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WHITE PAPER

# Balancing challenges on Environment with access to medicines in Europe

## Impact assessment of policy options for Pharmaceuticals in the Environment and the use of **Extended Producer Responsibility** applied to human medicines

# CONTENTS

# EXECUTIVE SUMMARY

**Increasing pharmaceutical and chemical residues have been detected in urban wastewater due to several reasons, such as:**

- Growing populations and their increased density in large urban municipalities.
- Increase in the use of medicines to support people living longer, healthier and more productive lives.
- Evolving analytical detection techniques that measure smaller concentrations of active pharmaceutical ingredients (APIs) contained in medicines.
- Convergence of effluents in urban wastewater treatment plants that have not been upgraded or are lacking network design for the population they serve.

Due to the nature of medicines and the mechanism of action of their active substances, that intentionally interact with biological systems, some have been identified as presenting a potential environmental concern. However, evidence-based studies led by independent organisations, academia, regulators, and the Pharmaceutical Industry suggest that **less than 10%** of the APIs **could pose a potential risk to the environment**[1] and that most drugs (> 80%) indicated a low environmental risk for the endpoints assessed in a European context.[2] Indeed, the vast majority of APIs are effectively removed in wastewater treatment plants and minimal concentrations reach surface waters. The risk of these APIs to the aquatic compartment is assessed via other pharmaceutical legislation in Europe, which is currently being strengthened.

**less than**
**10%**
of APIs
**could pose a potential risk to the environment**

**The highest percentage of APIs that find their way into the environment is a result of pharmaceutical use by individuals (through excretion or Wash-off), while smaller proportions are due to improper disposal.** The Industrial Emissions Directive already covers manufacturing processes and does not exclude APIs, thus providing an existing regulatory mechanism to control the potential for API releases from manufacturing facilities.

Much like in the case of other contaminants of emerging concern, the application of Extended Producer Responsibility (EPR) to human medicines has been mentioned as a source of financing for the upgrade of Urban Wastewater Treatment Plants (UWWTPs) to align with European Union targets.

[1] Küster and Adler (2014) https://royalsocietypublishing.org/doi/10.1098/rstb.2013.0587
[2] Gunnarsson, et al (2019) https://www.sciencedirect.com/science/article/pii/S0160412019309493

Before applying EPR to all human medicines, it is crucial to consider that:

## 1. Human medicines cannot be regulated like other commodities

Access to medicines is a fundamental component of the full realization of the right to health, therefore, human medicines cannot be considered as any other commodities. Active pharmaceutical ingredients contained in medicines are a special case of essential chemical and biological molecules that treat patients and save lives. This fact calls for a different policy approach than the one being considered for other goods or chemicals. Any measures to reduce the environmental impact of human medicines must consider and differentiate them as essential and critical public goods. Patient access to medicines, which have been deemed safe and effective by the regulators should not be hindered in any way.

Furthermore, the complexity of medicines for human use and the limits of the current scientific and technological progress must be considered. Changing the design of an API (e.g., to make it more biodegradable) could reduce the pharmacological efficiency. Medicines are a healthcare tool available to society that is not easily replaced by other technologies. In addition, **any policy measure must be accompanied by an impact assessment of its consequences for patient access to medicines**. It is of the highest importance to avoid any limitation of patient access to the medicines they need.

## 2. EPR is already applied for unused and expired medicines

EPR is already applied to human medicines in some EU countries in the form of take-back schemes for unused and expired medicines. These measures are using resources and financial support of supply chain stakeholders, including the pharmaceutical industry.

The intention of using EPR as a policy option, in general, is:

i) to ensure the separate collection and recyclability of a product (or a part of it),

ii) to incentivise the production and use of greener alternatives, and

iii) to make manufacturers responsible for the end phase of a product's life-cycle.

With medicines, however, it is hard, if not impossible, to envisage such activities as the evolution of innovation, technology and science have not made it possible (or resource-efficient).

So far, EPR as a policy option has been applied to tangible products or materials (usually part of an item), and its use at the molecular level is unprecedented.

## 3. Use of EPR on human medicinal products to finance UWWTPs upgrade is disproportionate

The Pharmaceutical Industry acknowledges the importance of wastewater treatment to protect surface waters and as an essential part of demographic concentration in large urban areas. In fact, the establishment of the UWWT industry has followed a User-Pays Principle (UPP) in its financing to treat general residues of the population that would otherwise become toxic to the environment and jeopardise human health. Thus far, wastewater operations and developments, be they public or private, have relied largely on investment by national and local governments much like other public interest infrastructure. While there is understandable pressure on the wastewater industry to become more efficient, to integrate circular economy principles, and to ensure their pathway towards sustainability, the cost burden to achieve this cannot be allowed to shift disproportionately to the health and pharmaceutical sector whose priority is to respond to the needs of the patients.

To a large extent, APIs are already efficiently managed by WWTP (Waste water treatment plant) and only a few APIs, that are not effectively removed, could pose a potential risk to the environment. Pharmaceutical residues are only a fraction of the substances that an improved wastewater treatment would control. Other product manufacturers ("free riders"), which are harder to identify, would benefit from any additional investment into WWTP infrastructure and technology, as it would also remove other substances which may be toxic, persistent or hazardous in the environment.

The application of EPR to human medicines to finance upgrades in wastewater treatment plants is complex due to the following:

- The acknowledged data gaps on the risks, sources and traceability of active ingredients (or their metabolites),
- The unclear attribution of responsibility surrounding the use of human medicines, and
- The unprecedented consideration of the molecular level as part of a product.

EPR, if applied to human medicines, would be disproportionate as APIs are not the only chemicals that are being released into the environment through wastewater. The Pharmaceutical Industry would essentially be taxed to address several unrelated challenges of wastewater treatment and to support WWTP upgrades, which would provide a solution for so many other contaminants of emerging concern from non-pharmaceutical sources.

## 4. EPR provisions on medicines at EU level could potentially conflict with the national competence for healthcare systems and endanger access to medicines

Health systems In the EU are varied and reflect different societal choices. For that reason, primary responsibility for health protection and, in particular, healthcare systems, continues to lie with the Member States.

Within a Polluter-Pays Principle, pollution control is assigned to the polluters, who can absorb costs without excessive setback to their own or other actors' interests. It is unclear whether, having medicines manufacturers pay, meets this condition because these provisions will induce external costs with an indirect burden on health systems and patients.

Having medicines manufacturers pay for WWTP upgrades, for instance, could incentivize the cost recoup through higher prices for human medicines, aggravating the national pharmaceutical budget, or result in the withdrawal of a medicine in markets where such requests are made or in which that product would no longer be economically viable.[3]

Patients that have to pay out of pocket for certain classes of medicines or that are financially insecure would have reduced accessibility to needed medicines if prices were increased. Some examples of more vulnerable categories of patients potentially affected would include, for instance, chronic pain patients reliant on pain medication, mental health patients reliant on anti-depressives, female patients reliant on hormonal treatments, children and hospital patients receiving anti-infective treatments. Given the clinical importance of these medicines, diminished access to them will have a real health impact.

[3] Nijsingh et al. (2019) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6833301/

## 5. Misalignment between Environmental policies and Pharmaceutical and Industrial strategies

Inappropriate EPR would translate into a *de facto* tax which would disproportionately impact patients using the medicines affected by the measure, contradicting the European Pharmaceutical Strategy goal of reducing access inequalities. It would also have a negative impact on the EU's goal to enhance the resilience of pharmaceutical supply, a key asset for Europe's competitiveness, health and preparedness for future health crises.

Access of patients to medicines is already restricted in many instances in Europe due to budget control measures or due to high co-payments (out-of-pocket expenses for patients). Inappropriate EPR tax for human medicines would exacerbate inequities in access to medicines, which the Commission is working to reduce in the Pharmaceutical Strategy for Europe.

## 6. EU law does not support the application of EPR to human medicines

According to legal experts, an environmental levy on medicinal products for human use would question the primary European law as well as secondary environmental law. The use of EPR for APIs in medicinal products, derived from the Polluter-Pays Principle (PPP), brings attached several concerns for this particular case. The steering concept of comprehensive product responsibility is hardly applicable to medicinal products for human use.

The introduction of the EPR levy would challenge the precedence of the pharmaceutical legislation, as *lex specialis*, over other cross-sectorial legislation, as *lex generalis*. Moreover, it is questionable whether the European Union has legislative competence to apply this levy on human medicines.

*The WHITE PAPER Balancing challenges on Environment with access to Medicines in Europe - Impact assessment of policy options for Pharmaceuticals in the Environment and the use of Extended Producer Responsibility applied to human medicines* further explores policy options, the proportionality and adequacy considerations of Extended Producer Responsibility applied to APIs, namely to finance the upgrade of urban wastewater treatment plants, as well as the impacts such policy would have on healthcare systems.

## BACKGROUND

Medicines are used to prevent, treat and cure diseases, and thereby add value to society by allowing people to live healthier, longer, autonomous and productive lives. As a principle, medicines are essential to human health and safety, which makes accessibility to them critical.

Evolving science and increasingly sensitive detection methodologies have been able to find increasing numbers of contaminants of emerging concern at lower levels in the environment, particularly in wastewater, including traces of pharmaceutical residues.

Overall, there are three main pathways by which APIs can reach the environment:

- **Manufacturing of medicines**
  This pathway occurs in limited surface waters but could result in higher environmental concentrations in specific locations (hotspots). In Europe, due to emission regulations, only trace levels can be attributed to waste from production sites. Also, heavy sanctions exist for spills with environmental consequences.
- **Improper disposal**
  A fraction comes from expired or unused medicines that are not correctly disposed of (e.g. direct disposal to the sewer via sink or toilet).
- **Patient use**
  The main emission source of APIs to the environment is the excretion by patients into the wastewater treatment systems. It accounts for the highest proportion of the total amount of pharmaceutical substances reaching the environment and affects all surface waters that receive wastewater effluents. The residues may include both metabolites and unchanged APIs.

**The exact percentage of these fractions in each pathway can vary depending on the characteristics of the active substance, geography, season and wastewater treatment technology in place.**

The Pharmaceutical Industry remains committed to working with all partners along the value chain of medicines and the EU institutions, to addressing environmental concerns while responding to patient needs and to ensuring access to medicines.

Based on the understanding that any measures aimed to reduce pharmaceutical residues in the environment must not jeopardize patients' access to appropriate treatments, an Eco-Pharmaco-Stewardship programme was put in place over a decade ago by the major European trade associations for pharmaceutical products (AESGP, EFPIA, and Medicines for Europe), and is continuously improved and extended.

The elements of the Eco-Pharmaco-Stewardship programme are:

- Better understanding of risks for the environment and data collection with IMI projects iPiE and PREMIER
- Improving the future evaluation of medicines relating to their environmental risks with a reflection on *Policy Options for an Extended Environment Risk Assessment*
- Making sure that manufacturing operations have increased safety standards with a *Technical Guidance on Responsible Manufacturing Effluent Management*
- Awareness campaign on the correct disposal of expired or unused medicines in different countries in Europe, named MedsDisposal.

Because human medicines have a critical role in protecting and promoting both individual and public health, the responsibility for Pharmaceuticals in the Environment should lie with the many different stakeholders and beneficiaries in addition to the pharmaceutical industry, including the healthcare system, individual patients, and society as a whole.

Access to clean water and sanitation is a human right and key to preventing poor health. In that sense, the treatment of wastewater is a target under the United Nations Sustainable Development Goal 6 – Water and Sanitation, with direct contributions or impacts to SDG 3 – Good Health and Wellbeing, to SDG 12 – Responsible Consumption and Production, SDG 14 – Life below water and SDG 15 – Life on land.

In Europe, societal evolution has made use of technology to treat urban effluents which, in turn, allowed for even greater population concentrations in cities. Wastewater treatment plants have been the solution to centralising the treatment of otherwise unsafe human biological waste.

So far, this has been done as a collective effort, through solidarity, under a User-Pays Principle, without imposing responsibility on manufacturers of ingestible goods, namely food and drinks, as these are also essential for survival and well-being.

In 2018, Wood PLC published a report showing that 11.3% of urban wastewater treatment plants in the EU still do not even have secondary treatment ("Support to DG Environment's evaluation of the UWWTD"). Furthermore, the report details concern that the UWWTD has not adequately addressed even traditional water quality issues such as dissolved oxygen deficits and nutrient pollution associated with high levels of nitrogen and phosphorus discharges. These deficiencies could impact the ability to meet the European water quality objectives of the Water Framework Directive. Traditional water quality deficits must be managed before addressing other pollutants such as micropollutants.

The European Union already requires Member States to *ensure that appropriate collection systems are in place for human medicinal products that are unused or have expired*.[4] However, the extent of the implementation of take-back schemes for human drugs is still quite different among European countries. Public promotion and education of take-back schemes could improve to bring better results.

Even if some materials are included in some already existing EPR regulations, these usually correspond to a component of a larger item that should be correctly disposed of (e.g. glass, paper, tyres).[5] Today, there is no model that would deal with EPR at a molecular (or active product ingredient) level also as it is conceptually difficult to set up such an EPR model for molecules.

Much like in the case of other contaminants of emerging concern, it has been pointed out that EPR should apply to pharmaceuticals as well.

**However, pharmaceuticals are a special case that call for a different approach than that of other goods or chemicals.**

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[4] Article 127b of Directive 2004/27/EC

[5] *Development of Guidance on Extended Producer Responsibility (EPR) [2014]* https://www2.deloitte.com/content/dam/Deloitte/fr/Documents/sustainability-services/deloitte_sustainability-les-filieres-a-responsabilite-elargie-du-producteur-en-europe_dec-15.pdf

# DEFINITIONS AND PRINCIPLES

**Polluter-Pays Principle** is a key element underpinning European environmental policy. It stipulates that the waste producer should bear the costs of waste management in a way that guarantees a high level of protection of the environment and human health.

Polluter-Pays Principle and **Extended Producer Responsibility** are often used interchangeably in debate – although, technically, EPR is a specific application of the PPP.

## Definition of Extended Producer Responsibility (EPR)

The OECD defined EPR as an environmental policy approach in which a producer's responsibility for a product is extended to the post-consumer stage of a product's life cycle. In practice, **EPR involves producers taking responsibility for collecting end-of-life products, and for sorting them before their final treatment, ideally, recycling.** EPR schemes can allow producers to exercise their responsibility either by providing the financial resources required and/or by taking over the operational and organisational aspects of the process from municipalities. They can do so individually or collectively.

EPR policy is consistent with the Polluter-Pays Principle in so far as financial responsibility for treating end-of-life products is shifted from taxpayers and municipalities to producers and, ultimately, consumers. However, **EPR policy alone does not aim to achieve a full internalisation of environmental costs; the task of establishing an environmental price for a wide range of environmentally diverse waste streams makes this impractical.** EPR policy nevertheless aims to provide producers with incentives to internalise environmental costs throughout the product life-cycle, including at the design stage. **EPRs seek to provide incentives to producers to (re)design products and packaging to facilitate their end-of-life management, and to avoid using materials that may pose risks to human health or the environment.** Without this, some products can require significant amount of resources before they can be recycled.

SOURCE: *(OECD, 2016) Extended Producer Responsibility*
https://www.oecd.org/environment/waste/extended-producer-responsibility-9789264256385-en.htm

In the European Union, extended producer responsibility is mandatory within the context of the WEEE [waste electrical and electronic equipment], Batteries, and ELV Directives, which put the responsibility for **the financing of collection, recycling and responsible end-of-life disposal** of WEEE, batteries, accumulators and vehicles on producers. The Packaging Directive also indirectly invokes the EPR principle by requiring Member States (MS) to take necessary measures to ensure that systems are set up for the collection and recycling of packaging waste. Additional waste streams for which producer responsibility organisations have been most commonly identified within the European Union include tyres, waste oil, paper and card, and construction and demolition waste. However, **a much broader range of waste streams are subject to obligatory or voluntary producer responsibility systems in some MS, including:** farm plastics, medicines and medical waste, plastic bags, photo-chemicals and chemicals, newspapers, refrigerants, pesticides and herbicides, and lamps, light bulbs and fittings.

SOURCE: *(BioIS/Deloitte for DG Environment, 2014) Development of Guidance on Extended Producer Responsibility (EPR)*
https://ec.europa.eu/environment/archives/waste/eu_guidance/pdf/Guidance%20on%20EPR%20-%20Final%20Report.pdf

Thus far, EPR has been used to avoid concentration in the environment of residues or products at the end-of-use, by fostering their collection and redirection to proper elimination (ex. glass, paper, plastic, oil, batteries, tyres, cars, electronic equipment).

It is a key feature of EPR policies that they transfer responsibility for a product's end-of-life environmental impact to the original producer and/or seller of that product, thereby preventing waste, improving the reusability of old items and recycling of waste.

A second reason for the application of EPR, according to OECD (2001), is "the provision of incentives to producers to take into account environmental considerations when designing their products".

The **User-Pays Principle**[6] (UPP) is the variation of the Polluter-pays principle that calls upon the user of a natural resource to bear the cost.

Governments worldwide adopt the User-Pays Principle in relation to many public services. The principle involves those actually using or consuming the service to pay for it even if those services might have previously been available without charge. The UPP promotes more responsibility and accountability in relation to the environment and the consumption of increasingly scarce resources.

## EPR applied to pharmaceutical waste – unused and expired medicines

### There are many reasons why drugs can become waste

- **No-effect, adverse reactions and/or therapy change:** Prescribed drugs prove to be unsuitable for treatment and are consequently abandoned, or the treatment is changed.
- **Non-adherence:** Patients have a poor record in taking their medication.
- **Recovery or deceased:** Patients recover more rapidly than foreseen or decease.
- **Stockpiling and/or expiring:** Patients may stock pharmaceuticals for 'just-in-case', which leads to medicines reaching their expiry date before being completely utilised (in particular over-the-counter pharmaceuticals and non-prescription drugs). Stockpiling and potential expiry is not only an issue in households but also in public buildings, hotels, marine vessels, societal institutions, prison systems and military bases where drugs are commonly stored in case of emergencies but only used infrequently.
- **Prescription or purchasing error:** Patients may be prescribed or may purchase the wrong pharmaceuticals. Over prescribing can also lead to medicine waste.

SOURCE: *(OECD, 2022) Management of Pharmaceutical Household Waste*
https://www.oecd.org/environment/management-of-pharmaceutical-household-waste-3854026c-en.htm

While EU legislation often sets the framework for EPR in different areas, Member States have different understandings on how it is applied and who is defined as the "polluter".

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[6] https://www.eea.europa.eu/help/glossary/eea-glossary/user-pays-principle

Take-back schemes are in place in most European Member States even if not all correspond to EPR projects. Public investment has also been drawn at the national or local level, under the general attributed responsibility for waste management. This has been, so far, a Member State prerogative to decide upon.

It is important to understand at this point that a medicine, as commonly understood under EU law, is a product that comprises the full drug formulation, pharmaceutical form, ancillary devices, different layers of packaging and information, which are in place after years of development of quality, safety and efficacy for patients and citizens in the EU.

## Household disposal practices vary among (OECD) countries

> Separate collection systems help avoid environmental leakage caused by flushing unused or expired medicines in the drainage, or by mixing those with solid household waste, that is destined for landfill without leachate collection. **A variety of different collection schemes, take-back systems and stewardship programs are in place in OECD countries that aim to recover and manage waste pharmaceuticals. These can differ in many ways, including the scope of medicine waste covered, financing, collection routes, legislation and recovery efficacies.** On-site receptacles at pharmacies constitute the most common collection system. Some programs rely only on government funding while others are financed by contributions from the pharmaceutical industry or from pharmacies that provide support on a voluntary basis or driven by extended producer responsibility (EPR) legislation.
>
> In some countries, such as the Netherlands, Finland and Poland, drug take-back schemes are implemented in the form of voluntary approaches. Pharmacies and the pharmaceutical industry implement these systems driven by their corporate social responsibility commitments. Other motivating factors are pressure from consumers or pre-empting regulatory requirements.
>
> **Household disposal practices vary among (OECD) countries, critical drivers being the availability of drug take-back systems and the public awareness of these systems. Whilst a share of unused and expired medicines is returned to pharmacies and collection points, disposing of them in solid waste bins or down household drains remains common practice in most OECD countries.** In some OECD countries, where most MSW [Municipal Solid Waste] is incinerated in state-of-the-art facilities, disposal via solid household waste is one of the recommended disposal routes (e.g. Germany). Disposal via the toilets and sinks, is commonly advised against.
>
> SOURCE: *(OECD, 2022) Management of Pharmaceutical Household Waste*
> https://www.oecd.org/environment/management-of-pharmaceutical-household-waste-3854026c-en.htm

EPR has also been applied in the case of human medicines, as several take-back schemes have been put in place in EU Member States to avoid disposal of unused or expired medicines through solid waste or water effluents. Some of these take-back schemes were established and financed by the different stakeholders of the medicines value chain – manufacturers, wholesalers, and pharmacies – under their social and environmental responsibility programs, by setting up initiatives for Producer Responsibility Organizations (PROs).

Although, in theory, EPR is an individual responsibility, in practice, obligated companies often come together to form PROs to gather fees to finance the collection and treatment of the waste stream and organise the functioning of the system.

## Which Member States already apply EPR to Pharmaceuticals?

It is important to note that European waste legislation currently gives a global framework for the implementation of EPR in Europe. **The Member States and their respective legislation are responsible for the implementation of EPR, including regulating the operational aspects of EPR.**

Despite EPR being, in theory, an individual obligation, in practice producers often exert this responsibility collectively. **In collective schemes, a Producer Responsibility Organisation (PRO) is set up to implement the EPR principle on behalf of all the adhering companies (the obligated industry).** PROs potentially exert three main functions: financing the collection and treatment of the product at the end of its life (targeted waste stream) by collecting fees and redistributing the corresponding financial amounts; managing the corresponding data; organising and/or supervising these activities.


SOURCE: *(BioIS/Deloitte for DG Environment, 2014) Development of Guidance on Extended Producer Responsibility (EPR)*
https://ec.europa.eu/environment/archives/waste/eu_guidance/pdf/Guidance%20on%20EPR%20-%20Final%20Report.pdf

Most European countries have special medication disposal schemes in place in order to prevent pharmaceuticals from ending up in the environment.

Some of these schemes are financed by joint stakeholder EPR, such as **France** (Cyclamed), **Portugal** (Valormed) and **Spain** (Sigre).

SOURCE: *MedsDisposal.EU*
http://medsdisposal.eu/

Several countries and provinces, such as France, Spain and Portugal have pursued an EPR approach to managing household medication. By obliging pharmaceutical companies to collect and destroy unwanted pharmaceuticals that they have put on the market, EPR shifts the economic and organisational burden of unused drugs collection and disposal from the government to the pharmaceutical industry. As a result, EPR implements the "producer pays principle", moving waste management costs from taxpayers to producers. Companies can internalise these costs in the price and can, in theory, provide services more cost-efficiently.


**EPR systems in pharmaceutical waste streams are commonly organised as collective producer responsibility schemes (CPRs), where producers pay a contribution to a producer responsibility organisation (PRO), which manages the collection and safe disposal of UEM [Unused and Expired Medicines].**

SOURCE: *(OECD, 2022) Management of Pharmaceutical Household Waste*
https://www.oecd.org/environment/management-of-pharmaceutical-household-waste-3854026c-en.htm

The intent of applying EPR, however, with a purpose to incentivize greener products, is not always a realistic or a feasible option for human medicines.

## DISCUSSION

Pharmaceuticals are a particular case of substances of emerging concern, since they are used to prevent, treat and cure diseases, with significant impact on improving public health and economic power. Therefore, any environmental measures to be applied, need to consider and differentiate **human medicines as essential public goods**, access to which must not be hindered.

This is why, according to the pharmaceutical legislation (Directive 2001/83/EC), the environmental impact must not constitute a criterion for the refusal of a marketing authorisation for medicinal products for human use. Instead, potential environmental risks posed by medicines should be assessed by the competent medicines authority and specific arrangements to limit their impact should be considered on a case-by-case basis.

APIs are an important healthcare resource that cannot be wasted or wrongly used. For that reason, the doses and durations of treatments are already calculated to optimise specific treatments, ensure patient safety, and avoid waste.

The physiological nature of the action of medicines, that treats the origin of a disease or its symptoms, may sometimes have unintended consequences on other species. Medicines interact with human biological systems in complex ways, and their formulation ensures APIs are administered and delivered where they are needed in the human body. Medicines represent decades of medical and pharmaceutical science that make them a healthcare tool for society that is not easily (or cheaply) replaced, if possible, at all.

Therefore, environmental policies to pressure the development and use of greener versions of other general products may not be applicable in the case of pharmaceuticals in the same way as in other sectors. Also, there may not be alternative medicines available that have the same efficacy and safety for a particular patient. The complexity of medicines for human use and the limits of the current scientifical and technological progress must be considered. Changing the design of a pharmaceutical compound can have impacts on the pharmacological aspects. Still, the pharmaceutical industry is committed to studying and finding new active ingredients, assessing impacts on the environment, and deploying mitigating measures that can avoid concentrations in the environment that could pose a risk to wildlife and biodiversity.

## Where does the responsibility really lie?

Medicines are some of the most powerful tools in helping people all over Europe to live longer, healthier, and more productive lives. European citizens use medicines to prevent illness, treat disease and mitigate symptoms. But there are many factors to take into consideration between the need and the use of a medicine. There is a science-based process of decision and shared responsibility between patients and healthcare professionals that leads to the use of pharmaceutical products (Figure 1).

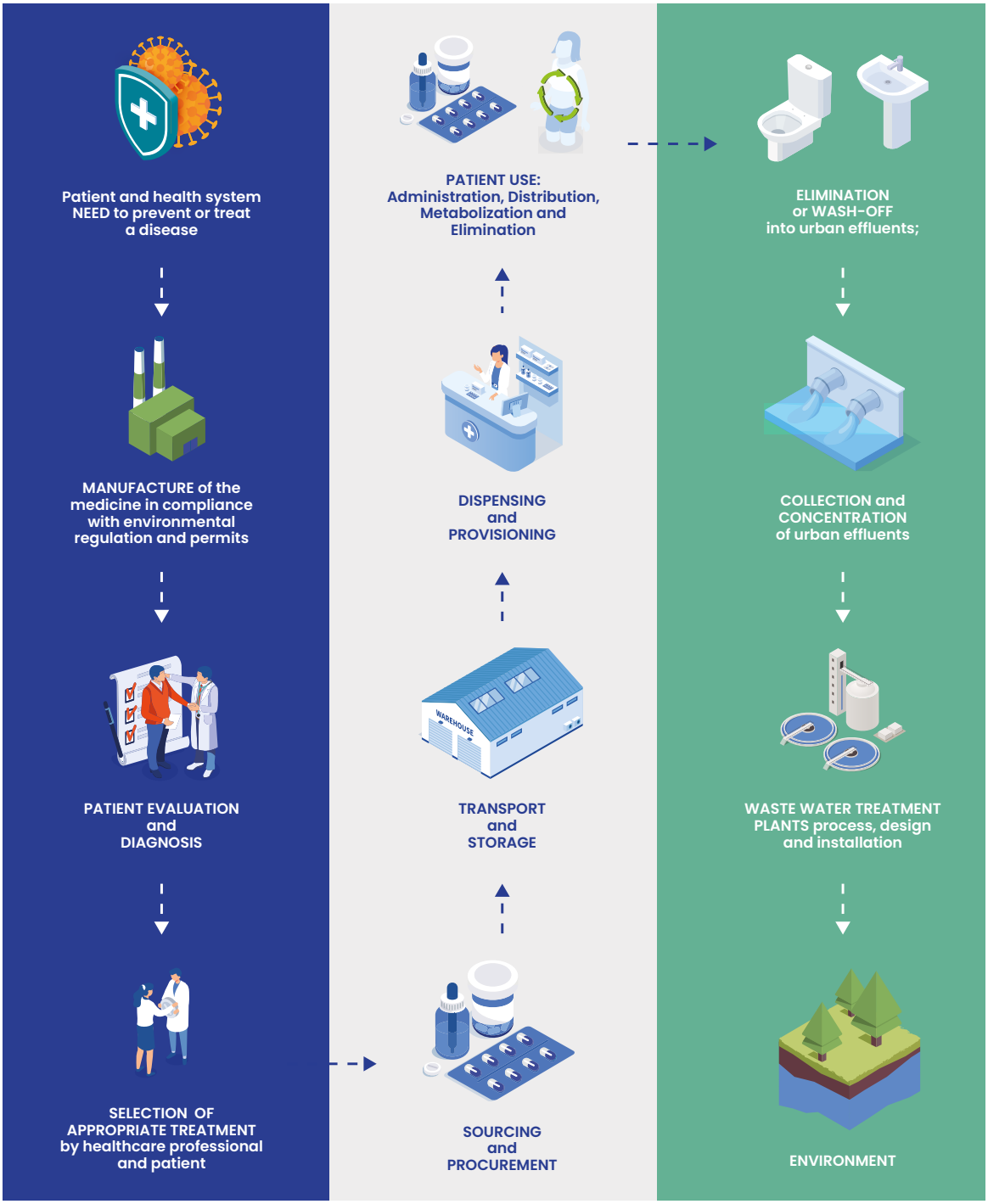



**Figure 1:**
Responsibility for APIs can be attributed to many stakeholders even beyond the lifecycle of a medicine

This process encompasses diagnosis, clinical necessity, and appropriateness of a medicine, culminating in its activity on human physiological pathways. Eventually, after use and excretion (or wash-off for topical medicines), residues are centralised in urban effluent management systems and might face different wastewater network designs, installations, and processes, before eventually reaching the environment.

Therefore, incentivizing prudent use and prescription of pharmaceuticals should remain a priority for all healthcare systems.

Pharmaceuticals have a special role in addressing the right to healthcare, by promoting individual and public health, and in ensuring the sustainability of health systems. There are many beneficiaries of medicines in addition to the producers. It needs to be considered that many healthcare factors and decisions contribute to the choice and use of medicines. For that reason, it is considered that there is a shared responsibility along the supply chain and lifecycle of a medicine.

Although some APIs of human medicines are detected, it does not mean that their concentration is harmful or is at a polluting level. A number of studies have concluded that, at the extremely low levels found in drinking water, pharmaceuticals do not present a significant risk to human health.

## Pharmaceuticals in drinking water


**Trace quantities of pharmaceuticals in drinking-water are very unlikely to pose risks to human health because of the substantial MOE or margin of safety between the concentrations detected and the concentrations likely to evoke a pharmacological effect.**

Concerns over pharmaceuticals should not divert the attention and valuable resources of water suppliers and regulators from the various bacterial, viral and protozoan waterborne pathogens and other chemical priorities, such as lead and arsenic.

SOURCE: *(WHO, 2012) Pharmaceuticals in drinking-water*
https://www.who.int/publications/i/item/9789241502085

In fact, many pharmaceuticals are removed from wastewater in part or fully by WWTP technologies and only few pharmaceuticals, that are not effectively removed, pose a potential risk to the environment.

## Traces of pharmaceutical residues in wastewater

**The consumption phase is considered to be the biggest contributor to the emissions of medicinal products into the environment, notably through excretions** and incorrect disposal of unused medicines through sinks and toilets.

Once in wastewater, **treatment can partly eliminate or remove medicinal product residues, but some traces are still detectable in effluents** as well as in the receiving surface and groundwaters. The residues remaining after wastewater treatment **depend on the composition of the medicinal product, wastewater treatment process, and initial concentrations in the influent**. For example, Ibuprofen, which is present in significant amounts in wastewater influents, is reduced by 60 to 96%, while Carbamazepine removal rates are much lower.

The mechanisms of transformations and transfer in the environment lead to the exposure of biota and constitute a potential risk for ecosystems. Although the scientific assessment of ecotoxicological effects of medicinal products on organisms is less developed compared to pesticides for example, it is becoming increasingly clear that some medicinal products, in particular anti-parasiticides, anti-mycotics, antibiotics and (xeno)estrogens, pose environmental risks in specific exposure scenarios. […] **For a range of other pharmaceuticals, environmental risks can be rather negligible, due to low environmental persistence and ecotoxicity of the compounds.**

SOURCE: *(BioIS, 2013) Study on the environmental risks of medicinal products*
https://ec.europa.eu/health/sites/health/files/files/environment/study_environment.pdf


Furthermore, through secondary and more stringent treatment, some chemicals (other than N and P), **including pharmaceuticals, are partially or entirely removed** depending on their behaviour in the process, whereas **other chemicals are effectively not removed** from the influent to the WWTP.

SOURCE: *(EC, 2019) Evaluation of the Urban Waste Water Treatment Directive*
https://ec.europa.eu/environment/water/water-urbanwaste/pdf/UWWTD%20Evaluation%20SWD%20448-701%20web.pdf

The centralisation of urban wastewater infrastructure and operations can result in hotspots of pharmaceuticals in surface water just downstream of wastewater treatment plants. A WWTP operator that fails to take steps to improve the removal of pharmaceutical residues from wastewater may also qualify as **polluter by omission**, and thus, under Polluter-Pays Principle, be required to take such steps or help fund them.

## Traces of pharmaceutical residues in wastewater

In effect, not only manufacturers, authorization agencies, healthcare providers, physicians and patients may count as polluters. **A WWTP operator that fails to take steps to improve the removal of pharmaceutical residues from wastewater may also qualify as polluter, but by omission, and thus, under PPP, be required to take such steps or help fund them.**

Admittedly, omissions are not always considered causes of relevance for attributing (moral or legal) responsibility, but mostly count as such when they represent a failure to fulfil some prior obligation, i.e., in cases of culpable negligence. However, WWTP operators are arguably under such an obligation, since their socially sanctioned task is to help secure clean waterways. **A failure to contribute to this task by taking steps to mitigate pharmaceutical pollution may thus be construed as a relevant cause of the pollution.**

SOURCE: *(Malmqvist et al, 2022) Study on the environmental risks of medicinal products*
https://www.researchgate.net/publication/356987913_Pharmaceutical_pollution_from_human_use_and_the_Polluter_Pays_Principle

## Diverse challenges of WWTP towards a circular economy

WWTPs have several challenges nowadays. One of these challenges covers contaminants of emerging concern which are of diverse origin and not only pharmaceuticals. UWWTPs need to develop their operations to face these new challenges where innovation can play a crucial part. However, only a part of this technology could be targeting pharmaceutical substances. Even so, these technologies are not specific to APIs of human medicines and, in fact, would be solving other problems of chemicals, which are present in wastewater at higher levels than APIs.

### Acknowledged challenges of WWTPs?

Past decades have seen billions of euros invested across Europe in the collection and treatment of urban waste water to remove harmful microorganisms, oxygen-consuming substances and nutrients. **This investment means that most Europeans no longer need to worry about the quality of their drinking water or local waterways.** However, our understanding of the challenges faced by urban waste water treatment has improved, for instance, in our knowledge of climate change and of the presence of hazardous substances. As we address these, we can use the opportunity to implement more sustainable solutions for:

- Storm water management and adaptation to climate change
- Urban and rural wastewater treatment provision
- Improving resource and energy efficiency
- Contaminants of emerging concern
- Compliance with European Legislation
- Financing

**In urban areas it can be a challenge to find space to install new treatment plants or upgrade existing ones.** There can be public opposition to development near residential areas, owing to noise and odour concerns.

SOURCE: *(EEA, 2019) Urban waste water treatment for 21st century challenges*
https://www.eea.europa.eu/themes/water/european-waters/water-use-and-environmental-pressures/uwwtd/urban-waste-water-treatment

WWTP governance, research and development have led to more sustainable and energy self-sufficient operations. Even if most of the public WWTP are covered by public funding, it seems that the value of treated water could increase as it becomes eligible for re-use, under the aims of a circular economy and also taking into account water shortage due to droughts in consequence of climate change.

Wastewater has a huge potential for resource recovery regarding, for instance, algae biomass[7], minerals[8], fibres, polymers and other organic materials[9], which could make these operations valuable, marketable and profitable on their own. Still, water resources must be paid while remaining affordable. That is why the necessary upgrades and investments are currently financed through taxes, water tariffs and transfers from governments.

## Technology and WWTP network design to remove pharmaceuticals

The degree of pharmaceutical removal in WWTP highly varies depending on the physico-chemical properties of the APIs and the treatment process. **Advanced wastewater treatment processes, such as adsorption (powered or granular) via activated carbon, ozonation, filtration by nanofiltration or reverse osmosis membranes, have been demonstrated to effectively remove most pharmaceuticals.** These can achieve higher removal rates for pharmaceuticals in comparison to conventional secondary wastewater treatment (activated sludge processes, or other forms of biological treatment such as biofiltration).

However, advanced treatment technologies are generally more cost-intensive than traditional technologies and increase treatment costs by a factor of two to four, depending on technology and WWTP size (Bui et al., 2016[25]). Consequently, these technologies are not so commonly used for public WWTPs, though some countries have decided to upgrade some of their facilities. For instance, Switzerland implemented advanced wastewater treatment on a large scale using ozonation and granulated activated carbon technologies.

**Decentralised point-source effluent management from hospitals, healthcare facilities, elderly homes and pharmaceutical manufacturing sites may be another route for end-of-pipe treatment.** The high concentration of medicines, contrast media, cytostatics, antimicrobial resistant bacteria and pathogens in hospital discharges may provide a case for emission capture and treatment at source.


**Currently, legislation rarely holds hospitals accountable for non-clinical wastewater discharges and excreted pharmaceuticals.** Nonetheless, several newly built hospitals, for instance in the Netherlands, installed on-site treatment facilities on voluntary basis (Dutch Waste Sector, 2018[26]). Trials and pilot projects are also underway in Germany, Ireland and Switzerland (EurEau, 2019[27]).

SOURCE: *(OECD, 2022) Management of Pharmaceutical Household Waste*
https://www.oecd.org/environment/management-of-pharmaceutical-household-waste-3854026c-en.htm

[7] https://www.eureau.org/resources/publications/eureau-publications/6091-factsheet-on-products-from-waste-water-algae-biomass-1/file
[8] https://www.eureau.org/resources/publications/eureau-publications/6092-factsheet-on-products-from-waste-water-minerals-1/file
[9] https://www.eureau.org/resources/publications/eureau-publications/6093-factsheet-on-products-from-waste-water-fibres-and-polymers-1/file

> **In terms of possible technological response, advanced oxidation has proven to successfully remove active pharmaceutical ingredients from water, and can be used close to the main emitters (e.g. hospitals and clinics) together with actions to limit the input to waste water.**

SOURCE: *(EEA, 2018) Industrial waste water treatment – pressures on Europe's environment - EEA Report No. 23/2018*
https://www.eea.europa.eu/publications/industrial-waste-water-treatment-pressures


There is still no consensus as to which sort of technology would be most cost-effective in wastewater treatment to deal with substances of emerging concern. A rational assessment would be needed to evaluate the risk from the several contaminants at a local / regional level and to decide, then, which containment or elimination measures should be established. This principle is already applied in some countries, such as Switzerland, for assessing the wastewater network needs and to upgrading the necessary WWTPs, especially the ones close to hotspots.

Other product manufacturers (**free riders**) would benefit from the implementation of WWTP technology to remove pharmaceuticals, as it would also remove other organic chemical micropollutants that may have a risk to the environment but result from non-pharmaceutical sources. There is great difficulty in pinpointing responsible industries for some of the emerging contaminants – these include natural or synthetic chemical substances that have the potential to enter the environment causing adverse ecological or human health effects (e.g. natural excreted hormones and xenoestrogens; lifestyle drugs such as nicotine and caffeine; and drugs of abuse, such as cocaine).

According to the UN, the shift in residence of the human population from rural to urban areas, combined with the overall growth of the world's population, could add another 2.5 billion people to urban areas by 2050[10]. The impact of the population increase will surely bring added challenges for the growth of WWTPs, even to control naturally occurring substances, such as human hormones (endocrine disruptors).

**+ 2.5**
**BILLION PEOPLE**
to urban areas by 2050

It is, however, of challenging proportionality that, to achieve these common objectives, it will be up to a very limited number of industry sectors, including the pharmaceutical industry, producing essential and critical goods, to be taxed under an EPR principle. Especially when the costs are addressing several unrelated challenges of wastewater treatment, by supporting the WWTP upgrade, which can be a solution for so many other contaminants of emerging concern.

Currently, there is a discretionary planning and application of WWTP technical operating capacity, that should undergo frequent revision. Therefore, technology will not benefit or be applied to all WWTPs, nor will innovation necessarily favour high-cost solutions for effective removal.

Moreover, WWTPs already receive public financing aiming at the efficient and cost-effective removal of residues and emergent pollutants, and at investing in research, technology and innovation.

[10] https://population.un.org/wup/

## Industry gathers the science on PiE to be able to respond to future challenges

Medicines currently undergo an Environmental Risk Assessment (ERA) process prior to authorisation and, with the EU pharmaceutical legislative revision, that process will be further strengthened, adding to the expansion of knowledge regarding environmental risks.

Although some pharmaceutical substances lack environmental data since they were authorised in the EU before 2006, when ERA became mandatory, it is likely that only few pharmaceuticals detected in wastewater could have harmful consequences. One evaluation concluded that less than **10%** of the APIs **could pose a potential risk to the environment**[11] even when assuming worst-case scenarios of exposure and hazard.

**less than**
**10%**
of APIs
**could pose a potential risk to the environment**

The pharmaceutical industry, in cooperation with academia, regulators, public entities and the European Commission, has been working to close the knowledge gaps on the environmental risk of medicines, through the IMI/IHI project PREMIER[12]. By facilitating access to data and tools to regulators, environmental organisations and policy makers, a new standard for environmental protection across Europe can be adopted. The evidence-based information system and tools generated by PREMIER will give regulators, water managers, and the scientific community access to valuable knowledge that can be used to advance on the responsible use of medicines and mitigate impacts on the environment.

The **PREMIER**[13] project aims at addressing data gaps so we can expect, by 2026, to have a better understanding of the APIs that have a potential to pose a greater environmental risk.

PREMIER is built on the success of the previous IMI project iPiE[14], which has developed a technical model that draws on national drug consumption data to estimate the concentrations of pharmaceuticals in the environment across Europe. iPiE released an online tool, iPiE*SUM (iPiE Summary Database Search), that summarises the properties, environmental toxicity, and characteristics of APIs.

The iPiE project has produced a number of important scientific publications and technical tools, which will improve scientific knowledge of environmental hazards and risks of human medicines, will make risk assessment and prediction more powerful, and will support the prioritization of large numbers of APIs with lack of environmental data.

In terms of science, the project developed the following:

- A high-quality database on APIs, including mainly industry-sponsored studies for environmental fate, effects and behaviour of APIs, which had mostly not been publicly accessible before
- A high-resolution spatial model to predict exposure to pharmaceuticals in European surface waters (ePiE)
- Quantitative Structure-Property Relationships (QSPRs) to predict sorption, biodegradation, and bioconcentration of APIs

[11] *Küster and Adler (2014)* https://royalsocietypublishing.org/doi/10.1098/rstb.2013.0587
[12] https://imi-premier.eu/
[13] *PREMIER: Prioritisation and Risk Evaluation of Medicines In the EnviRonment*, running 2020-2026 with approximately 10M€ under IMI funding, 15 public partners (including EMA) + 10 industry partners.
[14] https://www.imi.europa.eu/projects-results/project-factsheets/ipie

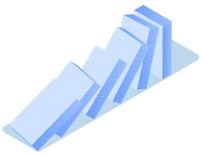
- A database that reflects the presence of pharmacological targets of APIs in environmental taxa (ECOdrug)
- Acute and chronic baseline models for effects in fish, invertebrates and algae
- Improvement of the fish plasma model for estimating critical environmental concentrations

It is also worth noting that a wealth of environmental exposure data exists in the published, peer-reviewed literature as well as in publicly available databases. Data shows, in the number of samples measured which contain pharmaceutical residues, that these are well below concentrations that cause ecotoxicological effects.

Also, recent new evidence[15] showed that the measured environmental concentrations reported in upper and upper-middle income countries (including countries of Europe), are comparatively lower, which must be attributed to the effectiveness of existing waste water treatment capacity and industrial effluent management practices and largely responsible disposal behaviour.

There remain, nonetheless, some **knowledge gaps** to focus on in the future, particularly on long-term exposure effects in very low concentrations and substance combination effects, which have not yet been studied.

## Unintended impact of applying EPR to pharmaceuticals



Health systems in the EU are varied and reflect different societal choices. For that reason, primary responsibility for health protection and, in particular, healthcare systems, continues to lie with the Member States (subsidiarity principle).

While EPR is a central criterion in managing the impact of manufacturing activities, pharmaceutical manufacturers must first and foremost ensure the safety, efficacy and quality of their products.

Within a Polluter-Pays Principle, by definition, pollution control is assigned to the polluters, who would absorb costs without excessive setback to their own or other actors' interests. It is unclear that, having medicines manufacturers bearing the costs meets this condition because these provisions will induce external expenses with indirect burden on health systems and patients.

Having medicines manufacturers pay for WWTP upgrades will surely incentivize the cost recoup through higher drug prices, aggravating the national pharmaceutical budget, or forcing them to leave markets where such requests are made or in which a product would no longer be economically viable[16]. Therefore, there could be unintended negative impacts on the availability of medicines, which would unfairly penalize patients who rely on these products for their health and wellbeing.

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[15] *Wikinson et al (2022):* https://www.pnas.org/doi/10.1073/pnas.2113947119
[16] *Nijsingh et al. (2019)* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6833301/

**Less than 10% of the APIs could pose a potential risk to the environment**[17] and most drugs (> 80%) indicate a low environmental risk for the endpoints assessed in a European context.[18] Again, it is unclear whether responsibility should befall on the manufacturers of APIs, on Marketing Authorisation Holders, on the supply chain stakeholders (including pharmacies) or on society as a whole in a collective effort through public investment, as it has been the case for UWWTPs until today.

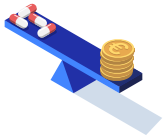
Even if EPR were to be applied, there is an added challenge in making a fair distribution of costs due to the scenario of **uncertainty** (relating to acknowledged data gaps) and of **relativity** (active pharmaceutical substances of human medicines are but a fraction of the micropollutant substances removed by improved wastewater treatment). It is also hard to pinpoint the exact origin of molecules used as APIs (and their metabolites) deemed to pose risk to the environment.

If a blanket environmental levy were to be applied to all pharmaceutical industry, this would increase the final purchasing price of medicines to both national health systems and to self-medicating patients and both of which are socially questionable.

Access of patients to medicines is already restricted in many instances in Europe due to budget control measures or due to high co-payments (out-of-pocket expenses for patients, where these exist). Any EPR tax under consideration for human medicines would exacerbate inequities in access to medicines which the Commission is working to reduce in the Pharmaceutical Strategy for Europe. This tax would disproportionately burden patients in the following categories:

- Elderly reliant on polimedication for non-communicable diseases.
- Cancer patients reliant on chemotherapy.
- Chronic pain patients reliant on pain medication.
- Mental health patients reliant on anti-depression medication.
- Female patients reliant on hormonal treatments.
- Children and hospital patients receiving anti-infective treatment.

These categories of the population are usually more economically challenged when compared to the European average. Costs would be transferred either through higher co-payments or direct costs (pain medicine and birth control are typically paid out of pocket, many chronic disease medicines include a co-payment) or through lower access as less expensive medicines could be withdrawn from the market due to the increased tax. Financing UWWTPs upgrade through the water bill to households would distribute costs equally between the sick and non-sick populations (or between men and women for birth control) and include protections for the lowest socio-economic categories of the population due to public service obligations.



The pharmaceutical industry believes that any possible changes to the EPR concept for tackling the issue of PiE need to take into account the fundamental right to healthcare[19] which is based on solidarity between the users and the non-users of the healthcare budget (between the sick and the healthy) and not to impose additional surcharges on patients for consuming medicines.

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[17] *Küster and Adler (2014)* https://royalsocietypublishing.org/doi/10.1098/rstb.2013.0587
[18] *Gunnarsson, et al (2019)* https://www.sciencedirect.com/science/article/pii/S0160412019309493
[19] https://fra.europa.eu/en/eu-charter/article/35-health-care

## Negative impact of EPR in price regulation of Generic Medicines

In Europe, **pharmaceutical pricing is regulated** and there are **limitations to the ability to adjust** pricing of medicines to account for increased operational costs. The intention of regulating pricing is to **protect patients' access to medicine** and **manage public health budgets**. Access to generic medicines is essential for that purpose. At the same time, market-authorization holders (MAHs) of generic medicines, are particularly vulnerable to the combined effect of increased cost due to new regulations such as EPR, incremental price reductions and price cutting measures, strong competition and price regulation that in most cases doesn't allow increases in the price of pharmaceuticals, even if there is an increase in operational costs.

To illustrate the potential unintended negative impact on availability of off-patent medicines due to application of the EPR, cost assumptions in the below graphic were based on real-world findings from Swedish wastewater treatment plants; the **cost of implementing techniques for advanced purification of drug residues was found to vary widely, but to be in the range of 0.5% to 4.5% of the total expenditure on pharmaceuticals**.

Allocation of the costs of the advanced purification techniques solely to the market authorisation holders may, in the worst case, lead to **up to 24% of the product lines falling below the cost of production**, as illustrated by Figure 2, posing challenges to MAHs' ability to continue marketing the products.

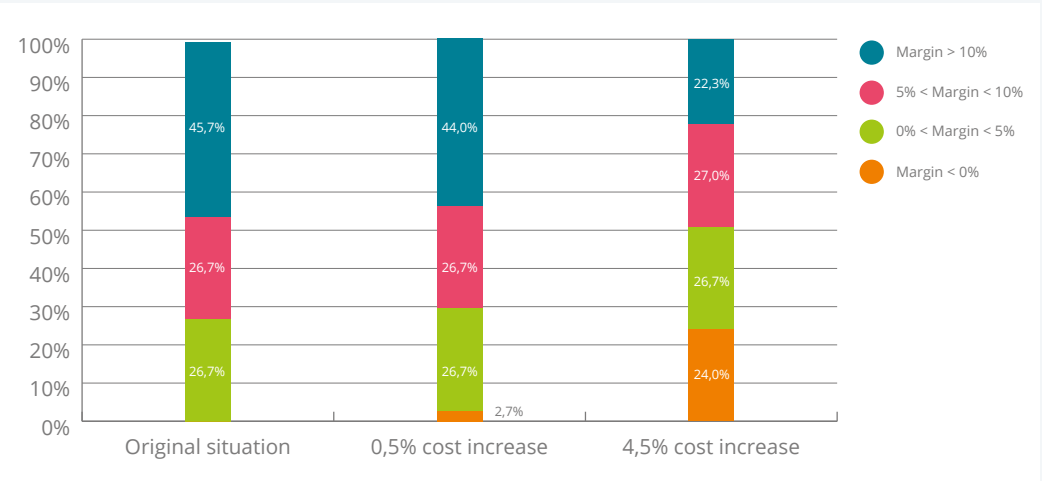



**Figure 2:**
Impact of 0.5% (middle) and 4.5% (right) cost increase compared to the basic situation (left)

SOURCE: *(Capgemini, 2020) New regulation and generic medicine shortages: Impact and solutions*
https://www.capgemini.com/nl-nl/wp-content/uploads/sites/7/2020/11/Report_New-Regulation-and-Generic-Medicine-Shortages_Impact-And-Solutions.pdf

## Legality of the application of EPR to pharmaceuticals

A special environmental levy on medicinal products for human use would violate primary European law and secondary environmental law. An EPR for medicinal products cannot be derived from the PPP for the particular case of pharmaceuticals. The steering concept of comprehensive product responsibility is not applicable to medicinal products for human use.

Medicinal products for human use are goods of a special kind and are subject to special laws. The public authority has a substantial interest in the development and existence of effective and high-quality pharmaceuticals with low side effects. From this formal perspective, pharmaceutical law is governed by special legislation, the Directive 2001/83/EC – the European Medicines for Human Use Code. By legal definition (Art. 1 No. 2 of Directive 2001/83/EC), a medicinal product for human use is "any substance or combination of substances presented as having properties for treating or preventing diseases in human beings".

They are not goods or services in a general sense and cannot be compared and treated equally with trace substances of, e.g., paints and coatings, cosmetics and detergents or debris from tire abrasion. Medicinal products are in a highlighted specific regulatory context of protection of people. The Directive 2001/83/EC regulates specifically the prerequisites for placing effective, high-quality and safe pharmaceuticals on the market.

The central element of the marketing authorization procedures for pharmaceuticals is the risk-benefit assessment: The therapeutic benefit of the medicinal products application is essentially assessed in relation to the application in connection with quality, safety and efficacy. Only if the benefit outweighs the risk, will the marketing authorization be granted for medicinal products for human use. The applicant for the marketing authorization must submit documents for the assessment of potential environmental risks, in order to be able to demonstrate potential hazards in connection with waste disposal.

However, in the case of medicinal products for human use, it would not be acceptable that a marketing authorization is refused because of potential environmental risks. Instead, mitigation measures are proposed to better control possible environmental impact.

From a formal perspective, pharmaceutical law is governed by special legislation and therefore excluded from the environmental sector. According to the legal principle *lex specialis derogat legi generali,* the more specific rule prevails over the more general rules. Therefore, the Pharmaceutical Directive 2001/83/EC takes precedence over cross-sectorial environmental provisions.

A special environmental levy on medicinal products for human use would also be in violation of predominant primary law. The use of an economic steering instrument customary in environmental law would counteract the priority of human life and health protection over other legal interests; especially since the requirement to design medicinal products in an environmentally friendly manner from the outset seems obvious but is frequently not even possible in the case of chemically synthesized active ingredients.

It is also questionable whether the European Union has legislative competence of its own to apply this kind of tax law or for any other levies.

A levy regulation based on Article 191(1) TFEU, pursuant to which the environmental policy of the Union must contribute to the preservation of the environment and the improvement of its quality, would violate European law in the field of pharmaceutical law – at least in the field of medicinal products for human use.

The introduction of extended producer and product responsibility in the field of medicinal products for human use is not comparable, e.g., with the regulatory content of waste or plastic product law.

Pursuant to the Waste Framework Directive (cf. Article 8 of Directive 2008/98/EC), the Member States may take appropriate environmental policy measures – accordingly also impose the financial responsibility in accordance with the Polluter-Pays Principle either partly or fully on the producer of the product (extended producer responsibility).

However, the management of waste, which may be harmful to the environment (e.g., sewage sludge), cannot be equated with the manufacture and marketing of medicinal products for human use. A conclusion by analogy would not be justified.

In humans, the environmental concern may not be used in the central risk-benefit assessment; steering effects intended under wastewater law must not impair the risk-benefit balance of pharmaceuticals, which is oriented toward human health, and certainly not by means of economic instruments.

As correct and important as economic instruments may be for the implementation of environmental protection concerns and sustainability considerations in the general economy, such arguments have no room in the development and production of medicinal products. Otherwise, this would entail the risk that compromises in the efficacy or safety would be made in the material development of pharmaceuticals in order to avoid micro-residues.

In other words: The Union lawmaker lacks a legitimate purpose to enforce an environmental policy measure by means of a European stimulated special levy in the field of medicinal products for human use at the municipal level.

By this, it is already clear with regards to the question of the legitimate reason that a steering instrument of water management must neither be used to disturb the sensitive risk-benefit balance under pharmaceutical law nor to possibly influence it to the detriment of human health. In this respect, the imposition of a financing burden for wastewater disposal based on secondary environmental law of the European Union represents an unjustified infringement of fundamental rights pursuant to Articles 15, 16, 17 and 20 of the Charter of Fundamental Rights of the European Union (CFR).

Moreover, the EU would interfere with the levy-related autonomy of the Member States and transgress its competences (ultra vires doctrine). Union law is faced with the competence problem in that the Union is not generally authorized to impose levies, i.e., taxes, contributions, fees or even special levies, purely on the basis of financial constitutional legitimacy. This is regularly one of the sensitive core competencies of the Member States. If there is no legitimate steering effect in this respect within the framework of extended product responsibility, the European legislature enters the controversial field of a possible competence shift of the Union into the core area of the Member States. This can be assumed if a European Urban Waste Water Treatment Directive or another secondary environmental regulation imposes mandatory levies in the Member States without being authorized to do so by a substantive competence title – and

as mentioned before the Union legislator lacks a legitimate purpose to enforce an environmental policy measure by means of a European stimulated special levy in the field of medicinal products for human use at the municipal level.

The rationale of a financing responsibility beyond legitimate environmental control purposes interferes with the levy-related autonomy of the Member States. Such a structurally significant shift can be assumed in any case in a justifiable manner only if the European Union issues binding tax regulations for the Member States, which, insofar, do not find a sufficient basis in an accessorily existing competence.

## Other options to EPR

### EPR and Design for Environment

> As compared with alternative policy instruments, an attraction of EPR is the incentive it creates for producers to **consider post-consumer waste-management costs when making decisions about product design and marketing**. Such "Design-for-Environment" incentives are an important part of the overall assessment of EPR, but their practical evaluation could be difficult.
>
> In fact, the original motivation for product take-back mandates, including the German packaging program, was to **provide incentives for producers to make changes to products that would reduce waste management costs**. Those changes would include **improving product recyclability and reusability, reducing material usage and downsizing products, and engaging in a host of other so-called "design for environment" (DfE) activities**.
>
> SOURCE: *(OECD, 2005) Analytical framework for evaluating the costs and benefits of EPR programmes*
> http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?doclanguage=en&cote=env/epoc/wgwpr(2005)6/final

Medicines are not recyclable or reusable items. Take-back schemes have been put in place in countries where waste is not incinerated, in order to reduce the amount that goes to wastewater or landfill.

Medicines are not "designed-for-environment". They are health tools that are designed to treat or prevent illness ensuring safety, quality, and efficacy to the patients that take them. Discovery and development of innovative medicines, that are both safe and effective, to supply healthcare unmet needs of the population, is difficult. Adding another layer of concern will hinder the drug design pathway and deprive Europeans of healthcare solutions.

Other policy measures should, therefore, apply, targeting the effective removal from the environment.

## EPR and non-EPR policy instruments

There are several different policy instruments, and variants of those instruments, that fall under the EPR umbrella. The following is a list of the most common instruments; it is not meant to be exhaustive but includes most of the policy tools used in practice:

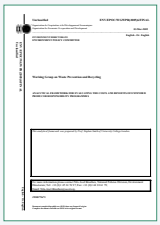
- Product take-back mandate and recycling rate targets
- Product take-back mandate and recycling rate targets, with a tradable recycling credit scheme
- Voluntary product take-back with recycling rate targets
- Advance recycling fees (ARF)
- ARF combined with a recycling subsidy

All of these policy instruments have the feature that they make the producer of a product financially or physically responsible for the end-of-life environmental impacts of the product he produces. In this sense, all could be considered EPR. **However, they have very different incentive effects and ultimately may lead to different environmental outcomes. Also, costs of the instruments may differ widely.**

**There are other policy instruments that governments may employ that can lead to similar outcomes to EPR but that do not focus upstream on producers.**
We list four such non-EPR instruments here:

- Landfill bans
- "Pay as you throw" pricing of waste collection/disposal
- Recycling subsidies
- Recycling investment tax credits

SOURCE: *(OECD, 2005) Analytical framework for evaluating the costs and benefits of EPR programmes*
http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?doclanguage=en&cote=env/epoc/wgwpr(2005)6/final



Still, all policy options target tangible material items that are possible to recycle. So far, the EPR concept has not been applied at the molecular level. The collection and subsequent recyclability of substances at the molecular level, such as pharmaceuticals, is still far from the reach of current science and technology.

## Other options to deal with PiE beyond end-of-pipe measures


While pharmaceuticals have undeniable benefits, countries struggle to address their potential impacts on drinking water quality, and ecosystem and human health. Pharmaceutical pollution challenges traditional water quality management, requiring new technologies in wastewater treatment and behavioural changes in industry, agriculture and health care sectors and society at large.

Current policy approaches to water quality protection are typically reactive; measures are adopted only when routine monitoring is in place and risks can be proven. Many country responses to the pharmaceutical problem have focussed on monitoring and end-of pipe measures (e.g. upgrading wastewater treatment plants and implementing public take-back programmes for unused and expired medicines). However, upstream, source-directed and use-orientated approaches are emerging, such as restrictions on the use of antibiotics in agriculture, green pharmacy and public environmental health campaigns.

SOURCE: *(OECD, 2019) Pharmaceutical Residues in Freshwater*
https://www.oecd-ilibrary.org/environment/pharmaceutical-residues-in-freshwater_c936f42d-en

# Good practices in WWTP upgrade for contaminants of emerging concern

Some countries have already had the initiative to carry out upgrade programmes for WWTPs to address Contaminants of Emerging Concern (CECs). Switzerland did not apply any EPR model but followed a User-Pays Principle instead.

## Upgrade of WWTPs in Switzerland

In 2014, the Waters Protection Act was revised, following agreement by Parliament, to further improve wastewater treatment for the removal of CECs (including pharmaceuticals). The revised Act involved three policy instruments:

i) a new technical wastewater treatment standard, and
ii) a nationwide wastewater tax, and
iii) public subsidies to fund technical upgrades of WWTPs.

The technical standard requires selected WWTPs to remove 80% of CECs from raw sewage, measured on the basis of 12 indicator substances, by 2040.

**The majority of the costs (75%) are financed by a new nationwide wastewater tax** of CHF 9 per person per year, which is earmarked in a federal fund to upgrade WWTPs. The remaining 25% of costs are covered by the municipalities. As WWTPs are upgraded and become operational, the municipalities are exempted from the tax.

Furthermore, a **national online survey indicated that the public were willing to pay the tax** for reducing the potential environmental risk of pharmaceuticals; the average willingness to pay per household was CHF 100 per year, generating a total annual economic value of CHF 155 m per year.


SOURCE: *(OECD, 2019) Pharmaceutical Residues in Freshwater*
https://www.oecd-ilibrary.org/environment/pharmaceutical-residues-in-freshwater_c936f42d-en

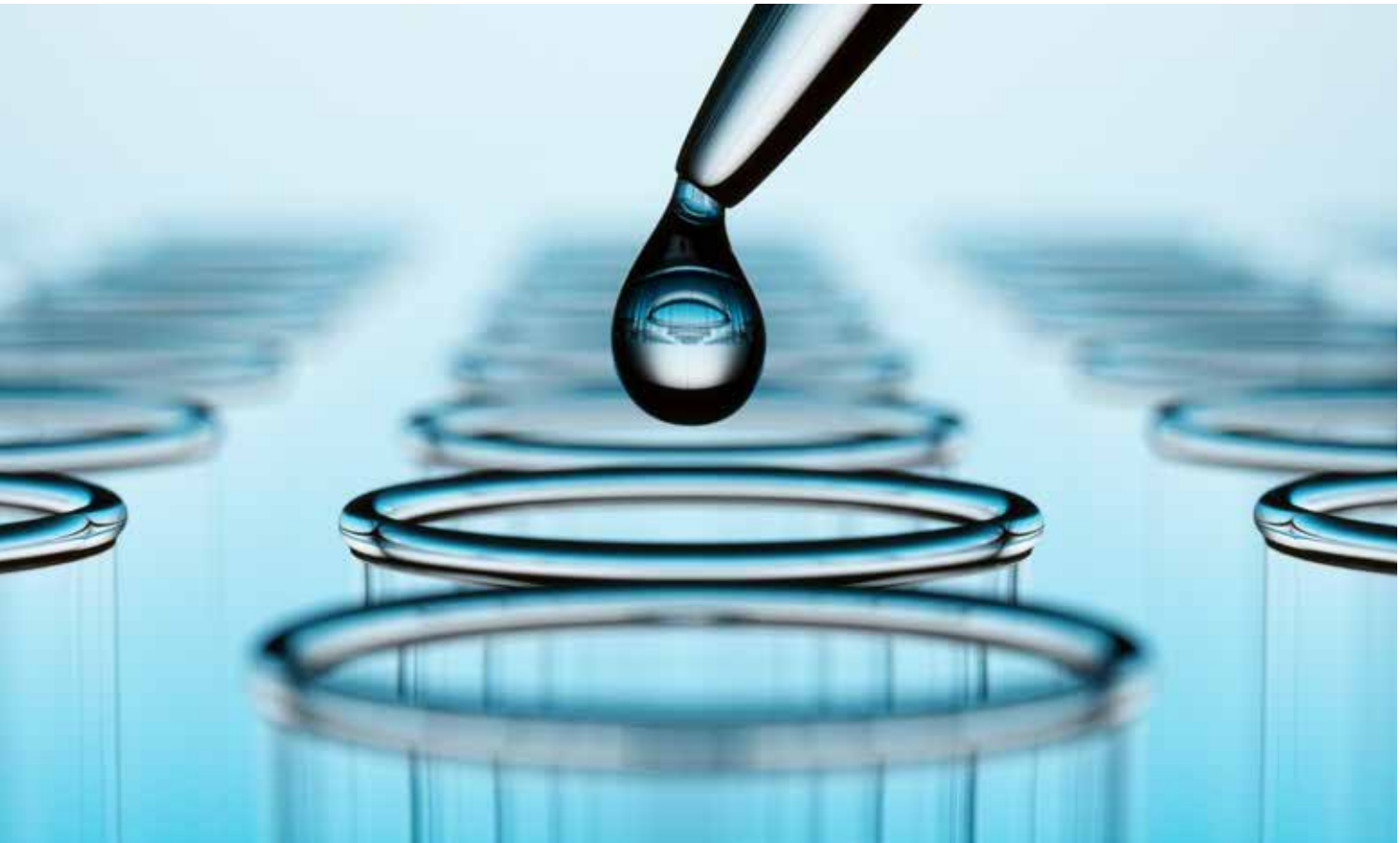
## Dutch “Chain approach” to PiE


In the Netherlands, a holistic “chain approach” is being used to address the issue of pharmaceutical residues (both human and veterinarian) in water. The programme started in 2016 and considers the entire cycle, from the source to the end of the pipe, and supports various stakeholders in their voluntary efforts to reduce pharmaceutical pollution in water.

When initiating the programme, four ‘rules of the game’ were established and agreed upon:

1) Patients must keep access to the medicines they need (i.e. medicines shall not be banned),
2) All actions taken in the pharmaceutical chain should have a pragmatic approach and should be aimed at solving problems (measures for the sake of appearances to be avoided),
3) All stakeholders act where they can, within acceptable costs, and
4) Stakeholders should not wait for other stakeholders to take the first step.

SOURCE: *(OECD, 2019) Pharmaceutical Residues in Freshwater*
https://www.oecd-ilibrary.org/environment/pharmaceutical-residues-in-freshwater_c936f42d-en



# CONCLUSION

The pharmaceutical industry remains committed to making a positive impact on the lives of patients while operating sustainably and continues to embrace the Commission's focus on delivering on the European Green Deal for a more sustainable Europe. We recognise that reducing our environmental footprint is an important step we can take to positively impact human health.

In addition to actively mitigating climate change and increasing focus on transitioning to circularity, the pharmaceutical industry is committed to playing a role in addressing pharmaceuticals in the environment and is actively engaged in minimising the impact of its activities on the environment, whilst remaining mindful of patient needs and ensuring access to medicines.

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 medicines.

Dialogue should be open and transparent, involving healthcare, social welfare, environment regulatory authorities, wastewater and pharmaceutical industries, patients, scientists and environmental NGOs, to aim for a constructive approach that can balance our shared ambition for clean water in Europe with our mission of securing access to healthcare for all.

Pharmaceutical residues **are only a small fraction** of the substances that an improved wastewater treatment would remove, allowing for an unfair model in which a great majority of polluting substances ("free-riders") would benefit.

The application of EPR to pharmaceuticals to finance wastewater treatment plants would need to be proportional, which is challenging:

- given the acknowledged data gaps both on the potential risks and on pinpointing the provenance of a pharmaceutical or its metabolites,
- given the unclear attribution of responsibilities addressing healthcare needs and medicines use, including responsibility by omission,
- given the limited feasibility of upstream options (e.g. "greener" pharmaceuticals) and potentially impose considerable costs on health systems and patients
- given the potential collateral benefit of improved removal of various non-pharmaceutical substances,
- especially, given the precedent of considering the molecular level as part of a product.

Having medicines manufacturers pay for WWTP upgrades will likely incentivize the cost recoup through higher medicine prices, aggravating the national pharmaceutical budget, or forcing them to leave markets where such requests are made or in which that product would no longer be economically viable. Therefore, there could be unintended negative impacts on the availability of medicines, which would unfairly penalize patients who rely on these products for their health and wellbeing.

By **negatively affecting patient access to medicines**, this measure would exacerbate inequities and contradict one of the main principles of the Commission's approach to Pharmaceuticals in the Environment, which states that any actions taken in this field must not jeopardise patient access to safe and effective pharmaceutical treatments.

Costs would be transferred either through higher co-payments or direct costs (pain medicine and birth control are typically paid out of pocket, many chronic disease medicines include a co-payment) or through lower access as less expensive medicines could be withdrawn from the market. It would also be misaligned with the goals of the European Pharmaceutical and Industrial strategies.

**There are clear legal opinions, data and evidence informing that EPR is not an adequate and proportionate** measure to deal with medicinal and pharmaceutical residues, in comparison with other options that have been proven to successfully address the issue.

- Legal opinion *Limits of Union law and Union constitutional law* regarding a special levy on medicinal products for human use (Prof. Udo Di Fabio)
- OECD *Financing Water Supply, Sanitation and Flood Protection*
- OECD *Management of pharmaceutical household waste*
- Government of The Netherlands *Reducing Pharmaceutical Residues in Water: A Chain Approach*
- Government of the Swiss Confederation *Optimization of Wastewater Treatment Plants*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