Civil society recommendations for improving the 2000 Orphan Regulation and the 2006 Paediatric Regulation

On the occasion of a special policy dialogue zooming in civil society organisations' recommendations to improve the 2000 Orphan Medicinal Products Regulation and the 2006 Paediatric Regulation, the **Association of European Cancer Leagues (ECL)**, the **European Fair Pricing Network (EFPN)**, the **European Public Health Alliance (EPHA)** and the **European Society for Paediatric Oncology (SIOP Europe)** teamed up to formulate concrete recommendations to deliver optimal treatment for children and those suffering from rare diseases, as **"one-size-fits-all" incentives do not lead to a sustainable and equitable pharmaceutical system.**

OUR GOAL

To foster the development and equal access to affordable medicines for children and patients with rare diseases, and bring the right medicines, at the right time, to the right people.

OUR PRINCIPLES

Patient-centredness

Changes in the legislative framework should be driven by public health and patients' needs.

Transparency

Disclosure of essential information is critical to increase transparency in P&R negotiations and increase public trust in the pharmaceutical system.

Accessibility

Any treatment, no matter if innovative or not, has no value until it reaches patients so that they benefit from it. Affordability is therefore a key element.

OUR JOINT RECOMMENDATIONS

1. Setting research priorities that target unmet medical needs

- Set an unambiguous and clear definition for the term 'unmet medical needs' (UMN), based on transparent and objective criteria. The definition should include but not be limited to the following: incidence **[1],** survival rates, existing alternative treatments, mortality and severity of the disease.

ECL Association of European Cancer Leagues

SIOPE SIOP Europe the European Society for Paediatric Oncology

epha european public health alliance

EFPN EUROPEAN FAIR PRICING NETWORK

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@EPHA_EU
@SIOPEurope

#LetsTalkAccess
#EUPharmaStrategy
#OrphanDrugs
#Meds4Kids

- Put patient-centredness and participatory decision-making at the heart of defining UMN. From a paediatric oncology perspective, it would be counterproductive to set fixed criteria in the legislation whilst defining UMN. It is essential that the definition of UMN is the result of a rich multi-stakeholder dialogue, which would ensure that UMN are better defined by disease.
- Urgently steer access to new and essential medicines for European children and adolescents with cancer, in line with the recent European Commission and European Parliament's findings. It is not acceptable that only 9 anti-cancer medicines have been authorised for a specific paediatric cancer indication in Europe since 2007, in contrast to over 150 for adult cancers **[2]**.
- Implement an approach to paediatric medicine development driven by a mechanism of drug action, disease biology and patient needs (this includes suppression of Article 11b of the Paediatric Medicine Regulation). This is vital in order to align the Regulations with science and unmet needs of children with cancer.
- Personalised medicines should not be handled as orphan medicinal products within the remit of the Regulation (EC) No 141/2000. The definition of personalised medicines should differ from the definition of orphan medicinal products.

2. Strive for future-proofed incentives and investments

- Create targeted incentives to support early-stage medicine development (e.g. for children) and ensure medicines with proven added value and medicines in areas where there currently are no treatments. Public and private investments should address and meet public health and patients' needs, with particular attention to children and adolescents with cancer and rare cancers with low survival.
- Create a system of rewards/obligations to cover knowledge gaps in basic research to address neglected diseases, guarantee the supply of medicines, and steer accessibility.
- Use alternative pull incentives that are publicly-funded, such as market entry or innovation rewards **[3]**.
- Incentives should be proportionate to the costs required to put a specific medicine on the market and to the return-on-investment. Hence, transparency and disclosure of costs to national authorities and payers is essential to stop blindfolded negotiations on price and reimbursement. To this end, with the revision of the two Regulations, the marketing authorization holders should report to the European Medicines Agency the annual revenues of the year and this could be implemented with the extended mandate of the Agency.
- Incentivise the 'First-in-Child' development **[2]** and marketed authorisation of medicines against specific paediatric biological targets for the treatment of children with life-threatening and debilitating rare diseases, such as paediatric cancers. In addition, reducing delays in starting the development of paediatric medicines and introducing tailored incentives should ensure the early start of paediatric cancer drugs development.
- Consider repurposing of existing drugs for treatments without viable markets. This can sometimes be done at low cost and has the potential to decrease both the time-frame and the costs.
- Assess the impact of the incentives already granted before extending the market exclusivity period. This could be done by looking at (i) the real added value brought by the new health technology applying a European Health Technology Assessment, and (ii) the impact of the new product into the market on pharmaceutical expenditure, and on health expenditures more broadly.

[1] See Gatta, G. et al (2017) 'Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet - a population-based study'. Lancet Oncology, 18 (8), 1022-1039. Available here: https://doi.org/10.1016/S1470-2045(17)30445-X

[2] See SIOP Europe and Childhood Cancer International-Europe's recommendations.

[3] As in many countries orphan medicines are fully paid for by the government or compulsory insurance schemes financed through social contributions, public payers might have an interest in subsidising product development for these indications with clear conditions attached, such as making products available at affordable prices for patients with rare diseases.

3. Set conditionalities to guarantee the correct implementation of the current Regulations and tackle the wide inequalities in availability, accessibility, and affordability in the EU

- Fully operationalise the market exclusivity review mechanism for OMPs to (i) enable the revocation of the orphan drug designation and (ii) evaluate the effects of the orphan drug designation on availability, affordability and accessibility.
- Foster legal conditions connected to incentives (e.g. supplementary protection certificates) with the goal of enhancing wide market availability. A unitary SPC would limit the fragmentation of the system and the lack of transparency especially from a cross-border perspective **[4]**. This will be essential to ensure that the level of incentives is linked to the actual availability, accessibility, and affordability of pharmaceutical products across the EU.
- Limit financial returns for orphan medicines that achieve high levels of sales, through truncated market exclusivity or partial refunds beyond a revenue cap, in instances where the exclusivity clearly leads to overcompensation. This will ensure that societies do not pay indirectly more than necessary to encourage the development of treatments for rare diseases.

4. Increase competition to reduce prices

- The European Commission together with Member States should investigate and address the (marketing) tactic of withdrawing off-patent drugs and reintroducing similar medicines with new indications and higher prices **[5]**. The revision of the Directive 2001/83 will be critical in this regard.
- The revision of the Regulations needs to address and discourage commercial practices that hamper competition, such as 'indication stacking', 'salami-slicing' and splitting common diseases into many artificial subsets (each of which could then be considered a rare disease and profit from orphan designation and other benefits).
- The European Commission and antitrust authorities should keep monitoring closely the acquisition of SMEs by large pharmaceutical companies that undermine fair competition.
- Discourage practices which extend market exclusivity, prolong intellectual property protection, lead to competition distortion and profit maximization, through strategic use of intellectual property rights, such as incremental patenting of existing products ("ever-greening" strategies).
- Promote generic competition for off-patent rare disease drugs. To this end, advanced market commitments and subsidies for non-for-profit manufacturers should be considered **[6]**.

5. Support research and scientific developments geared towards unmet patient needs

- Generously support and fund public and non-profit research centers and academia, as they play a pivotal role in identifying the scientific gaps, such as for pediatric cancers **[7]**. Currently, they cannot benefit from the fee waiver and scientific advice reserved to SMEs **[8]**.
- The European Commission should encourage Member States to make use of the diagnostic tools necessary to find out the most effective treatments with positive cost-benefit ratios. This would reduce avoidable harm to patients, improve treatment outcomes, and possibly reduce costs for national healthcare systems.
- Consider the societal value of cancer drugs and their impact on quality of life, as well as their short and long-term side effects, when assessing the added value of new health technologies.

[4] See the Evaluation of Regulation (EC) 469/2009 concerning the supplementary protection certificate for medicinal products.
[5] See the Pharmaceutical Sector Inquiry by the European Commission.
[6] See Jarosławski, S. and Toumi, M. (2019) 'Non-profit drug research and development: the case study of Genethon'. Journal of Market Access & Health Policy, 7(1). Available here: https://doi.org/10.1080/20016689.2018.1545514 & Davies, E.H. (2017) 'Affordable orphan drugs: a role for not-for-profit organizations'. British Journal of Clinical Pharmacology, 83(7), 1595–1601. Available here: https://doi.org/10.1111/bcp.13240
[7] Childhood cancer is still the leading cause of children's death by disease as survival rates in several hard-to-treat malignancies have plateaued. Up to 60% of the 500,000 paediatric survivors experience long-term adverse side-effects.
[8] See page 103 of the Joint evaluation of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.