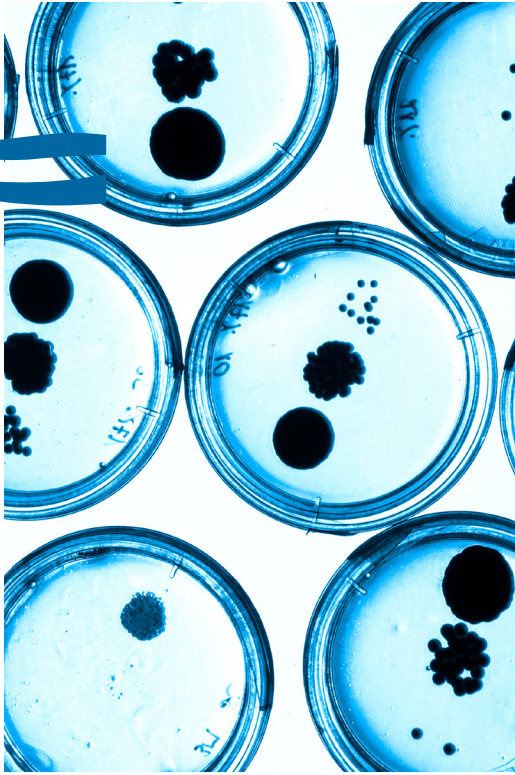


Antibiotic resistance: the importance of water



Antibiotic resistance is becoming one of the biggest threats to global health, with experts warning it will “nullify the progress of over a century of modern medicine”. Unrestricted and untraced use of antibiotics, and uncontrolled effluents from pharmaceutical manufacturing accelerate resistance to antimicrobials. Effective management of these sources combined with efforts to reduce demand for antibiotics are key to slowing this dangerous trend.

Antibiotics and bacteria – a dangerous arms race | The number of different bacteria developing resistance towards antibiotics is growing. In the European Union approximately 25 000 people die every year due to reduced efficacy of antibiotics. Globally, the number is estimated to be 500 000, of which 200 000 are new-borns.

This threatens the global healthcare system at its very core. Treatments such as chemotherapy, organ transplants and hip replacements may turn from life-saving to life-threatening. Common diseases like pneumonia have already become more difficult to treat. Since February 2017, the World Health Organization (WHO) has listed pneumonia as a disease that urgently needs new antibiotics.

If this trend continues there is a risk that 50 million people will die due to antimicrobial resistance by the year of 2050 according to a British report published by Jim O’Neill in 2016; 15 times more than today. The World Bank states that the societal costs in many countries will be large enough to significantly impact the global economy.

Mappings from institutes for infectious disease control around the world show a clear correlation between the amount of antibiotics consumed and the prevalence of antibiotic resistant bacteria. The situation is worsening since no new types of antibiotics have been discovered over the last 30 years.

Understanding the phenomenon – fungi, factories and farms | The phenomenon of bacteria developing a resistance to antibiotics does not per se relate to human activities. It is an evolutionary process happening in nature. Microorganisms such as fungi and bacteria are producing antibiotics to eliminate their competitors. Resistance becomes a way to protect oneself. This in itself is not alarming. However, the rate at which pathogenic

bacteria are exposed to antibiotics in low doses, due to presence in the environment, allows them to build resistance faster than new antibiotics can be developed.

In September 2016, antibiotic resistance was given attention in the United Nations General Assembly, as officials from 193 countries pledged to tackle this challenge. The accelerating resistance to antibiotics is driven by unrestricted and untraced use of antibiotics in humans, animals and agriculture, but also from uncontrolled effluents from pharmaceutical manufacturing. As resistance can spread quickly, the uncontrolled release of insufficiently treated wastewater locally will not only affect neighbouring areas, but also lead to consequences on national and global levels.

Up to 90 percent of consumed antibiotics end up in faeces and urine. They are then passed on to wastewater treatment plants, or often directly into water sources. Even when wastewater is treated, treatment plants are not designed to treat for pharmaceuticals. Wastewater is often recycled into water for irrigation or drinking water, without proper treatment this water can be an additional source of antibiotic exposure.

According to the Swedish Water & Wastewater Association, around 15 tonnes of antibiotics ends up in Swedish sewage sludge every year. This sewage sludge, once treated, is often used as an agricultural fertilizer. A research project in Skåne, Sweden, which will continue until 2019, will assess if this application of sewage sludge is increasing the presence of antibiotic resistant bacteria in the soil.



Other countries are even more exposed. The race towards cheaper pharmaceuticals have resulted in a large share of antibiotics being produced in low-income countries where factories lack sufficient wastewater treatment. This results in large quantities of antibiotics being discharged directly to the environment.

Joakim Larsson, professor and director of Centre for Antibiotic Resistance Research in Gothenburg, has published a number of studies that highlights the breadth of the problem. Not least in India, which together with China, produce the majority of all antibiotics. Outside of the wastewater treatment plant that receives water from 90 pharmaceutical manufacturers in Hyderabad, researchers found bacteria that had developed resistance to 30 out of 39 tested forms of antibiotics. The bacteria were not pathogenic but the resistance genes can be transmitted to other bacteria in the environment. Resistance genes can also be transmitted by animals drinking the water, irrigation or by people who are in contact with the water or the sediment.

Particularly worrying are the high levels of antibiotics targeting multiple types of bacteria (broad-spectrum antibiotics) that have spread to the groundwater and drinking water in the Hyderabad area.

Researchers have established that 50 percent of all travellers to India, and every third person who travels to Southeast Asia, return home carrying antibiotic resistant bacteria.

Manure from animals that have been treated with antibiotics can also be a source of antibiotic resistant bacteria which in turn are transferred to water sources. Studies have shown that antibiotic resistant bacteria can travel long distances in water.

Aquacultural production of fish and shellfish is increasing the levels of antibiotics in the water and promoting the development of resistant bacteria. Antibiotics are distributed through the food or are simply poured into the water where fish are cultivated.

The volume of antibiotics used in aquaculture varies between countries. Countries with low volumes such as Norway and Scotland are using 0.02 – 0.39 grams antibiotics for every tonne of fish. Chile on the other hand have the highest use of antibiotics, up to 33 000 times higher than practices of Norway and Scotland.

What can be done – examples from Northern Europe | Up to 60 percent of post-consumer antibiotics that pass through a treatment plant end up in sewage sludge, the remaining flows out with the treated water. There is observable growth in antibiotic resistant bacteria in post-treatment water. Wastewater treatment plants are therefore viewed as a source of spread of antibiotic-resistance to the aquatic environment.

To equip wastewater treatment plants with systems able to break down pharmaceuticals is one way to reduce the impact. Nykvarnsverket in Linköping, Sweden, is one of the first wastewater treatment plants that has introduced an extra step in the process to filter pharmaceuticals.

In Switzerland, there is a drive by the government to minimize pharmaceutical residues in surface water. 100 wastewater treatment plants will be equipped with an extra step to filter out pharmaceuticals in the treatment process over the next 25 years.

Another technique is to use enzymes that can break down anti-



Antibiotics while still in the toilet. Tailormade enzymes are merged into a block, which can be fastened to the toilet bowl. During the spring and summer of 2018 this method will be tested in 270 toilets at the Uppsala University Hospital in Sweden.

In Denmark, Nya Herlev Hospital outside of Copenhagen has invested in a treatment plant, which can be used for filtering both antibiotics and antibiotic-resistant bacteria (membrane-bioreactor in combination with ozone and activated coal).

Changing behaviours through demand | Large single buyers have a unique opportunity to change the emissions practice of pharmaceutical companies. Pharmaceuticals are often centrally

purchased, yet environmental criteria are rarely used in the product selection process. However, due to their purchasing power, countries like Sweden can apply pressure on manufacturers and suppliers to require environmental practice to be disclosed.

Environmental impacts are also missing in global standards like the Good Manufacturing Practice (GMP), where the focus is exclusively on quality and patient safety. Information on where pharmaceuticals, or their ingredients, have been produced are currently not required to be publicly available, although the site of production can be an indicator of environmental practice.

Solving the problem at its source

A lack of reliable access to clean drinking water results in the spread of diseases that often requires treatment with antibiotics, and thus, increases opportunity for their entry to the water supply. This includes 494 million cases of diarrhoeal disease in India, Nigeria, Indonesia and Brazil every year. According to WaterAid, the volume of antibiotics used to fight these diseases could be reduced by 60 percent if more people had reliable access to clean water and sanitation.

Clean water together with good hand hygiene are essential weapons in the fight against increasing antibiotic resistance.

If fewer people are infected with pathogenic bacteria the volume of consumed antibiotics will decrease. This will in turn reduce the risk of pathogenic bacteria developing antibiotic resistance, which would decrease the threat of a post-antibiotic era where common diseases such as pneumonia and sepsis can no longer be cured.

Challenges and opportunities for the pharmaceutical industry

Reducing emissions from antibiotics production is a special challenge, due to the strict regulation and certification that focuses on quality and safety, but does not cover environmental aspects. Under this framework, it is difficult, if not impossible, to effectively impose sustainability criteria on pharmaceutical products. Public procurers have difficulties formulating relevant and traceable criteria and often lack resources for systematic compliance control; subsidy or reimbursement schemes usually focus on lowest available price; and pharmacies lack access to relevant information in order to offer their customers an informed environmental choice for over the counter products. For the industry, this has led to fragmented approaches by buyers covering different fields of concern and different levels of expectation, and in consequence, growing resources being required for customer dialogue and audits.

Given the urgency of resistance against antibiotics as a global humanitarian threat and the need for future regulation, it is essential to improve the dialogue and mutual understanding between the supply and demand sides of pharmaceutical markets and to enable the development of effective tools for reducing emissions throughout the supply chain.

SIWI's engagement in the fight against antibiotic resistance

SIWI strives to improve the dialogue between industry, customers and regulators, and develops proposals for how to address the emissions of pharmaceuticals, especially antibiotics. Through the project REAP-effect (Reducing Emissions from Antibiotics Production through Resource Efficiency), financed by the Swedish Postcode Foundation, efforts focus on reducing emissions of active pharmaceutical ingredients from production sites. The project seeks to adapt, test and validate a methodology which will reduce the pollution by improved resource efficiency. The project will be carried out in India, where one of the biggest hubs of the pharmaceutical industry is located. The project will

Recommendations

- Businesses should be made aware of the advantages for engaging proactively and being ready for future market requirements and regulation.
- Public procurement is a market segment where piloting of new environmental criteria is possible. Using this operating space is also important to inform the other market segments about the effect of sustainability criteria.
- Cooperation with customers on sustainability criteria for antibiotics will enable harmonization between different types of buyers and market segments and a faster learning curve for both sides in the application of the criteria.
- Cooperation between suppliers will increase synergies in meeting customers' requirements and setting standards and benchmarks.
- End of pipe solutions will not solve the whole problem in an efficient way. Resource efficiency as a tool to reduce emissions should be the starting point.

be carried out in close collaboration with the UN-initiative Sustainable Procurement in the Health Sector, SPHS.

Other projects address the need for harmonized sustainability criteria for public procurers as well as other market actors.

A critical issue outside the supply chain is the role of clean and safe drinking water, sustainable sanitation and hygiene, that can reduce the need for antibiotics and improve health in multiple dimensions.