EHA's recommendations for the revision of the EU pharmaceutical legislation

A key opportunity to improve the availability of and access to medicinal products

The European Hematology Association (EHA) is the leading representative of hematology and hematology professionals in Europe. We are a not-for-profit, public-benefit organization with 8,300 members and an annual congress welcoming around 18,000 healthcare professionals each year. EHA supports career development and research, develops and harmonizes hematology education, and advocates for enhanced, affordable and equitable access to innovative therapies for patients with hematological disease across Europe.

The revision of the EU's pharmaceutical legislation should deliver a robust, future-proof legal framework that significantly improves availability and access to medicinal products across the European Union. Research and innovation are only worth the investment - public as well as private - if they reach patients.

Drug repurposing *Article 48, 2023/0131 COD*

EHA strongly supports drug repurposing as a means to improving access to and affordability of medicines across Europe. Repurposing can accelerate drug development by leveraging existing innovation and data. In the field of hematology, where there are many rare disorders with limited treatment options, this can create significant opportunities for underserved patients. In addition, repurposing entails lower costs than developing a novel medicinal product from scratch.

EHA supports the European Parliament's amendment to Article 48.1 extending the scope of the provision to all medicinal products and mentioning the submission of additional evidence by Marketing Authorization Holders (MAHs). Drug repurposing should cover all medicinal products. In addition, we ask for more clarity regarding the term "substantive evidence", and advocate for streamlined regulatory procedures related to drug repurposing.

Evidence generation plays a crucial role in the detection of new indications for authorized medicinal products, particularly when they emerge from off-label use. The focus of the European Medicines Agency (EMA) on monitoring safety signals could be complemented by the systematic collection of new and unexpected efficacy signals for off-label medicine use. We propose the establishment of a "Drug Evidence Watch" by the EMA to enable the monitoring and public dissemination of such signals. The latter could be supported by European research registries and not-for-profit entities, which are well-positioned to collect and generate real-world evidence (RWE). This approach could inform opportunities for drug repurposing and facilitate subsequent label updates, crucial to advance innovation and health outcomes.

EHA proposes the following amendments with a view to increasing transparency, incentivizing a centralized collection of valuable evidence, and facilitating the detection of possible new indications:

Article 48.4 2023/0131 COD (New)	
European Commission proposal	EHA's proposed amendment
Text proposed by the Commission	***The Agency shall establish and maintain a publicly accessible database to collect and publish information on new and unexpected efficacy signals for off-label drug use. This database can serve as a central resource for identifying therapeutic opportunities, supporting evidence-based decision-making, and facilitating the collection of high-quality real-world evidence (RWE) by leveraging European registries and contributions from not-for-profit entities.***

Hospital exemption — *Article 2, 2023/0132 COD*

The hospital exemption (HE) framework serves as an essential complement to the commercial pathway, particularly for therapies that may not be commercially viable due to the small patient population and/or an insufficient return on investment. This is attested by the fact that the development of Advanced Therapies Medicinal Products (ATMPs) is often highly dependent on public funding[1]. The hospital exemption therefore constitutes a legislative lifeline serving patients with unmet medical needs or requiring personalized treatment. Article 2 also reflects the reality that many ATMPs stem from clinical practice and are formulated closely to the patient.

HE approvals entail careful consideration by the Member State competent authorities, as permits are only accorded to ATMPs that foresee a benefit for the patient, meet regulatory requirements and are not inferior to the standard of care. To that extent, any limitations on the use of HE should be carefully evaluated and be kept proportional:

- The duration requirements of a hospital exemption cannot lead to the interruption or unavailability of patient treatment, nor create an unnecessary administrative burden for healthcare professionals that takes away from patient care or slows decision-making.
- HE should not be confined to cases where no medicine for that indication is approved (at EU level), as approval does not always translate to availability and access. ATMPs are often not available due to the marketing strategies of MAH, high prices, or negative reimbursement decisions and failed pricing negotiations.
- Clinical trials or compassionate use programs for a similar indication cannot qualify as reasons for not granting a hospital exemption approval. There is no guarantee that the

[1] Page 11: https://www.cancer.eu/wp-content/uploads/2023-03-23-Policy-paper_The-potential-for-academic-development-of-medicines-in-Europe.pdf

medicinal product being studied will be approved, nor that the patient can be included in the clinical trial in question; moreover, the final indication might be of narrower scope than initially foreseen.

EHA strongly supports the European Parliament's amendment allowing for the cross-border exchange of ATMPs prepared under hospital exemption, in cases of medical need (new Article 2.8 a). EHA also firmly supports the European Parliament's amendments regarding the creation of a publicly available repository on hospital exemption approvals (Article 2.6).

Article 2.1 2023/0132 COD	
European Commission proposal	EHA's proposed amendment
By way of derogation from Article 1(1), only this Article shall apply to advanced therapy medicinal products prepared on a non-routine basis in accordance with the requirements set in paragraph 3 and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient ('advanced therapy medicinal products prepared under hospital exemption').	By way of derogation from Article 1(1), only this Article shall apply to advanced therapy medicinal products prepared ~~***on a non-routine basis***~~ in accordance with the requirements set in paragraph 3 and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner and, ***where relevant, a hospital pharmacist***, in order to comply with an individual medical prescription for a custom-made product for an individual patient ('advanced therapy medicinal products prepared under hospital exemption').

Article 2.2 2023/0132 COD	
European Commission proposal	EHA's proposed amendment
The manufacturing of an advanced therapy medicinal product prepared under hospital exemption shall require an approval by the competent authority of the Member State ('hospital exemption approval'). Member States shall notify any such approval, as well as subsequent changes, to the Agency. The application for a hospital exemption approval shall be submitted to the competent authority of the Member State where the hospital is located.	The manufacturing of an advanced therapy medicinal product prepared under hospital exemption shall require an approval by the competent authority of the Member State ('hospital exemption approval'). Member States shall notify any such approval, as well as subsequent changes, to the Agency. The application for a hospital exemption approval shall be submitted to the competent authority of the Member State where the hospital is located. ***The duration of a specific hospital exemption approval shall be at least as long as the anticipated treatment period to ensure that each patient can complete their treatment without interruption. Ongoing national***

marketing approval procedures shall not disrupt the continuation of treatment for patients receiving care under the hospital exemption framework.

Reporting financial support *Article 57, 2023/0132 COD*

There are major differences between EU countries when it comes to their health budgets, reimbursement decisions and, consequently, access to medicines. More insight into the costs incurred during the research and development of medicinal products, as well as how these have been shouldered, is crucial for more fair and transparent pricing negotiations. Article 57, as proposed by the Commission, will not meet these objectives. Reporting obligations should be expanded to include financial support from charities and non-commercial organisations, as well as tax breaks. This information should be provided in an easily accessible manner.

EHA strongly supports the European Parliament's amendments requiring MAHs to disclose the full funding history, regardless of geographic origin, as well as any funding associated with acquired medicinal products (Articles 57.1 and 57.2a – point iii a). A clearer funding history will empower Member States to negotiate fairer drug prices for their markets.

Article 57.1 2023/0132 COD

European Commission proposal	EHA's proposed amendment
The marketing authorisation holder shall declare to the public any direct financial support received from any public authority or publicly funded body, in relation to any activities for the research and development of the medicinal product covered by a national or a centralised marketing authorisation, irrespective of the legal entity that received that support	The marketing authorisation holder shall declare to the public any direct ***or indirect*** financial support, ***including tax breaks***, received from any public authority or publicly funded body ***or charity***, in relation to any activities for the research and development of the medicinal product covered by a national or a centralised marketing authorisation, irrespective of the legal entity that received that support.

Defining unmet medical need *Article 83, 2023/0132 COD*

EHA supports an inclusive and future-proof definition of unmet medical need (UMN) that responds to the needs of patients. The following parameters should therefore be considered:

- Impact on the quality of life of the patient;
- Impact on disease severity, progression and duration;
- Availability of alternative treatments, as the standard of care is often not available or inaccessible to patients;
- Burden of illness on the patient, in terms of physical, psychological and social health, but also the burden on society and the healthcare system;

An assessment of whether a medicinal product qualifies as addressing an UMN cannot overlook patient reported outcomes (PRO) and patient experience data (PED).

Guidelines for application

The consultation process set out in Article 162 of the proposed Regulation (2023/0131 COD) states that patients and healthcare professionals can be consulted at the Agency's discretion. However, EHA urges decision-makers to make input from health professionals and patients mandatory in the formulation of the guidelines foreseen by Article 83.3. The insights of clinicians and patients – from across the EU, to account for regional differences – are crucial to ensure a framework that is viable and fit-for-purpose. In addition, a future-proof UMN framework will require periodic re-evaluations of the applicable parameters, in order to keep up with clinical and patient needs.

Article 83.1, 2023/0132 COD	
European Commission proposal	EHA's proposed amendment
A medicinal product shall be considered as addressing an unmet medical need if at least one of its therapeutic indications relates to a life threatening or severely debilitating disease and the following conditions are met: (a) there is no medicinal product authorised in the Union for such disease, or, where despite medicinal products being authorised for such disease in the Union, the disease is associated with a remaining high morbidity or mortality; (b) the use of the medicinal product results in a meaningful reduction in disease morbidity or mortality for the relevant patient population.	A medicinal product shall be considered as addressing an unmet medical need if at least one of its therapeutic indications relates to a life threatening or severely debilitating disease and the following conditions are met: (a) there is no medicinal product authorised in the Union for such disease, or, where despite medicinal products being authorised for such disease in the Union, the disease is associated with a remaining high morbidity or mortality, ***or a significant burden on patients and healthcare systems;*** (b) the use of the medicinal product results in a meaningful reduction in disease morbidity***,*** mortality***, progression, or severity, or provides a meaningful improvement in the quality of life*** for the relevant patient population.

Article 83.3, 2023/0132 COD	
European Commission proposal	EHA's proposed amendment
Where the Agency adopts scientific guidelines for the application of this Article	***The Agency shall adopt*** scientific guidelines for the application of this Article***, further***

it shall consult the Commission and the authorities or bodies referred to in Article 162 of [revised Regulation (EC) No 726/2004].	***specifying the parameters required for a medicinal product to be considered to address an unmet medical need. The guidelines should be precise, in order to create legal certainty, and be updated whenever required by evolving clinical and/or patient needs and in response to impact monitoring. For this purpose, the Agency*** shall consult the Commission, and the authorities or bodies referred to in Article 162 of [revised Regulation (EC) No 726/2004], ***ensuring comprehensive clinician and patient involvement in the consultation process.***

Regulatory incentives *Articles 80-82, 2023/0132 COD*

One of the key aims of the pharmaceutical reform is to boost research and innovation in Europe, ensuring adequate investment to meet current and future health challenges. However, it is vital to find a balance between promoting the development of innovative medicines and managing national healthcare expenditures. EHA therefore welcomes the Commission's proposed reduction of the baseline regulatory protection and supports making additional regulatory protection conditional on the fulfilment of requirements increasing the availability of innovative therapies for patients across the EU.

Bolster European R&D

Furthermore, incentives should be leveraged to encourage R&D within Europe. This is essential to respond to the unique needs of patients with blood disorders in the EU. Conducting research in the EU will enable pharmaceutical companies to better understand the genetic and environmental factors that contribute to blood diseases in the EU population, which will facilitate the development of more targeted and effective treatments. In addition, localized research and development can help build capacity in the EU to conduct clinical trials for new blood disease treatments. This would ensure that patients in the EU can participate in clinical trials and access the latest treatments as soon as possible (European Parliamentary Research Service, PE 697.197, 2021). It would furthermore bolster the EU's competitiveness, as well as its resilience and (strategic) autonomy. EHA therefore strongly supports the wording introduced by the European Parliament in the new Article 81.2ca.

Improve access

EHA welcomes the new provision on 'Reporting on access to medicinal products', introduced by the European Parliament in its position (article 86a). Having indicators to measure access, as well as a publicly available report assessing access and the barriers thereto, will be fundamental to ensure the value derived from innovation actually reaches the end users. Moreover, we welcome articles 58a and 58b of the EP's position, creating an obligation to

submit an application for pricing and reimbursement in all Member States (that have requested this) and introducing an EU access to medicines notification system.

Bolar exemption *Article 85, 2023/0132 COD*

The delayed entry of generics and biosimilars on the market is a loss for patients and detrimental to national health expenditures. Generics should be able to enter the market on 'Day 1' after the expiration of the proprietary rights of the reference medicine. However, that can only happen if all the preparatory steps can be taken beforehand. EHA welcomes Article 85, as extended in scope by the European Parliament in its position, and covering activities (including but not limited to studies and trials) conducted for the purpose of obtaining marketing authorization, undergoing health technology assessment, and obtaining pricing and reimbursement approval. The absence or weakening of the bolar exemption creates a *de facto* extension of regulatory protection.

Medicine shortages *Articles 2, 24, 116-8, 2023/0131 COD*

Medicine shortages constitute a major concern for patients and healthcare professionals across Europe and require collective efforts for prevention and mitigation. We welcome the Commission's timely decision to include a chapter addressing the 'availability and security of supply of medicinal products'.

EHA supports the proposed definition of shortages, and welcomes several measures included by the Commission in the draft legislation, as well as by the European Parliament in its position from April 2024, namely:

- The Parliament's amendment providing a definition of 'demand', which specifies when 'demand is satisfactorily met' (Article 2.14a, 2023/0131 COD). This is an important clarification to ensure the continuity of patient care.
- For critical medicinal products, the requirement for marketing authorization holders (MAHs) to transfer their marketing authorization to third parties, in case they decide to withdrawal it (Article 24, 2023/0131 COD);
- A requirement for MAHs to notify authorities at least 12 months in advance, in case of a permanent marketing cessation, or at least 6 months in advance in cases of a temporary suspension. These measures could help to ensure the supply of medicines (Article 116, 2023/0131 COD)
- A requirement for MAHs to draft a shortage prevention plan for any medicinal products placed on the market, and ensure that it remains updated, and the possibility for competent authorities to request a shortage mitigation plan (Articles 117 and 118.2, 2023/0131 COD)
- The Parliament's decision to include the Healthcare Professionals' Working Party (HCPWP) and the Patients' and Consumers' Working Party (PCWP) in the development of guidance for MAHs on how to set up a shortage prevention plan (Article 117, 2023/0131, COD).

While the Commission proposal and European Parliament's position set a benchmark for shortage management in the EU, practice shows that healthcare professionals retain an important role in terms of vigilance and addressing shortages. It is therefore essential that

they are informed about upcoming shortages in a timely manner, allowing them to determine the best course of action for their patients.

Declarations of Interest *Article 208, 2023/0132 COD*

The European Hematology Association (EHA) supports the requirement in Article 208 for regulators and experts involved in the authorization and surveillance of medicinal products to declare their financial interests annually. This measure will help ensure that regulators and experts are impartial and that their decisions are devoid of influence. Furthermore, EHA agrees with the European Parliament's position that these declarations should be updated as necessary and made available upon request.

However, EHA emphasizes that the purpose of declaring interests is to enhance transparency, not to exclude essential experts. Conflicts of interest should be managed rather than prohibited, especially in rare diseases where there are few experts across Europe. This approach ensures the quality and relevance of regulatory processes, including scientific advice, safety and efficacy evaluations, and clinical effectiveness assessments.