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On 20 March 2021, the CPME Board adopted the 'CPME Position Paper on the European Commission Pharmaceutical Strategy for Europe' (CPME 2021/011 FINAL).

Restoring balance in the pharmaceutical sector

European Doctors' Position Paper on the European Commission Pharmaceutical Strategy for Europe

The Standing Committee of European Doctors (CPME) represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues.[1]

Over time, trust in the pharmaceutical sector and its ability to promote the development of medical innovations while ensuring sustainable access has been eroded. Confidence in how this system works needs to be restored. The European Commission's Pharmaceutical Strategy for Europe offers a unique opportunity to deliver a policy that provides EU citizens with medicines that bring additional therapeutic benefits at a price they are able to pay.

[1]CPME is registered in the Transparency Register with the ID number 9276943405-41. More information about CPME's activities can be found under www.cpme.eu

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EXECUTIVE SUMMARY

Through the Pharmaceutical Strategy, the European Commission sets the right course of action towards fulfilling its primary mission in the pharmaceutical sector, which is to ensure patients' access to affordable medicines.

The Strategy correctly identifies the current problems facing the pharmaceutical system in the EU. It provides a sound basis for restoring balance in the pharmaceutical sector between public and private interests. A balance also needs to be restored in many aspects of the sector, e.g., between investment in high revenue generating areas and in those of unmet medical needs, or between savings in healthcare and ensuring the sector's emergency preparedness.

The ultimate success of the Strategy will depend on how the initiatives defined are implemented. The Commission must choose the right tools to deliver on its objectives across the four work strands.

To *"ensure access to affordable medicines for patients and address unmet medical needs",* the Commission must play a more active role in shaping health innovation, make all forms of public investment in the research and development process subject to concrete commitments and promote and facilitate transparency on net unit prices of medicines.

While bringing *"EU regulatory approval times onto par with those in other parts of the world"*, patient benefit and safety aspects must be adequately taken into consideration. At the same time, the Commission cannot overlook the overuse of the regulatory procedures for accelerated assessment. It must critically review the use of the PRIME scheme that facilitates market entry for medicines with limited information on their added therapeutic benefits and safety issues.

To *"enhance crisis preparedness and response mechanisms"* the EU needs to stop entrusting its health security to private companies. The EU should reconsider the interplay between public and private actors in biopharmaceutical research and development systems.

Finally, a key aspect of *"a strong EU voice in the world"* is the message this voice conveys. Working with third country partners, the EU should seek true global solidarity and promote high standards of governance in the public interest.

Undoubtedly, the implementation of many of the proposed changes will draw strong criticism from the beneficiaries of the current system in the EU and globally. These beneficiaries might perceive these changes as a threat to maintaining the current profitable status quo. The Commission should stand firm on its ambitions and defend its approach.

The Commission should recognise the role of healthcare professional, patient and consumer organisations and the importance of a balanced dialogue in introducing the proposed reforms – European doctors are confident that they can bring valuable knowledge and experience to this discussion and contribute to building a patient-centred EU pharmaceutical policy.

Key recommendations to the European Commission and EU Member States:

Play a greater role in providing directions for health innovation

Given that the public co-creates and is a major investor in health technologies, it should take an active role in defining directions for health innovation to create a system that is aligned with medical and social needs, rather than leaving it to be driven by commercial interests alone.

Review the current system of incentives and foster the use of alternative models to encourage health innovation

Following the premise that the Pharmaceutical Strategy is patient-centred, the current system of incentives based on intellectual property rights needs to be reshaped in the public interest, including ensuring better quality of patents and revising the Supplementary Protection Certificate system. Alternative models for encouraging innovation that decouple investment in innovation from medicine sales volumes and high prices should be further explored and implemented.

Promote transparency and increase cooperation in pricing of medicines

The information asymmetry between national authorities and pharmaceutical companies is disadvantageous for Member States and results in higher prices of medicines in Europe. By increasing transparency on net unit prices and joining forces in pricing negotiations, Member States can increase their bargaining power. The EU has a key role to play in achieving this goal.

Address structural, legislative and communicational problems leading to medicine shortages

The pandemic uncovered long-existing structural problems in the supply of medicines. While long-term organisational and regulatory changes are needed, short-term measures to mitigate the impact of shortages on patients, doctors and health systems must also be initiated.

Ensure the pharmaceutical sector's readiness to respond to health emergencies

Entrusting health security to private companies leaves Europe unprepared to respond to health emergencies. In times of health crises, the EU must be able to take decisions on how and when vaccines and treatments are manufactured and distributed, instead of leaving this to the discretion of the private sector. The pandemic has provided a fundamental lesson on the role of health security strategies and public health funding, calling for structural interventions.

Demonstrate leadership in protecting the public interest and seek true global solidarity

The EU should set high standards of governance in the public interest and address the systemic problems embedded in the global pharmaceutical sector that lead to inequality and generate a dynamic in which money drives innovation, prioritizing the interests of high-income countries instead of delivering relevant innovation to different regions and ensuring global access.

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1. DELIVERING FOR PATIENTS

The European Commission has taken the right approach in setting out objectives and actions to deliver on the Strategy's primary objective of improving patients' access to affordable medicines. Guided by this ambition, the Commission should seize the opportunity to reshape the system of health innovation, create a more beneficial cooperation with the private sector and improve Member States' and public health agencies' cooperation. Importantly, this can only be done by taking radical initiatives and challenging the current status quo.

1.1. PRIORITIZING UNMET MEDICAL NEEDS

1.1.1. Shaping directions of health innovation

The current research and development (R&D) system is biased towards high revenue generating diseases, leading to an increasing gap between real unmet medical needs (as a concept often misused and requiring a definition, see more under 1.1.3.) and investment.

Pharmaceutical companies often pursue low-risk strategies that can more easily bring commercial success, rather than developing innovations to address neglected areas. This has led to the proliferation of "me-too" medicines – those that offer little or no therapeutic advance on existing medicines but are sufficiently different to obtain patent protection.[2]

Consequently, the majority of medicines approved by the European Medicines Agency between 2000 and 2014 were modified versions of existing ones with no evidence of additional therapeutic benefits, while 95% of rare diseases remain without treatments.[3,4]

Play a greater role in providing directions for health innovation

The public sector is responsible for funding some of the highest risk research that leads to the most important innovations. However, as their exploitation, product development, pricing, and access are largely left to the discretion of industry, many of the promises of health technologies have not been fully translated into available and affordable clinical advances.

Given that the public co-creates and is a major investor in health technologies, the EU and national governments should take an active role in defining directions for health innovation to create a system that is aligned with medical and social needs, rather than leaving it to be driven by commercial interests alone.[5]

[2] Feldman R., *May your drug price be evergreen*, Journal of Law and the Biosciences, Volume 5, Issue 3, December 2018, pp. 590–647.

[3] Prescrire International (2015), *New drugs and indications in 2014…*, Volume 24 N° 159, April 2015, pp. 107–110.

[4] Marselis D., Hordijk L., *From blockbuster to "nichebuster"*, BMJ 2020;370:m2983, July 2020, p. 2.

[5] Mazzucato M., Li H. L., *A market-shaping approach for the biopharmaceutical industry*, UCL Institute for Innovation and Public Purpose, Working Paper Series (IIPP WP 2020-21), pp. 2-4.

Learn from previous initiatives and explore alternative approaches

To date, the EU has taken various measures to increase the development of medicines addressing neglected areas and "market failures", but they have only been partially successful. For example, although the Innovative Medicines Initiative (IMI)[6] has been operating for over a decade, according to a recent report, it has failed to invest in diseases where public funding is the most urgently needed.[7]

Additionally, the Orphan Regulation has been in force for more than twenty years, offering significant economic incentives for the development of medicines for rare diseases. Yet its evaluation points out that only 28% of registered orphan medicines are for diseases for which there were no alternative treatment options, while, as noted above, 95% of rare diseases remain without any treatment.[8]

The Commission needs to build on this experience when implementing the Innovative Health Initiative[9], IMI's successor, and reviewing the legislation on medicines for rare diseases and children (discussed further under 1.3.4.).

Besides this, the Commission could explore alternative approaches for increasing innovation in diseases that lack economic incentives, such as the ones covered by the Drugs for Neglected Diseases initiative, the Global Antibiotic Research and Development Partnership, or the Medicines for Malaria Venture and the Global Alliance for Tuberculosis Drug Development (see also under 1.2.1.).

1.1.2. Defining new approaches to tackle AMR

Antimicrobial resistance (AMR) poses a unique challenge in the pharmaceutical sector. Growing resistance to existing antibiotics and a lack of new ones leave patients and healthcare professionals facing diminishing treatment options. As investment in medicines intended to be used as sparingly as possible is commercially unattractive, the Commission correctly identified that a new approach is needed to find ways to improve the prudent use of antibiotics and support the development of new ones.

Assist Member States in implementing National Action Plans on AMR

One of the key elements in the prevention and control of AMR is the development of National Action Plans. The Commission should support Member States in implementing national strategies that place particular emphasis on strengthening antimicrobial stewardship programmes, fostering research on

[6] Innovative Medicine Initiative is a public-private partnership between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA) created to improve access to innovative medicines, particularly in areas where there is an unmet medical need.

[7] Global Health Advocates (GHA), Corporate Europe Observatory (CEO), *More private than public...*, Brussels, April 2020, pp. 9-12.

[8] Marselis D., Hordijk L., supra note 3, p.2.

[9] European Commission, *European Partnership for innovative health*, 2019.

infection prevention and control to improve health security, promoting optimal antimicrobial prescribing, and reflecting the One Health approach.[10]

Furthermore, communication and coordination between Member States plays a key role in developing joint actions. To improve their collaboration, the Commission should explore strengthening the mandate of the EU AMR One Health Network by aligning its work with the EU Presidencies and including environmental issues on its agenda, as recommended by the EU-JAMRAI.[11]

Promote prudent use of antibiotics

The prudent use of antibiotics, which means using them only when needed, in correct dose intervals and correct duration, is a crucial aspect of slowing down the spread of AMR. To control antibiotic consumption, only doctors and dentists should be entitled to prescribe them.

It is noteworthy that European doctors are aware of the key role that they play in controlling AMR.[12] However, a precondition for the prudent use of antibiotics is access to precise guidelines for antibiotic treatment.[13]

Encourage interdisciplinary education and professional training in the One Health approach

Cross-sectorial education and collaboration between doctors, veterinarians, dentists, pharmacists, and other health professionals, following the One Health approach, is particularly important in the context of AMR. The Commission should encourage and facilitate under and post-graduate education, as well as professional training that covers One Health, both in terms of content and format, in recognition of the interlinks between human health, animal health and the environment.[14]

Facilitate the transition of antibiotics from early clinical phases to commercialization through a tailored system of pull incentives

There is general consensus that both push incentives (subsidizing the overall development cost) and pull incentives (rewarding successful development) are needed to stimulate antibiotic development.[15]

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[10] Stakeholder Network on AMR, *Roadmap for action on Antimicrobial Resistance*, July 2020.

[11] EU-JAMRAI, *Policy brief: The need for a reinforced AMR One Health Network*, January 2021.

[12] The CPME report of November 2020 found that the vast majority of European doctors do consider antibiotic resistance when treating patients, including by providing advice on prudent antibiotic use to patients. More than 70% of them agreed to having good opportunities to provide advice on prudent use of antibiotics to individuals, but 45% of them are not able to give out advice or resources to patients because of insufficient time and no resources available. See: *What do European doctors know about antibiotic resistance?*, November 2020.

[13] The guidelines can also be used as a tool to inform the general public about when antibiotics should or should not be used. Thus, they could be used to decrease public demand for antibiotics. To this end, CPME defined a set of principles on the use of antibiotics in primary care. See: *Antibiotic Resistance: a CPME position paper*, April 2013.

[14] In order to promote this, CPME, along with other organizations representing dentists, pharmacists and veterinarians and our students' organizations, holds regional open debates on the implementation of One Health in undergraduate education. The last two workshops were organized in Paris and in Warsaw in 2018 and 2019. The next session focusing on professional training is planned as a webinar in the first half of 2021.

[15] The Transatlantic Task Force on Antimicrobial Resistance, *Pull Incentives for Antibacterial Drug Development...*, Clinical Infectious Diseases, Volume 65, Issue 8, Oxford University Press, October 2017, pp. 1378-1382.

Given that governments to date have largely provided only the former, there is a considerable lack of the latter to facilitate the transition of antibiotic products from early clinical phases to commercialization.

There are many examples of pull incentives,[16] and some European countries have already started to pilot some of them.[17] Of the various options, de-linkage models seem likely to stimulate innovation most effectively (see also the discussion under 1.2.1.).[18]

In addition, the Commission should support Member States in deciding which incentive is appropriate for a given country, how to implement it, and how much it will cost.[19] Notwithstanding this, the Commission should promote a European or global incentive programme that would pool resources and avoid duplications.

1.1.3. Increasing cooperation among public health agencies

The COVID-19 pandemic has highlighted the need and provided an opportunity to harness new collaborations among regulatory agencies, health technology assessment (HTA) bodies and payers to ensure timely generation of comparative data on medicines.[20] Similarly, improved cooperation among public health agencies can lead to more informed pricing decisions and convergence on key concepts and definitions.

Seek ways to increase clinical trials' efficacy and utility

Regulators should use their competencies, such as providing scientific advice as leverage to require companies to harmonise the designs and outcomes of clinical trials to make their comparison easier and to improve their utility for HTA bodies and payers.[21]

Furthermore, in the post-marketing period, regulators, with input from HTA bodies, should encourage companies to conduct randomised trials with an active comparator to demonstrate the added therapeutic benefit of their products.

[16] See e.g., Transatlantic Task Force on Antimicrobial Resistance, *Economic Incentives for Antibacterial Drug Development...*, Clinical Infectious Diseases, Volume 63, Issue 11, December 2016, Oxford University Press, p.1470.

[17] See examples from Germany, Sweden and the UK in: EU-JARMAI, *Incentivizing antibiotic access and innovation*, Policy Brief, January 2021.

[18] The application of a de-linkage system could directly benefit unmet public health needs by providing a predictable return on investment for products that satisfy predefined public health priorities. Moreover, it would promote prudent use of antibiotics by allowing research and development investments in successful products without requiring high product sales. In addition, contractual clauses could assure the products are priced reasonably and widely distributed. One major challenge of this system is the need for substantial upfront public investment.

[19] The current lack of such a support has been indicated in the EU-JAMRAI interviews with policymakers and AMR experts in ten European countries: EU-JARMAI, supra note 6, 2021.

[20] Naci H., Kesselheim A. S., et al., *Producing and using timely comparative evidence on drugs: lessons from clinical trials for covid-19*, BMJ 2020;371:m3869, October 2020, pp. 1-6.

[21] European Public Health Alliance (EPHA), *Recommendations: Unleashing innovation through regulatory reform*, October 2020, p. 4.

Encourage the generation of better evidence on medicines and increase its transparency

Payers should use their negotiating power to incentivise the generation of better evidence on new and existing medicines, for example, by explicitly including proven added therapeutic benefit in pricing and payment decisions.

Moreover, HTA bodies and payers across Europe should routinely disclose information on the comparative benefits and harms of new and existing medicines.[22]

Harmonize key concepts and definitions

A number of terms and concepts require common definitions that should be jointly developed by public health agencies in cooperation with relevant stakeholders.

The term "unmet medical need" is currently misused to justify innovation in more profitable areas that are not necessarily neglected and to benefit from accelerated approval procedures, while AMR, Alzheimer's disease or dementia remain largely unaddressed.

Moreover, the optimisation of the incentive system and the right functioning of the intellectual property rights framework require the definition of an "innovative medicine" as one that meets a previously unmet or inadequately met, substantive health need and offers enhanced effectiveness or other incremental benefit relative to existing therapeutic alternatives.[23]

Another example where cooperation is needed is in regard to medicine shortages and essential pharmaceuticals. These require a harmonised definition of what constitutes a medicine shortage and what are clinically essential pharmaceuticals. These definitions are necessary for the reporting system to function properly.

1.2. ENSURING ACCESS TO MEDICINES

1.2.1. Reviewing the system of incentives

Following the premise that the Pharmaceutical Strategy is patient-centred, the R&D system needs to be reshaped in the public interest. Instead of maintaining the status quo, the EU should seize this opportunity to foster the development of relevant health innovations – while improving their accessibility and affordability – by reviewing the system of incentives based on intellectual property rights (IPR). It is the EU's and national governments' responsibility to create a more beneficial cooperation with the private sector.

[22] Ibid., p. 6.

[23] Organisation for Economic Co-operation and Development (OECD), *Pharmaceutical Innovation and Access to Medicines* OECD report on Pharmaceutical Innovation and Access to Medicines, November 2018, pp. 27-30.

Identify the main problems with the current intellectual property rights system

The optimal functioning of the IPR system and competition is currently central to health innovation.

However, while the role of a strong IPR framework to incentivise investment is emphasised, its negative impact on knowledge sharing and scientific progress is often overlooked. A reinforced IPR system encourages actors to work in secrecy and isolation, leading to knowledge fragmentation and limiting the ability of science to be disseminated and translated into future innovation. It also results in wasted financial resources and duplication.

The development of COVID-19-related technologies can serve as an example of the system's shortcomings. While each company conducted research on vaccines and treatments only within the boundaries of its own proprietary technology covered by patents, combining the best elements of different platforms could result in much more suitable portfolio of adequate public health interventions.[24, 25]

Beyond the issue of knowledge appropriation, the current problems with the IPR system are that patenting is becoming increasingly wide (broadly defining a patentable subject matter), stronger (making it more difficult to license to third parties), and more upstream (patenting not only innovations, but also the tools and processes for research that might lead to these discoveries).[26] What is more, a strong and misused IPR system results in unaffordable monopoly medicine pricing that forms a major barrier to access, with a great impact on public (health) expenditure and patients' out-of-packet payments.

Improve the quality of patents by applying consistently high standards and rigorous assessment of patentability criteria

Patents should be granted only for genuine innovation and not for simple changes, for example, in chemistry or formulation that offer little or no therapeutic advance on existing medicines.

Moreover, patents should be narrow to protect only the area that is fundamentally new, and focused downstream to avoid tools and processes being privatised, while at the same time enabling licensing and diffusion.

[24] Torreele E., *Business-as-Usual will not Deliver the COVID-19 Vaccines We Need*, Society for International Development November 2020, p. 192.

[25] Similarly, once developed, the roll-out of mRNA vaccines has been slow, in part because the IPR to some of their advanced components e.g., Lipid nanoparticles or a special nucleotide (called a five-prime-cap), being a part of the mRNA instructions, were held by only a few companies.

[26] Mazzucato M., Li H. L., supra note 4, p.2.

Facilitate and encourage the use of different instruments to improve access to medicines during public health emergencies

In the context of public health crises, the EU should encourage national governments to more actively use policy instruments designed to improve access to medicines (see also further discussion under 3.3.2.). For that purpose, the Commission and EU countries should pursue the correctly identified objectives of the IP Action Plan to create fast-track procedures for issuing compulsory licenses, an emergency coordination mechanism, and to introduce a novel licensing system making critical IP available during health emergencies.

Explore and foster the use of alternative models of incentivising health innovation based on grants and prize funds

The Commission should more actively explore alternative models for encouraging innovation which, instead of relying on the IPR system, decouple investment in innovation from medicine sales volumes and high prices.

There are various systems that aspire to make R&D investments more cost-effective and responsive to public needs. They can provide a diverse set of alternative mechanisms for financing innovation, leading even to the elimination of monopoly and exclusivity.[27]

For example, if there is uncertainty about the end product's commercial application or if scientific progress is the main goal, grants can be used as incentives for all stages of research.

Furthermore, if the medical need is pre-determined and well-framed, R&D towards it can be incentivised through prize funds. Prize funds are payments for achieving specific results, either at regular milestones or at the end of a project.[28] The concept of prize funds is not new. This model has already been used by the Commission.[29]

Importantly, the prize system requires significant upfront public investments. Therefore, the Commission should engage in a constructive dialogue with Member States to ensure a robust budget for that purpose. This would not generate additional public spending, but a re-allocation of resources that are already dedicated to encouraging innovation through the IPR system. The difference, however, is that, unlike patents, which are granted regardless of the social value of the end product, prize-funded health technology always addresses a specifically identified medical need.

Furthermore, by including contractual conditions, the accessibility and affordability of the end products can be secured, as well as the sharing of knowledge resulting from the publicly-funded

[27] Unitaid, *An Economic Perspective on Delinking the Cost of R&D from the Price of Medicines*, World Health Organization, February 2016, pp. 13-45.

[28] One advantage of this incentive is that it allows multiple promising research proposals with different approaches to be undertaken simultaneously, rather than targeting only one proposal at a time, as in a grant-based model.

[29] In the past, the Commission awarded a €1 million prize to a German company for developing a point-of-care rapid test that can identify patients with upper respiratory tract infections that can be managed safely without antibiotics. The Commission also awarded a €2 million prize to a German company in 2014 for stabilising technology to protect vaccines against elevated temperatures or accidental freezing.

research. In this way, prize funds have a potential to progressively replace the granting of exclusive monopoly rights.

A number of initiatives have clearly demonstrated the value and potential of such models.[30] The Commission can build on these examples and apply them broadly.

1.2.2. Reviewing the system of the Supplementary Protection Certificate

The Supplementary Protection Certificate (SPC) provides up to five years of additional patent-like protection of a registered medicine upon expiration of the 20-year patent term. The SPC was designed to make up for years in which a patent could not be commercially exploited due to required regulatory procedures.

The Pharmaceutical Strategy and the IP Action Plan proposes to review the SPC system solely by simplifying the application process.

In our view, this approach is a major flaw in the Commission's plan. It could hinder the Strategy's objective of improving access to affordable medicines by reviewing the IP incentives framework.

Instead, a thorough revision of the SPC system is needed to assess whether additional exclusivity is necessary to cover industry R&D costs, considering its negative impact on access and €37 billion of extra spending.[31, 32]

While the profits from expanded patent protection for pharmaceutical companies are clear, the cost-benefit ratio of SPCs for the public can be questioned, particularly if they are granted for blockbuster medicines with unaffordable prices. For example, an analysis of medicines used in the treatment of hepatitis c and cancer suggested the SPCs were not needed for their manufacturers to recoup R&D investment. The analysis also found evidence of how the system hampered the medicines' accessibility.[33]

There are several recommendations on how the SPCs framework could be better designed to achieve its goal. These include the granting of a SPC being conditional on providing evidence that it is needed to cover R&D investment, creating procedures to revoke a SPC already granted if the investment has been recouped, or linking the entry into force of an SPC to a requirement on affordable pricing.[34]

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[30] For example, the need to address diseases that lack economic incentives has led to the creation of not-for profit product development partnerships, such as the Drugs for Neglected Diseases initiative (DNDi) in which public and private contributions pay for the cost of R&D upfront, rather than through sales of the resulting products, allowing the initiative to identify priorities based on public health needs and to offer products at sustainably low prices, while allowing knowledge and data to be broadly shared. Other initiatives based on this model include The Meningitis Vaccine Project (MVP), the Global Antibiotic Research and Development Partnership, the Medicines for Malaria Venture and the Global Alliance for Tuberculosis Drug Development.See: Médecins Sans Frontières (MSF), *Lives on the Edge...*, pp.28-32.

[31] European Commission, *EU incentives for the pharmaceutical sector...*, November 2020.

[32] Médecins Sans Frontières (MSF), *MSF welcomes EU pharmaceutical strategy...*, November 2020.

[33] Hu, Y., Eynikel D, et al., *Supplementary protection certificates and their impact on access to medicines in Europe...*, Journal of Pharmaceutical Policy and Practice, 13:1, January 2020, pp. 1-12.

[34] Medicines Law & Policy, *European Union Review of Pharmaceutical Incentives...*, June 2019, pp. 9-21.

The Pharmaceutical Strategy is an opportunity for the Commission to better balance the SPC Regulation's objectives to cover private investments into R&D and to benefit public interests. It must not be wasted by merely opting for simplification of the system.

1.2.3. Restricting deferred market launches

Member States are often in very different positions with regard to the availability of medicines for which a marketing authorisation (MA) has been granted by the European Medicines Agency. Although pharmaceutical companies benefit from a centralised MA procedure and economic incentives for the development of medicines, they often launch their new products at different times in different EU countries.

Subject the granting of a marketing authorisation to the obligation that medicinal products are launched in all EU countries at the same time

The Commission should tackle the problem of diverging market launches by linking the centralised marketing authorisation to a commitment on the part of pharmaceutical companies, i.e., once authorised, medicinal products have to be launched in all EU countries at the same time. Moreover, pharmaceutical companies should not be allowed to subsequently withdraw these products from particular markets for commercial reasons.

Take action to remedy unavailability of medicines caused by commercially-motivated decisions

A problem closely related to deferred market launches is discontinuation or withdrawal of effective medicines from particular (less profitable) Member States' markets. As there is a lack of transparency on their reasons, they are at least partly due to commercially-motivated decisions by the pharmaceutical companies.

Such practices can not only hinder equal access to medicines for all EU citizens and lead to medicine shortages, but also place Member States in different positions with regard to prices. If the availability of a specific product cannot be guaranteed, healthcare systems may be forced to introduce more expensive medicines or less effective alternatives. As observed by the Council of the European Union, the management of uncontrolled withdrawals is critical for continuity of care.[35]

The Commission should address this problem and take action to remedy the inequalities in access to medicines caused by the purely commercial motivations of private companies, as also requested by the European Parliament.[36]

[35] Council of the European Union, *Note from the Finnish Presidency...*, December 2019, p.8.

[36] *The European Parliament's resolution on EU options for improving access to medicines (2016/2057(INI))*, March 2017 p. 17 pt. 101.

1.2.4. Improving market entry of generics and biosimilars

As the use of generic and biosimilar versions of medicines leads to lowering costs of and increasing access to treatments, their immediate market entry after the expiry of patents on brand-name medicines is of crucial interest to the public.

Address the abuse of the IPR system to delay market entry of generics and biosimilars

The current IPR framework is often abused as patents of questionable quality are repeatedly granted for irrelevant "innovations" and unjustly extended (see also 1.2.1.). While patents are intended to incentivise relevant health innovation, they are often strategically misused to present a barrier to generic and biosimilar entry. The revision of the IPR system must also address deficiencies in the quality of the patent granting system, the creation of patent thickets and filing of numerous follow-on patents or the abuse of patent litigation procedures.[37]

The Commission should continue to focus on antitrust enforcement and investigate anti-competitive practices

The immediate market entry of generics and biosimilars can also be blocked by anti-competitive practices and illegal agreements between originator companies and generic manufacturers.

The Commission has recently decided to fine the pharmaceutical companies Teva and Cephalon for agreeing to delay for six years the market entry of a cheaper generic version of Cephalon's medicine after its main patents had expired.[38] This and three other previously concluded investigations[39] provide positive examples of the use of antitrust law as a tool to expose and penalise illegal practices that prevent patients and health systems from benefitting from lower medicines' prices earlier.

While the latest decision brings to an end the current cycle of the Commission's "pay-for-delay" investigations, the pharmaceutical sector must remain at the centre of regulators' attention. The EU antitrust enforcement should continue to complement other efforts to increase accessibility and affordability of medicines.

[37] European Generic medicines Association, *Patent-related Barriers to Market Entry for Generic Medicines in the European Union*, May 2008.

[38] European Commission, *Antitrust: Commission fines Teva and Cephalon €60.5 million...*, Press release, November 2020.

[39] One concerning perindopril, a cardiovascular medicine, one concerning citalopram, an anti-depressant, and one concerning fentanyl, a painkiller.

1.3. ENSURING AFFORDABILITY OF MEDICINES

1.3.1. Guaranteeing fair return on public investments

The public sector funds the highest-risk research and is most likely to discover medicines that offer significant therapeutic benefits over the existing ones.[40],[41] Furthermore, it provides private companies with numerous direct and indirect financial supports and incentives for R&D on medicines.[42] Moreover, private companies are increasingly developing medicines in partnership with public universities.

Recognition of these contributions has critical implications for the distributions of risks and rewards in the health innovation system. However, while the benefits for the private sector are tangible, it is questionable whether they yield a fair return on investment for the public, as the most pressing unmet needs remain unaddressed and high prices of patented innovative medicines are unsustainable for health systems and unaffordable for patients.[43]

Make all forms of public investment in the R&D process subject to concrete commitments

The Commission and national governments need to put in place concrete conditions for any kind of public funding or incentives.[44]

Such conditions should ensure that products resulting from public funding are priced fairly. A well-designed and enforced fair pricing condition could better ensure that EU citizens can afford medicines they helped to develop.

Moreover, it should be a requirement that the R&D costs of medicines that have benefited from public funding are transparent and include a breakdown between private and public investment. This would empower national authorities by reducing information asymmetry in pricing negotiations, enable informed discussion on what constitutes a fair price for these medicines and allow public accountability for the use of public resources.[45]

Furthermore, medicines that have been developed with financial support at the EU level should be available in all Member States at the same time.

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[40] For example, the method for generating monoclonal antibodies (MABs) was developed at the publicly funded UK Medical Research Council Laboratory of Molecular Biology in Cambridge. However, the technique has not been patented as its inventor did not patent the technique because he disapproved of the principle. Six of the ten drugs with the highest global sales of all time are MABs., See: Global Justice Now, *Pills and profits...*, October 2017.

[41] Prescrire, *Drug research: public funding, private profits*, Prescrire International, Volume 29 N° 221, December 2020, p.30.

[42] In the form of tax credits that enable companies to reduce the salary costs for staff engaged in R&D, a reduced tax rate on profits generated through innovative activities, capital to support the creation of biotechnology companies, and help with funding clinical trials. See: Global Justice Now, *Pills and profits...*, October 2017.

[43] Mazzucato M., Li H. L., supra note 4, pp.5-6. Moreover, public gains through the taxation system due to new jobs being generated, as well as taxes being paid by companies benefiting from the investments are offset in several ways (like tax avoidance, evasion and cuts), the knowledge spillovers hindered by fragmented patent rights (see more above) and the intended impact of increased domestic investment in R&D have hardly materialised, while stock buyback and dividends have increased.

[44] Ibid., pp.9-10.

[45] Global Justice Now, *Pills and profits...*, October 2017, p.41.

In addition, open sharing of data and knowledge obtained through public funding should also be encouraged.

Other examples of conditions that could ensure a return on public investment include holding part of the intellectual property rights to the technology developed, receiving royalties on the resulting product's sales, or a commitment to reinvest part of the company's profits in predefined economic activities or a public innovation fund.[46]

1.3.2. Improving transparency and Member States' cooperation on pricing of medicines

National decision making on pricing and reimbursement is hampered not only by a lack of transparency over the medicines' R&D costs, but also by the confidentiality of pricing negotiations in certain countries. Information asymmetry between national authorities and pharmaceutical companies is significantly advantageous for the latter and results in higher prices of medicines in Europe. By increasing transparency and joining forces, EU Member State can increase their bargaining power and find themselves in a much more favourable negotiating position. The EU has a key role to play in achieving this goal.

Promote transparency of national pricing negotiations

Pharmaceutical companies disclose the official prices set in different countries. However, these prices may differ significantly from the actual ones paid by national health systems, as pricing authorities often receive discounts or rebates based on a medicine's sales volume or performance. Importantly, these reductions in official unit prices are subject to confidentiality clauses and are not publicly disclosed. Consequently, national governments cannot know the real net prices paid by other countries. This can result in some EU Member States paying more for the same medicines than others for no particular reason, resulting in inequalities in access across Europe.

Promoting transparency on net unit prices would allow Member States to make more informed decisions. It could also lead to a level playing field for national governments with varying purchasing powers and market sizes, as well as for medicine manufacturers. Transparency is a precondition to ensure competition and a balanced market.[47]

Learn from regional initiatives and support existing platforms

There are already intergovernmental regional initiatives, such as Beneluxa and Valetta groups, which focus on sustainability and transparency, laying the groundwork for cooperation and information sharing between national governments.

[46] Mazzucato, M., *The Entrepreneurial State: Debunking Public vs. Private Sector Myths*, Penguin Books, DOI:10.1016/S1386-6532(09)70080-0, pp.164-166.

[47] See: *Joint Nordic Statement*, January 2021.

In addition, various existing information sharing platforms for public authorities, such as EURIPID[48] or the International Horizon Scanning Initiative (IHSI)[49] aim to mitigate the effects of information asymmetry.

EU countries should take advantage of these initiatives and learn from them to benefit from increased cooperation.

Follow up on the World Health Assembly's resolution of 2019 on transparency of markets for medicines, vaccines, and other health products

The Commission should lead national governments in taking concrete action following the World Health Assembly's resolution of 2019 which – despite the lack of strong norms and actions on several critical elements of transparency – is a positive first step to correct the power imbalance that currently exists during negotiations between governments and pharmaceutical companies on medicines.[50]

Draw lessons from the EU Vaccines Strategy and set high transparency standards in future joint public procurements

While all Member States speaking with one voice during the COVID-19 vaccine negotiations was an unprecedented success for the EU, the unjustifiable secrecy around these negotiations resulted in a self-inflicted crisis.

The Commission and Member States need to realise how joint procurement has benefited their bargaining power and analyse whether it has been fully exploited, and whether all possible public interest conditionalities have been included in the contracts. Drawing conclusions from this experience, options for improving and expanding joint negotiations in health emergencies should be discussed.

Importantly, Member States should use their bargaining power to demand high transparency standards in future joint procurements. Contracts with companies should include the condition of publication. Such an approach will change the dynamic in the negotiations, strengthening the negotiating power of governments.[51]

1.3.3. Strengthening cooperation on health technology assessment

Structured EU cooperation on health technology assessment (HTA), based on a comprehensive evaluation of clinical evidence, can enhance evidence-based decisions taken at decision-maker and doctor levels. However, the legislative process for the HTA Regulation has been stalled for years.

[48] See EURIPID Collaboration.

[49] See the IHSI Joint Horizon Scanning Database.

[50] World Health Assembly, 72, *Improving the transparency of markets for medicines, vaccines, and other health products*, World Health Organization 2019.

[51] Joint Statement, *Transparency is a fundamental pillar for the success of the EU Vaccines Strategy*, December 2020.

The Council of the European Union needs to reach a position on the proposal under the Portuguese Presidency and the trialogue between the EU co-legislators and the Commission should lead to the establishment of a regulation that will outline clear rules for high-quality joint clinical assessment and include sufficient provisions on transparency and independence to guarantee trust in the system and appropriate access by healthcare professionals and the public to HTA documents and reports.[52]

1.3.4. Revising the legislation on medicines for rare diseases and children

The Commission correctly notes that while the Orphan and Paediatric Medicines Regulations have increased the involvement of pharmaceutical companies in the development of medicines for rare diseases and for children, the current system of pharmaceutical incentives has numerous shortcomings.[53] The existing framework that does not provide adequate safeguards to protect against its abuse nor sufficiently stimulate innovation in areas of real unmet medical needs, and results in often unaffordable and unequally available treatments generating high profits, requires profound revision.

Introduce a corrective mechanism in the Orphan Regulation

While the main reason for the adoption of the Orphan Regulation was the presumed lack of profitability of medicines for rare diseases, in practice the actual economic considerations are never examined in granting orphan incentives to the industry or afterwards.[54]

At the same time, the Regulation does not provide for the practical possibility of withdrawing market exclusivity if a company charges prices that the public cannot afford, or if its revenues from the orphan product excessively exceed the value of its investment in it.

Therefore, the Commission should amend Article 8(2) of the Regulation to allow for withdrawal of market exclusivity for the above reasons, irrespective of the criterion that was used to obtain orphan designation.[55]

Introduce transparency requirements to allow definition of sufficient and excessive profitability or return on investment and review criteria for orphan designation

The provision of orphan incentives should be subject to a transparency requirement that would enable evidence-based decision-making. For one, the term “sufficient” used in Article 8(2) in the context of

[52] *CPME statement on the European Commission proposal for a Regulation on Health Technology Assessment (HTA) 2018/0018 (COD)*, 2018.

[53] See: *Commission Staff Working Document*, August 2020.

[54] Similar to the case of the Supplementary Protection Certificate (SPC) that was introduced based on the presumption that the period of product exclusivity after its marketing could not be sufficient to recoup the investment, the granting of a SPC is not dependent on the actual revenue or profit a pharmaceutical company obtains from that product (see the discussion under 1.2.2.).

[55] D. Marselis, L. Hordijk, supra note 4, p. 4.

profitability should be defined with knowledge of the actual costs of R&D incurred by developers to determine what is an "insufficient" or "excessive" return on investment.[56]

Furthermore, there is compelling evidence that the presumption that a medicine developed for no more than about 250,000 people is not profitable is false.[57] Soaring orphan medicine prices and extended periods of exclusivity through combining indications make orphan medicines among the most profitable in companies' portfolios. Based on these findings, the current prevalence threshold should be re-examined.

Explore the feasibility of tailored incentives in place of broadly granting extended periods of market exclusivity

The Commission should look for ways to introduce a new system of incentives that would limit the granting of market exclusivity extensions and provide tailored and proportionate rewards for relevant innovations (see the further discussion on pharmaceutical incentives under 1.2.1.).

Some of the potential solutions already discussed by the Commission are not suitable for achieving this goal. Transferable vouchers are not an efficient mechanism for promoting innovation[58] and should not be introduced, nor should the revision of the Supplementary Protection Certificates be limited to simplifying the procedure for granting them, but should include a thorough rethinking of the functioning of the current scheme (see the discussion under 1.2.2.).

Make the granting of incentives for medicines for children subject to specific criteria that reflect paediatric needs

Similar to the legislation on rare diseases, the Paediatric Regulation has not led to sufficient investment in developing innovative medicines for children in areas of real unmet medical needs and does not ensure equal availability across Europe.

Incentives for innovation in paediatric medicines should be conditional on ensuring that these medicines are marketed with a packaging suitable for paediatric use, offered in a safe and suitable form and with adapted package leaflets, with particular attention to dosage accuracy to avoid medication errors.[59] Moreover, they should encourage clinical trials for children to address the widespread off-label use of medicines in children.

[56] Medicines Law & Policy, *European Union Review of Pharmaceutical Incentives...*, June 2019, pp. 9-21.

[57] D. Marselis, L. Hordijk, supra note 54, pp. 2-3.

[58] The Transatlantic Task Force on Antimicrobial Resistance, supra. note 14, p. 1381.

[59] *Prescrire's response to the European Commission public consultation*, January 2021.

2. SUPPORTING THE EUROPEAN PHARMACEUTICAL INDUSTRY

2.1. ENABLING INNOVATION AND DIGITAL TRANSFORMATION

Digital technologies bring numerous opportunities for the development, authorisation and monitoring of pharmaceuticals.

Big data and real-world data can provide developers and regulators with new insights into, e.g., potential indications for new medicines or a different safety profile in certain patient subgroups. More frequent data collection can increase statistical power, and AI-based technology allows huge datasets to be analysed.

It can also lead to improved manufacturing processes, providing advanced analysis of production sites, reducing the costs of developing innovative medicines and optimizing the conduct of clinical trials while improving patient care throughout them.

Provide an adequate framework for the use of high quality, reliable and useful real-world data

Real-world data can provide useful supplementary information in the context of marketing authorisation processes and, in particular, post-approval surveillance activities. However, it should only be considered as complementary to randomized clinical trials and should under no circumstances be promoted as a replacement for these.

Importantly, an appropriate framework is needed to ensure the quality, robustness, reliability and usefulness of data collected, while guaranteeing the confidentiality and privacy of patient information. This requires the existence of an appropriate data governance model based on the WMA Declaration of Helsinki[60] and the WMA Declaration of Taipei[61].

Keep high evidence requirements for approval of advanced therapy medicinal products

The number of advanced therapy medicinal products (ATMPs) is increasing. Although they hold great medical promise, any pressure to obtain fast-track approval should be resisted and evidence requirements cannot be lowered as patient safety must be put before economic interests. Since ATMPs are authorised based on limited clinical trial data, the collection of real-world safety and efficacy data in the post-authorisation period is critical for monitoring and assessing these medicines.

Special emphasis should be placed on programmes assuring the quality, efficacy and safety (demonstrated by clinical data) of cell-based ATMPs at the time of administration.

[60] *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*, October 2013.

[61] *WMA Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks*, October 2016.

2.2. A SOUND AND FLEXIBLE REGULATORY SYSTEM

The Commission should uphold strong regulatory standards. Any revision of the regulatory procedures and approaches to the assessment of scientific evidence aimed at bringing "EU regulatory approval times onto par with those in other parts of the world" must be undertaken cautiously in order to adequately take patient benefit and safety aspects into consideration.

Review the regulatory procedures for accelerated approval

Different accelerated approval procedures, such as conditional marketing authorization[62], PRIORITY MEDICINES (PRIME)[63], accelerated assessment procedures[64] and approval under "exceptional circumstances" (EC)[65] have been overused in recent years. It is important that their use be limited to situations where no other medicinal alternative is available. A strictly regulated framework is indispensable to safeguard patient safety and health systems.

The Commission must critically review the regulatory procedures for accelerated approval by the EMA as such schemes facilitate market entry for medicinal products with limited information on their added therapeutic benefits and safety issues.

Improve the use of objective, transparent and independent product information in electronic format

The Commission's objective of improving the use of electronic product information (ePI) to expand access to medicine information using different media is desirable. Ensuring that product information is accessible to all, and in particular to patients/consumers with diverse abilities, is essential, and therefore ePI should never replace the paper version included in medicine packets.[66]

Importantly, it must be ensured that product information in electronic format – as in any other format – meets standards of objectivity, is transparent, independent and free of any advertising or commercial interests. In the context of the latter, it must be guaranteed that the very thin line between objective information and promotional advertising is clearly identified and that the existing and future ban on direct-to-consumer advertising is enforced.[67] Electronic push information should remain prohibited.

Moreover, when it comes to making ePI available through various technologies and applications, including mobile scanning technology on the medicine packet, a link to the official websites of the EMA and/or national competent authorities should be preferred.

[62] See: Conditional marketing authorisation.

[63] See: PRIME: priority medicines.

[64] See: Accelerated assessment.

[65] See: Exceptional circumstances.

[66] See *CPME response to public consultation on key principles for electronic product information for human medicines in the EU*, April 2019.

[67] See e.g., *CPME response to ENVI Committee vote on 'Information to Patients' report by MEP*, November 2010.

3. ENHANCING RESILIENCE

3.1. SECURE THE SUPPLY OF MEDICINES ACROSS THE EU AND AVOID SHORTAGES

The pandemic has brought home long-existing structural problems in the supply of medicines and highlighted shortcomings in current cooperation among Member States and EU coordination in preventing and mitigating medicine shortages. Rightfully, addressing this problem is one of the Commission's top priorities.

Many of these structural issues require organisational solutions and regulatory changes that need to be implemented gradually over time. However, the Commission must not overlook the critical importance of measures that can be put in place much more quickly to mitigate the impact of shortages on patients, doctors and health systems.[68]

Addressing these shortages must take place through targeted actions at the levels of communication, organisation and legislation.

Strengthen the resilience of medicines' supply chains, increase diversification of supply sources, and reduce Europe's reliance on third country manufacturing

Over the past year, there has been unquestionable evidence of the risks posed by overreliance on manufacturing sites located in third countries. The current model, in which certain essential medicinal products are manufactured externally and at just a few production sites, leaves Europe exposed.

The Strategy correctly identifies this problem and seeks ways to bring the production of essential medicines back into the EU (while safeguarding their affordability), to increase diversification of supply sources and to address the vulnerability and opacity of global supply chains, learning from the experience of COVID-19.

To this end, the Commission needs to gather more data on supply chains' risks in order to establish exactly where their vulnerabilities lie and how their resilience can be strengthened.

Furthermore, in order to ensure continuity of supply, pharmaceutical companies supplying medicines to the EU market should be able to demonstrate that their supply chain is resilient to a variety of shocks, including by not being overly dependent on one country or region, and provide contingency plans to help identify risks early and promote mitigation measures.
In this context, the Commission should explore the possibility of building on the example of the new EU law on corporate due diligence, currently under negotiation, to hold companies responsible for guaranteeing the robustness of their supply chains.[69]

[68] *Gemeinsame Stellungnahme der Bundesärztekammer und der Arzneimittelkommission der deutschen Ärzteschaft*, January 2021, pp. 9-10.

[69] The EU is currently preparing corporate due diligence legislation to hold companies accountable for harm caused to people and the planet by obliging them to identify, address and remedy any human rights or environmental standards' infringements within their supply chains. The Commission could build on this example and similarly require pharmaceutical companies to diligently review the actors in their supply chains and ensure they operate a "just-in-case" approach and are resistant to any disruption.

Improve monitoring and communication at EU level and establish a standardised reporting system and common terminology

Communication plays a crucial role in preventing and managing shortages. Early awareness of a supply problem and early identification of potential therapeutic alternatives may mitigate the possibility for adverse reactions endangering patient safety.

It is therefore critical to establish a standardised reporting system which gives guidance as to what, when and how to report. Producers and importers should be obliged to report existing or arising shortages to the national competent authorities and the EMA.[70] However, the reporting system will not function properly unless common definitions of a medicine shortage and clinically essential pharmaceuticals are agreed on (see also the discussion under 1.1.3.).

Information reported to the EMA should be made accessible to all competent authorities in Member States, who should then decide whether the information should be published or made available to the other supply chain actors (physicians, pharmacists and hospitals) in a user-friendly format.

Implement "just-in-case" operating models within supply chains and steer medicine distribution

One of the key elements for increasing the EU's resilience to external crises is to change the operating model of supply chain actors from "just in time" to "just in case". A coordinated stockpiling obligation for certain raw materials, active pharmaceutical ingredients and critical medicines would enhance the EU's preparedness for unexpected supply disruptions.

Stockpiling at the level of manufacturers and wholesalers should provide for a period of at least eight weeks. The amount of stockpiling at national level should be based on average consumption and suffice for at least four weeks for medicines used in intensive care.[71]

Additionally, strategic medicines should also be stockpiled at EU level under coordination of the EMA allowing for targeted interventions.

Furthermore, in case of ineffectiveness of other solutions, Member States should be allowed to temporarily ban the parallel export of medicines[72] in short supply or at risk of shortage, as this may help to avoid medicines' unavailability in their markets arising or being aggravated. Importantly,

[70] Moreover, an EU-wide reporting system requires an agreed electronic template to be used. The EMA should propose such standards in consultation with the users (i.e. producers, physicians, pharmacists, hospitals etc.) and competent authorities. This could follow the example of the Commission´s IMI (Internal Market Information System) communication tool.

[71] *Gemeinsame Stellungnahme der Bundesärztekammer und der Arzneimittelkommission der deutschen Ärzteschaft*, December 2019.

[72] By parallel trade, medicines can be exported from Member States where they are relatively cheaper to markets where their prices are higher.

applying such a measure must be justified, reasonable and proportionate to ensure a legitimate public interest, not to infringe on the principles of free trade and movement of goods within the EU.[73]

Lastly, to the establishment of a central European database on medicines supply to the EU market should be explored. This could include information on which country authorised the medicine, under which trademark, whether it was resupplied to or withdrawn from the market, and its supply status.

Revise national tendering procedures to include criteria other than price

The Commission should engage with Member States in a structured exchange of best practices on procurement procedures for medicines, issuing recommendations. Member States should be encouraged to apply other criteria than price in national tendering procedures, such as reliability of supply and the number and location of production sites.

One solution could be the creation of a label "medicine made in Europe" which national health systems could use as a requirement in tendering procedures.

Strengthen and enforce supply and reporting obligations

It should not be overlooked that medicine shortages are often the result of profit-oriented decision-making on the part of the pharmaceutical industry. The Commission therefore correctly notes the need to reinforce the obligation of continuous supply.

To this end, the current pharmaceutical legislation needs to be reviewed and the Community Code Directive 2001/83/EC clarified i.e., introduce enforcement mechanisms and sanctions (e.g., license withdrawal) to hold marketing authorization holders accountable.[74]

Empower the European Medicines Agency with a strengthened infrastructure and mandate beyond health crises

Given the supervision of medicines, input from national registries, and information from all agencies in Europe, the EMA is the body best suited to take responsibility for the European response to medicine shortages.

Although the proposal for extending the Agency's mandate (further discussed under 3.3.3.) is a step in the right direction, as the problem of shortages is not limited to crises, the EMA's competencies should also be extended beyond the context of health emergencies and major events.

Moreover, the Agency should be entirely publicly funded as a prerequisite to its independence.

[73] European Commission, *Infringement: Parallel trade of medicines*, Press Release, May 2018.

[74] *Community code relating to medicinal products for human use*, Directive 2001/83/EC, OJ L 311, 28.11.2001, November 2001.

3.2. HIGH QUALITY, SAFE AND ENVIRONMENTALLY SUSTAINABLE MEDICINES

The negative impact of the pharmaceutical sector on the environment is multifaceted and includes pollution linked to the production, transport and disposal of pharmaceuticals.[75]
While the problem is recognised by the Commission, the Strategy lacks concrete actions to address it.

The right balance between environmental protection and access to medicines needs to be achieved by increasing awareness and promoting prudent use of pharmaceuticals, informing patients about safe disposal methods for unused or expired medicines, supporting greener manufacturing, and reducing wastage and improving waste management.[76]

Increase environmental requirements for all actors in the pharmaceutical sector

It is the responsibility of the EU and national governments to set high environmental standards and to impose sanctions on pharmaceutical sector actors for non-compliance.

The Commission should strengthen environmental impact assessment requirements and demand that pharmaceutical companies invest to decarbonise every part of their value chain.

Moreover, the pharmaceutical industry should be more transparent about its policies and objectives throughout its entire supply chain and operations. Sustainability policy is now often seen as a side project or a PR strategy. But for environmental commitments to be truly effective, they should be integrated into an organisation's fabric and business model. The Commission can contribute to this objective by implementing the due diligence legislation.[77]

Include environmental criteria in national tendering procedures

The Commission should encourage Member States to include environmental criteria in national tendering procedures to stimulate market towards the production of environmentally friendly pharmaceuticals.[78]

Explore the possibility to extend the expiry dates of certain medicines

One other way to reduce pharmaceutical waste is to extend the expiry dates of certain medicines (particularly small molecules) that are often marketed for a much shorter time than their stability would allow for. To prove their actual stability, the duration of stability testing for these medicines should be extended. This could also prove to be helpful in tackling medicine shortages.

[75] A. Nawrat, *Are healthcare's sustainability goals bold enough?*, Pharmaceutical Technology, December 2020.
[76] Health Care Without Harm, *Safer Pharma*.
[77] See: Global Justice Now, supra note 45.
[78] Health Care Without Harm, *Health Care's Climate*, September 2019, p. 35.

3.3. ENHANCING EUROPE'S HEALTH CRISIS RESPONSE MECHANISMS

Future health emergencies may look different from the COVID-19 pandemic, and climate-related emergencies may become common in the European region in future.

What has become clear is that the 'just in time' rationale used in commercial sectors cannot be applied to health systems without severe risks. It is necessary to adopt a 'just in case' model. In the pharmaceutical sector, the 'just in case' model means that supply chains must be resilient, essential medicines stockpiled, and contingency plans and preparedness and response mechanisms developed on the part of the public and private sectors.

Over the last year, Europe has been paying the price for its failure to ensure the pharmaceutical sector's readiness to tackle health threats such as infectious diseases. The EU needs to rethink its health security policy and address the current shortcomings of the biopharmaceutical R&D system.

3.3.1. Ensuring the pharmaceutical sector's readiness

Entrusting health security to private companies operating solely for the purpose of making profit leaves Europe unprepared and unsuited to respond to health emergencies.

Responsibility for undertaking critically important biomedical R&D and advancing manufacturing capacities in the EU, left to the private sector, has been neglected, despite urgent concerns raised by the scientific community over the past decades.

Instead of de-risking the development process and providing market commitments without strings attached, the Commission should show leadership in shaping (and funding, including at late-stage) medical countermeasure R&D and ensuring access and equitable distribution.

In times of health crises, the EU must be able to take decisions on how and when vaccines and treatments are manufactured and distributed, instead of leaving it to the discretion of the private sector.

The pandemic has provided a fundamental lesson on the role of health security strategy and public health funding, calling for structural interventions.

3.3.2. Addressing intellectual property barriers during health emergencies

The Commission should facilitate and encourage the use of different instruments to improve access to medicines during health emergencies.

Encourage Member States to effectively use compulsory licensing

The Action Plan on Intellectual Property rightfully calls on Member States to ensure that their laws allow for the effective use of compulsory licensing.[79] However, a major impediment in this context is the fact that Member States can only take the advantage of this instrument in their domestic markets, as all of them declared themselves ineligible to import medicines manufactured in another country under a compulsory license by opting out of Article 31*bis* of the TRIPS Agreement.[80] The Commission should encourage Member States to opt back into the Agreement as importers.[81]

Encourage the sharing and pooling of intellectual property and introduce an effective framework for so-called march-in rights

The Commission should incentivise companies to share critical technology during health crisis and use public investment in innovation as leverage to encourage IP pooling through mechanisms established for this purpose, such as the COVID-19 Technology Access Pool (C-TAP) launched by WHO to voluntarily share knowledge, IP and data necessary for tackling COVID-19.[82]

The IP Action Plan also anticipates the creation of "a novel licensing system making critical IP available" during emergencies.[83] The Commission should seek to create an effective framework for march-in rights so that patents on specific technologies can be effectively ignored and additional licenses granted to other developers to guarantee that publicly funded IP is available in case of critical shortages.

3.3.3. Extending the mandate of the European Medicines Agency

The Pharmaceutical Strategy is intended to be a key pillar of a European Health Union, the Commission's overarching plan to improve the EU's health emergency management framework through increasing crisis coordination and empowering key health agencies.

Reports received by CPME from national medical associations indicate that this initiative is welcomed. In many instances, improved coordination at EU level would allow for better protection of EU citizens' health during the COVID-19 pandemic.[84] The need for revisiting existing approaches has also been recognised by European doctors in their Recommendations to the EU.[85]

[79] European Commission, *An intellectual property action plan to support the EU's recovery and resilience*, November 2019.

[80] Ch. Garrison, *Never say never...*, Medicine law and policy, April 2020.

[81] See *Open letter asking 37 WTO Members to declare themselves eligible to import medicines manufactured under compulsory license in another country, under 31bis of TRIPS Agreement*, April 2020.

[82] See *COVID-19 Technology Access Pool*.

[83] European Commission, *An intellectual property action plan…*, supra note 78, pp. 11-12.

[84] CPME, *CPME report on COVID-19 in Europe*, November 2020.

[85] CPME, *Pandemic Preparedness - European doctors' Recommendations to the EU*, November 2020.

The Commission rightfully proposes extending the mandate of the European Medicines Agency so that ad hoc processes and resources currently put in place for the Agency can be reinforced and formalised.[86] The EMA must not be forced to work in emergency mode and should be equipped with a better infrastructure and sufficient capacity in the future.

Empower the EMA to supervise medical devices during health crises

The Commission's proposal to give the EMA competences to monitor and advise on the supply of medical devices is a positive step. Given that health crises affect the development and supply of medicine and medical devices to a similar extent, it is logical not to duplicate efforts but to allow the Agency to address both areas.

The establishment of parallel Executive Steering Groups for medicines and for medical devices, and the inclusion of expert panels on medical devices within the Agency structure, should streamline the communication and cooperation crucial during crises and beyond. The EU co-legislators should recognize the added value of bringing the two areas closer together.

Define the most clinically relevant performance targets for vaccines and treatments to be measured in clinical trials

As of now, the EMA and other regulatory authorities are not empowered to require developers to comply with specific criteria or characteristics of medical countermeasures to become effective public health interventions.[87] Regulators cannot impose public health imperatives on developers. In the current R&D model, it is left to the discretion of companies to set the vaccine and treatment efficacy targets they will measure in clinical trials.[88]

The Emergency Task Force, with proposed competences to review clinical trial protocols and advise developers on conducting trials in the EU, could influence the setting of the most clinically relevant performance targets for medical countermeasures.

Ensure high standards of transparency by the EMA

During the COVID-19 pandemic the EMA has proactively shared data on approved vaccines and medicines as well as information on the conduct of the Agency's activities. The EMA also explained the

[86] Over the last year, the EMA has implemented different kinds of ad hoc measures to increase transparency and explain its regulatory activities to ensure continuous communication with and among Member States and developers, and also to provide scientific advice and recommendations.

[87] For example, the WHO published a Target Product Profiles for the purpose of developing COVID-19 vaccines in April 2020, but this remained aspirational.

[88] E.g., in the context of the COVID-19 pandemic, the WHO proposed a collaborative efficacy trial "Solidarity" to directly compare the performance of different vaccines. However, developers of the COVID-19 vaccine candidates preferred to compare their candidates to placebos and measure efficacy in different ways, making the results impossible to compare.

regulatory processes to the public. These approaches have been considered highly beneficial. The same level of transparency should be ensured in the future.

As it is proposed to formalise other ad hoc measures, the Regulation should also include a provision that all clinical trials data, based on which the Agency authorises medicines or vaccines, should be published, as should clinical trials' protocols on which the Agency advises, in line with the Clinical Trial Regulation.[89]

3.3.4. Establishing a new mechanism for R&D on medical countermeasures

The EU needs to take responsibility for shaping health innovation in the public interest and address the current shortcomings of the biopharmaceutical R&D system, while reconsidering the roles that public and private actors play in it.[90]

The Commission correctly recognises the need for a new mechanism responsible for health innovation related to preparedness and response to cross-border health threats. Regardless of the form and structure such a mechanism takes, if it is to resolve the current problems it must follow the below recommendations.

Ensure public governance and transparency

The new system responsible for R&D of medical countermeasures must be fully publicly governed in order to ensure that the directions of innovation identified will respond to real public health needs. Moreover, full public governance would allow for adequate cooperation with the private sector and coordination across the innovation chain to ensure the desired results are delivered and equally distributed.

Moreover, transparent management and decision making-processes, e.g., on public funding for research projects, interactions with private partners or the selection of health threats to be addressed, are essential to allow for public scrutiny, to build trust and confidence in the R&D system and ensure accountability.

Create significant funding for crisis-related health innovation

For the new mechanism to deliver on its expectations, it needs to be provided with substantial public resources. Only with a sustainable and flexible budget would it be able to develop a long-term strategy, invest actively and widely in high-risk projects, terminate unsuccessful programmes and reinvest.

[89] *Clinical Trial Regulation*, Regulation (EU) No 536/2014, L 158/1, 16 April 2014.

[90] F. Massimo, *Biomed Europa: after the coronavirus, a public infrastructure to overcome the pharmaceutical oligopoly*, CIRIEC working paper 2020/08, April 2020.

Ensure that the overarching objective of increasing health security takes precedence over any economic interests

Improving public health and health security should always be the primary objective of the new system. Increasing investment in and coordination of medical countermeasure R&D can have numerous positive economic impacts, such as a significant contribution to strengthening Europe's overall competitiveness in health innovation and attracting private investment. Undoubtedly, the EU should exploit the potential of the agency in this context. However, on no account must economic objectives take precedence over public health interests. The performance of the new mechanism must be judged on the benefits it brings to public health, not to business.

Define fair sharing of risks and rewards from the outset

The new system must provide equitable access, availability and distribution of medical countermeasures. To allow it to accomplish this mission, the sharing of risks and rewards of future innovations between the public and private sectors must be fairly defined from the outset. Any agreement or partnership with industry must be guided by the public interest and include conditions to ensure the availability and affordability of the technology developed, such as the provision of fair prices or broad access to technology and knowledge transfer.

4. ENSURING A STRONG EU VOICE GLOBALLY

Demonstrate leadership in protecting the public interest when cooperating with third country partners and international organisations

The EU must have a strong voice at international level in setting a high standard of governance in the public interest. Following the Pharmaceutical Strategy's premise of delivering access to affordable medicines, the Commission should stick firmly to its ambition, defend its approach at international fora and promote reforms to restore the balance between public and private interests in the pharmaceutical sector worldwide.[91]

This goal should also guide the Commission in its work with third country partners at the WTO, where it should lead efforts to fully operationalise TRIPS flexibilities[92] (see also discussion under 3.3.2.) and rethink its stance on intellectual property rights enforcement in low and middle-income countries so that it does not constitute a barrier to access to affordable medicines.[93]

[91] Understandably, the Commission's ambition to put the public interest ahead of private profits and the identification of affordability and accessibility as the primary goals of its Strategy has drawn strong criticism from the beneficiaries of the current system, the pharmaceutical industry, which is now pressuring the U.S. administration *"to continue to seek assurances that the problems (…) are quickly and effectively resolved"*, referring to different measures included in the Commission's Strategy that the industry perceives as a threat to maintaining the current highly profitable status quo. See: PhRMA, *SPECIAL 301 SUBMISSION 2021* pp. 241-244.

[92] See: Medicines Law & Policy, *The TRIPS Flexibilities Database*.

[93] Corporate Europe Observatory, *EU risks global public health in its protection of big pharma monopolies*, March 2021.

The EU should also actively seek global solutions to issues that can be most effectively addressed at international level, such as antimicrobial resistance or the environmental impact of pharmaceuticals, and be actively involved in the work of the WHO, e.g., on ensuring equal access to medicines worldwide.

The European Medicines Agency should continue its collaboration with other regulatory authorities in the International Coalition of Medicines Regulatory Authorities,[94] promoting high regulatory standards and ensuring the development of safe, high quality and effective medicines, e.g., by influencing the design and conduct of clinical trials so that they deliver the most relevant and comparable clinical evidence.

Seek true global solidarity

The COVID-19 pandemic proved to be a difficult test for EU global solidarity.
Over the past year, the Commission has repeatedly underlined its commitment to international cooperation and global solutions by, e.g., declaring COVID-19 vaccines a universal public good and providing funding for international mechanisms. At the same time, however, it has decided not to participate in the WHO COVAX Facility[95] that would have improved equitable access to vaccines worldwide, and to sign bilateral advance purchase agreements that have effectively limited the availability of vaccines in poorer regions.[96] In the case of the latter, the Commission, in at least one case, even agreed that the pharmaceutical company would have the final say on whether vaccine doses purchased by the EU can be donated or resold abroad.[97]

The EU should recognise that the current system to which it contributes often results in increasing inequality and generates a dynamic in which money drives innovation, prioritizing the interests of profit instead of delivering innovation that is relevant to different regions and globally accessible.

The Commission should address the systemic problems embedded in the global pharmaceutical sector to ensure that the development and allocation of essential pharmaceuticals is driven by medical and social needs, not profit, and governed by public mechanisms instead of being left to the discretion of private interests, particularly during health emergencies.

[94] See: *The International Coalition of Medicines Regulatory Authorities*.

[95] See: *COVAX - Working for global equitable access to COVID-19 vaccines*.

[96] For the discussion on how to ensure global access to COVID-19 vaccines, see, e.g., in: O.J. Wouters et al., *Challenges in ensuring global access to COVID-19 vaccines…*, Volume 397, March 2021, pp. 1023-1034.

[97] See: *The European Commission says Covid-19 vaccines should be global public goods*, Medicines Law & Policy, January 2021.