EPF call for continued focus on paediatrics in the new pharmaceutical legislation

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BACKGROUND AND KEY CONSIDERATIONS

Regulation (EC) No 1901/2006 on medicinal products for paediatric use aimed to facilitate the research, development, and availability of medicines for children aged 0 to 17 years[i]. Its main feature was the creation of a system of obligations, incentives, and rewards for manufacturers to encourage and enable research and development (R&D) of medicines for children, supported by a specific committee at the European Medicines Agency (EMA), the Paediatric Committee (PDCO). The PDCO's main role is to evaluate the content of paediatric investigation plans (PIPs) and related data, adopt opinions on medicines for paediatric use, and advise other institutions on issues related to paediatric medicines. Since its creation under the regulation, the PDCO has taken a central role in coordinating and enhancing the Agency's work on medicines for children and supporting broader EU through members' activities at country and national agency level.

The European Commission's proposal for a new general pharmaceutical legislation incorporates the Paediatrics regulation. EPF welcomes some of the proposed changes in the new text, such as increased flexibility of the clinical development plans and additional restrictions on waivers if the product's mechanism of action could be relevant for another disease in children. These measures could strengthen PDCO's capacity to push for needed paediatric developments. However, EPF notes that incentives remain limited, impacting notably paediatric developments in younger children. In addition, the new draft does not mandate regulatory representation of paediatric medicines at the CHMP or the creation by the CHMP of a dedicated working group on paediatrics[ii].

Consequently, EPF is very concerned about the disappearance of the PDCO as a result of the proposed EMA structure and the subsequent lack of an appropriate forum to discuss and assess PIPs. While we understand the focus on simplifying the system and strengthening the centralising role of the EMA, we are concerned that **the proposed change may lead to an unintended deprioritisation of paediatric medicines' R&D and less paediatric marketing authorisation applications (MAAs), ultimately denying access to essential medicines for neonates, infants, children, and adolescents across the EU.**

The disappearance of the PDCO poses a number of issues:

- Despite some progress since the implementation of the regulation, manufacturers remain reluctant to conduct paediatric studies, especially when they don't align with commercial interests. PDCO acts as an independent third party with broad representation and therefore has significant negotiating power when a development plan is submitted early. Without PDCO, it is unclear whether EMA will have **the leverage and resources to push for specific studies** before the submission of the MAA in adults, especially in the most underserved and complex populations, such as neonates. Of note, new expensive and complex medicines, such as gene therapies or antibodies, are generally not accessible if they are not authorised for each paediatric age-subset.
    - PDCO has a considerable workload, with more than 1300 procedures to manage each year, which increases automatically with the updates and modifications of the agreed development plans. This workload will increase with the new legislation as it will make it possible to mandate a PIP development outside of a medicine's indication. For each PIP, the PDCO plays a key role in the coordination of key dedicated working groups on paediatric formulations, preclinical developments for children, and innovative methodologies. Unless EMA receives significant

additional resources to take on this work, **it is unclear how the same level of focus, independence, coordination and oversight of paediatric assessments** will be ensured.

- PDCO experts have gained **extensive expertise and experience** in paediatric diseases, research, and medicines and in assessing paediatric development plans. Without a specific forum for discussion in the new system, this **expertise will likely not be updated and rapidly lost,** with member states' experts assigned to different tasks and topics. In addition, the loss of PDCO national experts will likely lead to further fragmentation. The current model ensures that each country is represented and can verify the implementation of the scientific requirements across the development process. PDCO national experts can also act as links between EMA, national authorities for medicines, and health technology assessment bodies to ensure authorised paediatric products actually become available at country level.
    - As a result, removing the PDCO may not address the alleged complexity of the EU system. On the contrary, **the increased direct workload could create even more administrative burden for the CHMP.** Instead, establishing a direct link between the PDCO and the CHMP, with dedicated paediatrics regulators at the CHMP, could ensure consistent and rapid scientific evaluation while avoiding duplicative assessments across the medicine's lifecycle.
        - Of note, **medicines' development poses similar challenges for the youngest and the oldest patients.** Populations at either ends of the age continuum face lack of access to medicines as formulations and dose recommendations (due to organ dysfunctions) do not encompass these vulnerable subgroups. Finding synergies through a "population approach" to medicines' assessment could provide an answer to increasingly pressing public health needs, as evidenced by the COVID-19 pandemic where age was a determining factor.
    - An additional challenge is that the work undertaken by PDCO experts is unpaid. The contribution of national competent authorities' (NCAs) experts is fully funded by the national agencies, and therefore **the few paediatric experts at national level are identified and exist because of the PDCO**. The solution should not be to remove the PDCO and free up resources for other tasks, but to establish a **sustainable financing model to retain PDCO members' expertise and prioritisation within NCAs**. This will certainly enhance the whole system and position the EU as a leader in this field.
- The disappearance of the PDCO also creates significant uncertainty regarding patient representation.
    - While some patients with expertise in paediatric medicines may be part of the CHMP, the absence of a cross-cutting paediatric working party means that patients cannot be involved early in the development process.
        - In particular, patients' and healthcare professionals' views **are essential to ensure studies are feasible and practical** (e.g. identifying recruitment issues, defining outcomes, etc.) **and they must be consulted.**
    - Meaningful patient participation requires hands-on evaluation work, which cannot be reduced to ad hoc consultation. Patient representatives build expertise through reviewing multiple applications and monthly interactions across committees. The disappearance of the PDCO means this continuous input and these opportunities for cross-learnings will be lost.
        - More broadly, the proposed shift to competency-based working parties could be very detrimental to patient representatives, whose expertise is based on lived experience and a practical understanding of new medicines' R&D. This practical experience should be recognised, with no narrow definitions, and patient representatives should have access to appropriate training and compensation.

RECOMMENDATIONS

- **Retaining the PDCO or a similar paediatric committee, with an adequate and sustainable funding model, decision-making power, and adequate representation at the CHMP,** would remain the best option to ensure continued focus on paediatric medicines in the new system.
    - **Most rare diseases affecting children still don't have treatment, and there remains an unmet need for appropriate and tested paediatric products for diseases affecting both adults and children**, leading to considerable inappropriate off-label use. Only a structured approach to paediatrics in the regulatory system can ensure that the issue remains top of mind for manufacturers.
    - In addition, a dedicated committee would ensure that patient representatives' unique perspective is included and embedded in the process.
- As an alternative if the co-legislators choose to maintain the proposed EMA's simplified structure, the system needs to ensure:
    - The creation, mandated by law, of a scientific working party under the CHMP with paediatric medicines/assessment of PIPs explicitly part of its mandate and with mandated participation of patients' and healthcare professionals' representatives. Given its heavy workload, this working party should reach an appropriate size with enough members. In view of the ageing of the European population and the need to improve diversity and inclusion in medicines' development, such a working party could reflect a broader "population approach". This would ensure that considerations related to specific population groups are fully integrated in medicines' development plans, and that medicines target the needs of all patients, from 0 to 100+ years old.
    - In addition to patients and healthcare professionals' representatives, specific NCA representatives with expertise in paediatric medicines must be involved in the CHMP to ensure the linkage between the PIP and the marketing authorisation process.

About EPF

The European Patients' Forum (EPF) is an umbrella organisation of patient organisations across Europe and across disease areas. Our 79 members include disease-specific patient groups active at the EU level and national coalitions of patients representing 19 countries and an estimated 150 million patients across Europe. www.eu-patient.eu

[i] European Medicines Agency

[ii] [ii] Article 150(2) of the proposed regulation only mandates "working parties with scientific expertise in the fields of pharmaceutical quality, methodologies, non-clinical and clinical evaluations" and a scientific advice working party.