Lilly's response:

Open Public Consultation on the revision of the general pharmaceutical legislation

28 September 2021 - 21 December 2021

Introduction

On 25 November 2020, the Commission published a Communication on a Pharmaceutical Strategy for Europe.

The Pharmaceutical Strategy identifies flagship initiatives and other actions to ensure the delivery of tangible results. As part of the implementation of the strategy, the Commission is evaluating the general pharmaceutical legislation[1] and assessing the impacts of possible changes in the legislation as described in the relevant inception impact assessment.

This public consultation aims to collect views of stakeholders and the general public in order to support the evaluation of the existing general pharmaceutical legislation and the impact assessment of its revision. It builds further on the public consultation conducted for the preparation of the pharmaceutical strategy for Europe. The replies to that consultation will be taken into account for the revision of the general pharmaceutical legislation. The present questionnaire should be seen as a continuation of that process.

In parallel, the legislation for medicines for rare diseases and children is being revised as well. Separate consultation activities have been carried out for that revision.

[1] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use
Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

Looking back

As mentioned in the Inception Impact assessment, the revision aims to tackle the following problems:

- Unmet medical needs and market failures for medicines other than medicines for rare diseases and children;
- Unequal access to available and affordable medicines for patients across the EU;
- The current legislative framework may not be fully equipped to respond quickly to innovation;
- Inefficiency and administrative burden of regulatory procedures;
- Vulnerability of supply of medicines, shortages of medicines;
- Environmental challenges and sustainability;
- Any other issues, which might emerge from the evaluation.

Q1 In your opinion, are there any other issues that should be addressed in this revision?

Lilly response:

While we support the responses of our trade associations (EFPIA, EuropaBio) to this consultation, we have sought to offer additional considerations, examples and COVID-19 pandemic learnings to date. Given the speed of drug and digital innovations, we propose ensuring that this revision not only creates an EU regulatory system that becomes more efficient, effective, and globally competitive, but also seeks to generate a broader R&D base and clinical trials footprint in Europe. Separately, the proposed measures are limited to advice on the classification of medicines, but should be broadened to drug/device combination developments. We also wish to emphasise the need to adapt the regulatory framework for certain categories of novel products and technologies, including platform technologies.

Q2 How has the legislation performed in terms of the following elements?

	Very well	Well	Moderately	Poorly	Very poorly	Don't know
1. Fulfilling its public health protection mission for patients and society.	X					
2. Promoting the development of new medicines, especially for unmet medical needs.		X				
3. Enabling timely development of medicines at all times, including during crises.			X			
4. Enabling timely authorisation, including scientific evaluation, of medicines in normal times.				X		
5. Enabling timely authorisation, including scientific evaluation during crises.		X				

6. Adapting efficiently and effectively to technological and scientific advancements and innovation.				X		
7. Ensuring medicines are of high quality, safe and effective.	X					
8. Addressing the competitive functioning of the market to support affordability.		X				
9. Ensuring the availability of generic[3] and biosimilar[4] medicines. [3] "Generic" is a copy of a medicine based on simple or chemical molecules. [4] "Biosimilar" is a copy of a medicine based on biological molecules.		X				
10. Ensuring that new medicines are timely available to patients in all EU countries.			X			
11. Ensuring that medicines stay on the market at all times and that there are no shortages.		X				
12. Ensuring that authorised medicines are manufactured, used and disposed of in an environmentally friendly manner.		X				

13. Ensuring that the EU system for development, authorisation and monitoring of medicines, including its rules and procedures, is understandable and easy to navigate.			X			
14. Attracting global investment for medicine innovation in the EU.				X		

Is there any other aspect you would like to mention, including positive or unintended effects of the legislation, or would you like to justify your replies?

We believe the flexibilities and accelerations applied during the pandemic, plus the unprecedented communication and cooperation with companies, should become standard, best practice to deliver faster access to all patients in Europe. This would help close the gap of a median of 426 days for the EMA to approve a new active substance vs 244 days in the USA (2021 CIRS, R&D Briefing 81). We acknowledge the multi-dimensional challenges in the EU regulatory system and the unique opportunity to resolve these. Reducing IP or creating conditions around IP will not address the common goal of equal, timely patient access. Instead, Europe needs to generate a level playing field across Member States to address national and sub-national hurdles and generate regulatory flexibility on a par with the US.

Looking forward

This section reflects on possible solutions to address the problems identified in the inception impact assessment mentioned in the previous section. Your contribution will help us in defining the way forward.

UNMET MEDICAL NEEDS

One of the aims of the strategy is to stimulate innovation and breakthrough therapies, especially in areas of 'unmet medical need'.

Regulators, health technology assessment experts and representatives of bodies responsible for reimbursing or paying for medicines ('payers') are discussing a definition or a set of principles for 'unmet medical needs'[5] in order to achieve the objectives of the general pharmaceutical legislation. The discussions reveal different perceptions of what is an 'unmet medical need'. Convergence on this key concept should facilitate the design of clinical trials, generation of evidence and its assessment, and the quick availability on the market of these

products and ensuring that innovation matches the needs of patients and of the national health systems.

The purpose of this question is to identify elements that are important in defining what is unmet medical need and in which areas of unmet medical need innovation should be stimulated.

[5] Please note that a similar discussion is taking place in the context of medicines for rare diseases and for children. The concept of 'unmet needs' in the context of rare diseases and children might be slightly differentiated compared to 'unmet needs' in the context of the general pharmaceutical legislation.

Q3 How important are the following elements for defining 'unmet medical needs'?

	Very important	Important	Fairly important	Slightly important	Not important	Don't know
1. Seriousness of a disease.	x					
2. Absence of satisfactory treatment authorised in the EU.	x					
3. A new medicine has major therapeutic advantage over existing treatment(s).	x					
4. Lack of access for patients across the EU to an authorised treatment.					x	
5. Other (please specify).						

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined elements, or would you like to justify your replies?

The definition of UMN should not be limited to areas where no treatments exist as unmet need can exist even if a treatment is available. The creation of a list of diseases of UMN would continuously change over time, and UMN will remain dynamic, with new treatments arriving and treatment guidance evolving. Defining UMN needs to be guided by science, HCP and patient perspectives. Concerning quick availability of products for UMN, 62% of medicines with a new, active substance were approved in the US by an expedited pathway verses only

9% for the EMA (2021 CIRS, R&D Briefing 81), illustrating the opportunity for the EMA to foster R&D for UMN through more agile, faster processes.

INCENTIVES FOR INNOVATION

The general pharmaceutical legislation guarantees the pharmaceutical innovator, typically a company, regulatory data and market protection for its new medicinal product. This data protection makes sure that another pharmaceutical company cannot re-use the proprietary data of the innovator for 8 years. Market protection makes sure that a generic or biosimilar medicine cannot be marketed until 10 years after authorisation. This dual protection shields a pharmaceutical innovator from generics or biosimilars on the market for 10 years. This protection is part of the EU system of incentives for innovation. The EU regime of intellectual property protection provides an additional protection coverage but is beyond the scope of this questionnaire and the revision of the general pharmaceutical legislation.

Q4 What do you think of the following measures to support innovation, including for 'unmet medical needs'?

	Very important	Important	Fairly important	Slightly important	Not important	Don't know
1. The current data and market protection periods for innovative medicines: 10 years of market protection, and 8 years of data protection.	x					
2. Provide different data and market protection periods depending on the purpose of the medicine (i. e. longer period of protection in areas of unmet medical need).					x	

3. Reduce the data and market protection periods to allow earlier access for generic and biosimilar medicines to the market.					x	
4. Introduce new types of incentives[6] on top of the existing data and market protection for medicines addressing an 'unmet medical need'. [6] Examples of new incentives are a transferable exclusivity voucher or a priority review voucher. A transferable exclusivity voucher would give the legal right to extend the protection time period of any other patented medicinal product, in exchange for the successful regulatory approval of a specified medicine for unmet medical need (e.g. an antibiotic). The voucher would be transferable or saleable, and may impact the turnover and profitability levels of other products in a developer's portfolio. A priority review voucher gives priority to the assessment of the application of the medicine in question or another medicine	x					

in the applicant's portfolio.						
5. Early scientific support and faster review /authorisation of a new promising medicine for an unmet medical need.		X				
6. Public listing of priority therapeutic areas of high unmet medical need to support product development by providing incentives.					x	
7. Require transparent reporting from companies about their research and development costs and public funding as a condition to obtain certain incentives.					x	
8. Other (please specify)						

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

Investing in high-risk areas such as Lilly has done in Alzheimer's Disease for over three decades, spending over $5 billion, depends on the certainty of strong, predictable IP incentives and rewards at the required point of investment. The setbacks we have had provide valuable, new scientific knowledge. RDP needs to remain predictable and at the current length to encourage further innovation. Requiring R&D cost reporting from companies will have a

stark negative effect because such costs would not recognise multiple setbacks in one disease area for a company; product development costs do not end at first indication market authorisation; and such an approach could perversely reward inefficiencies. Disclosing R&D cost would go against existing EU law on trade secrets and anti-competition.

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance (AMR) is the ability of microorganisms (such as bacteria, viruses, fungi or parasites) to survive and grow over time and no longer respond to medicines making infections harder to treat and increasing the risk of infections, severe illness and death. Antimicrobials include antibiotics, which are substances that fight bacterial infections. Overprescribing, overuse and inappropriate use of antibiotics are key drivers of AMR, leading to harmful health outcomes. The question below is intended to collect opinions on both the incentives for the development of new antimicrobials as well as possible option on their prudent use.

Q5 Should there be specific regulatory incentives for the development of new antimicrobials while taking into account the need for more prudent use and if so what should they be?

A looming global health threat like AMR requires creative reforms focused on priority pathogens. At the appropriate level, Transferable Exclusivity Extension (TEE) can attract long-term, sustainable private investment. A TEE should work in concert with existing IP incentives. TEEs can provide incentives for research areas where market mechanisms typically do not work. Alternatively, a subscription payment model, which enables access to innovative products for patients, provides budget predictability for payers, and provides a sustainable return on investment for the innovator company can be used. Lastly, a market entry reward (MER) can be an appropriate incentive, but not a substitute for, existing IP incentives to spur R&D investment and drive pipeline growth to market. A MER provides a predictable and reliable ROI for companies that successfully launch novel products, especially in areas of unmet need where traditional market incentives do not exist.

FUTURE PROOFING: ADAPTED, AGILE AND PREDICTABLE REGULATORY FRAMEWORK FOR NOVEL PRODUCTS

Novel products and innovative solutions continue to challenge the understanding of a "medicinal product" with low volume, and cutting-edge products (e.g. medicines combined with self-learning artificial intelligence) becoming a new reality. 'Bedside' manufacture of more individualised medicines changes the way medicines are produced. There are classification and interplay challenges with other medical products, such as medical devices and substances of human origin, or related to the combination of clinical trials with in vitro diagnostics/medical devices and medicines. In addition, certain cell-based advanced therapy medicines[7] are offered in hospital settings and are exempted from aspects of the pharmaceutical legislation. These developments offer possibilities for novel promising treatments and new ways of authorising and monitoring medicines but they are also testing the limits of the current regulatory system. They need to be addressed to unfold their potential while safeguarding the principles of high quality, safety and efficacy of medicines.

Digital transformation is affecting the discovery, development, manufacture, evidence generation, assessment, supply and use of medicines. Medicines, medical technologies and

digital health are becoming increasingly integral to overarching therapeutic options. These include systems based on artificial intelligence for prevention, diagnosis, better treatment, therapeutic monitoring and data for personalised medicines and other healthcare applications.

[7] Advanced therapy medicinal products (ATMPs) are medicines for human use that are based on genes, tissues or cells. They offer ground- breaking new opportunities for the treatment of disease and injury.

Q6 How would you assess the following measures to create an adapted, agile and predictable regulatory framework for novel products?

	Very important	Important	Fairly important	Slightly important	Not important	Don't know
1. Maintain the current rules.			X			
2. Create a central mechanism in close coordination with other concerned authorities (e.g. those responsible for medical devices, substances of human origins) to provide non- binding scientific advice on whether a treatment/product should be classified as a medicine or not.	X					
3. Make use of the possibility for 'regulatory sandboxes'[8] in legislation to pilot certain categories of novel products/technologies. [8] Some very innovative solutions fail to see the light of day because of regulations which might be outdated or poorly adapted for fast evolving technologies. One way to address this is through regulatory sandboxes. This enables nnovative solutions not already foreseen in regulations or guidelines to be live-tested with supervisors and regulators, provided that the appropriate conditions are in place, for example to ensure equal treatment. Regulatory sandboxes provide up-to-date information to regulators and supervisors on, and experience with, new technology, while enabling policy experimentation.	X					

4. Create adaptive regulatory frameworks (e.g. adapted requirements for authorisation and monitoring with possibility to adjust easily to scientific progress) for certain novel types of medicines or low volume products (hospital preparations) in coherence with other legal frameworks (e.g. medical devices and substances of human origin [9]) and respecting the principles of quality, safety and efficacy. [9] Substances that are donated by humans such as blood, plasma, cells, gametes, tissues and organs and are applied as therapy. Some substances of human origin can also become starting materials to manufacture medicines.	X					
5. Introduce an EU-wide centrally coordinated process for early dialogue and more coordination among clinical trial, marketing authorisation, health technology assessment bodies, pricing and reimbursement authorities and payers for integrated medicines development and post- authorisation monitoring.					X	
6. Other (please specify)						

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

We believe the biggest opportunity is to improve the regulatory timelines, to enable rapid patient access to medicines without compromising safety. Expedited regulatory tools are key to an agile system and although some are available in the EU, their use is limited in comparison to those offered in other countries. Companies developing COVID-19 products experienced swift and proactive engagement from the EMA, for example, which supported clear medicine development plans. The FDA used a very timely process under the emergency use authorization (EUA) procedure; an equivalent is needed in Europe. The role of the regulator and its decision making is already complex, and their decisions should focus on their core role of assessing the efficacy, quality and safety of new medicines.

Q7. Do you think that certain definitions and the scope of the legislation need to be updated to reflect scientific and technological developments in the sector (e.g. personalised medicines, bedside manufacturing, artificial intelligence) and if so what would you propose to change?

Given the speed of drug and digital innovations, we need to ensure the EU regulatory system becomes and remains more efficient, effective and globally competitive. This includes modernisation of the EU regulatory system e.g. supporting cloud based submission, decentralised clinical trials (DCTs). DCTs and hybrid trials have been essential during COVID-19. Beyond the pandemic, DCTs can increase study enrolment and retention, increase participant diversity and improve data quality. The legislation and regulatory system should also be better connected in support of diagnostics and drug/device combination developments. There is also a need to adapt the regulatory framework for certain categories of novel products and technologies, including platform technologies and digital health. As clinical research is global, international regulatory cooperation for emerging technology such as AI should be fostered, particularly between the EU and US.

REWARDS AND OBLIGATIONS RELATED TO IMPROVED ACCESS TO MEDICINES

Some medicines and therapies do not always reach patients in all EU countries, so patients in the EU still have different levels of access to medicines, depending on where they live. Even if a medicine received an EU-wide authorisation, companies are currently not obliged to market it in all EU countries. A company may decide not to market its medicines in, or decide to withdraw them from, one or more countries. This can be due to various factors, such as national pricing and reimbursement policies, size of the population and level of wealth, the organisation of health systems and national administrative procedures. Smaller markets in particular face challenges for availability and supplies of medicines.

Q8 How would you assess the following measures to improve patient access to medicines across the EU?

	Very important	Important	Fairly important	Slightly important	Not important	Don't know
1. Maintain the current rules which provide no	X					

obligation to market medicines in all EU countries.						
2. Require companies to notify their market launch intentions to regulators at the time of the authorisation of the medicine.					X	
3. Introduce incentives for swift market launch across the EU.					X	
4. Allow early introduction of generics in case of delayed market launch of medicines across the EU, while respecting intellectual property rights.					X	
5. Require companies to place – within a certain period after authorisation – a medicine on the market of the majority of Member States, that includes small markets.					X	
6. Require companies withdrawing a medicine from the market to offer another company to taker over the medicine.					X	
7. Introduce rules on electronic product information to replace the paper package leaflet.	X					
8. Introduce harmonised rules	X					

for multi-country packages of medicines.						
9. Other (please specify). **Lilly:** Adhere to and enforce 180-day timeframe for P&R per EU Transparency Directive	X					

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

Lilly is working to file for P&R within 2 years of MA across the EU27 to improve patient access, national P&R systems permitting. Given a medicine's launch is at national level, any EU P&R obligation beyond Transparency Directive (TD) enforcement of the 180 days would not be within EU control and would add uncertainty. External reference pricing, P&R process, value assessment, system readiness and sub-national approval are major root causes of delay e.g. Italy has a 100 day difference to access in oncology (Rada, M. 2017). Possible solutions include free/non extra-territoriality of pricing and enforcing the TD. Length of exclusivity is impacted by R&D risks and national policies and timelines on P&R, making certainty of predictable IP incentives key at the required point of investment.

ENHANCE THE COMPETITIVE FUNCTIONING OF THE MARKET TO ENSURE AFFORDABLE MEDICINES

The affordability of medicines has implications for both public and household finances. It poses a growing challenge to pay for medicines in the majority of Member States. Often, innovative medicines have higher prices, while there are growing concerns among stakeholders about the real-life effectiveness of some medicines and related overall costs. This puts the budgetary sustainability of health systems at risk, and reduces the possibilities for patients to have access to these medicines. Generics and biosimilars[10] of medicines which no longer benefit from intellectual property protection (off-patent medicines) may provide accessible and affordable treatments. They also increase the availability of alternative treatment options for patients. They may also increase competition between available medicines. However, experience shows that there are still barriers for medicines entering the EU market, including for generics or biosimilars.

[10] "Generics" are copies of medicines based on simple or chemical molecules; "biosimilars" are copies of medicines based on biological molecules.

Q9 In your view, to what extent would the following measures support access to affordable medicines?

	To a great extent	To a certain extent	No change	Very little	Not at all	Don't know
1. Maintain the current rules.		X				
2. Stimulate earlier market entry through a broader possibility to authorise generics /biosimilars despite ongoing patent protection ('Bolar exemption')[11]. [11] The Bolar exemption allows companies to conduct research on patent protected medicines under the condition that it is with a view to apply for a marketing authorisation for a generic.			X			
3. Create a specific (regulatory) incentive for a limited number of biosimilars that come to the market first.			X			
4. Introduce an EU-wide scientific recommendation on interchangeability for specific biosimilars.				X		
5. Introduce other, non-legislative measures, such as joint procurement to reinforce competition while addressing security of supply and				X		

environmental challenges.						
6. Other (please specify). Multi-winner procurement frameworks	x					

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

Lilly recognises the need for healthcare sustainability, and we support a smooth transition to generics and biosimilars once the IP exclusivity expires. Lilly supports appropriate exemptions from patent infringement for activities related to seeking regulatory approval, that facilitate efficient approval while preserving the integrity and function of the patent and regulatory review systems. Bolar should not be expanded to cover P&R because it would further undermine the patent system. The more steps, such as P&R activities, that are exempted from infringement during patent term, the less opportunities there will be to resolve a patent dispute pre-launch. Allowing P&R activities under Bolar would result in uncertainty to patients, payers and companies.

REPURPOSING OF MEDICINES

Repurposing is the process of identifying a new use for an established medicine in a disease or condition other than that it is currently authorised for. Repurposing of older (off-patent) medicines constitutes an emerging and dynamic field of medicines development, often led by academic units and medical research charities, with the potential for faster development times and reduced costs as well as lower risks for companies. This is because repurposing commonly starts with substances that have already been tested and many have demonstrated an acceptable level of safety and tolerability. The objective is to identify the opportunities and address any regulatory burdens to facilitate repurposing of off-patent, affordable medicines.

Q10 What measures could stimulate the repurposing of off-patent medicines and provide additional uses of the medicine against new diseases and medical conditions? Please justify your answers.

Repurposing existing substances must be based on sound evidence of safety and efficacy. Gathering the evidence will require regulatory and scientific expertise, time and financial resources, and there must therefore be adequate incentives to make the investment. When the patent conditions are fulfilled, a second medical use patent would be available. In other cases, regulatory exclusivity will be essential. Each of these incentives must, however, be fully recognised and respected by the national reimbursement policies (possibly through indication-based coverage). In order to be effective, steps should be taken to prevent off-label or cross-label prescription undermining the incentives. In general, just like pharmacy or hospital compounding, off-label (and cross-label) use should only occur when there is a specific health need for patients, and not be based on economic considerations.

SECURITY OF SUPPLY OF MEDICINES

Shortages of medicines and the vulnerabilities in the pharmaceutical supply chain continue to be concerns in the EU. Shortages of medicines can have serious impacts on patient care. Under the current pharmaceutical legislation, pharmaceutical companies and wholesalers must, within the limits of their responsibilities, ensure a continued supply of medicines once they are placed on the market in the EU. Companies must also notify national authorities at least two months before an expected shortage or planned market withdrawal.

Q11 What is your view on the following measures to ensure security of supply of medicines in the EU?

	Very important	Important	Fairly important	Slightly important	Not imporatnt	Don't know
1. Maintain the current rules.				X		
2. Earlier reporting of shortages and market withdrawals to national authorities in a common format.		X				
3. Companies to have shortage prevention plans.	X					
4. Companies to have safety stocks.				X		
5. Monitoring of supply and demand at national level.	X					
6. Introduce a shortage monitoring system at EU level.	X					
7. Require companies to diversify their supply chains, in particular the number of key suppliers of medicines and components.					X	
8. Companies to provide more information to regulators on their supply chain.			X			
9. Introduce penalties for non-compliance by companies with proposed new obligations.					X	
10. EU coordination to help identify areas where consolidation in the supply chain has reduced the number of suppliers.			X			
11. Other (please specify) European stocks / shortage monitoring system based on a common definition of shortages and a common reporting format.	X					

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

Lilly's global monitoring and risk mitigation systems allow us to determine the supply of medicines to meet our obligation to patients. Policies that mandate changes to global supply chains e.g. location, sourcing or inventory, could distort the security and reliability of the supply. Stockpiling could limit capacity to adjust to demand, put patient needs at risk and may lead to medicines expiry. Supply and demand uncertainty is proportionate to time: the longer the period of time, the greater the uncertainty, in addition to detracting resources away from ensuring reliable supply. Therefore, a meaningful timeframe of notifications to authorities on anticipated/potential shortage is 4-6 weeks. The existing European Medicines Verification System should be used to track supply and shortages.

QUALITY AND MANUFACTURING

Medicines manufactured for the EU market must comply with the principles and guidelines of good manufacturing practice (GMP). GMP describes the minimum standard that a medicines manufacturer must meet in their production processes. GMP requires that medicines are of consistent high quality, are appropriate for their intended use and meet the requirements of the marketing authorisation or clinical trial authorisation.

Q12 What is your opinion of the following measures to ensure manufacturing and distribution of high quality products?

	Very adequate	Adequate	Neutral	Less adequate	Not adequate	Don't know
1. Maintain the current rules.	x					
2. Strengthen manufacturing and oversight rules.			x			
3. Adapt manufacturing rules to reflect new manufacturing methods.	x					
4. Include selected environmental requirements for manufacturing of medicines in line with the one health approach on antimicrobial resistance[12]. [12] The one-health approach is a holistic and multi-sectorial approach					x	

to addressing antimicrobial resistance since antimicrobials used to treat infectious diseases in animals may be the same or be similar to those used in humans.						
5. Increase Member State cooperation and surveillance of the supply chain in the EU and third countries.			x			
6. Strengthen and clarify responsibilities of business operators over the entire supply chain on sharing information on quality, safety and efficacy.		x				
7. Other (please specify)						

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

An average Lilly product, from procurement of raw materials through production, may use about 800 different ingredients, components, and materials which are procured globally across about 150 vendors. Because Lilly's supply chain is global, we can be flexible and adapt resources and supplies to ensure our medicine is available at the right time for each patient. More flexible regulatory systems would support the manufacturing and supply of innovative medicines including aligning regulatory practice, creating a more agile system for variation changes and changes of API sources, and making use of and expanding existing MRAs (i.e. EU US MRA on GMP inspections). This would support contingency planning in companies.

ENVIRONMENTAL CHALLENGES

While access to pharmaceuticals is a priority, it is also important that the environmental impacts of those pharmaceuticals are as low as possible. The environmental risk assessments (ERAs) is currently not taken into account in the overall benefit/risk analysis which influences

the delivery of a marketing authorisation (MA) of a medicine. ERA can influence risk management measures. Yet, ERA results are not decisive in the MA process.

Q13 How would you assess the following measures to ensure that the environmental challenges emerging from human medicines are addressed?

	Very important	Important	Fairly important	Slightly important	Not important	Don't know
1. Maintain the current rules.		x				
2. Strengthen the environmental risk assessment during authorisation of a medicine, including risk mitigation measures, where appropriate.			x			
3. Harmonize environmental risk assessment by national regulators, including risk mitigation measures.	x					
4. Increase information to the health care professionals and the general public about the assessment of environmental risks of medicines.			x			
5. Allow companies to use existing data about environmental risks for authorisations of a new medicine to avoid duplicating tests.	x					
6. Other (please specify).						

Is there any other aspect you would like to mention, for example on the potential economic, social, environmental or other impacts of the outlined measures, or would you like to justify/elaborate your replies?

It is critical to ensure that any environmental policies under consideration here or in other EU legislation do not impede the discovery of and access to new, innovative medicines. Such

policies risk incoherence, e.g. putting the environmental risk assessments (ERAs) into the benefit/risk analysis; having HCPs consider ERAs when prescribing; implementing EPR schemes to reduce micropollutants, and restricting PFAS by REACH. On the reuse of data for a MA, while data can be shared, risks still need to be assessed since exposure will change. To require an evaluation of the manufacturing processes in the ERA would result in duplicative regulation and duplicative enforcement.

Q14 Is there anything else you would like to add that has not been covered in this consultation?

1) While this revision is a once in a generation opportunity to revise the framework for pharmaceuticals, we propose ensuring non-legislative options and policies are available in the coming years to allow for adjustments as science evolves and regulatory challenges emerge. 2) Ensuring the smooth implementation of the Clinical Trials Regulation and its portal, without harming the patent ecosystem, is key to ensure the EU competes with the increasing number of trials conducted in Asia, which grew from 14% (2009-2013) to 34% in 2020 (IQVIA). 3) Supply chain resilience can be strengthened through policies that seek to create a rich life sciences community and enable Europe to be a location of choice for pharmaceutical investment, such as ensuring a vibrant talent pool in STEM and complementary technical partners (SMEs, universities, etc.).

Q15 In case you would like to share a document that substantiates your replies, please upload it below (optional).