ECL-EFPN Reflection paper on the revision of Regulation (EC) No 141/2000 on orphan medicinal products

The Access to Medicines Task Force of the Association of European Cancer Leagues (ECL) and the European Fair Pricing Network (EFPN), appreciate the opportunity to contribute to the European Commission's stakeholder consultation on the revision of Regulation No 141/2000 on Orphan Medicinal Products and Regulation No 1901/2006 on Paediatric Medicines.

We also thank PPMI Group (PPMI), the Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus (FGB), and Asklepios for the opportunity to participate in a focus group discussion on 23 February 2022.

Following up on the conversation, with this **summary,** ECL and EFPN aim to provide the European Commission and the focus group discussion's organisers with an **overview of our reflections**. We do not provide input on the first question addressed by the consultants on supplementary protection certificate (SPC), as paediatric medicines fall outside our remit.

ONE SIZE FITS ALL INCENTIVE IS NEITHER SUSTAINABLE NOR FAIR

We understand that the European Commission is leaning towards the **modulation of incentives that ECL and EFPN fully support.** Citing the Staff Working Document, we stress that "*a graduation/differentiation of the incentives to the magnitude of rarity or the scale of investment needed may enable incentives to be focused better on therapeutic areas that are neglected or where a bigger investment is necessary.*" We believe that, if the European Commission wants to steer R&D investments and research projects toward disease areas with high unmet medical need, the Regulation should consider: **survival rate**, impact on **quality of life**, the existence/absence of **alternative therapeutic options**.

Incentives

We believe that **accountability and transparency** are the foundations of mutually trusting relationships between pharmaceutical companies and the European Commission. Thus, **incentives should be linked to (i) conditionalities and (ii) R&D cost transparency** because the main objective of incentives is to steer investments and research efforts toward areas where the expected return-on-investment is not sufficient**. Incentives are not meant to lead to overcompensation.**

For ECL and EFPN, the 10-year market exclusivity (**ME**) is the key aspect of the Regulation's revision. The EU has the longest ME duration and yet the US is considered as the gold standard despite its 7-year exclusivity for orphan drugs. Hence, **there are other pivotal elements besides 10-year ME** that lead companies to invest more in the US than in the EU. It is worth looking at the UK dynamics following Brexit. Despite being a smaller market compared to the EU, a UK Biotech Financing Report, published by the BioIndustry

Association (BIA) and Clarivate shows that 2021 was the highest year on record for investments into biotech and life sciences companies, with an increase of 60% in private and public financing (largely coming from overseas) compared to 2020. The UK is renowned for its well-resourced and prosperous research environment, and world-class universities and research centres.

Rewards

ECL and the EFPN believe **rewards,** (incl.SPC), **should be granted only when robust evidence** about the patient-benefit value is provided. This can happen when the following two conditions are met :

1. The product must be launched in all EU member states.
2. The product must come with a fair and sustainable price tag that allows national authorities to reimburse it.

We would also like to highlight the importance of making information on the effects of the incentives publicly available.
The Commission has been exploring the use of **vouchers**. Our understanding is that this tool is already being used e in the US and, it does not seem to be effective. Moreover, attendees of the focus group discussion on 23 February, including pharmaceutical company representatives, were sceptical about vouchers. **We suggest re-framing existing incentives and rewards without adding other layers of complexity or any additional incentives.**

We invite you to **read and consider** our **joint recommendations** at this link **bit.ly/2QyqFZ3**

Addressing Unmet Medical Needs

We noted at the focus group discussion that there is no general agreement on maintaining the 10-year duration of ME. Shortening its duration may facilitate the entrance into the market of other stakeholders, such as **academia and not-for-profit research centres**. When it comes to **generics and biosimilars**, there is great potential to reduce the costs of pharmaceuticals. Yet, as reported in this article, "*drugs treating rare diseases may be at elevated risk of insufficient generic competition because generic manufacturers may avoid niche markets and prioritise drugs treating more prevalent conditions*". We would recommend the European Commission explore and better understand the options to reduce the price by facilitating the availability of generics and biosimilars in rare diseases.

ECL and the EFPN believe that the maximum duration of ME should be granted to companies and non-commercial entities that:

1. Demonstrate to be working on a molecule that could treat a rare disease with high unmet needs (e.g., no treatment options available) AND
2. Demonstrate high risks of having low/no profit from their product once placed in the EU member states (transparency is needed) AND
3. The product would be launched in most/all EU member states with an affordable price tag.

Thus, the maximum duration of market exclusivity should be reserved to incentivize (i) R&D in areas with unmet need and (ii) equal access across EU member states.
If insufficient (clinical) added benefit for patients are demonstrated for a product enjoying the full package of incentives compared to alternatives during the 10-year ME, the market exclusivity should be shortened.

LOOKING FORWARD

Personalised medicine should not lead to the breakdown of cancer in many subsets. Treatments for these subsets with a clear clinical benefit must reach patients, but not necessarily via the Regulation.

As an example, the paper produced by the European Cancer Patient Coalition (ECPC) on pancreatic cancer reports that there are 7 rare cancers of the pancreas. Advancements in science help researchers find better cures, less invasive treatments, and a more targeted approach to fight cancer. However, if the trend is a constant discovery of new forms of cancer within the same category, and all are entitled to the full package of incentives, the healthcare systems cannot cope with such a burden in the years and decades to come. Indeed, the pharmaceutical industry has dozens of new health technologies in the pipeline. "*Precision medicine increasingly dominates in oncology where targeted therapies account for almost all of research, and over* ***40% of the pipeline is for rare cancers*** *where next-generation biotherapeutics — including cell and gene therapies – are increasingly being deployed*." (IQVIA, 2022).

NEW MEDICINES DEVELOPMENT MODELS REMAIN TO BE EXPLORED AND REGULATED

Incentives and scientific advice reserved to SMEs should be extended to academia and not-for-profit research centres. The positive contribution of charities and non-for-profit research centers to science cannot be indeed disregarded. According to this article, in 2018, the German Cancer Research Center (DKFZ) ran a total budget of €280 million and the Netherlands Cancer Institute invested around €80 million into research. Transformative medicines often come from discoveries supported by public or not-for profit funding.

Past public policy changes led to the monopolization of the pharmaceutical industry in the last 20 years so we think that it is imperative to (i) break the monopolistic system run exclusively by the pharmaceutical industry and (ii) support and advance development of medicines by academia, non-profit research organisations and non-commercial entities. There are positive examples of academically developed new therapies brought to patients in a timely manner: the Hospital Clínic de Barcelona developed a CAR-T cell therapy treatment with donations of €1.8mn from companies, foundations, associations and individuals. The drug aims to fill an unmet need and offer advantages from local production at a cost less than a third of that of commercial CAR-T-cell therapies. This is the first "academic" CAR-T-cell therapy to achieve EMA PRIME status and a price tag of €89,000. In some instances, the objective seems to be to bypass the pharmaceutical companies, but initiatives such as the Association of Corporate Counsel (ACC) in Italy seek collaboration with the industry.

We believe that the European Union should aspire to make **Europe a global hub for life sciences and innovation, in which (i) private and public funding are allocated in a transparent way and handled with accountability, and (ii) incentives are awarded only if robust evidence is provided.** It is, therefore, worth exploring how a functional, fair, and transparent **public-private partnership** could be a way forward.

About the ECL Access to Medicines Task Force

Established in 2016, the ECL Access to Medicines Task Force (A2M TF) connects 30 national and regional cancer societies in 25 European countries, representing over 570 million Europeans. It aims to make safe and effective medicines available to all cancer patients in Europe, by insisting on accessibility, availability, affordability and increased transparency related to medicine prices, ultimately leading to sustainability of healthcare systems. The Task Force strongly believes in the power of constructive dialogue. We urge all stakeholders to push for accessibility to high quality treatments, improving both survival and the quality of life of cancer patients.

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About the European Fair Pricing Network

In November 2020, ten European Cancer Societies launched the European Fair Pricing Network (EFPN) – the first-ever EU-wide collaborative network to improve transparency, access and affordability of cancer medicines for the benefit of cancer patients. EPFN has invested €1 million to team up with the Netherlands Cancer Institute (NKI) and the Organisation of European Cancer Institutes (OECI) to shed a light on medicine pricing and translate findings into evidence-based policy asks for national and European decision-makers.

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