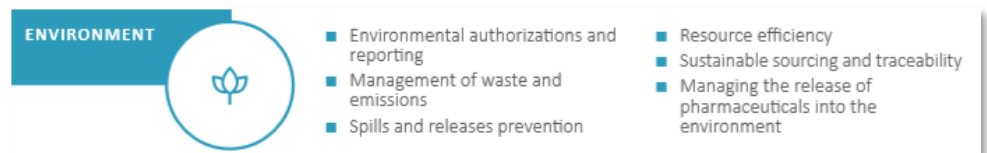


PSCI Position Statement on PiE and AMR

24th March 2020

Pharmaceuticals in the environment (PiE) are an important issue and the subject of increasing focus by the media, governments, NGOs and the wider public. In recognition of this growing importance, the Pharmaceutical Supply Chain Initiative (PSCI) has a dedicated Sub-Team working on the PiE issue. This Sub-Team aims to provide members and suppliers with materials and training to help improve their capability in managing their environmental emissions of pharmaceuticals during manufacturing operations. The purpose of this position statement is to highlight the relevance of the PiE issue along the supply chain and the availability of these resources.

Human and veterinary medicines bring enormous societal benefits, supporting public health and ensuring a safe food



Overview of PSCI Principles on Environment

supply. One of the unintended but inevitable results of delivering life-changing medicines to patients is that pharmaceutical residues can find their way into the environment. Most residues in the environment are a result of patient and veterinary use and the inappropriate disposal of unused medicines. Unintended release of pharmaceuticals in manufacturing emissions represents a minor yet potentially important environmental source that is controllable and has the potential to be further minimised.

At a local level it is recognised that manufacturing discharges can cause localised 'PiE hotspots' unless they are adequately assessed and controlled. Reports of active pharmaceutical ingredients (APIs) in surface water downstream from pharmaceutical manufacturing in the European Union, the United States, India and elsewhere indicate concentrations have reached mg/L levels when wastewater discharges are not sufficiently controlled at facilities, highlighting the importance of effective control of API emissions from manufacturing, both in bulk API production and product formulation^{1, 3}.

Another important element of PiE is the potential contribution to the spread of anti-microbial resistance (AMR)³. The use, overuse and misuse of antibiotics in humans and animals is the largest contributing factor to the development of AMR. However, there is concern that when antibiotic residues in the environment are sufficiently high, they could create a selection pressure to favour the development of resistance². In particular, elevated concentrations of antibiotics downstream of some manufacturing facilities could potentially contribute to the evolution and selection for resistance in environmental and pathogenic bacteria³. Industry has acknowledged this issue and has committed to work collaboratively^{4, 5, 6} to understand and minimise the impact of antibiotics on AMR from emissions across our supply chains.

Pharmaceutical Supply Chain Initiative (PSCI) Principles

The PSCI is a group of pharmaceutical and healthcare companies that share a vision to establish and promote responsible practices to continuously improve social, health, safety and environmentally sustainable outcomes within our supply chains. The PSCI Principles state that “any waste, wastewater or emissions with the potential to adversely impact human or environmental health shall be appropriately managed, controlled and treated prior to release into the environment. This includes managing releases of active pharmaceuticals into the environment (PiE)”⁷.

The PSCI promotes control of pharmaceuticals in wastewater effluent using a risk-based approach to ensure that pharmaceuticals in surface waters do not exceed predicted no effect concentrations (PNECs). PNECs are chosen to protect aquatic organisms in surface water as well as humans or wildlife that use surface water from harmful effects of pharmaceuticals. PNECs are also set to minimise the risk of development of AMR in environmental bacteria from the presence of antibiotics in surface water.

To promote good wastewater effluent management, several tools have been developed that can be applied throughout the supply chain (see below).

Assessment tools

During supplier evaluations PiE-specific questions are incorporated into the PSCI [assessment and audit tools](#).

Capability building

PSCI has a range of resources, publicly available on the PSCI website, to drive good practices in the management of APIs at manufacturing sites to minimise the impact of PiE and AMR. These include:

- A 4-part webinar series designed to spread awareness of the PiE issue and communicate best effluent management practices. These were originally presented in 2016 to 2018 in India and China specifically for suppliers to the pharmaceutical industry:
 - o [Managing APIs in manufacturing effluent Part 1 - 27th Jan 2016](#)
 - o [Managing APIs in manufacturing effluent Part 2 - 15th June 2016](#)
 - o [Managing APIs in manufacturing effluent Part 3 - 25th October 2016](#)
 - o [Managing APIs in manufacturing effluent Part 4 - 10th July 2018](#)

- A webinar on the issue of AMR and how to calculate predicted environmental concentrations (PECs) of APIs in receiving water bodies (e.g. rivers, lakes and the sea) and where to find publicly available PNEC values for APIs:
 - o [Anti-Microbial Resistance Webinar 23 July 2019](#)

- A [technical deep dive seminar](#) exploring and providing training on the key issues and how sites can manage the release of APIs into the environment which took place at a Supplier Conference in Hyderabad, India in September 2019.

- A [PEC:PNEC calculator tool](#) launched in July 2019 that enables manufacturing facilities to calculate their wastewater effluent discharges based on site-specific parameters and compares estimated surface water concentrations (PECs) to the PNEC discharge targets for their APIs. Guidance on how to use the PEC:PNEC calculator tool was also given at the AMR Webinar in July 2019 (see above). Additional guidance for using the tool can also be found by accessing the key [resources on PNECs](#) link.



Deep dive seminar on PiE and AMR held in Hyderabad in 2019

A [common manufacturing framework to tackle anti-microbial resistance](#) document on managing antibiotic waste is also available from the AMR Industry Alliance along with a [list of PNEC values](#) for a wide range of antibiotics⁵.

Bringing experts together

Within PSCI, we have established a dedicated Sub-Team focused on PiE and AMR. Specialists drawn from member companies are represented in the group and contribute their knowledge and insights, enabling the group to effectively draw on the best practices and technical expertise from across the industry and a wide portfolio of pharmaceutical products.

By working closely with stakeholders on PiE, the Sub-Team ensures that activities reflect the latest science. Whilst PSCI does not define standards or discharge targets, the members of the Sub-Team do work closely with organisations that carry out such activities – including the AMR Industry Alliance Manufacturing Group, the European Federation of Pharmaceutical Industries and Associations (EFPIA), Medicines for Europe, Association of the European Self-Care Industry (AESGP) and the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) – to help promote best practice into the supply chain.

Looking ahead

The PSCI will build on the success of previous supplier seminars and webinars to deliver more focused training sessions on PiE/AMR.

For more information

If you wish to access PSCI's resources and events in relation to PiE, AMR or any other responsibility issues, you can access them via our [website](#) – visit the Resources section and search for topics of interest, or the Events section for upcoming and recent events and webinars. Information is also distributed via our mailing list and regular newsletters. If you wish to find out more about our work in this area, then please contact the PSCI Secretariat at info@pscinitiative.org.

References

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2. Bengtsson-Palme J, Kristiansson E, and Larsson DJ., 'Environmental factors influencing the development and spread of antibiotic resistance', *FEMS Microbiology Reviews*, 42(1), 2017, fux053.
3. Larsson DJ., 'Pollution from drug manufacturing: review and perspectives', *Philosophical Transactions of the Royal Society B: Biological Sciences*, 2014, 369:20130571.
4. AMR Industry Alliance Shared Goals, Common Manufacturing Framework and Antibiotic Discharge Targets, available at: <https://www.amrindustryalliance.org/shared-goals/common-antibiotic-manufacturingframework/>
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6. The Association of the European Self-Care Industry Position on PiE, available at: <https://aesgp.eu/articles/aesgp-releases-its-position-on-antimicrobial-resistance>
7. PSCI Principles v2.0 (2019), available at: <https://pscinitiative.org/viewResource?resource=1>