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EurEau Position Paper: Pharmaceutical legislative package

EurEau supports the Commission's approach to promoting environmental protection coupled with access to medicines. While the proposal offers long-overdue advances in controlling pollution from pharmaceuticals at the source, it must go further in curbing excessive use of over-the-counter medicines, take into account risks posed by metabolites and transformation products, and provide further transparency for environmental risk assessments.

1. Introduction and general comments

EurEau welcomes the proposed Pharmaceuticals Directive and Pharmaceuticals Regulation. We support the Commission's ambition to improve access to medicines across the EU, an ambition which must go hand in hand with environmental protection.

The proposal's environmental provisions form the cornerstone of the Commission's Strategic Approach to Pharmaceuticals in the Environment, whose holistic supply-chain approach has already led to the proposal of end-of-pipe measures such as quaternary treatment requirements for many urban wastewater treatment plants in the proposed revision of the Urban Wastewater Treatment Directive (91/271/EC, UWWTD) as well as new environment quality standards (EQS) for pharmaceutical active substances in the Groundwater Directive (2006/118/EC, GWD) and Environmental Quality Standards Directive (2008/105/EC, EQSD). In addition, the revised Drinking Water Directive (2020/2184, DWD) also introduced active pharmaceutical ingredients (API) such as beta-estradiol to its watch list, which some Member States have complemented with additional APIs in their transposition, for instance azithromycin and diclofenac in the case of Spain.

This latest legislative proposal, which regulates the authorisation and marketing of pharmaceutical products, complements these downstream measures with indispensable control at source of pharmaceutical pollution.

Pharmaceuticals, when released to the aquatic environment, can pose risks to nature and public health. The European Commission therefore proposed new requirements for many Urban Wastewater Treatment Plants to remove 80% of certain substances by this pathway in the UWWTD revision. This new requirement has come alongside the creation of an Extended Producer Responsibility (EPR) scheme for producers of pharmaceuticals and

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cosmetics. EurEau reiterates its support for EPR as proposed by the Commission in the current UWWTD revision, in line with the Polluter Pays Principle.

While such end-of-pipe measures are needed to ensure the comprehensive protection of water bodies and drinking water resources, they are not sufficient on their own and cover only one of multiple pathways for pollutants to enter the aquatic environment. Control at source remains the most effective way to tackle pollution, in particular micro-pollutants such as pharmaceutical residues. We welcome the long-overdue application of this principle, enshrined in the Treaties, to the marketing of medicines in the EU.

The proposal offers a more meaningful role for Environmental Risk Assessments (ERAs) in the authorisation process for medicines in the EU, particularly by requiring that environmental risks identified by the ERA are sufficiently addressed before a product is authorised. Furthermore, if risks are expected, ERAs will have to be conducted for substances authorised before 2005, though existing ERAs will not be updated to specify how the environmental risks of products already on the market are to be addressed. Regrettably, the proposed texts do not grant either the public or drinking water and wastewater operators full access to ERAs, although our sector needs this information to conduct its own risk assessments under the DWD and UWWTD (under revision).

Moreover, in order to get a full picture of potential impacts on human health and the environment, assessing the specific risks posed by pharmaceuticals when going through drinking water and wastewater treatment processes should be made an integral part of the ERA.

We also welcome the ban of over-the-counter sales for products containing substances among the most harmful categories (PBT, vPvB, PMT, vPvM[1]), although this essential control-at-source measure should apply to additional substances in order to bring coherence with the revised EQSD.

2. EurEau's detailed position

From our initial analysis, the main topics under discussion in the Directive and the Regulation are: environmental risk assessments, the use of environmental criteria for marketing authorisations and the prescription status of products containing environmentally harmful substances.

Where they overlap, we have grouped our comments on the Directive (which concerns national marketing authorisations as well as other topics such as prescription status) and on the Regulation (which concerns EU-wide centralised marketing authorisations).

[1] PBT: Persistent, Bioaccumulative and Toxic; vPvB: very Persistent and very Bioaccumulative; PMT: Persistent, Mobile and Toxic; vPvM: very Persistent and very Mobile.

Benefit-risk balance (Article 4, Directive)

While we welcome the expanded definition of environmental risk assessments (see below), we consider that the benefit-risk balance should also take into account environmental risks, in addition to risks relating to the quality, safety or efficacy of the medicinal product. While this is particularly relevant to the Commission's objective of combating anti-microbial resistance (AMR), it would also bring the proposed Directive in line with the equivalent definition in Regulation (EU) 2019/6 (Veterinary Medicinal Products Regulation).

Environmental risk assessment for new products (Articles 4 &. 22 and Annex II, Directive; Article 6, Regulation)

We strongly welcome the changes to the contents of environmental impact assessments (ERAs) to include risk prevention, limitation and mitigation measures. Under current legislation, ERAs for pharmaceutical products must identify the risks posed by the product and its use, but do not have to offer measures to address those risks. The proposal requires applicants to specify how they intend to avoid or limit emissions to air, water and soil and justify that these are appropriate and sufficient, bringing pharmaceuticals legislation in line with the control-at-source principle enshrined in Article 191 TFEU.

We consider, however, that ERAs should take a full view of environmental risk and specifically address potential impacts not just of substances present in the pharmaceutical product but also of their **metabolites and transformation products**. To do this, it is necessary to assess the effects of standard wastewater treatment processes on a product's active substances and their metabolites. The effects of drinking water treatment processes must also be investigated in order to assess potential risks to public health due to the release of the medicinal product in the environment (specifically water resources used for the production of drinking water). The proposed Directive should specifically ensure that no product is authorised if it can disrupt the ability of water services to supply clean drinking water or discharge treated wastewater safely into the environment.

Moreover, some active substances, in particular substances classified as **mobile and persistent**, can pass unabated through ordinary treatment processes, meaning that end-of-pipe measures are not sufficient to prevent these substances from harming the environment through wastewater discharges, or public health through drinking water supply. We fully support the requirement to specify in the ERA whether these substances (PMT and vPvM) are present in a pharmaceutical product. We also welcome this requirement for substances classified as PBT, vPvB, and as endocrine disruptors. The new hazard classes as laid out in the 1272/2008 Classification, Labelling and Packaging (CLP) Directive (currently under revision) should be taken into consideration as well to create coherence within the European legislative framework, especially when it comes to the protection of the environment from chemicals and pharmaceutical substances.

Environmental risk assessment for existing products (Articles 23 & 22.6, Directive)

We welcome the requirement to conduct an environmental risk assessment for all pharmaceutical products currently on the market, including those authorised before 30 October 2005, when ERAs became part of the authorisation process.

However, we call upon the European Medicines Agency (EMA) to consult drinking water and wastewater operators when setting the scientific criteria for the identification of products as potentially harmful under Article 23.2. The impact of drinking water and wastewater treatment on active substances and the ability of water services to remove these substances must be taken into account in the scientific criteria and resulting prioritisation of ERAs. This is a procedure that is also common in other chemicals authorisation legislation, such as the Plant Protection Products Regulation (1107/2009)[2].

Moreover, while we recognise the limits of institutional capacity to clear the backlog of ERAs created by this Article, the Directive should specify a maximum timeframe for ERAs to be submitted as part of the EMA programme referred to in Article 23.1. This timeframe should not exceed **10 years**. This would provide transparency and insights for all actors involved, including drinking water and wastewater operators who will rely on these ERAs for their own risk assessment obligations under the DWD and UWWTD (under revision).

Finally, the proposed Directive does not provide for an update to the ERAs of products authorised since 30 October 2005 to bring them in line with the new requirements set out in the text. The assessments conducted for these products, while they identified environmental risks, did not have to specify any measures to mitigate those risks. **We call for existing ERAs to be updated** or, at the very least, complemented by an addendum identifying risk mitigation measures and justifying that these are appropriate and sufficient, **in line with Article 22.3**.

In this regard, the requirement laid out in Article 22.6 to update ERAs in the event that new information arises, particularly from the monitoring of water bodies under the Water Framework Directive (2000/60/EC, WFD), is welcome and necessary but not sufficient as the greatest benefit could be achieved if all ERAs from after 2005 would be updated.

Publication of environmental risk assessments (Article 43.5, Directive; Article 16.3, Regulation)

We welcome the requirement, as part of the centralised procedure laid out in the proposed Regulation, for the EMA to publish a European public assessment report (EPAR) containing a summary of the ERA, and the assessment of the ERA by the Agency. The equivalent requirements laid out for national procedures in the proposed Directive are much more limited, however, as competent authorities need only publish an assessment report

[2] Guidance document on the impact of water treatment processes on residues of active substances or their metabolites in water abstracted for the production of drinking water; EFSA Journal 2023; 21 (8):8194.

containing comments on the ERA.

For both legal texts, we call for further transparency by requiring the **publication of the ERA in its entirety**. At the very least, drinking water and wastewater operators should be given access to the full ERA, so that they can take its findings into account in the course of their own risk assessment obligations under the DWD and the UWWTD (under revision).

In addition, we support further transparency for the public by ensuring that **medicines which pose a significant risk to the environment display a warning** to this effect on their packaging. The warning should be clear and easily understandable, for example by using a traffic-light system. This will enable the public and healthcare professionals to make informed choices between alternative treatment options.

Conditional authorisation (Article 44, Directive; Articles 19 & 20, Regulation)

We welcome the possibility, under the proposed Directive, for competent authorities to grant conditional authorisation provided that post-authorisation ERA studies or other further investigations of environmental risk are conducted.

We call for these provisions to be replicated in the proposed Regulation, where the EMA can require an authorisation holder to conduct a post-authorisation ERA study to further investigate risks to the environment (Article 20.1.c) but not make the authorisation conditional upon the result of these studies.

For the sake of control at source but also of legislative coherence, we consider that the Regulation should be aligned with the Directive on this matter, by empowering the EMA to grant conditional authorisations subject to further ERA studies under Article 19.

Refusal of authorisation (Article 47, Directive; Article 15, Regulation)

We strongly support the inclusion of **environmental risks as grounds for refusing a marketing authorisation**, as is already the case for veterinary medicines under the Veterinary Medicinal Products Regulation. We fully agree with the proposal that ERAs must be complete and sufficiently substantiated, and that any risk identified in the ERA must be sufficiently addressed by the applicant before an authorisation is granted. Adding these criteria to the grounds for refusal listed in this article is indispensable to controlling pollution from pharmaceutical products at the source while simultaneously creating an incentive for the production of greener and more sustainable medical products.

Medical prescription (Article 51, Directive)

We strongly support the prescription requirement (i.e. ban on over-the-counter sales) for medicines containing active substances classified as **PBT, vPvB, PMT or vPvM** and welcome the explicit reference to environmental protection to justify this requirement.

This requirement should further be applied to **priority substances** listed in Annex I of the **Environmental Quality Standards Directive** (2008/105/EC, EQSD). The presence of just one of these substances in a water body at levels above the relevant EQS can cause that water body's chemical status to be downgraded, as a breach of a single parameter constitutes a failure to reach good chemical status under the WFD. As some of these substances are very difficult to treat through end-of-pipe measures, strong control at source is needed to curb their excessive use and thereby limit their environmental harm to ensure compliance with the WFD.

We strongly recommend that **endocrine disruptors** should also be included under this Article, in line with their inclusion in Article 22.2 of the proposed Directive. We recognise, however, that emergency contraceptives (commonly known as the 'morning-after pill') should be exempted from this requirement as their immediate availability is essential to the protection of reproductive health.

At the very least, advertising for products containing priority substances and endocrine disruptors must be prohibited under Article 177 of the proposed Directive.

Suspending, revoking or amending authorisations and withdrawal from the market (Articles 195 & 196, Directive)

We support the introduction of **environmental grounds** for competent authorities to suspend, revoke or amend a marketing authorisation, or to prohibit the supply and withdraw a product from the market in cases of serious risk to the environment. This provides an important safeguard in cases where environmental risks become known only after a product has been authorised. It also constitutes a logical complement to provisions in Article 22 on updating ERAs and in Article 23 on ERAs for medicines authorised before 30 October 2005.

Withdrawal of a product by the authorisation holder (Article 24, Regulation)

We welcome the obligation for the authorisation holder to declare its reason for suspending the marketing of a medicinal product or otherwise withdrawing it from the market, in particular if that reason is linked to a serious risk to the environment. This reason should be communicated immediately by the EMA to drinking water and wastewater operators so that they can take appropriate measures to address legacy pollution by this product. The information should also be shared with the public so that patients already in possession of this product can act accordingly.

Regulatory sandbox (Articles 113 & 114, Regulation)

While we understand the need to leave regulatory room for life-saving innovation, we must ensure that these provisions are not used to circumvent the need for appropriate environmental risk management. While we welcome the requirement to outline measures to mitigate environmental risks in the sandbox plan under Article 113.7.c, **we urge extreme caution in the application of derogations to marketing authorisations** as laid out in Article 114.3. We strongly believe that no product should see its manufacturer exempted from submitting a complete and substantiated ERA, including risk prevention, limitation and mitigation measures before receiving a marketing authorisation.

Further reading

To read more about the chemical status of European waters regarding pharmaceutical substances from household wastewater proposed EU legislation in this area and measures to be done to improve the situation in our common waters, see past publications from EurEau and its members:

EurEau Position on Environmental Quality Standards (EQS) for pharmaceuticals

Waste water treatment pains: Svenskt Vatten Report on pharmaceuticals in our water environment.

About EurEau

EurEau represents Europe's drinking and wastewater sector. We encompass 37 national water services associations including public and private operators from 32 countries.

Together we promote access to safe and reliable water services for Europe's citizens and businesses, the management of water quality and resource efficiency through effective environmental protection.

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