HYBRID CONFERENCE

Pharmaceuticals in the Environment

Current Challenges and Tomorrow's Solutions to Protect Wildlife

SUMMARY REPORT

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Introduction

Disease treatment relies on effective pharmaceuticals. Yet, there is overwhelming evidence that pharmaceutical residues are found in the environment and that these residues have a negative impact on wildlife and knock-on effects on wider ecosystems. Various recent studies[1] have shown that some pharmaceuticals such as antibiotics, painkillers or cancer treatments, even at very low concentrations, have direct effects on wildlife. For example, fish exposed to low concentrations of certain antidepressants have been found to change their behaviour in ways that could affect their survival and oral contraceptives based on natural or synthetic estrogens cause feminisation of fish and amphibians. These findings are even more worrying if one considers that environmental concentrations are likely to increase as the population ages and grows.

To tackle one issue, one must first understand its main causes. In 2019, the European Commission[2] identified three main ways in which pharmaceuticals reach the environment:

- through the discharge of effluent from wastewater treatment plants, containing excreted pharmaceuticals as well as unused pharmaceuticals thrown away into sinks and toilets, despite the existence of collection schemes;
- through the spreading of animal manure;
- through aquaculture, in which pharmaceuticals are often dispensed with the animal feed.

Yet, this information alone is not enough. More information is needed to understand and evaluate the environmental concentrations and the resulting levels of risk of certain pharmaceuticals[3]. Several studies and initiatives have gone a long way in this regard (e.g., the Swedish FASS System[4], the first

[1] Wojnorowski et al. 2021; Czarny et al. 2017. 1 Dzieweczynski, TL et al. 2016. J Exp Biol. 219: 797-804. "Pharmaceuticals pollution of the world's rivers », February 2022.
[2] European Commission, Communication on the European Union Strategic Approach to Pharmaceuticals in the Environment, pages 2-3.
[3] European Commission Communication on the European Union Strategic Approach to Pharmaceuticals in the Environment, page 4
[4] Wennmalm A, Gunnarsson B. Pharmaceutical management through environmental product labeling in Sweden. Environ Int. 2009 Jul;35(5):775-7. doi: 10.1016/j.envint.2008.12.008. Epub 2009 Feb 3. PMID: 19193440.

truly global study of pharmaceuticals in freshwater[5], the PREMIER Project[6], and the 'Pharmaceuticals in the Water Environment' tool[7]), but obstacles remain to fulfil Europe's zero-pollution ambition.

What are the remaining challenges, and what measures should the EU consider? Answers to these questions and other are paramount these days as the European Commission is working on a proposal for a regulation to revise the pharmaceutical legislation to strengthen provisions for environmentally sustainable pharmaceuticals – a proposal which will be later discussed in the Parliament and in the Council.

It is against this background that the Pharmaceuticals in the Environment (PiE) Conference 2022 took place. Initiated by Mithra and hosted by MEPs Sirpa Pietikäinen and Cristian Silviu Bușoi, the conference brought together representatives from the industry, water sector, academia and EU institutions to engage in a fruitful discussion on the issue of pharmaceuticals in the environment. The list of the speakers as well as their biographies can be found here.

Welcome Speech by MEP Busoi

At the European Parliament, Mr. Busoi, Member of the European Parliament and ITRE Committee Chair, worked on a resolution which built on the Approach proposed by the Commission: "My colleagues and I specifically called on the Member States and the Commission to support research, development, and innovation in the field of pharmaceuticals that are equally effective for patients and intrinsically less harmful for the environment. So, it is both my pleasure and honour to be here today with representatives of the industry who succeeded in developing greener pharmaceuticals. Because of my work as Chair of the Committee on Industry, Research and Energy, I know that this is a process that often comes rid with difficulties".

He declared himself to be aware of the need to act in a preventive manner and eager to learn what policy-makers should take into account when drafting the new regulation. As for the approach to be taken, he made his position very clear: "it is time to be ambitious", stating that he would "stand for strong measures to reduce the discharge of pharmaceuticals in the environment".

Key takeaways from the panel discussion

The panel discussion, titled "The direct effects of pharmaceuticals on wildlife, knowledge and policy gaps & solutions to support research and innovation to achieve the Zero Pollution Ambition", produced some interesting points for discussion.

Upstream measures should be the priority

Prof. Kestemont, Full Professor at the University of Namur, argued that increasing the efficiency of sewage treatment plants is not financially sustainable, and that efforts should thus be focused on upstream solutions, such as developing pharmaceuticals that are sustainable by design and making sure the wider public understands the importance of properly discarding pharmaceuticals. Of the same idea was Mr Loebel, Secretary General of EurEau, who, while recognising the role that his sector can play, highlighted that starting point must be the precautionary principle.

[5] Wilkinson J. et al. Pharmaceutical pollution of the world's rivers, PNAS, Vol.119, No. 8 (2022)
[6] https://imi-premier.eu/
[7] NHS Highland website, news, "New data tool launched to help researchers understand the effects human medicines have on Scotland's environment | NHS Highland

Mr Fontaine, Chief Commercial and External Affairs at Mithra, noted that the industry has been seeking to reduce its environmental footprint for a long time. However, designing environmentally sustainable pharmaceuticals adds an additional challenge to the research process. Ms Simon-Hettich, Head of Early Chemical and Preclinical Safety at Merck Group, added that many inter-association activities have been taking place in the last decade, and research projects have been carried out together with EU institutions.

From a policy point of view, Mr Stielstra, Deputy Head of Unit Sustainable Freshwater Management at DG ENV of the European Commission, noted that the strategy documents produced by the European Commission recognise the importance of the design stage. They are aware of the need to follow up with the legislation too, but developing legislation takes time.

Carrots, sticks or a combination of the two?

This month, the European Commission has started delivering on the above-mentioned commitments with the publication of the Proposal for a revision of the Urban Wastewater Treatment Directive. During the impact assessment, it was found that "92% of the toxic loads European urban wastewater treatments have to deal with come from either the cosmetic or pharmaceutical sector". The proposal suggests introducing an extended producer responsibility system for these sectors so that these can financially and fairly contribute to the very costly water cleaning work.

Mr Loebel reported that the water sector strongly supports the proposal. The industry, however, is more cautious: Ms Simon-Hettich warned that "the scheme will not solve the problem overnight, as people will still need to take the medicines". Moreover, she added, "the vast majority of pharmaceuticals are detected in amounts well below any concentration that may pose risks", and many of the commitments made in the Green Deal were made before the several crises we are facing broke out.

On a similar note, Mr Fontaine pointed out that a piece of legislation coming with sanctions is missing the other side of the coin : "Where is the support to accelerate this innovation? If you are a good student, where is the reward to further encourage the transformation?". Smaller companies like Mithra, he argued, need support to continue being part of the transition.

Mr Loebel recognised that more action is needed on that side too, e.g., making it easier to bring such compounds to the market by revising the general pharmaceuticals legislation. However, the responsibility for the substances that cause problems cannot be borne by wastewater treatment plants alone. Mr Stielstra replied that it has been calculated that such a system would not have a significant impact on the price of pharmaceuticals. As for the carrots for the industry, he mentioned the opportunities of the Horizon Programme.

Should the precautionary principle prevail?

As Prof. Kestemont explained, various data gaps remain, especially regarding cocktail effects of different compounds. Because of these gaps, Mr Stielstra stressed the importance of the precautionary principle. Even more so because, he noted, "legislation is very reactive: it takes a long time before it is in the law books, and even more time before the Member States implement it". In a more pessimistic vein, MEP Pietikäinen argued that the real precautionary principle is not actually applied, because we are not looking at long-term effects. The real question, in her view, is how the EU institutions could get close to that principle.

Of a totally different opinion is the industry, which favours an approach that does not forbid substances for which we do not know the impact yet. Ms Simon-Hettich noted that since 2006 every pharmaceutical is associated with an ERA, and products marketed before that have also undergone testing. She argued that data is available, and it shows that the environmental concentrations are usually well below any effect concentration. In her view, it's more a problem of communication rather than a problem of a lack of data.

Q&A session

The audience invited the panellists to look at the six recommendations of the forum on PiE of the European Federation of Academies of Medicine (FEAM) organised on March 22nd.

The audience also steered the discussion towards obstacles and incentives to the development of environmentally friendly compounds. Ms Simon-Hettich explained that from a chemical and scientific point of view the difficulty has to do with the balance between stability and degradability: "to make a compound a drug, this must stay in the body for a certain amount of time to exert its pharmacological effectiveness. This stability, on the contrary, is not beneficial to be degraded in the wastewater treatment plants. In addition, it is these days already extremely difficult to find new compounds that can modify a receptor or an enzyme in the body that are then able to cure diseases… And once we have found a drug, it might not be easily degradable".

Mr Fontaine added that when companies file for a new medicine at the European Medicines Agency, an Environmental Risk Assessment (ERA) needs to be conducted. Nevertheless, a good result today does not lead to any kind of accelerated registration. Similarly, when a medicine that is therapeutically equivalent and more environmentally friendly needs to be registered in different countries, it is not given any specific access advantage. An interesting idea that could be explored is the voluntary environmental classification system proposed in Sweden. Mr Loebel also regretted that the conclusions of the ERA are not considered in the authorisation as is done for veterinary pharmaceuticals and recognised that this translates into a disadvantage for those who bring innovative substances to the market. He argued that pricing could also be a solution to influence patient choices.

Attendees from the German Environment Agency called for a change in the legislation to make the ERA and risk mitigation measures mandatory during the authorisation procedure. They maintained that the Swedish idea is hard to implement because of the lack of data, as the legislation never took into account the problem of the substances put on the market before the ERA was introduced in 2006. As a possible solution to this problem, they drew the attention to an attempt which is currently discussed for veterinary medicines: the "monograph system on active pharmaceutical substances" which rests on the idea that we should have in the future a system of shared responsibility and values of all marketing authorisation holders marketing the same active substances, because from an environmental perspective we are interested in the active substances rather than in the single products. Ms Simon-Hettich, however, pointed out that data was collected within the PiE Task Force under the umbrella of the pharmaceutical industry organisation, so maybe it is simply a matter of communication. Representatives from the German Environment Agency replied that the data should be publicly available for all interested stakeholders.

Finally, Mr Stielstra had the chance to talk about the upstream solutions proposed by the legislation: EU institutions simply tell the Member States what concentrations they need to achieve and leave it

to them to decide what the most appropriate means are. However, further ideas such as the ones discussed today could be considered.

Closing remarks by MEP Pietikäinen

MEP Sirpa Pietikäinen wrapped up what she described as an “highly interesting discussion” and stated that “pharmaceuticals cannot be exempt from the general ambition for our industries”. Finally, she called on the Commission to “look at the cost of non-action, because quite often we see that when you need to do something new, it’s going to cost money for the industry and the consumers, but then if you don’t do anything, the price you pay is 10 times the initial investment”.