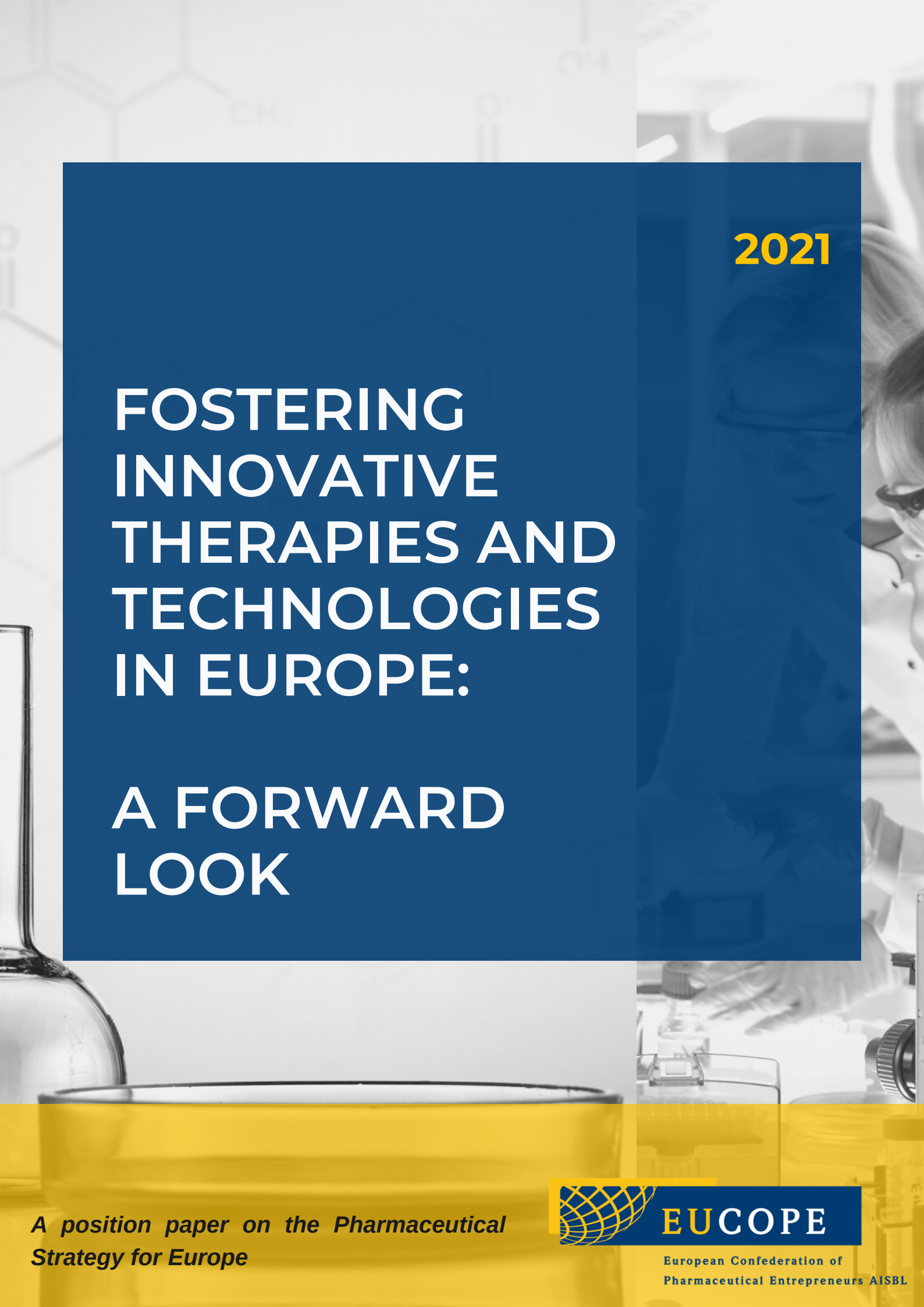

2021

FOSTERING INNOVATIVE THERAPIES AND TECHNOLOGIES IN EUROPE:

A FORWARD LOOK

A position paper on the Pharmaceutical Strategy for Europe

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

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FOSTERING INNOVATIVE THERAPIES AND TECHNOLOGIES IN EUROPE

EUCOPE Position on the Pharmaceutical Strategy

EXECUTIVE SUMMARY

The healthcare sector is constantly evolving, with manufacturers delivering innovative therapies to improve patient outcomes. To ensure that the European healthcare sector is responsive to the rapid technological developments and societal challenges of our times, the European Commission has outlined an ambitious policy agenda to reform the future healthcare landscape.

EUCOPE's position paper responds to the main actions proposed in the Commission's Pharmaceutical Strategy for Europe and presents concrete measures from the point of view of small to midsized developers of pharmaceuticals and medical technologies.

It is essential to **future proof the legislative framework** and continue **promoting research and technologies that reach patients,** while building on and maintaining a distinct Regulation and Directive. EUCOPE is supportive of the Commission's goal to **increase access to affordable medicines**. Encouraging access through European mechanisms **should recognise the diversity of the Europe's healthcare systems** governed by different Member States and the political challenges this presents. Stringent requirements that attach market launch conditions to incentives are no solution, as the European pricing and reimbursement environment is highly heterogeneous.

EUCOPE welcomes the Commission's commitment to **rare disease patients**. To support innovation across the healthcare sector, the **incentive framework should be strengthened** to account for the hurdles faced by especially smaller innovative companies. EUCOPE also welcomes continued dialogue to address the broader area of **unmet medical need**. EUCOPE supports the Commission's aim to reach a common understanding of unmet medical need, which is sufficiently broad and not limited to the absence of treatment options.

The proposed **simplification of the regulatory system, while upholding high standards, is welcomed**. The COVID-19 experience has demonstrated the impact of a **streamlined and accelerated approval process** which could be considered as an incentive for centrally approved therapies.

EUCOPE welcomes the Pharmaceutical Strategy's ambition to create a holistic, patient-centred and forward-looking environment for pharmaceuticals and medical technologies. **Therefore, we call for:**

Increasing access to innovative therapies

1. Based on the heterogeneity of Member States, **differential pricing with confidential prices should be considered as an effective solution** to provide wider access to affordable medicines.
2. The European Commission should build on the lessons of the COVID-19 pandemic when it comes to the unprecedented collaboration between stakeholders and the EU institutions, such as the Structured Dialogue, to facilitate a greater exchange of views between national competent authorities and industry stakeholders.
3. **Joint work on HTA at EU level could do much to tackle access delays**. To do so, it must prevent duplicative or repeat assessments, provide the required flexibility that is needed for specific products such as OMPs and ATMPs and provide broad access to joint scientific consultations.
4. For the sake of legal certainty and regulatory efficiency we suggest the targeted revision be based on the existing legal acts and **maintain the coexistence of both a general Regulation (for centralised marketing authorisations) and a general Directive (for decentralised/national marketing authorisations).**

Delivering for patients: Fulfilling unmet medical needs

5. **The incentives framework should be strengthened** in order not to risk significantly lowering the number of new medicines being developed and negatively affect the attractiveness of Europe as a region for innovation.
6. **Incentives are a crucial way of steering development into areas of unmet need** – a predictable and attractive incentive system is needed to foster medicine development. While market exclusivity, regulatory data protection and SPC should remain the main tools, additional incentives must be carefully designed to incentivise developers to go into areas where standard innovation models alone might not be effective.
7. **Proposed measures should be coherent with the EU IP Action Plan** which aims to decrease complexity and costs associated with the EU IP system. The introduction of a unitary European SPC as an option based on the Unitary European Patent would be a significant contribution in this respect. Harmonisation of intellectual property and tech transfer policy could help further commercialise EU-funded research and innovation and generate value locally. Any proposed revisions of the system of incentives should ensure these are based on predictable, adequate and effective enforcement of intellectual property rights, including expeditious remedies such as preliminary injunctions by the court.
8. **Multi-stakeholder dialogue is required to assess UMN** since a rigid definition e.g. an approach designed for specific patient populations, would not be well suited for identifying UMN across a wide range of disease areas. UMN is highly dependent on the scope and the value framework in which it is used based on different stakeholder preferences and responsibilities. The concept of UMN should therefore be considered within the broader value framework of each stakeholder (e.g. patient, health care professionals, scientific community, industry, regulators, payers, and broader society).

Supporting a competitive and innovative European Pharmaceutical Industry

9. **Incentives must not be linked to an obligation to launch.** Market launch depends on the structure and requirements of each individual Member State. For small and midsized companies it is particularly difficult to navigate the different systems in a given time frame due to their operational and financial limitations.

10. **Linking incentives to a declaration of R&D costs will prove unfeasible.** Developing products is a complex process with a high failure rate and methodologies cannot capture the R&D costs incurred and investments. Consequently, linking the incentives system to the aforementioned obligations would substantially weaking the EU's ability to attract and promote innovation.
11. Any efforts to bring generics or biosimilars to the market is clearly an objective. This should be done while maintaining the highest scientific standards and should not put the already balanced system of regulatory incentives and IP rights at risk.

A sound and flexible regulatory system

12. Further streamline evidence and data requirements between EMA, national HTA bodies, and payers for authorisation and HTA procedures, including reimbursement decisions.
13. **Increase use of Real-World Evidence (RWE) with evidence requirements coordinated with national HTA bodies** in order to link evidence requirements in accelerated approval processes with evidence requirements for national pricing or reimbursement procedures.
14. Encourage establishment of national disease registries for management of RWE.
15. **Advanced diagnostics and AI require rationalised funding and business incentives** that provide stimulus for investment and opportunities for public-private collaboration that can foster innovation and support for commercialisation.
16. **GMO requirements for ATMPs should be harmonised** with the aim to remove GMO requirements for cell therapies manufactured with vectors that have been established as safe.

Enhancing resilience: Diversified and secure supply chains

17. Efficient use of existing obligations should take precedence to imposing additional obligations which might be impossible to achieve, in particular for small to midsize companies. Efforts to support production for the EU should be carried out with incentives-driven reforms, which encourage advanced manufacturing capabilities for certain critical products.
18. HERA could play a supporting role by carrying out horizon scanning, providing risk sharing in the form of public-private partnerships and incentives in preparation for future cross-border health threats.

EUCOPE – the European Confederation of Pharmaceutical Entrepreneurs

EUCOPE is Europe's trade body for small to midsized innovative companies working in the field of pharmaceuticals and medical technologies.

Based in Brussels, EUCOPE gives voice to more than 900 research-orientated innovative companies and associations active in research and development of pharmaceuticals, biotechnologies and medical devices.

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THE EUROPEAN CONFEDERATION OF PHARMACEUTICAL ENTREPRENEURS

In this position paper we provide the views of our members in response to the proposed actions of the European Commission as presented in the 25 November 2020 Pharmaceutical Strategy for Europe.[1] Each chapter briefly summarises some of the actions proposed by the Commission before providing context on how the actions are likely to affect industry. We then propose concrete suggestions for the implementation of the Strategy. Each chapter corresponds to a section within the Pharmaceutical Strategy.

EUCOPE aims to ensure that the Pharmaceutical Strategy provides for a legal framework that is relevant for future innovative technologies, while providing conditions that ensure the European Union remains an attractive place to invest, research and develop medicinal products. In order to achieve this, **it will be key to strengthen the incentives framework while avoiding harmful obligations and to collaborate with industry to ensure the regulatory framework is responsive to the rapid development in healthcare technologies.**

1. MEDICINES – A STRONG ECOSYSTEM AT AN IMPORTANT CROSSROADS

The Pharmaceutical Strategy aims to create a future proof regulatory framework and support industry in promoting research and technologies that reach patients to fulfil their therapeutic needs. It will address market failures (e.g. discovery of novel antibiotics) and take into account weaknesses exposed during the COVID-19 pandemic. The Strategy paves the way for both legislative and non-legislative action around challenges facing the pharmaceutical sector, a sector which is a major contributor to the EU economy in terms of creating highly skilled jobs and investment in innovation. The Pharmaceutical Strategy forms part of the new Industrial Strategy for Europe[2] which aims to make EU industry more competitive globally and enhance Europe's strategic autonomy by being an "…industrial innovation strategy at heart."

Europe is home to a rich innovation ecosystem with start-ups, world-class research institutions, top universities for life sciences and many small and midsized pharmaceutical and biotech companies. However, we often see challenges in scaling up pre-clinical and clinical research to deliver innovative medicines for Europeans. The COVID-19 pandemic provided a number of lessons for governments and pharmaceutical companies alike, nonetheless it has also demonstrated the strength of European innovation in health technology with the most successful vaccines being developed in Europe. The pharmaceutical industry played a significant role in reducing the societal and health burden of the COVID-19 pandemic and enabling the return to normal life for Europeans. One of the crucial lessons to take away from this pandemic is the value of supporting an ecosystem for pharmaceuticals and medical technologies where a number of

[1] COM(2020) 761 – Pharmaceutical Strategy for Europe
[2] COM(2020) 102 – A New Industrial Strategy for Europe

small and midsized companies can dedicate time and resources to developing innovative therapies or prophylactics and partner with larger companies when necessary.

1.1 INCREASING ACCESS TO INNOVATIVE THERAPIES

EUCOPE supports the goal of the European Commission to increase access to affordable medicines for patients across the EU. As indicated by the Commission, there are various factors that impact access to medicines across Member States. While respecting Member State competence in defining their own health policies, the Commission can play a role in facilitating engagement between all stakeholders to improve access and continue to promote an attractive environment for innovation. The unequal access to affordable medicines in Member States is a product of more than 27 different pricing and reimbursement procedures, national and regional HTA bodies, health insurance systems and health budgets and large differences in spending power, fiscal policies, and healthcare priorities. Differential pricing with confidential prices, that allow for the provision of price discounts, should therefore be considered as an effective solution to provide wider access to affordable medicines.

These political and economic challenges need to be taken into account when choosing the most appropriate tools to foster access to medicines in the EU, whilst guaranteeing affordability, in particular the differences among the national health systems in terms of clinical practice, epidemiology and patterns of medicine usage, as well as their pricing and reimbursement systems.

To ensure that the Pharmaceutical Strategy sets realistic and achievable goals, the main focus should therefore be on those areas where the European Union currently has the required competencies to enact legislative measures. The COVID-19 pandemic has demonstrated an unprecedented collaboration between stakeholders and the EU institutions. Since many of the issues that the European Commission has included for priority are multifactorial, and some are outside of the competency of the European Union, we propose that the European Commission aim to facilitate greater dialogue between the relevant national authorities, industry and regulators at EU level.

Joint work on health technology assessment at the EU level can provide greater and more timely access to innovative therapies and medical technologies. However, for this to be achieved, duplication of work between Member States must be avoided at all costs. Joint work will only be successful in tackling delays to access insofar that it prevents duplicative or repeat assessments, provides the required flexibility that is needed for certain products, such as Orphan Medicinal Products (OMPs) and Advanced Therapy Medicinal Products (ATMPs) and provides each sponsor the chance for joint scientific consultation.[3]

[3] Eucope.org “EUCOPE’s statement on EU HTA Portuguese presidency compromise”, https://www.eucope.org/wp-content/uploads/2021/03/eucopes-statement-on-eu-hta-portuguese-presidency-compromise.pdf [Date of Access 25.05.2021]

- Based on the heterogeneity of Member States, **differential pricing with confidential prices should be considered as an effective solution** to provide wider access to affordable medicines.
- The European Commission should build on the lessons of the COVID-19 pandemic when it comes to the unprecedented collaboration between stakeholders and the EU institutions, such as the Structured Dialogue, to facilitate a greater exchange of views between national competent authorities and industry stakeholders.
- **Joint work on HTA at EU level could do much to tackle access delays.** To do so, it must prevent duplicative or repeat assessments, provide the required flexibility that is needed for specific products such as OMPs and ATMPs and provide broad access to joint scientific consultations.

1.2 TARGETED APPROACH TO THE REVISION OF THE PHARMACEUTICAL LEGISLATION

EUCOPE fully supports the European Commission's targeted approach to reviewing the legislation as it will enhance regulatory simplification and efficiency. The review should be undertaken with considerable care and be limited to those shortcomings and topics identified in consultation with stakeholders. This will facilitate a constructive and focused review while avoiding any unintended consequences or duplication in adapting the legislative framework.

The targeted approach should be pursued on the basis of the existing legal acts, i.e. maintaining both Directive 2001/83/EC and Regulation (EC) No 726/2004, amending them where necessary. The dual marketing authorisation system consisting of the Directive for decentralised/national procedures and the Regulation for the centralised procedure, ensures a comprehensive framework covering the entire lifecycle of medicinal products. Having been continuously updated over two decades, this dual system is well-established and should be maintained. It secures the suitable allocation of tasks to the respective competent authorities and eliminates competition hurdles especially for small and midsized companies.

The Regulation is the appropriate type of legal act to regulate the EMA as a European Agency and the centralised marketing authorisation as an EU uniform procedure, and the Directive remains the suitable and preferable legal act to regulate the national/decentralised authorisation procedures for marketing authorisations issued by national competent authorities. The Directive takes into account existing legal structures at Member States level as well as administrative procedures and experiences of national regulators. The legal uncertainty and increased administrative burden which is associated with a transition from a Directive to a Regulation – e.g. to be observed in the course of adapting Member States' laws in the field of veterinary medicinal products to the new Regulation (EU) 2019/6 – should be avoided.

- For the sake of legal certainty and regulatory efficiency we suggest the targeted revision be based on the existing legal acts and **maintain the coexistence of both a general Regulation (for centralised marketing authorisations) and a general Directive (for decentralised/national marketing authorisations).**

2. DELIVERING FOR PATIENTS: FULFILLING UNMET MEDICAL NEEDS

The European Commission proposes to revise the legislation regulating medicines for children and rare diseases to improve the therapeutic landscape and address unmet needs. In the Roadmap for the revision of the general EU pharmaceutical legislation, the Commission specifies its aim to reach a common understanding on Unmet Medical Needs (UMN) to stimulate innovation and breakthrough therapies beyond medicines for rare disease and children.

This presents an opportunity to significantly strengthen the EU incentives system by drawing lessons from what works as well as the current shortcomings or market failures which occur with antimicrobial resistance (AMR), medicines for children and rare diseases or technologies which have not yet seen sufficient commercialisation. For EU industries to remain competitive and resilient, it is key to have a solid incentives and intellectual property (IP) framework in place which encourages industry to continuously adapt and innovate, and which allows companies to commercialise products and ultimately make them available to the patient. The EU pharmaceutical regulatory framework must provide predictable regulatory pathways for innovative therapies that work in unison with the IP framework, Health Technology Assessment (HTA) and national market structures for access to medicines.

The end goal should be that clinically relevant innovative medicines can seamlessly be evaluated on clinical aspects linked to effectiveness that support reimbursement decisions.

Proposed measures should be coherent with the EU IP Action Plan.[4] The plan aims to decrease complexity and costs associated with the EU IP system and the proposed introduction of a Unitary European Supplementary Protection Certificate (SPC) as an option based on the Unitary European Patent would be a significant contribution in this respect. Harmonisation of IP and tech transfer policy could help further commercialise EU-funded research and innovation and generate value locally. Any proposed revisions of the system of incentives should ensure these are based on fair, adequate and effective enforcement of IP rights, including expeditious remedies such as preliminary injunctions by the courts.

2.1 CURRENT GAPS IN THE RARE DISEASE AND PAEDIATRIC ENVIRONMENT

Medicines for rare disease and paediatrics were early-on identified as in need of incentives to spur sustained research and development of new therapies, and while the recent Commission review concluded that the incentives have proven effective, significant challenges still remain.[5] There are more than 6-7,000

[4] COM(2020) 760 – Making the most of the EU's innovative potential – an intellectual property action plan to support the EU's recovery and resilience
[5] De Jong, Thyra et al (2019): "Study to support the evaluation of the EU Orphan Regulation". *Final report July 2019*. Technopolis Group.

known rare diseases globally and 95% of these do not yet have an authorised treatment option. The journey for those patients for whom there are available treatments is still far from simple, as the treatments are rarely transformative or curative.[6] Not all patients respond to treatments in the same way, something which holds especially true for rare disease, and consequently the availability of a single authorised OMP does not completely alleviate unmet need for a given disease area. This also means that any incremental innovation, i.e. innovation over a number of subsequent products being brought to the market, potentially makes an important contribution to addressing unmet needs.

Evidential uncertainty and differing requirements along the lifecycle of OMPs and paediatrics, from development to launch, pose significant hurdles, especially to smaller innovative companies whose main focus is treatments for these patient groups. In disease areas with few patients globally, there are enormous issues related to scattered and scarce data. These barriers, together with the heterogeneity of the disease (the high degree to which biological mechanisms in rare and paediatric diseases are not yet fully understood), negatively impact Research & Development (R&D) and regulatory approvals and can lead to different speeds of development. The absence of incentives for these companies could therefore risk significantly lowering the number of OMPs and Paediatric Medicines being developed, or in some cases threaten the survival of companies which solely produce them.[7]

- **The incentives framework should be strengthened** in order not to risk significantly lowering the number of new medicines being developed and negatively affect the attractiveness of Europe as a region for innovation.
- **Incentives are a crucial way of steering development into areas of unmet need** – a predictable and attractive incentive system is needed to foster medicine development. While market exclusivity, regulatory data protection and SPC should remain the main tools, additional incentives need to be carefully designed to incentivise developers to go into areas where standard innovation models alone might not be effective.
- **Proposed measures should be coherent with the EU IP Action Plan** which aims to decrease complexity and costs associated with the EU IP system. The introduction of a unitary European SPC as an option based on the Unitary European Patent would be a significant contribution in this respect. Harmonisation of intellectual property and tech transfer policy could help further commercialise EU-funded research and innovation and generate value locally. Any proposed revisions of the system of incentives should ensure these are based on predictable, adequate and effective enforcement of intellectual property rights, including expeditious remedies such as preliminary injunctions by the court.

[6] EURORDIS Rare Barometer: 7500 respondents: 69% of rare disease patients had received treatment for their rare disease, only 5% had received a transformative treatment approved for the entire European Union

[7] Eucope.org (2020): "Study: Economic & Financial Challenges of Developing Orphan Drugs", https://www.eucope.org/study-economic-financial-challenges-of-developing-omps/ [Date of Access 15.04.2021]

2.2 ADDRESSING UNMET MEDICAL NEEDS

The European Commission will aim to establish a common understanding of 'Unmet Medical Need' (UMN) beyond rare diseases through development of either criteria or a definition. The interpretation of what constitutes 'unmet medical needs' however varies in content and has different meanings depending on different stakeholders' perspectives (e.g. patients, developers, clinicians, regulators, HTA, payers) as well as to whose need one refers (e.g. individual or societal). The complete absence of a treatment option is not sufficient to determine UMN for a given disease area - disease severity, burden of illness and impact on the quality of life of patients as well as indirect costs for families and caregivers are also essential elements.[8] Further, a narrow definition of UMN could run the risk of disincentivising innovation in a disease area. For example, the first direct acting anti-viral in Hepatitis C would have been considered to have 'fulfilled' the UMN and pan-genotypic treatment regimens (acting against every genotype) could have been disincentivised.

- **Multi-stakeholder dialogue is required to assess UMN** since a rigid definition e.g. an approach designed for specific patient populations, would not be well suited for identifying UMN across a wide range of disease areas. UMN is highly dependent on the scope and the value framework in which it is used based on different stakeholder preferences and responsibilities. The concept of UMN should therefore be considered within the broader value framework of each stakeholder (e.g. patient, health care professionals, scientific community, industry, regulators, payers, broader society).

3. SUPPORTING A COMPETITIVE AND INNOVATIVE EUROPEAN PHARMACEUTICAL INDUSTRY

The European Commission proposes to revise the system of incentives and obligations in the pharmaceutical legislation, address market competition considerations to improve access to generic and biosimilar medicines and initiate a pilot project to understand the root causes of deferred market launches. The European Commission also proposes to implement non-legislative measures together with Member States to improve transparency to establish the R&D costs of medicines. Finally, the Commission proposes to optimise the supplementary protection certificates system to make it more transparent and efficient, as foreseen in the Intellectual Property Action Plan.

[8] Eurordis.org (2021): "Eurordis response to the European Commission Inception Impact Assessment (IIA) on Paediatric Medicines and Orphan Medicinal Products", http://download2.eurordis.org/documents/pdf/EURORDIS_Response_IIA_OMP_2021.pdf [Date of Access 22.04.2021]

EUCOPE supports novel rewards to complement market protection, especially in areas of high medical need. However, a tailored system that links incentives with placing products on the market in all or most Member States or so called 'transparency' of R&D costs would weaken the possibility for the incentives to be effectively granted.

Making incentives conditional upon market launch in most or all Member States would jeopardise business sustainability, especially for small and midsized companies. Market launches are typically determined by the length and heterogeneity of pricing and reimbursement processes in Member States. Different systems are used to inform reimbursement decisions, which pose a challenge to companies and impacts their ability to launch EU wide. Differences in market launches depend on the length and resources needed for the procedure, varying data requirements which might off set the financial benefit, different comparators that affect the achievable price and impedes value optimisation and willingness or ability to pay. Heterogenic pricing and reimbursement procedures and the resulting obstacles have a particularly profound impact on small and midsized companies as they face greater operational and financial limitations. Protracted procedures along with increased financial and data requirements more easily off set achievable price and any financial benefits, severely increasing the risk associated with broadening their commercial scope to other countries. Therefore, in many cases small and midsized companies first test and establish their business in a limited number of countries.

Measuring, and disaggregating R&D costs of an individual medicine is very complex for companies that have more than one product under development and would contribute to increased costs in terms of monitoring and reporting. Developing products is a highly complex process with a high failure rate and methodologies are unlikely to capture the true R&D costs and investments for any given product. It would not be feasible for payers to audit this data and companies would be incentivised to inflate their development expenses, potentially making R&D less efficient. Consequently, a system of IP incentives that is linked to R&D costs would substantially weaken the EU's ability to attract and promote innovation and do more harm than good.

Any efforts to bring generics or biosimilars to the market is clearly an objective but it should not put the already balanced system of regulatory incentives and IP rights at risk. The uptake of generics and biosimilars is determined by the Member States healthcare systems and therefore does not fall within the EU legislators' competence.

- **Incentives must not be linked to an obligation to launch.** Market launch depends on the structure and requirements of each individual Member State. For small and midsized companies it is particularly difficult to navigate the different systems in a given time frame due to their operational and financial limitations.
- **Linking incentives to a declaration of R&D costs will prove unfeasible.** Developing products is a complex process with a high failure rate, and methodologies cannot capture the R&D costs incurred and investments. Consequently, linking the incentives system to the aforementioned obligations would substantially weaken the EU's ability to attract and promote innovation.
- Any efforts to bring generics or biosimilars to the market is clearly an objective. This should be done while maintaining the highest scientific standards and should not put the already balanced system of regulatory incentives and IP rights at risk.

4. A SOUND AND FLEXIBLE REGULATORY SYSTEM

The European Commission proposes to simplify legislation and create regulatory attractiveness with the aim to reduce regulatory approval times and costs. This involves addressing challenges related to the interplay of medicines and devices. The revision will also include giving regulatory authorities more power to adapt on their own initiative the terms of marketing authorisations on the basis of scientific evidence. The Commission will also find ways to increase support and accelerate product development and authorisation in areas of unmet need through the incorporation of the EMA's priority medicines scheme (PRIME) or similar mechanisms in the regulatory framework. Finally, the Commission proposes to adapt regulatory requirements applicable to medicines for human use that contain or consist of genetically modified organisms (GMOs).

The proposed simplification is welcomed and particularly important for small and midsized companies. Any effort to allow regulatory authorities to adapt on their own initiative terms of marketing authorisations must include procedures for adequate consultation with Marketing Authorisation Holders (MAHs) to provide predictability. MAHs should for example not be forced into accepting new indications for which there may be a limited or no business case due to low demand or lacking reimbursement.

The centralised authorisation procedure can be made more efficient by shortening the time to Committee for Medicinal Products for Human Use (CHMP) opinion by streamlining the steps of the assessment process, including rolling review features and by shortening the time for the Commission to issue a decision. Better alignment between the CHMP and the Committee for Orphan Medicinal Products (COMP) could expedite

the decision processes for OMPs. Further simplification could be achieved by allowing the EMA to grant the OMP designation rather than the European Commission, which would save time by streamlining the designation process.

We view strengthened cooperation between EMA and national HTA bodies as key to further streamlining the evidence requirements for authorisation and HTA procedures. The number of joint procedures could be increased by funding the EMA Scientific Advice Working Party-HTA Parallel Consultation management, i.e. the precursor to the Joint Scientific Consultation of the EU HTA Regulation. Without proper resourcing, joint scientific consultations cannot be made available as needed and consequently the joint clinical assessments are less likely to align on relevant methodologies, evidence and endpoints. This, in turn, would increase the likelihood of a discontinued joint clinical assessment and lead to duplication of work and lost time as the joint assessment would have to be restarted with an updated dossier.

- Further streamline evidence and data requirements between EMA, national HTA bodies, and payers for authorisation and HTA procedures, including reimbursement decisions.

4.1 ACCELERATED PROCEDURES

Streamlined regulatory processes and expedited pathways that build on the experience with PRIME, EMA expedited approval and rolling review for vaccines during the COVID-19 pandemic with earlier and more interactions with developers, early assurance of accelerated assessment and decreased regulatory burden could prove effective incentives. EUCOPE strongly supports the EMA's intent to invest the necessary resources to streamline the current scientific advisory platforms, so that product-driven advice can address multiple development options effectively. In this regard, PRIME should be appropriately resourced.

With regard to the current functioning of PRIME, we note that the first marketing authorisations for products designated as eligible for PRIME were only granted in June 2018; hence it is essential to review the performance of the scheme after 3 and 5 years, to ensure that it delivers the expected impact on public health (i.e. faster priority medicines to market).

To ensure that all applicants would continue to see the benefit of using the scheme, a fast lane approach should be designed for PRIME products. This would include: shorter timeline for eligibility and kick-off meeting, continuous access to the EMA contact person and a rolling opportunity to receive advice on product development. In addition, the possibility to seek Rapporteurs' views on scientific matters would be a welcome addition.

ATMPs are frequently at a disadvantage in accelerated assessment procedures due to the extensive questions with limited time to answer requests for supplementary information – earlier dialogue and more upfront information could be helpful to elucidate relevant questions.

4.2 FUTURE PROOFING OF THE LEGISLATION

The European Commission proposes to revise the legislation to adapt to cutting-edge products, scientific developments (e.g. genomics or personalised medicine) and technological transformation (e.g. data analytics and digital tools) and provide tailored incentives for innovation.

EUCOPE supports future proofing the legislation in preparation of new innovative ways in which medicines and other health technologies are developed and evidence is generated. The adaptation of the existing legislation to innovative approaches to developing medicines should include a stronger recognition and use of Real-World Evidence (RWE).

This is especially important in areas where evidence is limited, such as rare diseases, and should be considered an effective complementary approach in addressing and resolving uncertainties that cannot be answered with traditional clinical trials. The EU should clearly spell out the applications for which RWE would be suitable to provide clarity and guidance.

We encourage establishing a European medicines regulatory network '*regulatory modernisation initiative*', appropriately funded by users-fees that can evaluate and reform regulatory science programmes with measurable outcomes negotiated between regulators and industry.

TRUST4RD Tool for Reducing Uncertainties in the evidence generation for Specialised Treatments for Rare Diseases	RWE4Decisions REAL WORLD EVIDENCE
A tool for reducing uncertainties in the evidence generation for specialised treatments for rare diseases (OMPs). Commissioned by the Belgian federal body of social security INAMI/RIZIV and developed through multi-stakeholder dialogue. Aims to reduce uncertainties through iterative and informed dialogue among stakeholders, with continuous review of uncertainties as evidence is generated.	A multi-stakeholder initiative that builds on TRUST4RD Acknowledges that collection of Real-World Evidence (RWE) is a shared responsibility, to inform decisions for highly innovative technologies. Brings together HTA authorities, payers, regulators, patient representatives, researchers, clinicians and industry. Establishes a learning network on RWE involving stakeholders, to realise the potential of RWE to inform HTA decision-making.

EUCOPE is actively involved in resolving uncertainties in HTA decision-making

Natural history studies and single-arm studies in diseases where patient numbers are low or where there is otherwise a large degree of uncertainty, such as for innovative technologies can hugely benefit from post-licensing evidence generation through registries and other observational methods. It is important that the EMA provides adequate advice and supports regulatory science initiatives that increase the suitability of such evidence for regulatory decision-making. This is an area where international collaboration (e.g. with the U.S. Food and Drug Administration (FDA) can be of particular benefit, as well as cross-stakeholders' collaboration with partners such as HTA bodies and healthcare professionals.

In the following section we would like to touch upon some groups of advanced technologies where there is a need for special attention and where there is a need for specific regulatory provisions. Advanced technologies such as Artificial Intelligence (AI) and genomics have the potential to drive personalised

medicine approaches, deliver vastly improved patient outcomes and should be supported by a sound regulatory framework that can bring these technologies to the market.

4.2.1 ADVANCED DIAGNOSTICS

When it comes to advanced diagnostics, e.g. DNA arrays, High-throughput Sequencing, Comprehensive Genomic Profiling, Whole Exome Sequencing and Whole Genome Sequencing their value is not sufficiently recognised. Funding is insufficient and support not well suited to increase their role in the clinical setting, resulting in clinical practices not keeping up with the accelerating cycle of innovation in novel diagnostics.

Regulatory bodies should provide more dialogue opportunities so that advanced diagnostic companies can obtain guidance on available regulatory pathways and early evidence generation, which in turn will enable manufacturers to shape studies to meet regulators' evidence requirements. Future regulatory frameworks should allow the flexibility to accommodate product improvements with genomic test panels by including the most up-to-date scientific knowledge, while ensuring that the tests are safe, effective and accurate and the feedback of advanced diagnostic companies should be taken into account in the development of regulatory frameworks.

4.2.2 ARTIFICIAL INTELLIGENCE

Digitalisation and AI inclusion will require defined standards for data collection and exchange with incentives for organisations and vendors to align on the common data standards as well as the promotion of data interoperability and exchange protocols, with the European Health Data Space (EHDS) potentially playing a central role.

The EU will need clear guidance on quality requirements for validation processes and it will be paramount that any proposed regulation or guidance documents do not represent a further barrier to the adoption of AI services, but rather act as an accelerator to stimulate innovation, to the benefit of the EU competitiveness, and ultimately, to the benefits of European patients.

4.2.3 NANOMEDICINES

To ensure the pharmaceutical legislation remains up-to-date and can adapt to emerging complex therapies, such as nanomedicines, a review of the therapies which should be authorised via the centralised procedure is needed. This could for example involve a mechanism for regularly reviewing technological developments in the context of the centralised procedure.

4.2.4 ADVANCED THERAPY MEDICINAL PRODUCTS

It would be highly desirable to harmonise the Genetically Modified Organism (GMO) requirements for medicines that contain GMOs such as ATMPs. Currently, the classification from the EMA's Committee for Advanced Therapies (CAT) does not necessarily prevail over the advice from national authorities, which can bring confusion about the requirements for development, manufacturing, control and use of such products. For ATMPs such as gene and cell therapies manufactured with vectors which have been established as safe, removal of GMO requirements should be considered as occurred for COVID-19 treatments during the pandemic.

- **Increase use of Real-World Evidence (RWE) with evidence requirements coordinated with national HTA bodies** to link evidence requirements in accelerated approval processes with evidence requirements for national pricing or reimbursement procedures.
- Encourage establishment of national disease registries for management of RWE.
- **Advanced diagnostics and AI require rationalised funding and business incentives** that provide stimulus for investment and opportunities for public-private collaboration that can foster innovation and support for commercialisation.
- **GMO requirements for ATMPs should be harmonised** with the aim to remove GMO requirements for cell therapies manufactured with vectors that have been established as safe.

5. ENHANCING RESILIENCE: DIVERSIFIED AND SECURE SUPPLY CHAINS

The European Commission proposes to revise the pharmaceutical legislation to enhance security of supply and address shortages through specific measures including stronger obligations for supply and transparency and earlier notification of shortages and withdrawals and proposes the creation of an EU Health Emergency Response Authority.

With the COVID-19 crisis, the pharmaceutical sector demonstrated the potential for being a driving force for economic recovery and a key factor for healthcare systems' resilience. Any changes proposed to enhance security of the pharmaceutical supply chains should include a data-driven, structured dialogue with the private sector as well as other relevant actors involved in the value chain to ensure supply chain resilience and security.

Manufacturers, distributors, and traders of medicines should prioritise ensuring supply at their point in the supply chain, with early notification being the most efficient solution to ensure medicine supply. The definition of a shortage in the case of autologous ATMP for instance differs from that in other areas, since such products are not supplied in the usual way, in bulk to pharmacies.

Europe's innovative pharmaceutical industry already has a strong inherent resilience since 76% of active pharmaceutical ingredients used in the manufacture of innovative medicines in Europe is being sourced in the EU with another 11% originating in the US. Only about 9% is currently sourced from Asia, including from South Korea and Japan.[9]

The proposal to establish a European Health Emergency preparedness and Response Authority (HERA) is a welcome continuation of the dialogue and commitment to public-private partnerships that has defined the response to the COVID-19 pandemic. While HERA can play an important role to provide horizon scanning and public-private partnerships to counter serious cross-border health-threats, it cannot be seen as the sole solution to drive research and investments in niche markets. General and tailored incentives are necessary to reduce the risk of early investment, reduce redundancy and costs and create predictability in the market. Since HERA will need to work within an existing framework, with a strengthened role for both the EMA and the European Centre for Disease Prevention and Control, it will be important that the authority does not introduce additional burdens but rather streamlines existing reporting systems and other existing measures.

- Efficient use of existing obligations should take precedence to imposing additional obligations which might be impossible to achieve, in particular for small and midsized companies. Efforts to support production for the EU should be carried out with incentives-driven reforms, which encourage advanced manufacturing capabilities for certain critical products.
- HERA could play a supporting role by carrying out horizon scanning, providing risk sharing in the form of public-private partnerships and incentives in preparation for future cross-border health threats.

[9] EFPIA.eu (2021) "EFPIA statement following the call with EU Commissioner Kyriakides", https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-statement-following-the-call-with-eu-commissioner-kyriakides/#_ftnref1 [Date of Access 21.06.2021]