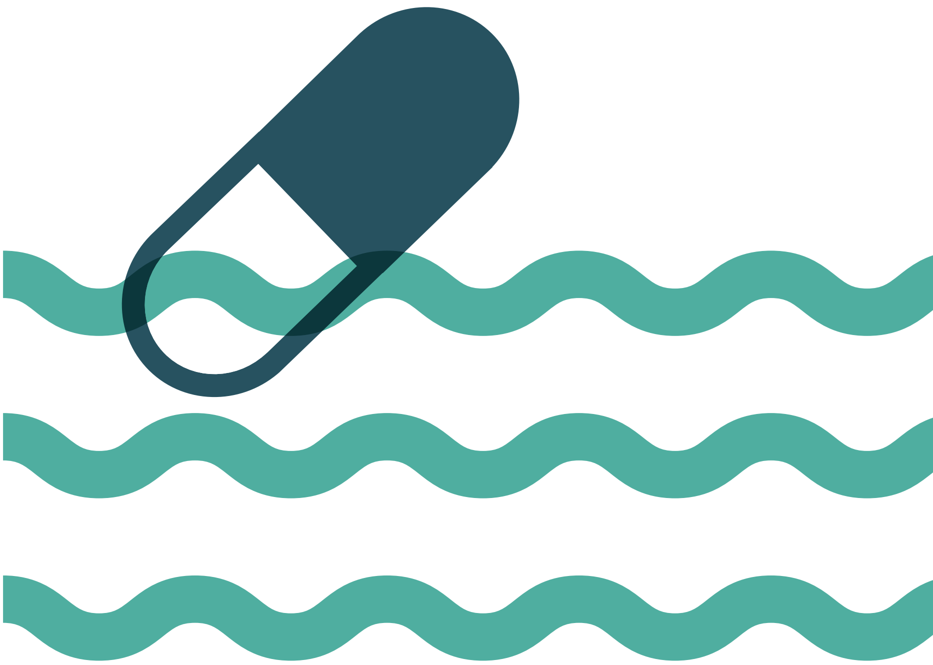
Engage in collaborative, cross-sectorial efforts with public authorities, healthcare procurers, knowledge centres, academia, and the private sector to research and develop tailored solutions.

04 RAISE AWARENESS

Increase public understanding of the issue and inform patients of actions they can take to ensure safe disposal of unused and expired medicines.

05 LEVERAGE YOUR INFLUENCE

Leverage the moral authority and purchasing power of the healthcare sector to promote the development of greener pharmaceuticals and advocate for legislative solutions that drive a rapid transition towards zero pollution.



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