EPF's Response to the European Commission's Public consultation on the EU Pharmaceutical Strategy

15 September 2020

Part 1. International dependency and manufacturing

The EU is increasingly dependent on active ingredients originating from outside the EU. This has implications, including as regards increasing the risk of quality issues and shortages of medicines. The recent outbreak of COVID-19 shows that a disruption in the pharmaceutical products supply chain originating from outside the EU could present a major health security issue.

1. What type of EU action or initiative do you consider helpful to incentivise the production of active pharmaceutical ingredients for essential medicines (e.g. antibiotics, oncology medicines) in the EU?

The EU should encourage sufficient collection of blood plasma, preferably from voluntary non-remunerated donors, within the EU to become less dependent from US paid plasma donors for plasma products and especially immunoglobulins. The dependency rate is now approximately 75%. The COVID-19 pandemic may cause shortages of immunoglobulins in the next year , and the available immunoglobulins may go to those countries who can afford high prices for these products. This is a topic relevant for the revision in the coming years of the EU Blood Directive.

2. What action do you consider most effective in enhancing the high quality of medicines in the EU? (1 choice)

- ❑ Stronger enforcement of the marketing authorisation holder responsibilities
- ❑ Increased official controls in the manufacturing and distribution chain
- X Other (please specify)
- ❑ I don't know

Please elaborate your answer

We believe MAHs should have more responsibility for overseeing manufacturing chains, as these are becoming quite complex. Increased controls through official inspections are also relevant. A further quality improvement strategy should be to develop a strategy to embed meaningful patient involvement in medicines r&d.

Part 2. Access to affordable medicines

A shortage of a medicine occurs when there are not enough medicines in a country to treat every patient with a given condition. Shortages can have a big impact on patients if their treatment is delayed because there is no alternative, or the alternative is not suited to their needs.

3. Are you concerned about medicines shortages in the EU?

- X I am concerned
- ❑ I am not concerned
- ❑ I have no particular opinion

If you wish, please elaborate your reply

> Shortages affect patients' safety, health and quality of life. They often affect long-established, off-patent and cheap medicines that are still needed by patients and for which good alternatives may not exist. Tackling them requires a range of tools depending on the reasons. It will be critical to understand patients' experience on shortages and their impact: patient involvement in policy is vital. Patients should also be able to report shortages to national and EU competent authorities.

4. Which actions do you think would have the biggest impact on reducing shortages in the EU? Max. 3 choices

- x Stronger obligations on medicines producers, and other players in the supply chain to ensure medicines are available
- x Transparent information exchange among authorities on medicine stocks available in each country
- x Increased cooperation among public authorities/national governments on shortages
- ❑ Multi-lingual packaging and electronic product information leaflets facilitating purchasing in different countries
- ❑ Providing incentives to companies to increase the production of medicines in the EU
- ❑ Inform on and make available to patients suitable substitutes for medicines that are at risk of shortage
- ❑ Other (please specify)

Please elaborate your reply.

> We believe all options are relevant. Medicines producers should have both incentives and obligations to ensure availability. Authorities need to co-operate more but also provide more transparent information to patients and the public on availability, including marketing status, and

shortages. They should work closely with patient organisations to gain information about shortages experienced by patients and ensure effective communication.

Innovative medicines have to undergo a centralised EU-wide marketing authorisation. Companies often initially market them in a limited number of EU countries. It can take several years before patients in the other EU countries have access to those products.

5. Do you think that companies that apply for and receive an EU-wide marketing authorisation should be required to make that product available in all EU countries?

- x I agree
- ❑ I neither agree or disagree
- ❑ I disagree
- ❑ I don't know

If you wish, please elaborate your reply

Inequity in access to medicines is a major cause of health inequalities. Disparity in patients' access to new medicines persist both among and within EU countries. Inequalities in access to medicines are contrary to the EU Charter of Fundamental Rights, the EU Treaties' commitment to the principle of well-being, and the fundamental European values of equity, solidarity and good quality in healthcare. Please refer to the attached paper for more details.

In recent years, there has been an increase in the number of medicines withdrawn from the market upon decisions by the manufacturers.

6. Do you have an opinion on the reasons for these market withdrawals?

- ❑ Yes
- X No

If yes, please elaborate

There are a number of reasons why manufacturers withdraw products, some of them commercial. It would be important to conduct an EU study to understand the access barriers experienced by patients in all countries across the EU. This should include a mapping of all the different reasons for lack of access.

7. Are you aware of patients not receiving the medicine they need because of its price?

X Yes

❑ No

If you wish, please elaborate your reply

Patients should not suffer financial hardship as a result of seeking treatment, but in reality they do. A price may be unacceptable to national agencies, leading to no reimbursement. Medicines also form a significant part of patients' cumulative out of pocket costs. A recent study found 1/4 patients postponed and 1/10 did not buy prescribed medicine because of price (see last question). Many patients with multiple chronic diseases have to choose to get only some part of their treatment.

8. Do you think that medicine prices are justified, taking into consideration the costs associated to their development and manufacturing?

❑ Yes

❑ No

X I don't know

If you wish, please elaborate your reply

We believe it is sometimes, though not always, the case. Costs of development and manufacturing are unknown; estimates vary from USD314m to USD2.8bn with a recent one at USD985m counting failed trials (Wouters et al, 2020). More transparency on costs of R&D, including company and public investments, and pricing, would help to judge whether the price of a specific medicine is justified. The benefit to patients must also always form part of this assessment, with meaningful patient input.

High prices for new medicines put pressure on public health spending. The costs for research and development are not publicly disclosed, and there is no agreement on how to calculate such costs. In certain cases, some EU countries join forces to increase their negotiating power when discussing prices with pharmaceutical companies. Individual pricing decisions in some EU countries may affect others. As an example, some EU countries limit the prices of medicines by linking that price to average prices in other EU countries (we call this "external reference pricing"- ERP). Because of ERP, a pricing decision in one EU country can inadvertently affect the prices in others. Once patents and other forms of market protection expire, generic and biosimilar medicines can enter the market and compete with the existing ones, this also typically brings down prices. Finally, there are plans to strengthen support to EU countries to work with each other on the clinical effectiveness of new medicines compared to existing alternatives, simply put how much better a medicine works compared to another one. This is part of the so called "health technology assessment "process.

9. What are the most effective ways the EU can help improve affordability of medicines for health systems?

- X Support the EU countries in better assessing and/or evaluating the value of medicines, meaning the effectiveness of a (new) medicine compared with existing ones
- x Help EU countries share experiences and pool expertise on pricing and procurement methods
- ❑ Better coordination among EU countries to ensure that pricing decisions taken by one EU country do not lead to negative impacts on patient access in another EU country
- ❑ Facilitate, market entry and a healthy market functioning for generics and biosimilars
- X More transparency on how the cost of a medicine relates to the cost of its research and development
- ❑ There should be a fair return on public investment when public funds were used to support the research and development of medicines
- ❑ I don't know
- ❑ Other

Please explain

A fundamental part of better evaluation of medicines is embedding meaningful patient involvement. Mechanisms for patient involvement especially in HTA and horizon scanning must be strengthened, both nationally and at EU level. With any policies it is always necessary to mitigate against negative impact on patients' access.

Part 3.Innovation in early development and authorisation

The European Commission actively supports health research and development through various funding mechanisms (e.g. Multiannual Financial Framework, Horizon 2020, Innovative Medicines Initiative partnership) and through collaborations between academia, healthcare systems and industry. Furthermore, the EU pharmaceutical legislation includes incentives to stimulate the development of innovative new medicines in areas such as paediatric and rare diseases; and market exclusivity rights to industry.

10. What actions at EU level do you consider most effective in supporting innovative research and development of medicines?

- X Make the legislative framework more adaptive to new technologies and advances in science
- X Provide more public funding for research
- ❑ Support (including through funding) private-public partnerships
- ❑ Support (including through funding) the creation of start-ups in medical research
- ❑ Foster research collaboration between universities, research centres and industry
- ❑ Provide research and development incentives in the form of intellectual property or market exclusivity rights for pharmaceutical companies investing in research
- ❑ Simplify the requirements for the conduct of clinical trials
- X Other (please specify)
- ❑ I don't know

Please explain

Patient involvement in trial design, understanding patients' unmet needs, non-IP incentives for r&d.

Expected return on investment in research and development for the pharmaceutical industry depends also on the expected volume of sales; this seems to be one of the root causes of limited availability of certain medicines (e.g. medicines for rare diseases or medicines for children).

11. What do you consider are the most effective actions related to research and development of medicines in areas where there are limited or no therapeutic options (unmet needs)?

- ❑ Provide market protection (protect a new medicine from competition)
- ❑ Provide intellectual property protection
- ❑ Provide data protection (protection of the data related to a medicine's clinical trials)
- X Agree on a common understanding on what are the areas of unmet need in the EU
- X Funding more targeted research at EU level
- ❑ Funding more targeted research at national level
- ❑ Provide national schemes to support companies economically

❑ I don't know / no opinion
X Other (please specify)

Please explain

Defining unmet needs with patients & co-producing r&d with patients.

The health sector is becoming more digitised, thanks to the increased availability and collection of health data from sources such as electronic health records, patient and disease registries and mobile apps (i.e. real world data) and through the use of artificial intelligence (AI) (i.e. systems that display intelligent behaviour and the use of complex algorithms and software in the analysis of complex health data). These developments, combined with real world data are transforming health, including the discovery of medicines.

12. Which opportunities do you see in digital technologies (such as artificial intelligence and use of real world data) for the development and use of medicines?

Improving the understanding of disease mechanisms and associations; discovery or validation of new biomarkers for personalised medicine; and for medicines safety monitoring. Digital tools use to increase efficiency of clinical trials, improve patient experience, safety and retainment in trials, if co-designed to meet their needs. RWD to monitor outcomes over time and better capture patients' needs and priorities, improve benefit-risk assessment and adherence through the lifecycle of medicines.

13. Which risks do you see in digital technologies (such as artificial intelligence and use of real world data) for the development and use of medicines?

Inappropriate access/use of data by third parties; undermining confidentiality and privacy; poor informed consent mechanisms; breaches of fundamental/patients' rights; risk to human autonomy. AI depends on the quality of data and wrong decisions may have serious consequences, raising questions of accountability, liability, and redress. Biases in data (collection) can introduce biased or discriminatory results that replicate biases found in society. AI diagnostics may lead to overdiagnosis and overtreatment. Lack of transparency in governance can lead to lack of trust.

Continuous manufacturing, advanced process analytics and control, 3D printing and portable / modular systems, may revolutionise the way medicines are manufactured.

14. Are you aware of any obstacles in the EU in taking advantage of technological progress in the manufacturing of medicines?

- ❑ Yes
- ❑ No
- X I don't know

Clinical trials are investigations in humans to discover if a new medicine is safe and effective. Clinical trials can also be used to test if a new treatment is more effective and/or safer than the standard treatment. Finally, so called "pragmatic clinical trials" can be conducted to compare the safety and effectiveness of different standard treatments in real world setting.

15. How could clinical trials in the EU be driven more by patients' needs while keeping them robust, relevant and safe for participants?

- ❑ By providing more national support for the conduct of so-called "pragmatic trials" with the aim to optimise treatment to patients
- X By better coordination for larger trials comparing different treatment strategies (covering medicines and other treatments such as surgery, radiotherapy, physiotherapy)
- ❑ By providing support for non-commercial organisations to conduct clinical trials in fields where financial interest is weaker
- X By involving patients' experiences in early phases of medicine design (e.g. factor-in how the disease affects their lives and develop medicines to target symptoms that are particularly important to patients)
- ❑ By designing more trials that collect information on medicine tolerability or the impact of a treatment on the quality of life
- ❑ By taking into consideration during the design of a trial the burden of trial participation on patients' life
- X Other (please specify).

Please specify

Mechanisms to ensure meaningful patient involvement in all R&D.

Certain medicines are developed based on genes, cells or tissue engineering. Some of these products are developed in hospitals. These are covered by the notion of advanced therapy medicines.

16. Is the current legal framework suitable to support the development of cell-based advanced therapy medicines in hospitals?

- ❑ I strongly agree
- ❑ I partially agree
- ❑ I disagree
- X I don't know

Part 4. Environmental sustainability of medicines and health challenges

Residues of several medicines have been found in surface and ground waters, soils and animal tissues across the Union. As of yet, no clear link has been established between medicine residues present in the environment and direct impacts on human health. However, the issue cannot be ignored and there is a need for a precautionary approach.

17. What actions at EU level do you consider most effective in limiting the negative environmental impact of medicines?

- X Cleaner manufacturing processes
- ❑ Enhanced application of the polluter pays principle
- X Review the way the Environment Risk Assessment of a medicine is conducted and its consequences on the authorisation process
- ❑ Clear labelling of environmental risks to allow informed choices among equivalent therapeutic options
- ❑ Reference to environmental risks in advertising for over-the-counter medicines
- ❑ Make medicines known to pose an environmental risk available by prescription only
- X Strict disposal rules for unused medicines
- ❑ Prescribe medicines only when it is absolutely necessary (more prudent use)
- ❑ Medicines dispensed to patients in the quantity actually needed (e.g. number of pills, volume of solution)
- ❑ Enhanced wastewater treatment if certain residues could be better removed
- ❑ Other (please specify)

Please explain

Patients' medical needs should always take precedence.

Antimicrobial resistance (AMR) is the ability of microorganisms (such as bacteria, viruses, fungi or parasites) to survive and grow in the presence of medicines. It reduces progressively the effectiveness of antimicrobials and is caused, among other things, by extensive and improper use of antimicrobial medicines. Antimicrobials include antibiotics, which are substances that fight bacterial infections. AMR can lead to problems such as difficulties to control infections, prolonged hospital stays, increased economic and social costs, and higher risk of disease spreading. AMR is one of the most serious and urgent public health concerns.

18. Which actions do you think would have the biggest impact on fighting AMR concerning the use of medicines for patients?

- X More prudent use of antimicrobials (if necessary through restrictions on prescriptions)
- ❑ Improve the treatment of wastewater and/or manure to lower the levels of antimicrobials
- X Raise citizens' and healthcare practitioners' awareness by informing them on appropriate use of antimicrobials and the correct disposal of unused medicines
- ❑ Introduce an obligation to use diagnostic tests before prescribing antimicrobials, for example to verify whether it is a bacterial infection before prescribing antibiotics and to define the most adequate antibiotic
- ❑ Public finance research and innovation on new antimicrobials, their alternatives and diagnostics
- ❑ Encourage public health campaigns that prevent infection through better general health including increased immunity
- ❑ Encourage public health campaigns that prevent infection through the use of vaccines
- X Encourage better hygiene measures in hospitals
- ❑ Other (please specify)
- ❑ I don't know

Please explain

For any restrictions exemptions should be in place to ensure patient's medical needs are met.

Innovation in antimicrobials is limited. For example, no new classes of antibiotics have been discovered for decades. Restricting the use of antibiotics to minimise the risk of developing resistance is a commercial disincentive for investment, as potential investors are concerned that their investment will not be profitable.

19. Where, in your view, should the EU focus its support for the creation of new antimicrobials or their alternatives?

- X Support academia for researching/discovering new antimicrobials or their alternatives
- ❑ Support industry for developing new antimicrobials or their alternatives
- ❑ Provide specific support to small and medium-sized enterprises (SMEs)
- X Other (please specify)
- ❑ I don't know

Please explain

Develop new kinds of incentives that will ensure affordability and universal access.

Health threats such as the coronavirus disease test the limits of public health systems, the pharmaceutical industry and of the pharmaceutical legislation. From the beginning of the coronavirus (COVID-19) pandemic, the EU has taken measures to coordinate a response, which includes actions ensuring the availability of medicines.

20. How has the coronavirus (COVID-19) pandemic affected you in relation to access to medicines and treatments?

Patients across the EU have been affected by disruptions in healthcare. In many countries, digital solutions have been put in place (e.g. e-prescriptions, teleconsultations) but access to these is unequal. While some medicine shortages have been observed, the severe impact has been in not having access to diagnosis, medical consultation or planned treatment. Studies already suggest these disruptions may result in thousands of excess deaths and morbidity. Their impact needs to be better understood.

21. In your opinion and based on your experience, what can the EU do to prepare for and manage such a situation better in the future in relation to pharmaceuticals?

Collaborative mechanisms to develop new diagnostics, vaccines, medical technologies and treatments swiftly and ensure equitable access and affordability. Roll-out of digital tools to enable e-prescriptions and access to prescribed medications without physically attending clinic or pharmacy, ensuring cross-border distribution chains are free from bottlenecks (e.g. labelling). Better tools to prevent and manage temporary shortages when e.g. repurposing existing treatments for pandemic use. Ensuring patient involvement in policy design to avoid unintended negative impacts.

Summary questions

22. While the Commission is working on improving the EU pharmaceuticals framework, which areas of work do you find most urgent? (max. 3 choices)

- X Improve patients' access to medicines
- ❑ Reduce shortages
- X Help national authorities ensure affordability for patients and increase health systems sustainability
- x Support innovation for unmet needs
- ❑ Use of digitalisation to develop medicines
- ❑ Help reduce anti-microbial resistance
- ❑ Reduce the dependency on essential active ingredients and medicines
- ❑ produced outside the EU
- ❑ Environmental sustainability of medicines
- ❑ I don't know
- ❑ Other (please specify)

Please explain

Antimicrobial resistance is also an essential priority.

23. If you were asked before the coronavirus (COVID-19) pandemic, would you have responded differently to any of the previous questions?

- ❑ Yes
- X No
- ❑ I don't know

If yes, please explain how your responses were influenced by the COVID-19 pandemic.

Patients' access challenges to medicines, including shortages, were well known already before the pandemic. Please see the uploaded EPF paper and our previous work on access.

24. Is there anything else you would like to add that has not been covered in this consultation?

Involving patients through the R&D cycle and in policy is key to fully understanding unmet needs and assessing value of new medicines. Patient involvement must start from defining needs and setting priorities, research questions, co-designing trials, to benefit-risk assessment and post-marketing monitoring of safety and effectiveness. Patient involvement in HTA and pricing/reimbursement at national level should be fostered through guidance and best practices.

References for Q7:

- WHO (2019) Can people afford to pay for health care? New evidence on financial protection in Europe
- Finnish patient associations study (2018): https://psori.fi/wp-content/uploads/2018/04/Selvitys-pitk%C3%A4aikaissairauksien-kustannuksista-2018.pdf

The EPF position paper 2020 on which our answers build can be accessed at : *https://www.eu-patient.eu/globalassets/library/position-papers--briefings/position-paper---pricing---finalversion.pdf*