2022-05-25

European Pharmaceutical Committee - ad hoc-working group on the EU strategic approach on PiE

Sub-group of the AMR One Health network on National Action Plan - meeeting 31 May-1 June

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Active pharmaceutical substance may reach the environment

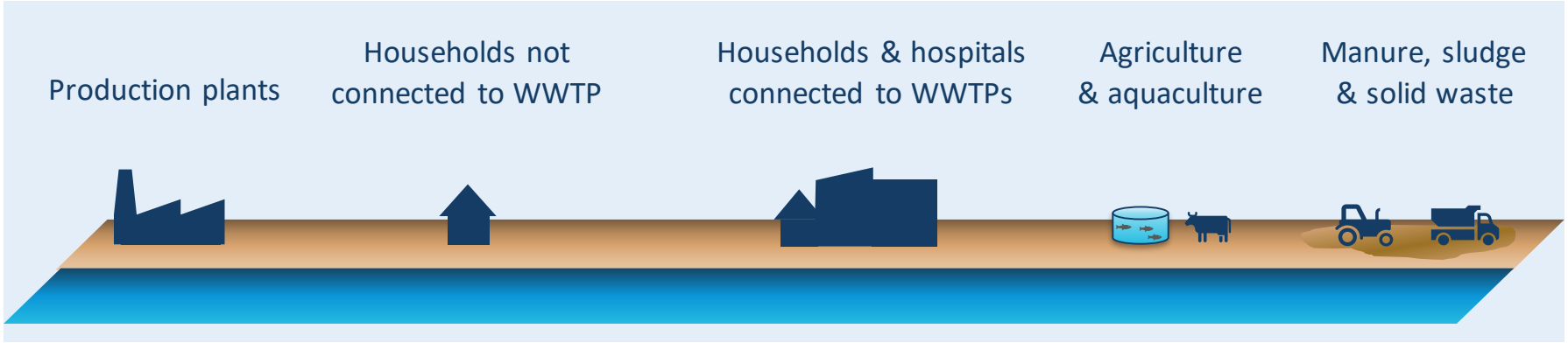


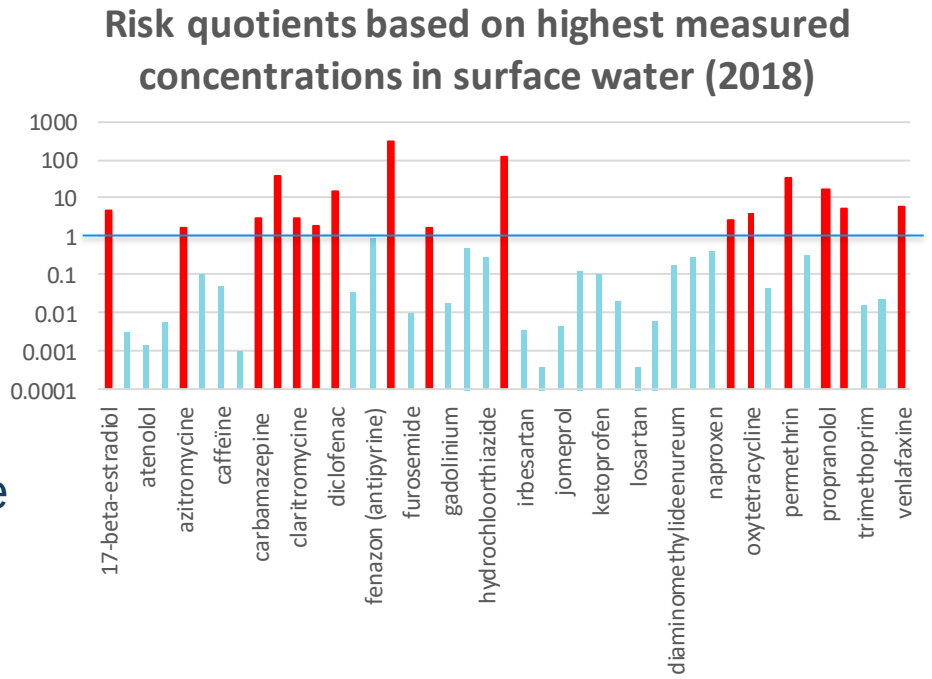
Image: Knowledge Centre on Pharmaceuticals in the Environment at Swedish MPA

- Chemical mixtures are present in our waters
- Ecosystems related to water resources may therefore be exposed to mixtures during their whole life-cycle
- Antimicrobial agents pose an additional risk by adding pressure towards increased antimicrobial resistance

Conclusions from NL inquiry - RIVM-briefrapport 2020-0088

(C.T.A. Moermond et al.)

- At least 190 tonnes of API residues reach Dutch surface water annually
- 16 of 43 measured APIs had a risk quotient (RQ) exceeding 1 (based on highest measured concentrations), indicating potential risk for aquatic organisms
- Dutch surface water environments are potentially at risk of adverse effects



COM Pharmaceutical Committee – work based on the EU strategic approach on PiE

An ad-hoc working group has been established to address parts of the “EU Strategic Approach to Pharmaceuticals in the Environment“ – human only

- Seven sub-working groups established (human medicines)
- Recommendation, guidelines and propose measures and/or further actions - Mars 2024
- All, more or less, have impact also on use of *antimicrobial medicines*
- Concept paper due to the revision of EU pharmaceutical legislation (Directive 2001/83/EC)

Overview of the action plan of the working group

	Topic		Outcomes	Participants
1	Promote the development of guidelines for healthcare professionals on the **prudent use** of pharmaceuticals posing a risk to or via the environment	2020-2022	• Recommendations including exchange of best practices • Possible guidelines	Leader: NL Collaborators: CZ, ES, FI, FR, SE
2	Explore, in cooperation with relevant stakeholders, how environmental aspects could become part of **medical training** and **professional development programmes**	2020-2022	• Recommendations including exchange of best practices • Possible guidelines	Leader: NL Collaborators: CZ, ES, FR, NL, SE
3	Foster best-practice exchanges between Member States on how environmental considerations are taken into account in the **advertising and prescription** of medicinal products and the **choice of therapy more generally**, where appropriate	2021-2023	• Recommendations/ exchange of best practices	Leader: - Collaborators: To be decided at a later stage

Overview of the work in the sub-working groups

	Topic		Outcomes	Participants
4	Explore the possibility of **reducing waste** by optimising the package size of pharmaceuticals so that medicines can be dispensed in quantities better matching needs, and by safely extending use-by (expiry) dates so that fewer medicines that are still usable have to be thrown away	2020-2022	• Recommendations/ exchange of best practices	Leader: FR Collaborators: DE, EMA, ES, SE
5	Facilitate the exchange of best practices among healthcare professionals on the environmentally **safe disposal of medicinal products and clinical waste**, and the collection of **pharmaceutical residues** as appropriate	2021-2023	• Recommendations/ exchange of best practices	Leader: RO To be decided at a later stage Collaborators: NL, SE

Overview of the work in the sub-working groups

	Topic		Outcomes	Participants
6	Assess the implementation of **collection schemes** for unused pharmaceuticals and consider how their availability and functioning could be improved, how **to increase public awareness** of the importance of using them, and how **extended producer responsibility** could play a role in **reducing inappropriate disposal**	2020-Q3 2021	• Recommendations/ exchange of best practices	Leader: ES Collaborators: FI, NL SE
7	Provide recommendations on the actions under the **section 5.3 ("Improve the environmental risk assessment and its review** for the human medicines") that fall under the competence of the Member States	2020-2023	• Recommendations	Leader: DE Collaborators: AT, CZ, EMA, ES, IE, NL, SE, SI

Concept paper – background

Following the adoption of the pharmaceutical Strategy for Europe that also sets flagship actions to address the environmental challenges, the ad-hoc Working Group on pharmaceuticals in the environment (PiE WG) was also given the task to draft a concept paper on the environmental challenges regarding the revision of the EU pharmaceutical legislation (Directive 2001/83/EC*) on the following aspects:

1. Strengthening the environmental risk assessment (ERA) requirements and conditions of use for medicines and take stock of the results of research under the innovative medicines initiative;

2. Greener pharmaceuticals with respect *to antimicrobial resistance*

COM(2020) 761 final, 25.11.2020, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52020DC0761&from=EN

*medicinal products for human use

My conclutions from PiE - WG CP on pharmaceutical pollution, including *antimicrobial resistance*, in upcoming revisions of EU legislation

Emissions of pharmaceutical substances to the environment should be minimised during production, use and disposal to minimise effects of pharmaceuticals on the environment and reduce the risk of antimicrobial resistance

There is now a window of opportunity to address this in upcoming revisions of several EU legislative acts. In the upcoming legislation relating to medicinal products for human use

1) Several provisions related to environmental risk assessment (ERA) and conditions of use should be strengthened. In addition, related to regulation of waste there are several possibilities to reduce unnecessary waste
2) provisions in the legislation to minimize emissions of active substances during production (active substances and medicinal products) should be introduced

Minimize emissions of active substances during production

The upcoming revision of the Industrial Emissions Directive and the Urban Wastewater Directive could be used to act against pharmaceutical pollution within the European Union

Large portion of active substances and medicinal products are imported to the European Union

Therefore, to enforce environmental requirements that target emissions from production also in third countries, environmental requirements should be introduced in the legislations relating to medicinal products for human use and also in the legislation relating to Good Manufacturing Practices (GMPs). For this, several changes in the legislation relating to medicinal products for human use should be done, mainly:

- Introduce a definition of GMP that includes emission of active substances to the environment
- Empower the Commission to set Emission Limit Values for active substances during production
- A stepwise introduction would enable considering potential effects on availability and prioritising of actions, for instance by starting *with antimicrobials* (It should be noted that a strengthened ERA with publicly available environmental information (topic 2) would be a very valuable source of information when setting emission limit values)

A strengthened environmental risk assessment (ERA) and conditions of use

A developed, transparent, and publicly available ERA on medicinal products, and improved risk mitigation related to conditions of use, would be a very valuable source of information:

- when setting emission limit values (inter alia for active substances during production)
- when developing for instance national medical treatment recommendations that consider both the need of the patient as well as the environment (tool for prudent use)
- for risk mitigation measures
- for environmental prioritisation and monitoring

Legislation relating to medicinal products for human use – ERA and environmental information

Issues that hamper the availability and use of environmental information and ERA. Suggestions to address this;

- The ERA should be considered in the benefit/risk balance in the marketing authorisation process. Balanced against benefits of the medicinal product and unmet medical needs
- Include *risk of antimicrobial resistance in the ERA*
- Ensure transparency and publicly availability of ERA from future and approved medicinal products
- Introduce catch-up ERA for legacy products that lack information on environmental risk to fill large data gaps
- Link environmental legislation with pharmaceutical legislation for data exchange **such as to the Water Framework Directive and the Groundwater Directive**. A legal provision to list active substances in a central database should be introduced making ERA results and study endpoints publicly available
- Introduce possibility of re-evaluation of ERA for substances with a potential environmental risk or if new data emerges (linked to for instance monitoring/ ecopharmacovigilance of active substances)
- Further develop risk mitigation conditions, for instance by introducing a new provision to impose risk mitigation measures or ERA studies as conditions to the marketing authorisation or Specific Obligations