WORKING PAPER 26

Water and pharmaceuticals – a shared responsibility

Many of the tools required to create a future with no negative environmental impact from pharmaceuticals are already available. This paper suggests that combining efforts along the whole pharmaceutical life cycle will not only be key to for sustainable development but also lead to increased transparency and understanding between stakeholders.

SIWI SWEDISH WATER HOUSE

Content

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Summary

The Swedish Water House, (SWH), Cluster Group for Water and Pharmaceuticals at the Stockholm International Water Institute, (SIWI), initiated a process to highlight key imperatives that could contribute to national and global reductions in the amount of pharmaceutical substances that enter water resources. We have concluded that a holistic solution is needed, where all stakeholders in the pharmaceutical life cycle co-operate, and that Sweden's extensive experience and competencies constitute a substantial resource in this regard. Many of the tools required to create a future with greatly reduced negative environmental impact are already available – it is more a matter of pushing the "green button" for the greatest overall benefit. Combining efforts along the entire pharmaceutical life cycle, including production, procurement, consumption, and wastewater treatment, will not only be key for sustainable development, but also lead to increased transparency and understanding between stakeholders catalyzing positive change.

Why water and pharmaceuticals?

Biologically active pharmaceutical ingredients, (APIs), are designed to affect various processes in the human body. The ability to interact with biological processes means that pharmaceuticals also influence other animal species. Manufactured to be stable enough to reach and interact with the relevant organ, many pharmaceuticals are not easily biodegradable and can remain in the environment for considerable periods of time.

The main emissions of pharmaceutical residues arise from their use. These substances, or their metabolites, are excreted and flushed down the toilet. The built-in resistant nature of APIs is a challenge for the standard wastewater treatment plant (WWTP). In conjunction with instances of insufficient treatment of effluent from pharmaceutical manufacturing processes, and improper disposal of unwanted/unused drugs or pills that have passed their expiration date, APIs have become ubiquitous micro pollutants in our waters, and are becoming a growing concern around the globe.

A growing number of scientific studies demonstrate the unwanted effects of APIs on organisms that are not their primary target. Hormonally active substances and antibiotics are most commonly seen as the groups of greatest concern due to their impact on the reproductive health of organisms, and through the evolution and dissemination of antibiotic-resistance. But even anxiolytics such as oxazepam have been proven to cause behavioural changes in fish species that might lead to disruption of food webs. The environmental effects of different substances are not only dependent on specific physiological effects, but also on the persistence and potential for bioaccumulation.

Pharmaceutical products are essential to modern healthcare, and their use is likely to increase in the future due to a growing ageing population. Source control approach must be sought when facing challenges posed by chemical substances, since end-of-pipe solutions alone do not provide sustainable solutions to the problem, and advanced treatment technologies lead to increased costs and energy consumption.

The holistic solution is made up of several parallel tracks involving stakeholders at different levels: all elements of the challenge need to be addressed, including authorities, the pharmaceutical industry, pharmacies, doctors, consumers, and WWTPs, (Figure 1). It proposes legislative measures as well as voluntary actions: all parties should play an active role in such a strategic approach, taking ownership and accepting responsibility.

Recognizing the concerns of environmental problems due to pharmaceutical pollution in Sweden, SIWI and SWH brought together Swedish expertise and stakeholders covering the entire pharmaceutical life cycle. The resulting Cluster Group on Water and Pharmaceuticals provided a unique opportunity to address these issues, and to identify a common way forward.

It is presumed that all stakeholders share the vision of "No unacceptable releases throughout the pharmaceutical life cycle: Manufacturing-Use-Disposal." To prevent unacceptable releases to air, water and soil, several initiatives need to be undertaken by a variety of stakeholders.

Patient health may never be put at risk in favour of a choice of drugs based on their environmental impact. Patient health and safety overrule environmental considerations, and hence there is a challenge for the relevant stakeholders to balance this dilemma.

This synthesis report, together with policy briefs and a detailed report on procurement, are available on the Cluster Group website at: swedishwaterhouse.se/en/cluster-groups/water-pharmaceuticals/.

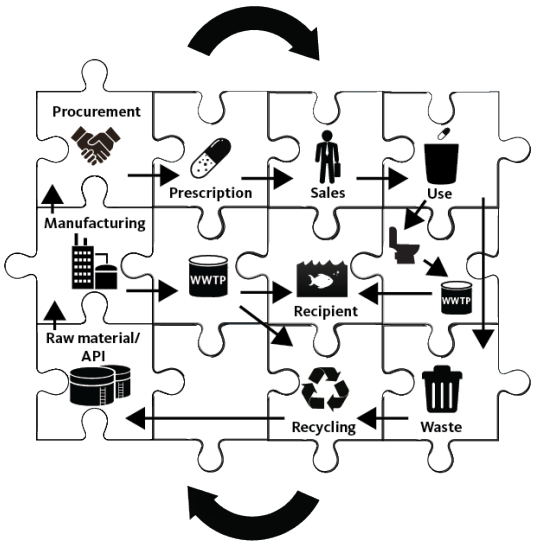

Figure 1. The pharmaceutical life cycle.

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- Sofia Schultz, Uppsala County Council

Reference Group

The following bodies advised the Cluster Group: the Ministry of the Environment and Energy, Swedish Environmental Protection Agency, Swedish Water & Wastewater Association, Medical Products Agency, The National Agency for Public Procurement, (a new authority; their role in the Cluster Group was initially filled by the Swedish Competition Authority), and Stockholm University/Mistra Pharma.

Timeline

25 April 2014 – First meeting.

17 September 2014 – Presentations by Cluster Group members.

25 November 2015 – Meeting.

23 January 2015 – Meeting.

5 March 2015 – Work plan agreed. Five focus areas are established.

10 June 2015 – Meeting.

30 June 2015 – Almedalen Week, Seminar, Water and Pharmaceuticals – Solutions for a Growing Environmental Problem.

22 September 2015 – Meeting.

4 November 2015 – Meeting.

9 December 2015 – Breakfast meeting, Swedish Parliament.

17 March 2016 – Final meeting.

12-13 April 2016 – Water and Pharmaceuticals Conference, Uppsala.

Pharmaceutical manufacturing

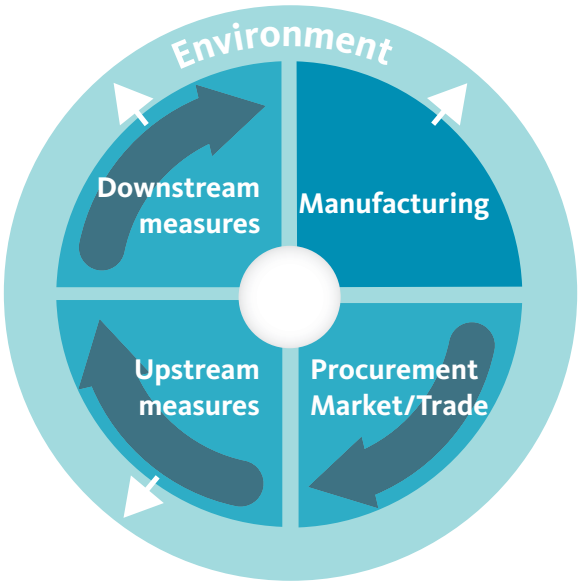
The three pharmaceutical industry trade associations – AESGP, (Association of European Self-Medication Industry), EFPIA, (European Federation of Pharmaceutical Industries and Associations), and EGA, (European Generic Medicines Association), have launched an initiative called EPS, (Eco-Pharmaco-Stewardship). EPS seeks to address environmental concerns while leaving patient access to medicines unimpeded. The programme, based on a life cycle approach, includes three main pillars:

1. Co-operation in R&D: Intelligence-led Assessment of Pharmaceuticals in the Environment (iPiE): As part of the iPiE-project, industry, academia and regulators will develop models to predict pharmaceutical substance properties and the associated environmental risk potential.

2. Managing discharges from manufacturing: The initiative will enable the sharing of best practices, benchmark operations, establish standards, and define control measures.

3. Extended Environmental Risk Assessment (eERA): Development of a scheme that will evaluate and limit the potential adverse environmental effects of new drugs, as well as "legacy" APIs, by establishing an ongoing monitoring system throughout product life cycles.

Pillar Two, managing discharges from manufacturing, could be a powerful tool to reach the "No unacceptable releases throughout the pharmaceutical life cycle: Manufacturing-Use-Disposal" vision. For the most part, the processes used to manufacture medicinal products are broadly similar all over the world. It therefore follows that potential losses into the environment from manufacturing facilities should also be equally controllable. However, this assumes a good understanding of environmental risks, and that the knowledge required to limit losses is uniformly available, and that necessary legislation is in place. In this effort, experts from several major manufacturers have shared experiences, developed a "maturity ladder" and associated guidance, to enable an enhanced understanding of existing methods, and the potential need for specific methodologies relative to the potential environmental risk posed by APIs and/or manufactured medicinal products. Manufacturing companies are encouraged to exchange knowledge of best practices for further developing the quality of their effluent control systems.



This work has resulted in the publication of an article entitled "A Risk Based Tool to Manage Active Pharmaceutical Ingredients in Manufacturing Effluent", in Environmental Toxicology & Chemistry. The article describes guidance intended to assist pharmaceutical manufacturers in assessing, mitigating and managing the potential environmental impacts of APIs in wastewater from manufacturing operations, including those from external suppliers. The tools in this publication are not a substitute for compliance with local regulatory requirements, but rather are intended to help manufacturers achieve the general standard of "no discharge of APIs in toxic amounts." The approaches detailed in the article identify practices for assessing potential environmental risks from APIs in manufacturing effluent, and outline measures that can be taken to reduce risks associated with the selective application of available treatment technologies. These measures are either commonly employed within the industry, or have been implemented to a more limited extent depending on local circumstances.

In addition to the EPS initiative, key players from the global pharmaceutical industry have backed the Pharmaceutical Supply Chain Initiative, (PSCI), with the aim of "creating a better supply chain in the pharmaceutical and healthcare industry." The PSCI is a group of pharmaceutical and healthcare companies that share a vision of better social, environmental, and economic outcomes. Collectively, PSCI members are able to share knowledge

and expertise, across the industry, to drive complex, global change more effectively than any single organization acting alone.

Much of the industry has united in PSCI to promote responsible supply chain management and better business conditions across the industry.

The Swedish National Pharmaceutical Strategy (NPS) was published in August 2011. It lists among its seven goals the need to encourage reductions in the environmental impact from pharmaceuticals. Its specific goal was to call for an action plan to address the environmental impact of medical products and pharmaceutical manufacturing:

Reduce the effects of pharmaceuticals on the environment both locally and globally
NPS encouraged voluntary improvements in the manufacturing of pharmaceuticals (task 7.2). It also proposed a review of ways to incorporate environmental considerations into the national reimbursement scheme (task 7.1).

7.1. Investigate the environmental aspects that should be considered in reimbursement of medicines (Lead: Ministry of Health and Social Affairs)
Analyze the framework of the national reimbursement scheme to take into consideration environmental concerns.

7.2. Encourage voluntary control of emissions from pharmaceutical factories (Lead: LIF)
Introduction of a voluntary environmental assessment of pharmaceutical products

The governmental Pharmaceutical and Pharmacy Inquiry, chaired by Sofia Wallström, recommended in its April 2013 report, (SOU 2013:23), that the Dental and Pharmaceutical Benefits Agency, (TLV), and/or the Medical Products Agency, (MPA), should be commissioned to evaluate if and how green economic incentives could be implemented in the generic substitution system. The report acknowledged the need for, and effort by the Research-based Pharmaceutical Industry in Sweden, (LIF), to propose an environmental assessment model to be used in such a green incentive programme.

LIF believes that a properly structured voluntary environmental premium programme would:
- Reward products contributing to reduced environmental impact from manufacturing operations
- Foster new and innovative approaches to encourage continuous improvement efforts
- Encourage company transparency through voluntary disclosure that can inform purchasing decisions

LIF delivered the proposal for an environmental assessment model, developed in collaboration with Swedish stakeholders and international pharmaceutical industry experts, to the Ministry of Health and Social Affairs at the end of June 2013. (A detailed description of the model is available as a PDF download here: skane.se/Upload/Webbplatser/Lakemedel/For_vardgivare/Lakemedelsforsorjning/Environmental_Assessment_of_Pharmaceutical_Products_Malmo_Oct_9_2013.pdf for a detailed description of the model).

Under the NPS Action Plan 2016, LIF has been commissioned to run a pilot study of the environmental assessment model developed 2011-2013 on OTC-products to evaluate, for instance, its applicability and user-friendliness. How results are validated and communicated to stakeholders are also to be evaluated. If such a pilot study on OTC-products is shown to be successful, the results could then be utilized in a system allowing for green economic incentives within the generic substitution system in accordance with recommendations in SOU 2013:23 (regeringen.se/rattsdokument/statens-offentliga-utredningar/2013/04/sou-201323/).

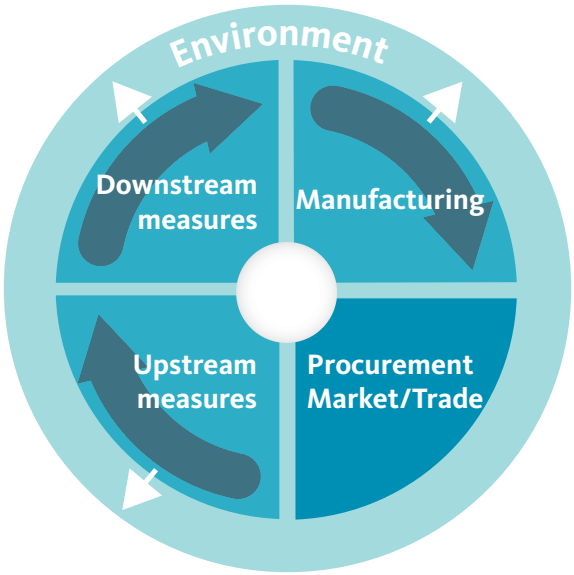
Recommendations
- Develop new business opportunities for industry, and build a market for pharmaceuticals with reduced environmental impact. Sweden is seen as a good pilot market for this.
- Develop a plan to take lessons learned from the pilot run on Over The Counter, (OTC), products to also incorporate prescribed pharmaceuticals in the assessment process, with special focus on the Swedish generic substitution system.
- Follow the development of the European Pharmaceutical Industry Initiative, EPS, and find ways to influence the programme to achieve "No unacceptable releases throughout the pharmaceutical life cycle: Manufacturing-Use-Disposal." The industry's effluent management must apply state-of-the-art wastewater treatment, (see chapter on Downstream Measures – Wastewater Treatment).
- Ensure that the development of tools for measuring and reducing pollution and resource consumption during the production of pharmaceuticals is aligned with the development of sustainability criteria for public procurement and private buyers to ensure broad application, and increased transparency and verification, (see chapter on Sustainable Procurement).
- Address the risk of anti-microbial resistance promotion from environmental releases.

Sustainable procurement

The total annual value of purchased prescription drugs in Sweden in 2015 was SEK 35.9 billion including pharmacies, (SEK 28.4 billion), and the public sector, (SEK 7.5 billion), (source: INSIKT, e-Hälsomyndigheten). The relatively low volume purchased by the public sector suggests a limited influence on suppliers. Currently, pharmacies have limited scope to require any aspect of environmental sustainability in their procurement due to the 2002 Pharmaceutical Reimbursement system. By contrast, Sweden as a whole has a leading role in this area due to its advanced sustainability policies, and the international influence of the sustainable procurement praxis. Therefore, the focus of the work was on the opportunities and processes available for the public sector to set and manage environmental procurement requirements. Setting similar requirements for pharmacies would require a review of the Pharmaceutical Reimbursement system.

The Swedish public sector encourages sustainable development. In that spirit, procurement of products and services are produced sustainably and under responsible conditions. The Swedish public sector has highlighted pharmaceuticals as a prioritized area in terms of social and environmental risks. While the general vision for sustainable procurement is clear, the recommendation is to develop concrete targets in dialogue and co-operation with the industry and other stakeholders. The Swedish public sector needs to further co-ordinate internally regarding requirements for sustainable procurement, partly to increase its influence, but also to make participation in the public procurement process more accessible to suppliers. It is further recommended that all actors in the public sector should develop common methods for follow-up with a view to further streamlining the process. Co-operation with respect to requirements and follow-up should also include a link to targets, risk assessments, and protocols for scenarios where stakeholders fail to meet agreed standards.

It is important to take into account industry conditions to understand where sustainable procurement and follow-up processes should be initiated. Creating a platform for dialogue and co-operation between the public procurement authority, industry, and other stakeholders enables a continuous and common understanding of challenges and opportunities arising during sustainable development programmes. The National Agency for



Public Procurement is suggested as the focal point and developer of such initiatives. Sustainable procurement of pharmaceuticals should be viewed as an iterative process where demands and follow-up evolve according to feedback and dialogue between stakeholders.

It is recommended that demands are put in proportion to what can be followed-up by the public sector. To follow-up set standards is fundamental to accredit the requirements and achieve desired effects. To set standards that are not followed-up has been proven not only detrimental to sustainable procurement as such, but also diminishes their overall legitimacy. Follow-up of set standards further contributes to clarify their business case to the industry, and is an area in need of increased resources and clearer co-ordination.

The lack of transparency to the general public within the pharmaceutical industry presents a huge challenge that restricts the number of options available for sustainability throughout the supply chain. Complex supply chains present further obstacles including traceability, limiting information **about** manufacturing origin, and how active pharmaceutical substances are manufactured. Transparency is also affected by the principle of public access to official records where confidentiality during public procurements cannot be guaranteed. Environmental information could be considered business sensitive, as could information regarding supply chains and internal

work processes. Another area requiring special consideration is the ability of parallel importers to meet current environmental and social standards. To date, parallel importers maintain limited capabilities to retrieve necessary knowledge about conditions throughout the supply chain. Procurement policies have to specify what part/parts of the supply chain need to meet environmental and social standards, which in turn puts greater demands on knowledge about what the supply chain looks like, and what the social and environmental challenges are.

Recommendations

In conclusion, a number of factors have been identified as important for relevant authorities to highlight in their future work on sustainable procurement. It is recommended that efforts be focused on:

- Creating opportunities for pharmacies to require sustainable public procurement of prescribed pharmaceuticals.
- Through dialogue and co-operation, develop the process of sustainable public procurement between authorities, pharmacies, public sector, industry and other stakeholders by:
  - Creating a platform for co-operation, (e.g. at National Agency for Public Procurement in Sweden)
  - Developing clear and shared criteria for sustainable procurement of pharmaceuticals
  - Developing clear and shared methods for follow-up including goals, risks, and protocols for scenarios where stakeholders do not meet set standards
  - Developing tools for sustainable procurement: risk assessment and follow-up
  - Investigating regulations regarding transparency and documentation
  - Clearly defining and communicating the legal framework for sustainable procurement to procurers and practitioners
  - Communicating the goals and purpose of sustainable procurement, (from vision to specific targets)
  - Co-operation with leading international stakeholders in sustainable procurement of pharmaceuticals, (e.g. academia, NHS, UNDP, HCWH, WHO)

Upstream measures to reduce emissions

Besides production sites for pharmaceuticals as point sources, the effluent from households via WWTP has been recognized as the main source for discharge of pharmaceuticals into the environment. Improving the treatment of pharmaceutical residues in wastewater would be one way to reduce emissions. Another key to minimizing the release of pharmaceuticals into the environment is to be found upstream, at the source of the pollution, and not only because treatment technologies require investment and lead to severely increased energy use and costs. Different examples of upstream interventions include:

Specific environmental impact or risk assessments:

- Research programmes for the development of easily degradable pharmaceuticals, and the introduction of standards for environmental labelling of pharmaceuticals.
- If possible from a patient health and safety standpoint doctors should prescribe more environmentally friendly pharmaceuticals.
- Apply environmental criteria during procurement/purchase of pharmaceuticals.

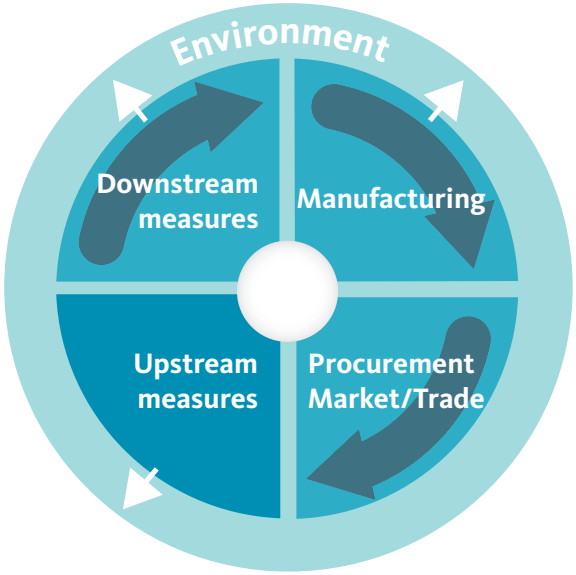
Point sources with high impact:

- Investigate the possible effects of additional wastewater treatment or avoidance of liquid discharge at point sources of specific pharmaceutical use at medical facilities, such as retirement homes, infection, psychiatric and oncology clinics.

Optimize and reduce total consumption of pharmaceuticals:

- Prescribe smaller start packs of medicine for first time users.
- Prescribe physical activity and other behavioural changes for healthier lifestyles.
- Increased public information regarding collection of unused or expired medicines.
- New business models, (e.g. for pharmacies), as health consultants instead of retailers.
- IT-based "E-health" tools for more efficient healthcare.

A pharmaceutical survey is currently being conducted by a member of the Cluster Group (IVL Swedish Environmental Research Institute) at a retirement home in Stockholm to determine whether there are any benefits of pharmaceutical surveys as upstream measures to minimize discharge of pharmaceuticals.



The noPILLS research programme (2015) presented evidence that the willingness among the general public and professionals of "doing the right thing" was widespread. However, the study also showed a lack of resources placed at their disposal to access data, information on patterns of use, exposure scenarios and potential hazards of pharmaceuticals. In their policy brief, Mistra Pharma recommend that environmental risk assessments, in addition to information regarding where pharmaceuticals are manufactured, should be made public for external review. Increased transparency would encourage companies to consider environmental responsibility throughout the supply chain.

The Swedish Association of Local Authorities and Regions (SKL) Pharmaceutical Committees compiles lists of several hundred recommended pharmaceuticals for common diseases, to be used by prescribers and patients. The initiative has already been proven to be effective in reducing healthcare costs, (e.g. Stockholm County Council, SCC), and is also highly recommended by the European Environment Agency as a practice to be extended across Europe.

LIF publishes environmental information on pharmaceuticals, including risk assessments, at fass.se.The environmental classification on this site is a self-declaration

system, meaning that each pharmaceutical company is responsible for the environmental information published on it. All such data published on the site are reviewed by an independent third party to ensure quality and coherence.

The environmental information on fass.se is used to perform a risk assessment of pharmaceutical substances. These assessments can be used to incorporate environmental considerations when county councils and regions develop their lists of recommended pharmaceuticals for common diseases to be used by prescribers. Use of the recommendation lists is not mandatory, but more than 80 per cent of the prescribed pharmaceuticals in the SCC are included on the lists. The recommendation lists primarily focus on medical benefits and side effects, but when multiple pharmaceuticals have the same benefits, the information from the environmental classification can be considered.

Although national agencies and authorities have recommended several upstream measures, and some have already been implemented at a regional level, the EU lacks a coherent implementation plan. To support decision makers, the outcomes of an increasing number of research projects in the field could be more useful if there was a European database dedicated to the profession.

Two MSc theses, (by Goran Jassim and Andrew McDonnell), under the Karolinska Institute Programme for Bioentrepreneurship, have been conducted to explore the potential for marketing "green pharmaceuticals."

Goran Jassim showed that there is a consumer/patient interest for "green pharmaceuticals." Andrew McDonnell's work concluded that a business case utilizing a well-known pharmaceutical product could give visibility and market reach. He also found that the incorporation of clear legislation is vital for green pharmaceuticals, and that third party verification, if possible, could provide a tool for market strategy and allow greater transparency.

Recommendations

- Educate and raise awareness in pharmacies, healthcare centres, hospitals, retirement homes, consumer associations and patient associations about the environmental risks associated with the use of medication – without compromising patient safety.
- Consumer associations could also play a role in raising awareness of how to dispose of unused and expired drugs properly.
- Promote and improve environmental risk assessment of pharmaceuticals more actively.
- Impose a prescription requirement on pharmaceuticals with high environmental impact.
- Further promote healthier lifestyles and physical therapy; if applicable, such an approach would be desirable to reduce the use of certain types of medicines.
- Recommend and promote the use of smaller starter packs when initiating medications, thereby reducing the risk of unused drugs being disposed by households inappropriately.
- Promote collection systems for unused/expired drugs. All EU member states have been required to provide collection systems for pharmaceuticals since 2004, but there is a significant lack of compliance.
- Consider alternative measures for handling excreted pharmaceutical waste. One option would be to collect urine and faecal matter in separate containers. This is especially important for people that lack basic access to sanitation.

Downstream measures – wastewater treatment

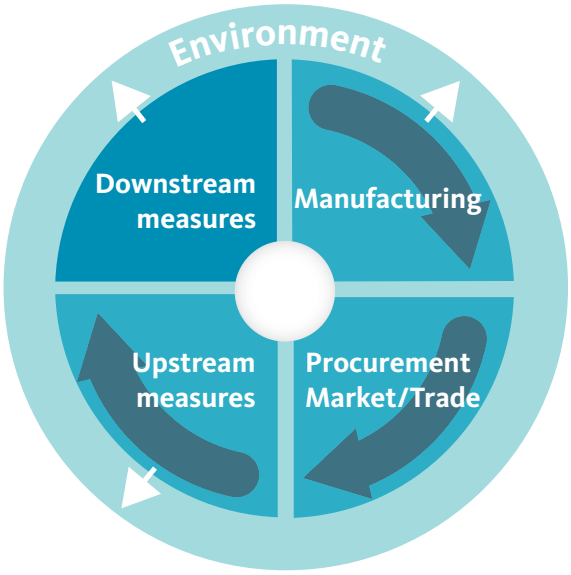
Wastewater treatment should be holistically addressed at source, rather than applying advanced, often energy intensive, treatments that require continuous and unsustainable upgrades, whenever new problems arise from other emerging pollutants, for removing pharmaceuticals at wastewater treatment plants. Many end-of-pipe solutions do not solve the environmental problem – rather, they only shift focus. Furthermore, it would result in decreasing public awareness and decision makers losing interest in the challenges the water sector faces.

The precautionary- and polluter-pays principles are key elements underpinning European environmental policy. The public debate in the 2013 review of the Priority Substances Directive has shown diverging opinions when it comes to identifying who is the polluter in the case of pollution originating from pharmaceuticals.

To reduce emissions, discharges and losses of pharmaceutical products to the aquatic environment, there is a need for coherent actions at several different levels.

Solve the challenge in a sustainable way – with the two necessary parallel tracks – upstream work and advanced wastewater treatment technology. The WWTP is the last step between the urban area and our waterways, but for us to achieve a sustainable society, the WWTP can never be the only step. In order to cope, a number of measures are required to find the most efficient upstream approach possible to enable everyone, from the small countryside household to the urban apartment complex, to cope with the leakage of pharmaceuticals into the environment. Anything that poses a negative impact on the environment in the long run, will also pose a negative impact on humans in the long run. Wise use of pharmaceuticals should always be at the centre of discussion.

We have reached a point today were we have a pretty good idea of how to most effectively treat wastewater containing pharmaceutical residues. Different treatment protocols have different efficiency rates and significantly different costs and energy requirements. Since energy consumption can increase between two to 10 times compared with current treatment technology, it is important to weigh the need for WWTP efforts with other environmental objectives, such as energy and climate change. The environmental objectives can be helpful for prioritizing treatment plants with the highest output of



environmentally harmful pharmaceutical residues in their effluent.

In terms of advanced wastewater treatment in sensitive receiving water scenarios, the most promising additional treatment processes applied to remove pharmaceutical residues from conventionally treated wastewater is low dose ozonation, with subsequent purification of residues through a biological treatment process, or filtering through activated carbon. Processes only applying activated carbon filter treatment have also shown positive results. These treatment processes are also able to clean water containing several other groups of organic pollutants. If a reduction in consumption patterns can be made of the most used, and also of the most resilient environmentally harmful drugs – through instruments for better use of pharmaceuticals such as preventive measures, pharmaceutical surveys, prescription requirements for environmentally harmful drugs, (see the chapter on Upstream Measures) – significantly less energy intensive biological treatment steps could be used. One such technique is the Moving Bed Biofilm Reactor (MBBR). It is claimed that MBBR methods can remove drugs from wastewater without causing adverse effects for the aquatic environment.

Recommendations

- Publically promote the fact that end-of-pipe treatments alone do not solve environmental problems. Pharmaceutical substances can be eliminated in WWTPs only partly even with additional treatment steps. Remember that households outside sewer network as well as sewer overflows also play a role.
- When advanced wastewater treatment may be considered, as for sensitive receiving waters, activated carbon and ozonation are considered the most promising methods for the removal of pollutants. MBBR technology is also a promising approach for tackling many pharmaceuticals. Best results are achieved by using a combination of an oxidation technique, (e.g. ozone treatment), and a supplementary adsorption technique, (activated carbon filtration). The average removal rate of all pharmaceuticals using these two techniques is between 80 and 90 per cent.
- There is a need to study removal technologies aiming to develop cost- and energy-efficient and sustainable methods of pollutants removal. Water utilities are already doing a lot of research related to such treatment technologies.

More information:

- about pharmaceuticals and the environment from the Swedish Environmental Agency: naturvardsverket.se/Sa-mar-miljon/Manniska/Miljogifter/Organiska-miljogifter/Lakemedel/
- about pharmaceuticals and environment from the Swedish Agency for Marine and Water Management: havochvatten.se/hav/fiske--fritid/miljohot/farliga-amnen/lakemedel.html
- about pharmaceuticals and environment from Swedish Medical Products Agency: lakemedelsverket.se/overgripande/Om-Lakemedelsverket/Miljoarbete/Om-lakemedel-och-miljon/
- about WWTP and treatment strategy from the Swedish Water & Wastewater Association: vav.griffel.net/filer/SVU-rapport_2014-16.pdf svensktvatten.se/FoU/SVU/Rapporter/Rapport-sida-dold/SVU-rapport-2015-09t21/?utm_source=nyhetsbrev&%20utm_medium=epost&%20utm_campaing=SVU-rapport-2015-09sida&utm_source=idrelay&utm_medium=email&utm_content=SVU-rapport%2B2015-09&utm_campaign=nyhetsbrev
- EurEau: EurEau's Contribution to the European Commission Strategic Approach on Pharmaceuticals in the Environment: eureau.org/administrator/components/com_europublication/pdf/d127f-8273bad53d568242fdc3a3c9f26-2014.05.26_PP_on_Pharmaceuticals.pdf

Monitoring pharmaceuticals in water

Pharmaceuticals occur globally in the environment, and not only in industrialized countries. A global review of available data showed a varying occurrence of a range of pharmaceuticals in 71 countries all over the world. Data availability is greater in western countries, but is also increasing in low and middle income countries. In most countries, certain pharmaceuticals prevail at concentrations above PNEC in surface waters, indicating a risk for adverse ecotoxicological effects in these locations. Different pharmaceutical groups have been in focus in different UN regions, for example antibiotics in Asia and estrogens in Africa. Urban wastewater discharge is the dominant emission pathway, while discharge from manufacturing can result in very high levels. Pollution with antibiotics can have effects on resistance development, with potentially global implications, despite the local nature of discharges. The accessible data on production or consumption used for this global survey is not sufficient for regional analysis of relevant pharmaceuticals.

To establish a baseline for Sweden, monitoring and screening data from different county councils were reviewed. This uncovered an urgent need for a coherent national protocol for analysis of pharmaceutical substances in water matrices. The investigation revealed how different interests, methods, needs, and budgets for analysis amongst county councils limit the comparability of results. About half of the 59 studies published between 2002 and 2013 used for the baseline analysis, had to be disregarded due to significant lack of comparable information. Sufficient information for a baseline for about 100 active substances was found, but the lack of systematic and coherent measurements, and the variety of times, points and laboratories involved led to a large variation in the final results. Nevertheless, an estimate of occurrence of the substances on the European Watch List was made available.

The Nordic Council of Ministers has conducted a survey of available data on pharmaceuticals, (and personal care products), in Nordic waterbodies, and reached similar conclusions. A large amount of data is available, but a systematic approach and a risk-based prioritization for monitoring of substances with environmental concentrations above PNEC is needed. The report suggests the collection of international data in an online database to enable countries to follow trends and observe effects of other nation's contingency actions.

Photo: iStock

Pharmaceutical pollution levels in European rivers assessed: Concentrations of three pharmaceuticals, (ethinylestradiol, estradiol and diclofenac), have been mapped in a recent study of European rivers. Researchers predict that levels of ethinylestradiol, a contraceptive and hormone replacement drug, could exceed the suggested environmental quality standards in the EU Water Framework Directive in 12 per cent of the total length of Europe's rivers.

Working group on environmental indicators within the Swedish National Pharmaceutical Strategy: To improve the quality and coherence of environmental monitoring, a working group under the National Pharmaceutical Strategy has suggested a list of 22 substances that should be monitored. This list covers a range of substance categories, and is based primarily on already available time-series, the new European Watch List, and suggestions from a network of county councils. General criteria for substances to be added to the list were relatively large volumes being used, and the suspicion of negative environmental impacts.

Political initiatives addressing the problem (specifically monitoring)

- National Pharmaceutical Strategy states in the chapter on environmental aspects that indicators are needed.
- The Swedish Environmental Objectives cover several

water and chemicals related areas that serve as a base argument for tackling the problem of pharmaceuticals in the environment.
- The Swedish Generation Target and the Policy Coherence for Development, (Politik för global utveckling, PGU), serve as a base argument for not exporting environmental and health risks to other countries.
- The European Watch List requires monitoring of a range of substances. The Swedish Agency for Marine and Water Management has gone one step further and established national maximum levels for some of the pharmaceutical substances based on the suggestions that led to the Watch List.
- Several initiatives in the Baltic Sea region are starting to focus on pharmaceutical pollution and seek upstream solutions to reduce prevalence in the Baltic Sea. These include HELCOM, the EU Strategy for the Baltic Sea Region etc.

Enabling conditions and political recommendations
- A systematic and unified approach with an agreed priority list will increase the quality of monitoring, and make it more cost efficient. But still, the programme needs to be funded through continuous monitoring initiatives and co-ordinated with the monitoring of priority chemicals according to the EU Water Framework Directive. The value of monitoring increases significantly when its continuity and quality lead to statistically usable time-series. This information is crucial for evaluation of success or failure of interventions.
- Co-ordination on a national level is necessary, although implementation can be commissioned to regional administration and/or consultants. Additionally, transboundary co-operation, for example on a European level, or generally between neighbouring countries, will improve data comparability.
- Until more knowledge about cocktail effects of pharmaceuticals, (also in combination with other pollutants), is available, precautionary risk margins are especially important in environmental risk assessment as implemented by risk factors of up to 1,000 in the calculation of predicted no effect concentrations (PNEC).
- Growing knowledge about effects and prevalence must lead to a decision making process:
  - To define maximum levels for wastewater recipients (taking into account cocktail effects of substances with similar modes of action, if possible).
  - To prioritize those WWTPs in most urgent need of advanced technology.

Recommendations
- Quality requirements: Current screenings and attempts to obtain an overview of the occurrence of pharmaceuticals in the environment must be co-ordinated and lifted to systematic monitoring, with clear description of the task and quality requirements/methodological standards if usable time-series are to be produced.
- Decision making process: Following the working group's process, priority substances should be identified based on available time series, legal requirements and relevance of the substance groups, (e.g. antibiotics, hormones, bioaccumulation risk, high volume products on domestic market, key products for domestic industry). A mechanism for revision should be included to adapt to new knowledge about the environmental effects of specific substances.
- Environmental risk assessments should be developed further to take biological effects of pharmaceuticals into account beyond the current focus on ecotoxicity that is derived from chemicals regulation.

Acronyms

AESGP	Association of the European Self-Medication Industry
API	Active Pharmaceutical Ingredients
eERA	Extended Environmental Risk Assessment
EFPIA	European Federation of Pharmaceutical Industries and Associations
EGA	European Generic Medicines Association
EPS	Eco-Pharmaco-Stewardship
EU	European Union
FASS	Farmacevtiska Specialiteter i Sverige (Pharmaceutical Specialties in Sweden)
HCWH	Health Care Without Harm
HELCOM	Baltic Marine Environment Protection Commission
IKEM	Innovation and Chemical Industries
iPiE	Intelligence-led Assessment of Pharmaceuticals in the Environment
LIF	The Research-Based Pharmaceutical Industry
MBBR	Moving Bed Biofilm Reactor
MPA	Medical Products Agency
MSc	Master of Science
NHS	National Health Service
NPS	Swedish National Pharmaceutical Strategy
OTC	Over-The-Counter
PGU	Policy Coherence for Development (Politik för global utveckling)
PNEC	Predicted no-effect concentration
PSCI	Pharmaceutical-Supply Chain Initiative
R&D	Research and Development
SEK	Swedish Krona
SIWI	Stockholm International Water Institute
SKL	Swedish Association of Local Authorities and Regions
SOU	Swedish Government Official Reports
SWH	Swedish Water House
TLV	Dental and Pharmaceutical Benefits Agency
UNDP	United Nations Development Programme
WFD	EU Water Framework Directive
WHO	World Health Organization
WWTP	Wastewater Treatment Plant

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About the SIWI Swedish Water House Cluster Group Water and Pharmaceuticals

SIWI Swedish Water House has brought together Swedish experts and stakeholders in pharmaceuticals and water management. The aim was to promote recommendations for more effective implementation of environmental regulations limiting pharmaceutical pollution. Representatives from SIWI Swedish Water House, Innovation and Chemical Industries (IKEM), Apotek Hjärtat, Pfizer Health AB, Fresenius-Kabi, The Research-Based Pharmaceutical Industry (LIF), Stockholm County Council (SLL), Swedish Environmental Research Institute (IVL), Käppalaförbundet, Uppsala University Hospital, and Uppsala County Council are core members of the group.

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