EUCOPE

European Confederation of Pharmaceutical Entrepreneurs AISBL

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THE ORPHAN MEDICINES REGULATION - THE WAY FORWARD

The European Commission recently published its Staff Working Document ("SWD") analysing the strengths and weaknesses of the Orphan Medicinal Product (OMP) Regulation.[1] Below, EUCOPE, the European association for small to medium-sized companies in the field of pharmaceuticals and medical technologies, outlines **ways to strengthen the EU environment for the development of OMPs.** EUCOPE focuses on the OMP Regulation itself, the pharmaceutical regulatory framework more broadly, Health Technology Assessment (HTA) and national market structures for access to OMPs.

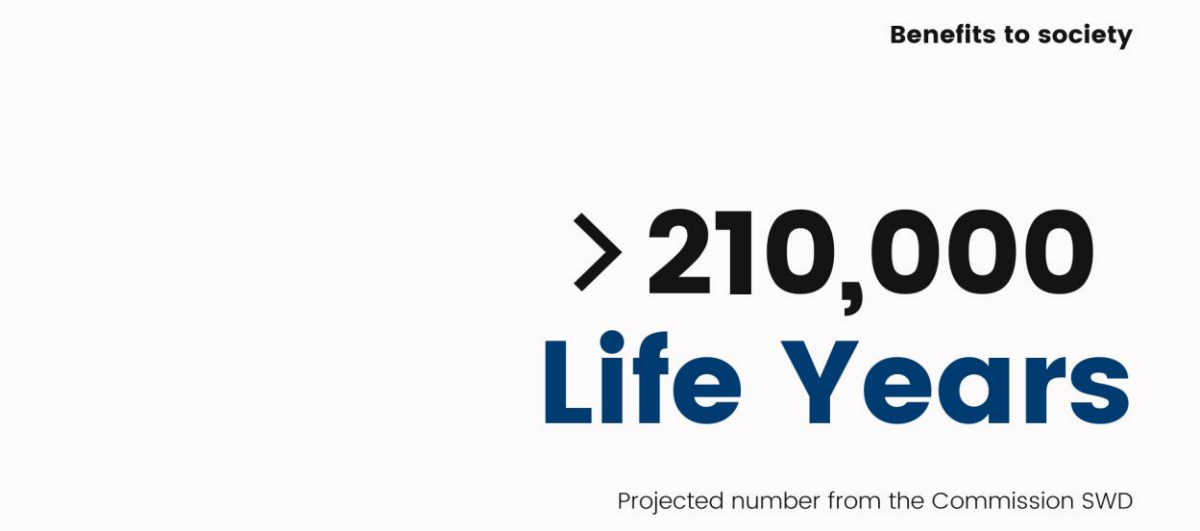
ELEMENTS FOR THE DEVELOPMENT OF OMPS ARE INTERDEPENDENT AND MUTUALLY SUPPORTIVE. EUCOPE CALLS FOR A MULTI-STAKEHOLDER ENGAGEMENT AND A HOLISTIC APPROACH TO STRENGTHENING THESE ELEMENTS. THIS WILL IMPROVE ACCESS FOR PATIENTS AND STIMULATE INNOVATION IN EUROPE.

(1) The OMP Regulation has created effective incentives for the development of new medicines against rare diseases.

Since 2000, the number of EU-authorised OMPs increased from eight to 182.[2] The SWD and its supporting study confirmed that the Regulation is effective.[3] The Regulation has helped companies to bring OMPs to market in many different disease areas and has also stimulated competition, a sign of a functioning model and market.

[1] While the evaluation covers both the Paediatric and Orphan Regulations, we focus here on the OMP Regulation.
[2] The Commission SWD refers to 142 approved products by the end of 2017. The European Medicines Agency lists 182 orphan medicines – Source: EMA website: https://bit.ly/3709zcn - accessed on 12 October 2020.
[3] Commission SWD, page 100.

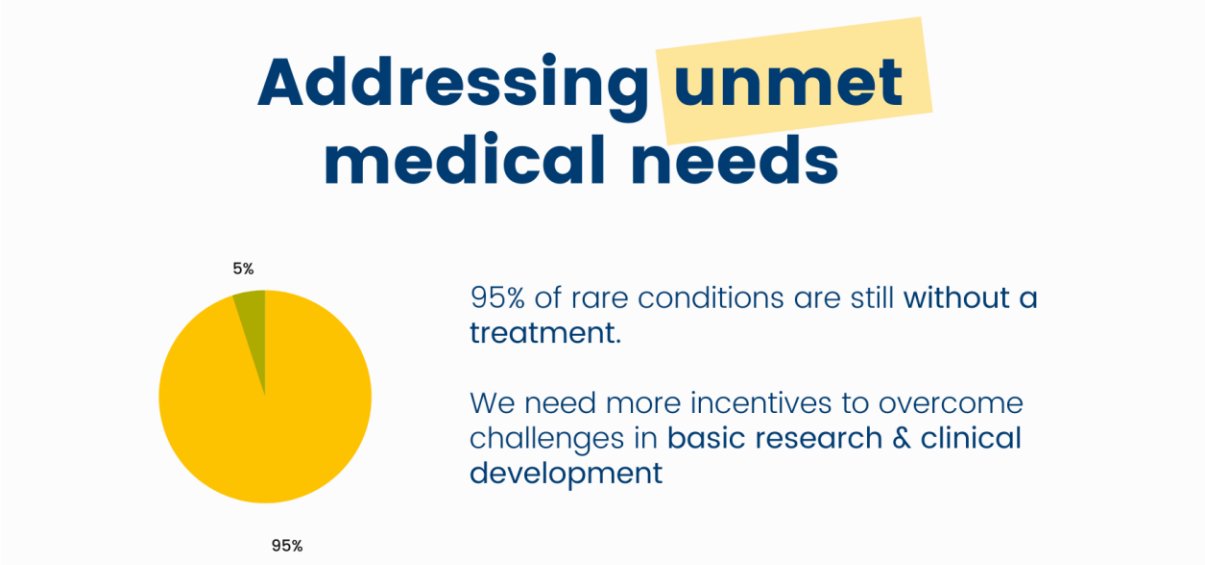
This competition, in turn, led to additional and differentiated therapies becoming available to patients.[4] Profits from products can be reinvested into subsequent and additional R&D. However, 48% of OMPs have revenues of less than EUR 10mln in the EU,[5] and investment in the development of OMPs remains risky and far from immediately profitable. The SWD confirms that additional costs to society of OMP development are very limited,[6] while additional benefits to patients and society are very substantial (from 210,000 to 440,000 life years).[7] In Europe, the overall cost of OMPs is estimated at around 7% of pharmaceutical spending;[8] about EUR 10.5bn per year.



However, 95% of rare conditions are still without an authorised treatment, so it is critical to improve the European regulatory, scientific and financial incentives eco-system for OMP development. There are 6,000 rare diseases globally and 95% of these do not have an authorised treatment option. However, there is a very uneven distribution of patients within that spectrum of rare diseases. 400 of the 6,000 are responsible for 98% of rare disease patients. Only 149 of the 6,000 rare diseases account for 77-81% of patients.[9] In order to

[4] NB: We are sceptical of any regulatory model that would disincentive further development in orphan conditions where a treatment is already authorised. This will not be in the best interest of patients to have research re-directed into other areas once a treatment option has been made available. A second treatment may not only offer a better risk-benefit profile, it could even be curative. We are sceptical of any regulatory model to only develop medicines for disease areas where there is no single treatment option. It would not be in the best interest of patients to have research re-directed into other areas once a treatment option has been made available. A second treatment may not only offer a better risk-benefit profile, but it could also even be curative.
[5] Commission SWD, page 67.
[6] Commission SWD, page 64.
[7] The Commission SWD assesses the benefits in Quality-Adjusted Life Years (QALYs) which is a measure from health economics.
[8] For 2017, the OMP share was estimated to be at 7.2%, or approximately 10.5 billion euros against the approximately 147 billion euros spent in total in medicines. Source: https://ojrd.biomedcentral.com/articles/10.1186/s13023-019-1246-7 - accessed on October 12, 2020.
[9] Nguengang Wakap, S., Lambert, D.M., Olry, A. *et al.* Estimating cumulative point prevalence of rare diseases: analysis of the

better address unmet medical needs and identify new solutions, there is a clear need for a better understanding of the underlying issues for this skewed distribution.



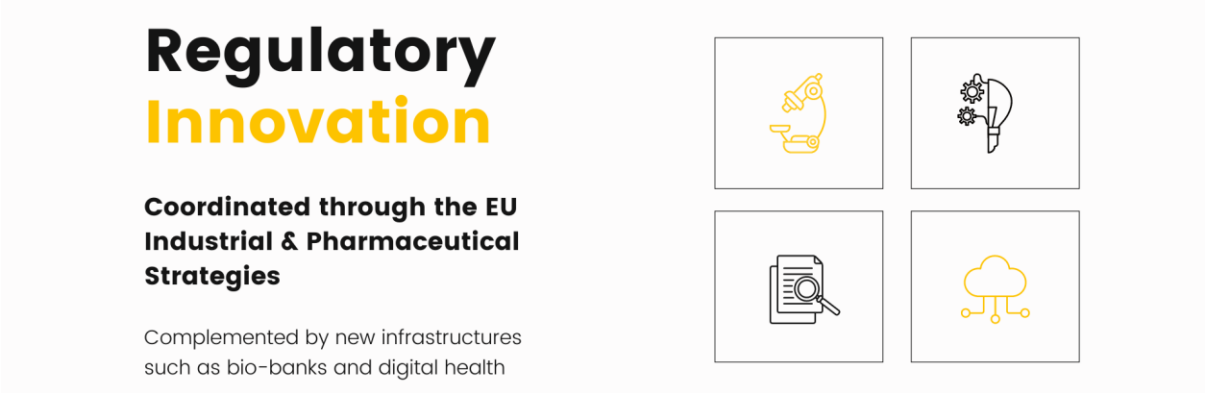
To better address all rare diseases, we need a multi-pronged approach, including a quantum leap in the funding of new research.

***EUCOPE recommendation**: Lack of research and funding hinders our knowledge of the +6,000 rare diseases. EUCOPE encourages policymakers to develop more incentives for biopharmaceutical companies active in rare diseases. These could include a special set of incentives to overcome challenges in basic research and clinical development.*

***(2)* We need regulatory and HTA framework flexibility to foster innovation. Flexibility should be coordinated and supported through the EU Industrial and Pharmaceutical Strategies, and the biopharmaceutical sector should stay at their core.**

Incentivising R&D only goes so far in tackling the significant unmet medical need in rare diseases. In disease areas with few patients globally, there are enormous issues related to scattered and scarce data, which negatively impact on R&D and regulatory approvals, and delay patient access.

Orphanet database. *Eur J Hum Genet* **28,** 165–173 (2020). https://doi.org/10.1038/s41431-019-0508-0 , figure 4. Accessed at https://www.nature.com/articles/s41431-019-0508-0 on Oct 12, 2020.



To tackle this, we need more acceptance of Real-World Evidence (RWE) and closer European collaboration on HTA. We need a better framework and closer alignment on requirements from EMA committees, and a forward-looking strategy that builds on the lessons from the COVID-19 crisis as regards regulatory flexibility. The EU shall adopt the proposed HTA Regulation, provided the final compromise doesn't lead to requirements duplication and strengthen the collaboration between Regulators, national HTA bodies, and payers on evaluation and access. This should all be underpinned by dedicated strategies for the biopharmaceutical sector, and follow-through on the European Commission's commitment[10] to allocate more resources to key EU Agencies such as the EMA.

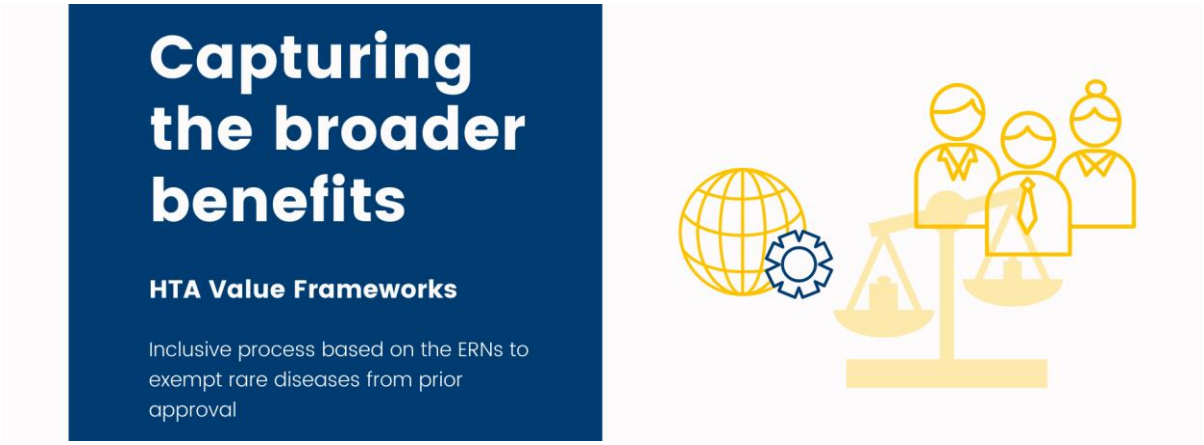
***EUCOPE recommendation**: We must build on the past twenty years of scientific and regulatory developments and on the lessons from the COVID-19 pandemic to optimise and streamline regulatory pathways for OMPs. As noted in our position on the Pharmaceutical Strategy for Europe, regulatory innovation should be complemented by new infrastructures such as biobanks and pan-European diseases registries, e-health systems, and public-private partnerships in the areas of RWE.*

(3) Access to OMPs should be made more inclusive. Investment in rare disease patients is an investment in society.

The SWD highlights that OMPs are not equally accessible to patients in all EU countries. Access is a shared responsibility and requires an aligned approach between all stakeholders, with Member States playing a crucial role. In the case of rare diseases, there are specific access obstacles on top of those experienced in more common disease areas. Not all EU countries currently have the expertise and specialised treatment centres to diagnose and treat

[10] The Commission is expected to extend the mandate of EMA and the ECDC on November 11 link.

all rare diseases. EUCOPE believes that the European Reference Networks (ERNs) can play a crucial role in developing better models and solutions to provide faster access to treatments, for all patients, across national borders. However, actions at EU level can only address these challenges in a limited way, as access to medicines is primarily a Member State competence.[11]



The quality of Member States policies, plans and strategies for rare diseases vary greatly; as do HTA processes for the evaluation of OMPs. Indeed, only some countries have distinct processes for OMPs in place.[12] Germany is a good example of where OMPs are subject to specific rules.[13] Unfortunately, this example is quite isolated, and many Member States operate rules that result in less access to OMPs.

EUCOPE recommendation: *Member States, the European Commission, patients, healthcare professionals, and industry should jointly develop pilots with the ERNs to exempt rare diseases from the need for prior approval before seeking diagnosis or treatment in a different EU country. We call for more consistent and widespread support across Member States to develop and implement the HTA Value Frameworks (VFs), which capture the broader benefits the OMPs bring to patients and their families, health systems, the economy, and society.*

[11] EU multi-stakeholder cooperation such as Orph-Val brings a clear added value in defining common criteria for assessing orphan medicines in pricing and reimbursement processes
[12] For instance, in England, Scotland, and Germany
[13] The rules provide an automatic benefit status to medicines that receive the marketing authorisation as an orphan medicine https://ojrd.biomedcentral.com/articles/10.1186/s13023-019-1078-5 access on October 12, 2020.

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