

CARE FOR PEOPLE & OUR ENVIRONMENT





OUR COMMITMENT: open and constructive engagement with all stakeholders involved

We remain committed to working with all partners along the value chain of medicines and the EU institutions, in order to address environmental concerns while responding to patient needs and ensuring access to medicines. This is a paramount objective of our industry.

Multiple initiatives under the Eco-Pharmaco-Stewardship have contributed over the last couple of years to improving scientific understanding, finding new ways to detect the trace amounts of Pharmaceuticals in the environment (PiE), understanding their impact, prioritising APIs posing a potential risk to the environment and also further reducing discharges from manufacturing plants. As an industry, we are striving to continually enhance our processes to deliver life-saving treatments in ways that are also protective of the environment.

Medicines and vaccines are some of the most powerful tools in helping people all over Europe to live longer, healthier and more productive lives. Today, people in the EU live up to 30 years longer than they did a century ago¹. Since the 1990s, deaths from cancer have fallen by 20% and recent pharmaceutical innovation means 90% of people living with Hepatitis C can be cured through a 12-week course of medicine. Over the past 20 years, EMA has authorised 190 new treatments for around 142 rare diseases².

By embracing evolutions in science, technology and integrating sustainable solutions across our entire value chain, **our companies are committed to improving people lives while working sustainably.**

One of the unintended but inevitable results of delivering these medicines to patients is that trace amounts of Active Pharmaceutical Ingredients can find their way into the environment at all stages of the product's life-cycle.

The European pharmaceutical industry, represented by AESGP, EFPIA and Medicines for Europe is **committed to continue playing an active role in addressing concerns around risks associated with Pharmaceuticals in the Environment (PiE)**. Minimising the impact of medicines on the environment while safeguarding access to effective treatments for patients is a critical issue across all sectors of healthcare. We believe that a collaborative approach allows us to increase our mutual knowledge and understanding on how to proactively address any potential risks imposed by the presence of pharmaceuticals in the environment.

The industry is committed to playing a pivotal role in addressing concerns regarding pharmaceuticals in the environment (PiE) and is actively engaged to address risk. To this end, industry developed the Eco-Pharmaco-Stewardship (EPS) framework that applies the widely accepted principles of product stewardship and is implemented across the industry and with broader stakeholders in the healthcare and environmental sectors.

People in the
EU live up to

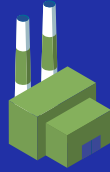
30+

**YEARS
LONGER**
than they did a
century ago

¹ The Pharmaceutical Industry in Figures 2020 https://www.efpia.eu/media/554521/efpia_pharmafigures_2020_web.pdf

² 2000-2020: 190 OMPs (some no longer have an active orphan-status) for around 142 rare diseases. Orphan Medicines Figures 2000- 2020 (europa.eu)

Source of pharmaceuticals



Industry



User/Patient



Farms

Pathways into the environment



Environment

- In Europe only trace levels can be attributed to waste from production.
- A smaller fraction comes from the expired or unused medicines that are not correctly disposed of.
- The largest part is a result of normal patient and consumer use and excretion into wastewater treatment systems. The exact percentage however varies, depending on the medicines characteristics.

We embrace the EU Commission's focus on the Green Agenda and a more sustainable Europe. Proactive management of PiE has been a driving force behind the creation of the Inter association **PiE Task Force and the Eco-Pharmaco-Stewardship (EPS)** initiative in 2015. We are proud of the contribution we have made and note that our EPS strategy contributes to **many shared goals and actions of the EU institutions and political agenda**. Furthermore, the industry activities are aligned with the United Nations Sustainability goals³ 3, 6, 9, 12, 14 and 17 on good health, clean water, industry and infrastructure, responsible consumption, life underwater, and partnerships respectively.

SUSTAINABLE DEVELOPMENT GOALS



The pharmaceutical industry supports the 2019 **European Union Strategic Approach to Pharmaceuticals in the Environment**⁴, a holistic lifecycle approach to minimising the impact of PiE by encouraging stakeholders to lead and promote exchange of best practices.

We broadly support that the implementation of the **Pharmaceutical Strategy for Europe**⁵ encompasses policy areas to ensure environmental sustainability of the supply chain of pharmaceuticals. This links to the **2019 Commission Strategic Approach** to PiE with a focus on challenges and opportunities in relation to their practical implementation, with many of its actions aligned with the activities industry has identified to effectively reduce possible environmental impacts of their operations.

It is encouraging that the Commission's approach recognises the added value of several industry initiatives which increase awareness and promote the responsible use of human and veterinary pharmaceuticals. These include the **AMR Industry Alliance**⁶, which has developed a framework for assessing and promoting safe discharge targets for antibiotic manufacturing and the **#medsdisposal**⁷ campaign established to improve the collection of unused or expired medicines. Moreover, innovative risk-based frameworks such as our extended **Environmental Risk Assessment (eERA)** model and **research initiatives such as IMI iPiE and IMI PREMIER** recognise the importance of bringing different stakeholders together to address the ongoing concerns around PiE.

³ <https://sdgs.un.org/goals>

⁴ https://ec.europa.eu/environment/water/water-dangersub/pdf/strategic_approach_pharmaceuticals_env.PDF

⁵ published in November 2020 https://ec.europa.eu/health/sites/default/files/human-use/docs/pharma-strategy_report_en.pdf

⁶ <https://www.amrindustryalliance.org/>

⁷ <http://medsdisposal.eu/>

The Pharmaceutical Supply Chain Initiative (PSCI)⁸ and the IAI PiE Task Force developed the Responsible Manufacturing Effluents Management Guidance, an internal set of principles promoting responsible supply chain management and best practice across the industry.

The industry continues to coordinate its efforts, under the Eco-Pharmaco-Stewardship, striving to ensure patient access to medicines while appropriately considering environmental aspects and focusing on areas where we believe we can most effectively reduce the potential environmental risks that might result through our activities:

FILLING THE KNOWLEDGE GAP THROUGH FURTHER RESEARCH AND INNOVATION



To make the most impactful change and to address remaining scientific knowledge gaps, the pharmaceutical industry has engaged with public partners from universities, regulatory agencies, patients and small/medium-sized enterprises under the Innovative Medicines Initiative (IMI).

IMI⁹ is the world's largest public-private partnership in the life sciences between the European Union and EFPIA, with project consortia pursuing the goal of developing the next generation of vaccines, medicines and treatments by improving research practice; getting new healthcare solutions to patients faster; and improving health outcomes thanks to new tools, methodologies, research infrastructure and big data, including a focus on sustainability and the environment.

The outcomes of the **IMI iPiE¹⁰ - Intelligence-led Assessment of Pharmaceuticals in the Environment project** (2015-2019) enabled consortia members, in collaboration with EMA, to develop a prioritisation framework to help identify those medicines that are most likely to present a risk for the environment¹¹. This multi-stakeholder project created a publicly accessible database on environmental information including more than 2000 studies for hundreds of existing Active Pharmaceutical Ingredients and other science-based tools¹² to identify the risks that medicines pose across Europe. Environmental risk assessments were conducted for over 120 previously untested APIs, with full EMA environmental datasets using country specific consumption data under worst case exposure scenarios, that indicated potential risks were limited to less than 5% of medicines and a few mechanisms of action.¹³



To further improve environmental data and also our capacity to prioritise, predict and assess potential environmental risk of yet untested medicines, we continue our research under the current **IMI PREMIER project (Prioritisation and Risk Evaluation of Medicines In the Environment)**, which kicked off in 2020. The aim is to improve models that can predict the exposure and the effects of APIs. The outputs may also be applied to screen new APIs to advance drug candidates for development that are less likely to be problematic from use and disposal, and in development to target environmental testing needs.¹⁴ PREMIER will also increase the transparency and accessibility of environmental data to all stakeholders through an intelligent digital assessment system. We believe this will largely contribute to several actions proposed by the EU Strategic Approach to PiE, such as facilitate identification of potential environmental risks associated with APIs earlier in development or explore the feasibility of greener drug design.



Furthermore, the next cross-sectorial **health innovation partnership (Innovative Health Initiative - IHI)** also offers the opportunity to consider future projects to improve environmental impacts.

⁸ <https://pscinitiative.org/home>

⁹ <https://www.imi.europa.eu/>

¹⁰ <http://i-pie.org/> See also for more information about the project results - Burns et al. ; L. Gunnarsson et al 2019; Verbruggan. The Oldenkamp et al..

¹² <https://www.tandfonline.com/doi/abs/10.1080/10937404.2018.1465873>

¹³ ePiE = exposure model

¹⁴ <https://www.sciencedirect.com/science/article/pii/S0160412019309493>

Further information the composition, budget and on achievements of the iPiE project concluded in 2019 and the PREMIER project that launched in September 2020 are updated regularly online.



IMPROVING CURRENT ENVIRONMENTAL RISK ASSESSMENT

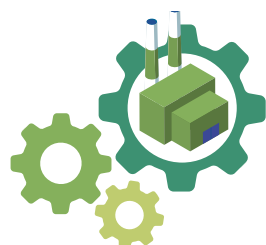
The industry welcomes the EU Strategic Approach to PiE as it identifies several actions by which the EMA, in collaboration with Member States, can facilitate better exposure assessment and environmental risk management within the current system of environmental risk assessment (ERA).

We believe that the ERA should be reviewed and, if necessary, updated throughout a product's lifecycle to reflect the latest information on the medicine's potential impact on the environment, while avoiding duplications of submissions for off-patent drugs. However, the focus should be on the APIs entering the environment and not on medicines, as a single API can be used in multiple medicines. Regulatory, academic and industry resources and associated environmental mitigation strategies should be prioritised on those APIs that pose a potential risk to the environment. This is why we have been working on the concept of the **Extended Environmental Risk Assessment (eERA)**.

The refinement of the existing ERA process for medicines would ensure that they remain up-to-date and relevant, capturing new reliable environmental toxicity data and measured environmental concentration. Newly available data from research can play an important role in the refined ERA process, extending beyond marketing authorisation. The ERA of a medicine is currently performed by companies either as part of a new marketing authorisation, line extension or when marketing authorisation for an existing product is expected to increase the environmental exposure of the API. The ERA must be performed to evaluate potential risks of medicines to the environment and ensure adequate precautions are taken where specific unacceptable risks are identified.

The eERA concept aims to:

- adjust exposure predictions as usage figures become available to better reflect patient use, including all medicines with the same API;
- collate published measured environmental concentrations for that API in appropriate environmental compartments (e.g. surface water) and conduct semi-probabilistic ERAs to determine 'real world' environmental risks¹⁵;
- update the effects profile, as relevant and reliable laboratory findings and/or observations in the field linked to an adverse outcome become available;
- undertake targeted post-approval commitments that may include environmental monitoring to refine potential risks identified at the point of authorisation; and
- consider risk mitigation options either through general regulatory provisions such as regional management activities, nationally or locally, if certain hot spots are concerned.



RESPONSIBLE MANUFACTURING EFFLUENT MANAGEMENT

Overall, the contribution of pharmaceutical manufacturing to PiE is minor¹⁶ and less significant compared with patient use and inappropriate discharges. However, potential impacts may occur on a local scale when manufacturing emissions of wastewater treatment plant (WWTP) discharges are inadequately¹⁷ managed. Therefore, there is room for improvement by the application of a risk-based approach.

Access to more advanced environmental information generated under the iPiE and PREMIER IMI projects and development of the extended Environmental Risk Assessment (eERA) opens new opportunities for identifying issues relating to manufacturing emissions.

¹⁵ Such as e.g. <https://www.astrazeneca.com/sustainability/environmental-protection/pharmaceuticals-in-the-environment.html>

¹⁶ Tischler, L., Buzby, M., Finan, D. S., & Cunningham, V. L. (2013). Landfill disposal of unused medicines reduces surface water releases. *Integr Environ Assess Manag*, 9(1), 142-154.

¹⁷ Caldwell et al (2015) A risk-based approach to managing active pharmaceutical ingredients in manufacturing effluent. *Journal of environmental Toxicology and Chemistry*, 35(4), 813 - 822.

This helps the pharmaceutical industry and WWTP operations to take measures where needed the most.

Appropriate risk-based measures to control the API emissions must be enforced during both manufacturing of APIs and during formulation into medicines for patient use. Ensuring the use of appropriate environmental risk management measures to adequately control manufacturing effluent emissions is the mission and the focus of pharmaceutical manufacturers already today¹⁸.

The pharmaceutical industry is continuously implementing initiatives and investment into projects which further address the potential risks of discharges of APIs and hazardous substances and reduce discharges from manufacturing plants through the exchange of good practices also inspired by solutions implemented by other industries. To this end, we have developed a **'maturity ladder' and the IAI PIE TF Responsible Manufacturing Effluents Management Guidance** that will help companies and their suppliers to gauge their performance and continuously improve. These establish a shared set of internal principles to guide the companies through the risk-based assessment of their wastewaters.

Additionally, many of our members are actively involved in the **Pharmaceutical Supply Chain Initiative (PSCI)**¹⁹, as part of a group of pharmaceutical and healthcare companies who have joined forces to promote responsible supply chain management and better business conditions across the industry.

Furthermore, we continue to monitor the issue of environmental impacts from the production of antibiotics and other highly active and/or hazardous substances. We have initiated several health-based commitments and are working, directly or via our member companies, through the **AMR Industry Alliance**²⁰ to manage potential risks. We have done this by supporting the implementation and application of the **AMR Alliance's common antibiotic manufacturing framework** and science-based PNEC targets for risk assessments to effectively control antibiotic releases from their operations and supply chain networks.

#MEDSDISPOSAL – EASIER THAN YOU THINK

The pharmaceutical industry stands ready to support the EU and Member States' communication activities and awareness raising campaigns on the appropriate use, storage and disposal of medicines. Most European countries have special medicines disposal schemes in place in order to prevent medicines from ending up in the environment. To visualise these, several healthcare stakeholders (industry, healthcare professionals and student organisations) jointly developed **#medsdisposal.eu**. This is an online communication campaign aimed at raising public awareness on the existing collection and disposal schemes emphasizing the fact that it is everyone's responsibility and it is easier than one may think.²¹

The disposal schemes for unused medicines have a great potential to eliminate some traces of PiE, (originating from incorrect disposal of expired or unused medicines), by implementing a cost-effective, efficient and straightforward take-back process. The pharmaceutical industry has been discussing with other partners along the value chain opportunities to further explore the potential of collection schemes for unused medicines since they are an important part of the solution to the ongoing discussion around the extended producer responsibility.



¹⁸ Caldwell DJ, Mertens B, Kappler K, Senac T, Journal R, Wilson P, Meyerhoff RD, Parke NJ, Mastrocco F, Mattson B, et al. 2016. A risk based approach to managing active pharmaceutical ingredients in manufacturing effluent. Environ Toxicol Chem 35(4):813–822. 10.1002/etc.3163 [PubMed]

¹⁹ <https://pscinitiative.org/home>

²⁰ <https://www.amrindustryalliance.org/>

²¹ <http://medsdisposal.eu/>



www.efpia.eu



www.aesgp.eu



www.medicinesforeurope.com