This document is a copy of the survey questions and it is intended to help you, or your organisation, gather relevant data to answer the survey provided on the link on the email. Please do not submit this document via email as a response to the survey, as this may result in your input not being recorded. Please note that the question numbers in this document are for internal routing purposes only and may not match the question number in the online survey questionnaire.

Study supporting the Evaluation and Impact Assessment of the EU general pharmaceutical legislation

Introduction

This survey is part of a study commissioned by the Directorate General for Health and Food Safety (DG SANTE) of the European Commission to support the evaluation and impact assessment for the revision of the EU general pharmaceutical legislation in the framework of the Pharmaceutical strategy for Europe. This is the first comprehensive review of the general legislation in more than 15 years, with the survey seeking both to capture the achievements of the 2004 revisions and to establish the refinements needed to bring the legislation up to date and ensure it is well-placed to meet the needs of Europe's citizens, health systems and pharmaceutical industry going forwards.

This survey covers the objectives of the general pharmaceutical legislation, Directive 2001/83/EC on the Community code relating to medicinal products for human use and Regulation (EC) No 726/2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency ("the legislation") and the elements of the future policy options for its revision.

Scope of the study

Regulation related to veterinary medicinal products are entirely out of scope for this study and provisions related to homeopathic and traditional herbal medicines, falsified medicines and advertising and information to patients are also out of scope. Similarly, specialised pharmaceutical legislations related to advanced therapy medicinal products, medicines for children and medicines for rare diseases are out of scope. Note that provisions relating to active pharmaceutical ingredients (APIs) and brokering of medicinal products are in scope for this study.

Privacy note

Your views and contributions will not be published directly as received; they will be published in the form of an aggregated summary report, or included in a wider policy document. You have the right to withdraw from the study at any time. For further information, please refer to our privacy statement.

Responding to this survey

The questionnaire is ambitious in scope and may take up to 1 hour to complete, however your input is critical to this once-in-a-generation review of the legislation. Your views thus matter greatly to the outcome, and we thank you for your time and consideration in providing a complete and careful response.

You do not have to answer all questions at once – answers will be stored at every page and you can return to the survey at any stage before completing it, provided the same device/browser is used and it is allowed for internet cookies.

If you have any questions or comments regarding this consultation, please contact the Technopolis study team by emailing us at pharma-legislation@technopolis-group.com.

About you / your organisation

A1. *Please select the option that best describes your organisation

- Civil society organisation (representing patients, consumers, and the environment)
- Academic/public and non-governmental research organisation
- Public authorities, agencies and healthcare payers
- Healthcare services
- Industry and business operators
    - Large enterprise (that employs more than 250 persons and has an annual turnover that exceed EUR 50 million)
    - SME (enterprise that employs fewer than 250 persons and has an annual turnover that does not exceed EUR 50 million)

A2. *Please select the country you are based in: [drop-down menu]

A3. *Please indicate which of the following match your organisation type:

- Industry association
- Developer of novel medicinal products (originator)
- Developer of generic medicine and biosimilars
- Fine chemical (API) manufacturer
- Contract research organisation
- Pharmaceutical wholesale & distribution
- Diagnostics and Medical Devices manufacturers
- Other – please specify: [Open]

A4. We would like to ensure that only unique contributions will be analysed in this targeted consultation. Therefore, we request you to provide the following information:

Name:

Organisation:

The effectiveness of the general pharmaceutical legislation

In the following questions we ask for your views on the extent to which the legislation has been effective in delivering its intended objectives since its implementation in 2005.

B1. To what extent has the legislation been effective in contributing to the following objectives?

	Very large	Large	Moderate	Small	Very small	Don' t know
1 Safeguard public health	X					
2Provide an attractive and robust authorisation system for medicines		X				
3 Provide resources and expertise to ensure timely assessment and authorisation of medicines at all times			X			
4 Enable timely access to medicines for patients and health systems		X				
5 Enable access to affordable medicines for patients and health systems		X				
6 Minimise inefficiencies and administrative burden of regulatory procedures			X			
7 Provide harmonised measures for improved functioning of internal market for medicines			X			
8 Ensure quality of medicines including through manufacturing rules and oversight of manufacturing and supply chain	X					
9 Enhance the security of supply of medicines and address shortages		X				
10 Provide clear and appropriate responsibilities to all actors throughout the lifecycle of medicines, including post-marketing obligations and oversight		X				
11 Ensure a competitive EU market for medicines		X				
12 Improve competitiveness of EU pharmaceutical industry on the global market			X			
13 Facilitate generic/biosimilar product entry to markets		X				
14 Enable progress in science, technology and digitisation for the development of high quality, safe and effective medicines			X			
15 Accommodate innovation for the development of complex and combination medicinal products			X			
16 Accommodate innovation for medicine manufacturing		X				
17 Attract pharmaceutical developers from outside the EU			X			

Reduce the environmental footprint of medicines		X				

B2. Please briefly describe the area in which the legislation has met your needs and expectations to the largest extent, compared to the situation prior to 2005, Please provide supporting data and evidence including weblinks if relevant. [Open]

EuropaBio believes the general pharmaceutical legislation has met many of the targets set in anticipation of the 2004 revision. The legislation has ensured that only safe, efficacious and high quality manufactured medicines are granted marketing authorisation.

In particular the co-existence of the different marketing authorisation procedures with centralised procedures (CP) for innovative medicinal products and DCP/MRP or national procedures for more mature products has created the right framework, in particular for SMEs with more limited resources that often seek more limited regional introductions.

For European citizens the pharmaceutical legislation has been valuable for access to innovative and biosimilar medicines with the introduction of CP and its scope extension in 2005 allowing for registration in all Member State (MS) countries including the smaller ones.

The legislation has also been a source of progress when it comes to the introduction of accelerated assessments or conditional marketing authorisation, it has increased the transparency of regulators' decisions through European Public Assessment Reports. It has improved the pharmacovigilance coordination on safety issues among MS contributing to improved public health.

The introduction of a standardised regimen of Regulatory Data Protection (RDP) across all MS has been a cornerstone of the improvement of the life sciences and biotechnology industrial ecosystem that should be preserved by all means.

When it comes to the availability and affordability of innovative medicines EuropaBio would like to stress that beyond the necessary acceleration of regulatory processes in the EU, pricing and reimbursement conditions are MS competencies that are not in the scope of the EU pharmaceutical legislation and should therefore not be evaluated for effectiveness of the legislation in this respect. The pricing and reimbursement choices and procedures should be dealt with at MS level to address country specificities.

Regarding the competitiveness of the life sciences and biotechnology industry, the focus point for the EU in its revision of the pharmaceutical legislation should be to regain its global leadership position as a primary source of health research, development and innovation, and as a strong cutting-edge industry, in order to maintain high quality care for all European citizens.

B3. Please briefly describe the area in which the legislation has met your needs and expectations to the smallest extent or not at all, compared to the situation prior to 2005. Please provide supporting data and evidence including weblinks if relevant. [Open]

The legislation, and subsequently the EU regulatory network, is less equipped to deal with the scientific and technological advances we have experienced since the legislative revisions in 2004. This puts the EU at a competitive disadvantage in comparison with other regions, in

particular with the US who remain a global leader in healthcare biotechnology. Many complexities exist for innovative biotechnology companies who wish to operate in the EU.

In light of new technologies and assessment methodologies future proper functioning of the regulatory network is crucial. Since the identification of biotechnology as a 'key enabling technology' in the 1990s, the EU's ability to retain or attract biotechnological development that translates to EU-first market launch medicines has dwindled. With the first widespread use of mRNA vaccines, healthcare biotechnology has now realised advances in medicine only theorised before-2004. In Europe, the healthcare biotechnology sector accounted for €29.9 bn or 86% of the total biotechnology industry in 2018, with a projected annual growth of of 4.1%, growing more than twice as fast as the EU information and communication sector (2.0%) and the overall economy (1.9%), making it one of the fastest growing innovative industries in Europe (EuropaBio/WifOR study, https://tinyurl.com/mrdbn2tc).

Resourcing of EMA and EU Regulatory Network

Adequate resourcing of the EU Network (EMA and the MS/NCAs) is necessary to increase the competitiveness of the EU. Reduction of timelines for assessment of medicines should be a core focus of the current review. Due to resourcing issues, and available expertise within the network, the provision of scientific advice to medicines developers, including SMEs, has not kept pace with other regions. Existing pathways to accelerated regulatory advice and assessment (Conditional Marketing Authorisation, Accelerated Assessment, PRIME) have improved the situation when compared pre-2004 when their introduction as part of the previous review was understood as a necessity to improve the networks competitiveness. There is however a need to further develop and enhance these pathways to ensure greater applicability, for e.g. in support of new indications (which may be addressing important unmet needs) as well as initial approvals. SMEs in particular rely heavily on scientific advice throughout the development lifecycle to reduce the administrative burdens they face in submitting marketing authorisation applications. Pathways for early dialogue with the different stakeholders (EMA/NCA/HTA) on appropriate study designs for evidence generation should be further strengthened.

Regulatory burden

In general there appears to be a broadening requirement for information which, in some instances, is redundant. There are many requests for information to be submitted that is already available in central database (e.g. repeating details in electronic application forms when most of the data requested has already been submitted previously). Increased efficiency could be found in making better use of contemporary IT and updated processes, supported by use of master data such as IDMP/SPOR and reference numbers, for e.g. MA numbers for marketed products or Unique Product Identifiers for research projects.

Review processes, use of RWE, and IT infrastructure

The EMA should have flexibility to adapt the review process to the nature and need of the product, this may include iterative submission of data for review, or expanded accelerated assessments. Adoption and uptake of new methodologies for data collection must continue in order to streamline and accelerate decision-making for precision medicines and speed up patient access. To achieve this, the underlying IT-infrastructure across the network requires improvement as part of the overarching EU digital transformation. Adequate databases, related data sharing protocols and data governance should be improved as part of a comprehensive digital strategy for medicine regulation (incorporating ongoing discussion on IDMP/DARWIN etc.). Updates to the systems should be done in collaboration with Member States, to avoid disconnect in the system.

Lessons learned from COVID-19

The COVID-19 pandemic has shown how regulatory systems can be optimised to speed up access (https://tinyurl.com/4ka77v72). Pathways for early dialogue with regulators and HTA bodies should be strengthened, which should also be introduced into appropriate study design. Expanded use of accelerated regulatory assessment based on the acceptance of staged submission of scientific evidence for new medicines and extension of indications led to the rapid introduction of vaccines and treatments. Improved capacity to provide rapid scientific advice, including through a flexible PRIME scheme with earlier access and including new extension of indications should be explored to future-proof the network. Remote inspection alternatives, and acceptance of decentralised and single-arm clinical trials offer a patient-centric approach leading to speedier access to novel technologies (https://tinyurl.com/5eupv6nd).

The relevance of the general pharmaceutical legislation

In the following questions, we ask you about the relevance of the legislation to each of the problems it was designed to address.

C1. How relevant is the current legislation, including its objectives and required actions, with regard to the following aspects?

	Extremely	Very	Moderately	Slightly	Not at all	Don' t know
Addressing current needs related to the development and authorisation of medicinal products in the EU		X				
Adapting to new therapies and their method of administration			X			
Ensuring the safety and quality of medicinal products	X					
Ensuring access to affordable medicinal products for those that need them		X				
Maintaining security of supply of medicinal products in the EU		X				
Maintaining resilience and responsiveness of health systems during health crises		X				
Minimising the impact of medicines on the environment through appropriate risk assessment		X				
Supporting successful digital and scientific transformation to meet the needs of medicinal product development and related technological developments			X			
Promoting the attractiveness of the EU system for developers compared to other jurisdictions			X			

C2. Please give an example of an aspect where the current legislation has been most relevant to your needs. Please provide supporting data and evidence including weblinks if relevant. [Open]

Reliable IP and RDP Frameworks

IP & incentives are critical to encourage long-term investments in high-risk, complex research & diversified product development (ATMPs, OMPs). Regulatory Data Protection provisions, 8 years of data protection, and 10 years of marketing protection provide the necessary conditions to allow innovation in Europe to grow. Biotechnology SMEs in particular rely on the parallel protections that IP and RDP can offer; IP protections on novel biotechnology attracts necessary capital investment to further R&D, while RDP allows for continued development and exploration of substances not yet approved but with treatment potential, improving the safety of approved medicines, and incentivising R&D within subpopulations.

Competitiveness

The current system has allowed for competitiveness, building in the necessary conditions in the previous review to improve the accessibility of biologics for example, which have the potential to contribute to the sustainability of health systems and increase the accessibility of certain medicines. At the same time, the system has maintained necessary conditions (IP/RDP above) which allow for development of novel treatments that offer vast improvements to the lives of patients and to the long-term financial sustainability of healthcare systems.

C3. Please give an example of an aspect where the current legislation has not sufficiently addressed your needs. Please provide supporting data and evidence including weblinks if relevant. [Open]

With reference to our response above at B3, we would reiterate the need for a forward looking pharmaceutical legislation, that is prepared for future scientific and technological advance. While the 2004 review helped to modernise the review and regulation of medicines in Europe, it lacked ambition in terms of technological-foresight. In comparing the two review periods, the 2004 review must be seen in the context of harmonisation of approach across the EU – the current review takes place, not only during a global pandemic, but as part of an ambitious agenda on behalf of the European Union and the Commission to modernise society for the next generation by way of the overarching green and digital transformations. The use of RWE will be of particular importance to complement the development of innovative medicines, for which only single-arm clinical studies are feasible to support registration, for example initial registration and extension of indication.

The Commission must seek to address the issues we face for next generation medicine development. EU affordability and access issues lie outside industry and EU control, where national pricing and reimbursement policies, and Member State health system organisation and administration remain a national competency. Thus, the focus of the review should be on harmonising the existing system, reducing timelines for review and inefficiencies and ensuring collaboration among all stakeholders.

Coherence of the general pharmaceutical legislation

In the following questions, we ask you to rate how well the legislation works internally and with other EU/international legislations and policies to achieve its intended objectives.

D1. How coherent is the general pharmaceutical legislation regarding the following aspects?

	Extremely	Very	Moderately	Slightly	Not at all	Don' t know
All elements of the legislation operating synergistically to achieve optimal results			X			
Linking with specialised pharmaceutical legislations (e.g. advanced therapy medicinal products, medicines for children and medicines for rare diseases)			X			
Complementing EU health-related legislations on (i) EMA fees		X				
(ii) Supplementary protection certificates		X				
(iii) Blood, cells and tissues			X			
(iv) Clinical trials			X			
(v) Medical devices and in-vitro diagnostics			X			
(vi) Genetically modified organisms					X	
Complementing other EU legislations and policies on (i) Data protection (e.g. GDPR)			X			
(ii) Digitalisation (e.g. Digital Single Market)			X			
(iii) Intellectual Property		X				
(iv) Environment (e.g. REACH, industrial emissions)		X				
Sustainable Development Goals		X				

D2. Please briefly comment on the aspect(s) where the current legislation has been most coherent. Please provide examples supported by data and evidence including weblinks if relevant. [Open]

EuropaBio considers that various legislative initiatives listed above are generally coherent with the general pharmaceutical legislation but would like to highlight the following aspects:

- The interplay of the legislation with the Blood Tissue and Cells, Advanced Therapy Medicinal products and Clinical Trial Regulation is of particular importance to EuropaBio's members in order to achieve effective and accelerated access to innovative medicines, a strong alignment should be achieved in order to avoid future disconnects overlaps or interpretation gaps at Member States level.
- On the EMA fees, it is essential that this agency and the EU regulatory network are properly funded and appropriately resourced to deliver on the increased tasks requested and to address the additional regulatory complexities in an environment of fast scientific development and deployment of digital tools (see also above, B3).

D3. Please briefly comment on the aspect(s) where the current legislation has been least coherent. Please provide examples supported by data and evidence including weblinks if relevant. [Open]

On GMOs, EuropaBio would reiterate a previous call, made in collaboration with EFPIA and ARM, to exempt ATMPs in clinical development from the EU GMO legislation; "Complying with GMO requirements is complex, varies significantly across EU Member States and is leading to delays to clinical trials with ATMPs. Such delays and varying implementation of the GMO legislation makes the EU less attractive as a region to conduct clinical trials with investigational gene therapies. This is detrimental to EU patients, since their timely access to these transformative potentially curative medicines is delayed" (https://tinyurl.com/yv7ydruh). Developers' ability to conduct R&D on ATMPs containing GMOs is hindered by the fragmented applications of the Deliberate Release and Contained Use directives. Mechanisms to harmonise the current system (guidelines, common application forms) have not reduced the complexity of the system or reduced the administrative burden on developers. Furthermore, due to the parallel GMO assessments, ATMP developers will not reap the benefits of a harmonised clinical trial procedure under the Clinical Trial Regulation, as GMO assessments naturally remain a Member State competence given the current system.

Flexibility in conducting clinical trials, and in clinical trial design, is also necessary to support future development of ATMPs and novel biotechnology derived medicines which focus on small populations (for e.g. rare disease patients) where RWE can supplement clinical trials, or for the conduct of decentralised clinical trials (https://tinyurl.com/5eupv6nd).

The added value of the general pharmaceutical legislation

In the following questions, we ask you about the value resulting from the EU legislation that is additional to what could be achieved at national levels.

E1. Please provide your view on the balance of EU level actions and national actions arising from the legislation.

	Very large	Large	Moderate	Small	Very small	Don' t know
To what extent has the legislation struck the right balance between action at EU level and national level?		X				
To what extent has the EU intervention in the context of the COVID crisis struck the right balance between action related to the legislation at EU level and national level?		X				
In the absence of EU level action, to what extent would Member States have had the ability to put in place appropriate measures?				X		

E2. In your opinion, what has been the most significant added value resulting from EU level actions stemming from the legislation compared to regional, national and international actions alone? Please provide examples supported by evidence. [Open]

The main purpose of the regulation of medicinal products has been to safeguard public health. The EU legal framework has guaranteed high standards of quality and safety and efficacy of medicinal products. It has also facilitated over the years the development of a biotechnology and life sciences ecosystem and the trade of medicinal products.

The creation of the European Medicines Agency has established strong procedures for central authorisation, supervision and pharmacovigilance of medicinal products that need today to be further enhanced and adapted to new technologies and digital requirements while accelerating the speed of regulatory approvals.

The coordinating role of the EMA has ensured rapid communication of information on pharmacovigilance concerns to healthcare professionals in Members States and the safety announcements of the national competent authorities.

The agency has also provided technical and scientific support in order to improve cooperation between the Member States, international organisations and third countries on scientific and technical issues relating to the evaluation of medicinal products. This work can be enhanced through continuous efforts for stronger regulatory harmonisation at international level.

The access to genetic and biosimilars in EU markets has been facilitated while preserving strong IP rules vital for the biotechnology industry.

E3. In your opinion, what has been the most significant added value resulting from EU level actions stemming from the legislation in response to COVID-19 compared to regional, national and international actions alone? Please provide examples supported by evidence. [Open]

The most significant added value of the legislation has been the possibility in justified cases like COVID-19, to meet unmet medical needs of patients, to grant a marketing authorisation prior to the submission of a comprehensive clinical data under the condition that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. The COVID-19 emergency situation has created the conditions of a marketing authorisation for vaccines and therapeutical treatments in record times. The broad definition of 'unmet medical needs' in this context has clearly been pivotal to this flexible approach. For the purpose of conditional marketing authorisation (Commission Regulation (EC) No 507/2006) unmet medical need means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Union or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.

The COVID-19 situation has also highlighted the need for clear guidance from the EU on how to conduct clinical trials in these particular circumstances. During the crisis, Member States issued different sets of rules , adding administrative burden and delays in clinical trials.

All the lessons learned from this COVID-19 experience should be drawn on in the review of the pharmaceutical legislation. How can the EMA learn from the COVID-19 fast track development support and approval of medicines and vaccines to accelerate its regulatory procedures so that marketing authorisations of safe, effective and high-quality treatments of the future can be granted as efficiently as possible?

This reflection has the potential to accelerate every step of the regulatory pathway of innovative medicines while ensuring robust scientific opinions are reached. Measures like rapid scientific advice through which developers receive prompt guidance and direction on the best methods and study designs to generate robust data on efficacy and safety as well as on the manufacturing and control process could be applied more routinely. Accelerated assessments and iterative submission of data could significantly contribute to efficiency and

more rapid authorisations reducing the standard timeline for the evaluation of an innovative medicine.

These various rapid procedures should also be made available in the context of extensions of indications of already approved medicines, which are being investigated to target other unmet needs and where the support of these pathways may be needed more than the initial indication.

For compassionate programmes that are set up at the level of individual EU Member States, to give patients access to treatments that are still under development and that have not yet received a marketing authorisation EMA could routinely provide scientific recommendations as to how these medicines should be used, to support a harmonised EU-wide approach.

The efficiency of the general pharmaceutical legislation

We will now explore the efficiency of the legislation from your perspective, i.e. the balance of costs and benefits resulting from the 2004 revision of the legislation. Please consider costs and benefits for your organisation owing to the introduction of the following measures:

- Definition of medicinal product adapted to account for **new therapies** and their method of administration and the new pathway for biosimilar medicines
- Expansion of the **scope of the centralised procedure**, both mandatory and voluntary
- Introduction of **accelerated assessment** procedure and conditional marketing authorisation and shortened decision-making procedure for granting of centralised marketing authorisation
- Changed composition of EMA's scientific committees and mandate to provide **scientific advice** to applicants to the centralised procedure
- Introduction of the **decentralised authorisation** procedure and optimisation of mutual recognition procedure for nationally authorised products together with optimised referral procedures
- Harmonisation of data protection period, additional data protection for new indications and introduction of **the 'Bolar' provision**
- Withdrawal of obligation to renew marketing authorisation every five years and introduction of **sunset clause** on validity of marketing authorisation
- Changes to documentation requirements, including **environmental risk assessment** (ERA)
- **Harmonised application** of good manufacturing practice (GMP) for active substances
- Reinforcement of inspections and increased coordination by introducing new tools (EudraGMDP)

Please separate out pharmacovigilance related costs if you are providing them in your responses below.

Please note that special legislations related to paediatric and orphan medicines, and falsified medicines are out of scope for this study and costs and benefits should not be part of the considerations below.

We would like to understand how costs incurred by your organisation related to the lifecycle of human medicinal products have been affected by the changes in the EU general pharmaceutical legislation introduced in 2005, and how these costs evolved to 2019. We understand that there are other reasons why the level of costs might have changed, please explain your answers briefly after each section.

F1. Please provide an estimate of the **one-off adjustment costs** your organisation incurred to comply with the 2004 revisions of the EU general pharmaceutical legislation. These expenses – paid once and not repeated – could be related to capital investment in new systems and infrastructure, commissioning external studies, running training programmes, etc. which had not been part of your usual operating activities.

Estimate of total One-off Costs (in Euros): [Open]

Please briefly describe these costs, when they occurred, providing examples where possible. [Open]

Given the timeframe for completion of this survey, EuropaBio were not in a position to gather information on this section (F1-12 inclusive).

F2. Please provide an estimate of the **additional ongoing DIRECT costs** your organisation had to spend in order to comply with the 2004 legislative revisions. These ongoing direct costs could be related to additional regulatory reporting obligations, payment of new fees and the introduction of other administrative expenses, including changed staff costs. Please also include in your overall estimate any savings that resulted from the simplifications introduced in the 2004 revisions.

Estimate of additional annual direct costs (in Euros) in 2005: [Open]

Estimate of additional annual direct costs (in Euros) in 2019: [Open]

Please briefly describe the main cost items and the drivers of these costs, providing examples where possible. Please also note where administrative cost savings were made possible by the legislative changes. [Open]

F3. Please provide an estimate of the **additional ongoing INDIRECT costs** your organisations had to spend in order to comply with the 2004 legislative revisions. These ongoing indirect costs could be related to any necessary changes in the wider operation of your company throughout the medicine lifecycle.

Estimate of additional annual indirect costs (in Euros) in 2005: [Open]

Estimate of additional annual indirect costs (in Euros) in 2019: [Open]

Please briefly describe the main cost items and the drivers of these costs, providing examples where possible. Please also note where operational cost savings were made possible by the legislative changes. [Open]

F4. Please provide an estimate of the **number of human medicinal product lines** that your organisation was working with in the following years.

Number of human medicinal products in 2005: [Open]

Number of human medicinal products in 2019: [Open]

To what extent did the costs and benefits related to the 2004 revisions of the EU general pharmaceutical legislation affect your company's product development decisions? Please illustrate your answer with data and examples where possible.

F6. To what extent did the 2004 revisions result in a reduction in regulatory burden? Please illustrate your answer with data and examples where possible.

F10. To what extent do you consider the additional costs incurred to comply with requirements of the 2004 revisions proportionate to the additional benefits realised across stakeholders, considering both monetisable and non-monetisable costs and benefits?

	Very large	Large	Moderate	Small	Very small	Don' t know
To what extent do you consider the costs of the legislation proportionate to its benefits for industry?						X
To what extent do you consider the costs of the legislation proportionate to its benefits for society i.e., health system and patients?						X
To what extent do you consider the costs of the legislation proportionate to its benefits for all stakeholders?						X

Please explain your response. [Open]

Given the insufficient time to collect quality data EuropaBio cannot furnish an answer to this question.

F12. Please describe the main opportunity you see for improving the balance of overall costs and benefits (including non-monetisable aspects). Please be specific and provide any evidence you can to support your answer (including weblinks if necessary). [Open]

Future policy measures: Incentives to support innovation for unmet medical needs

The following sections explore concepts that will underpin the future revision of the general pharmaceutical legislation in response to the new Pharmaceutical Strategy for Europe. The first set of questions explores measures for medicines in areas of unmet medical needs to foster their innovation, facilitate their approval, availability and access to them.

G1. Please rate the expected impact of each of the following policy measures **on supporting innovation** in particular to address unmet medical needs, UMN. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Reduction in the period of regulatory protection for any new medicinal products that **do not address a** UMN					X	
Additional period of regulatory protection for **new medicinal products that address an agreed UMN**		X				
A further period of regulatory protection for new medicinal products that address an agreed UMN and where the data package includes **evidence from a comparative trial** to help decision makers along the value chain (i.e. medicines regulators, HTA bodies and pricing and reimbursement authorities)			X			
Additional period of regulatory protection for robust evidence generated to support the **repurposing of an existing medicinal product** to address an agreed UMN		X				
Additional period of regulatory protection for new medicinal products targeting agreed UMN where there is **a demonstrable market failure** (i.e. the estimated total cost of product development is greater than the anticipated sales returns for that product)			X			
Transferable 'priority review voucher'** earned by developers of new medicines approved for use in the treatment of an agreed UMN			X			
Permit breaking of regulatory protection (e.g. compulsory licensing) under exceptional circumstances of urgency and insufficient coverage by authorised medicines to address UMN					X	
Codification of the PRIME (priority medicines) scheme*** within the legislation, ensuring the EMA will continue to provide enhanced advice and early dialogue with the developers of medicines that promise to address an UMN (including for repurposing medicines)			X			
Establishment of a binding system for scientific assessment of evidence relevant to the repurposing of off-patent medicines addressing an UMN						X
Simplification of the obligations for not-for-profit/ non-commercial entities (e.g. academic) to become marketing authorisation holders for medicinal products addressing UMN (including for repurposing medicines or hospital preparations)					X	

Other (please specify):						

1. * criteria for unmet medical need are being agreed on by regulators, HTA bodies and pricing and reimbursement authorities in Europe. These will consider conditions beyond paediatric and rare diseases
2. ** a transferable voucher allows a medicine developer to transfer certain benefits (e.g. priority review by authorities) to other products (including those not addressing 'unmet medical need').
3. *** the Priority Medicines (PRIME) scheme is a voluntary scheme through which the EMA offers early and proactive support to medicine developers to optimise development plans and speed up evaluation of medicines that target a UMN. The aim is to make these medicines available to patients as early as possible.

You may provide further comments regarding your responses above. [Open]

Further insight is required to the criteria which the Commission may propose to establish UMN, as such our responses above must be considered speculative.

Broad UMN criteria to support innovation

A narrow, prescriptive understanding of UMN will stifle innovation to the detriment of patients. Criteria should not be limited to diseases without any authorised treatments but should go beyond and apply also to conditions where available treatments have limited efficacy, significant side-effects or are very burdensome for patients. Only a broad conception will encourage R&D in all areas where there is UMN. To seek to reduce criteria may undermine stable investment in ongoing or future R&D life cycles which aim at developing treatments for the betterment of patients. UMN should be patient-centric and relevant criteria agreed in a multi-stakeholder forum of patients, caregivers, regulators, healthcare professionals, industry, HTA bodies, payers, etc., and must be carefully balanced against the need for predictability and reliability for drug developers, taking into account lengthy drug development processes.

Incentivise research

Elements which EuropaBio believe can spur innovation in healthcare biotechnology are those which seek to introduce new incentives, and build on the suite of existing incentives which underpin high-risk-failure R&D lifecycles in Europe. The stability which incentives bring to the R&D market cannot be underestimated (biotechnology exports and imports result in a significant trade surplus for the EU of €22.3 bn in 2018, EuropaBio/WifOR study figure 16 https://tinyurl.com/mrdbn2tc). EuropaBio supports efforts to introduce new incentives to attract cutting-edge research programmes, and encourage first-launches of products in the EU.

Clarify the hospital exemption

Bedside manufacturing by way of the hospital exemption should be limited (https://tinyurl.com/2p9uvsz5) and the relevant legislative provision clarified. Academic/hospital/non-commercial entities should be brought within the centralised procedure, and encouraged to explore pathways which maximise the accessibility of their products across the EU and ensure equal standards are applied to all products across the EU. Fragmentation of the centralised procedure only serves to diminish the system currently in place and, in the long run, potentially undermine its authority.

Reliable IP and RDP Frameworks

Breaking of regulatory protection (e.g. compulsory licensing), must also be clearly understood as a dilution of intellectual property protection. Within the context of UMN, as currently understood, there do not exist exceptional circumstances of urgency and insufficient coverage by authorised medicines to address UMN. Any reduction or dilution of RDP may prove

detrimental to sustaining future innovation, where RDP provides a necessary parallel protection to companies who conduct lengthy R&D as already mentioned at B2 and C2. Rather than potentially damaging the relationship between EU and industry, more understanding should be sought as to the necessity for strong IP and regulatory protections and their role and function in delivering innovative R&D, and in turn treatments to patients.

Future policy measures: Incentives and obligations to address antimicrobial resistance

Antimicrobial resistance is a multifactorial problem partly due to excessive and inappropriate use of antimicrobials. Development of novel antimicrobials is an example of unmet medical need, given the lack of therapeutic options to address antimicrobial resistance. This section explores specific measures for stimulating both innovation for new antimicrobials and their prudent use.

H1. Please rate the expected impact of each of the following policy measures **on stimulating innovation for new antimicrobial medicines**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Transferable 'exclusivity' vouchers* (independent and in addition to regulatory protection) to stimulate innovation for antibiotic development	X					
Additional market protection period for companies that hold a marketing authorisation for a novel antimicrobial			X			
Introduction of a 'play or pay' model – Either a company develops novel antimicrobials itself or pays into a fund to support their development					X	
Other (please specify):						

4. * A transferable voucher allows a medicine developer to transfer certain benefits (e.g. market exclusivity) to other products (including those not addressing antimicrobial resistance)

You may provide further comments regarding your responses above. [Open]

Fighting AMR needs the right incentives to encourage further research and innovation and implementation of a strong Public Private Partnership to create market conditions that today do not exist. It is important to have an EU-list of priority pathogens that guide developers to target the right unmet needs, as well as an alignment on the value demonstration amongst all concerned stakeholders (regulators, HTAs, payers). Economic models that apply to conventional treatments do not apply to new antimicrobials as they must be reserved in last resort. Innovative approaches to incentivise R&D in conditions which do not meet the traditional volume-based business model are required to reverse the market failure. For stewardship of existing antibiotics, effective use should be widely promoted and aimed at both

healthcare professionals and citizens to address general health threats and to reduce environmental impact

H2. Please rate the expected impact of each of the following policy measures **on stimulating prudent use of antimicrobials**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Tighten prescription requirements for antimicrobials		X				
Harmonisation of summary of product characteristics (SmPC) for nationally authorised antimicrobials to support prudent prescription practices and good antimicrobial stewardship			X			
Optimisation of the package size for antimicrobials to correspond to the typical recommended treatment dose and course of treatment			X			
Mandatory use of diagnostics to confirm presence of microbial infection before prescribing antimicrobial medicine		X				
Require companies to develop a lifecycle management plan for antimicrobials as part of marketing authorisation to set out a coherent strategy for prudent use, disposal, stewardship monitoring and reporting			X			
Establish monitoring system for data collection on human antimicrobial use and potentially environmental aspects		X				
Stricter rules on disposal of antimicrobial products by healthcare professionals		X				
Other (please specify):						

You may provide further comments regarding your responses above. [Open]

Future proofing: adapted, agile and predictable regulatory framework for novel products

The EU general pharmaceutical legislation aims to remain relevant and continue to enable innovation for the development of high quality, safe and effective medicines in the future. To this end, elements of flexibility and adaptability may need to be introduced in the regulatory scope and requirements. This section explores specific policy measures for accommodating emerging technologies, new models and processes throughout the lifecycle of medicines in a revised regulatory framework.

I1. Please rate the expected impact of each of the following policy measures **on supporting the future proofing of the regulatory system in the EU**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Adapt the definition of medicinal product in the current pharmaceutical legislation, to address emerging technological developments and gaps		X				
Adapt the regulatory framework for certain categories of novel products and technologies, including personalised medicine, medicines that contain or consist of GMOs, platform technologies, or combined with artificial intelligence		X				
Adapt regulatory requirements for specific cell-based medicinal products (Advanced Therapy Medicinal Products [ATMPs]) to facilitate production in hospital setting while ensuring quality, safety and efficacy				X		
For less complex cell-based medicinal products, adapt and simplify the regulatory requirements for authorisation under the pharmaceutical legislation and allow authorisation by national competent authorities (NCAs)				X		
Provide a mechanism to exclude less complex cell-based medicinal products from the scope of the pharmaceutical legislation and transfer them to the blood tissue and cells (BTC) legislation with authorisation by BTC NCAs				X		
Introduce a central classification mechanism for advice on whether products are medicines or not (borderline issues), in coordination with other concerned authorities in particular related to medical devices and/or blood, tissue and cells (BTC) legislations		X				
Introduce a coordination mechanism for advice on classification issues with advisory bodies related to other EU legal frameworks (e.g. medical devices, BTC)		X				
Adapt the regulatory system to support the use of new concepts including adaptive clinical trials, real world evidence, and health data	X					
Allow broader use of regulatory sandboxes, especially in the context of the approval and oversight of complex/cutting-edge medicinal products	X					
Replace the environmental risk assessment of investigational medicines that contain or consist of GMOs, currently under GMO legislation, by an EMA or decentralised (national) GMO assessment, before a clinical trial in the EU can start				X		
All investigational medicines that contain or consist of GMOs continue to be subject to an environmental risk assessment, before the start of a clinical trial in the EU				X		
Adopt a risk-based approach to determine when a specific environmental risk assessment is required for investigational medicines that contain or consist of GMOs, before the start of a clinical trial in the EU		X				
Other (please specify):						

You may provide further comments regarding your responses above. [Open]

Further insight is required on the applicable criteria or frameworks applicable to a number of questions and terms above ('less complex cell-based medicinal products', 'central classification mechanism', 'coordination mechanism', and the approach for adaptation of the regulatory system and use of regulatory sandboxes), as such our responses above must be considered speculative.

Avoid increased complexity between the BTC and ATMP legislation

EuropaBio consider the ATMP legislation fit for purpose and note it is outside the scope of this study. Proposals which seek to remove 'less complex cell-based products' from the scope of the ATMP Regulation, or to provide a mechanism for their classification by NCAs, are concerning given the Blood Tissue and Cells legislation already includes cell therapies which are 'minimally manipulated'. Furthermore, as previously mentioned at G1, we caution against fragmentation of the regulation of medicines within the EU – for example expanding the scope of activity of NCAs – where national interpretations may create further complexities for patients to access medicines that are otherwise assessed within a centralised procedure benefiting all EU patients.

GMO/ATMP requirements

GMO requirements currently applied to ATMPs/medicinal products are not fit for purpose, given the intent of the deliberate release/contained use directives were developed for agricultural products. As previously mentioned above at D3, developers' ability to conduct R&D on ATMPs containing GMOs is hindered by the fragmented applications of the Deliberate Release and Contained Use directives (https://tinyurl.com/yv7ydruh). Establishing derogations which would alleviate the regulatory burden on ATMP developers, particularly for established products for which it is clear there is no risk to the environment (i.e. ATMPs which employ AAV/LVV/RVV and/or are replication incompetent), would improve the attractiveness of the EU as a region to conduct R&D and subsequent clinical trials.

Clarify the hospital exemption

As previously outlined: bedside manufacturing by way of the hospital exemption should be limited (https://tinyurl.com/2p9uvsz5) and the relevant legislative provision clarified. Academic/hospital/non-commercial entities should be brought within the centralised procedure, and encouraged to explore pathways which maximise the accessibility of their products across the EU and ensure equal standards are applied to all products across the EU. Fragmentation of the centralised procedure only serves to diminish the system currently in place and, in the long run, potentially undermine its authority.

Clinical trials

Necessary evolution of clinical trials to support development of novel medicines requires acceptance, and proper guidance on the use, of alternative designs (e.g. single-arm trials with external controls) and fit-for-purpose RWE for regulatory benefit-risk assessment to drive clinical development and provide pivotal evidence of treatment benefits of new therapies, to complement possible evidence gaps (https://tinyurl.com/4ka77v72). Flexibility in conducting clinical trials, and in clinical trial design, is also necessary to support future development of ATMPs and novel biotechnology derived medicines which focus on small populations (for e.g. rare disease patients) where RWE can supplement clinical trials, or for the conduct of decentralised clinical trials (https://tinyurl.com/5eupv6nd).

Future policy measures: Incentives and obligations related to improved access to medicines

Access to medicines is currently not equal across the EU Member States and population groups. It is an important multifactorial challenge and incentives and legal obligations are required to address this challenge and support improved access to medicines in the future. This section explores the likely impact of potential policy measures in this direction.

J2. Please rate the expected impact of each of the following policy measures **on supporting improved access to medicines in the EU**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don't know
Expand the "optional scope"* of the centrally authorised procedure to all and any type of medicinal products (with some limitations), allowing applicants to request assessment through this route		X				
Introduce changes to conditional marketing authorisation to provide early access tools and accelerated assessment procedures. These may relate to exceptional circumstances, compassionate use, conditional indication, and prospective planning of studies	X					
Facilitate introduction of 'multi-country packs' with labelling that allows medicines to be marketed in several Member States with the same packaging	X					
Require marketing authorisation holders (MAHs) to notify regulators of their market launch intentions through a roll-out plan during the authorisation process for all centrally authorised medicines			X			
Allow early entry of generics in the EU market if a centrally authorised medicine is not launched in all Member States within 5 years of granting the marketing authorisation				X		
Allow additional period of regulatory protection if a medicinal product has been placed on the market in all Member States within 6 years of authorisation			X			
Require MAHs to place a centrally authorised medicine on the market in the majority of Member States (small markets included) within a certain period from authorisation					X	
Require MAHs to launch products in the majority of national health systems (including small markets) within a certain period from authorisation, where 'launch' means application for national reimbursement					X	
Require MAHs applying through mutual recognition/decentralised procedure (MRP/DCP) to include small markets					X	
Allow any Member State to opt-into a pending MRP/DCP procedure				X		

Require MAHs to keep a centrally authorised medicine on the market for five years after placing it on the market					X	
Codify a procedure for rolling review of products addressing UMN, allowing assessment of data for promising products as they become available i.e. before the formal submission of a complete marketing authorisation application		X				
Establish an EU system for emergency use authorisation of medicines		X				
Establish emergency use authorisation via national measures but based on EU scientific advice and under specified conditions			X			
Other (please specify):						

* "Optional scope" is defined in Article 3(2) of the Regulation (EC) No 726/2004

You may provide further comments regarding your responses above. [Open]

Availability of medicines

EuropaBio caution against measures which seek to impose on MAH an obligation to launch and/or maintain a product on a market, this will not tackle issues of availability. Launches depend on pricing and reimbursement decisions which are taken at a national level, as such Member States themselves should strive for more similarities in their HTAs and payers' requirements in order to lower the administrative and financial burden related to pricing and reimbursement, thereby accelerating patient access to new treatments. It is important to note that, in addition, launch is not possible in some countries due to a lack of infrastructure or experience, existing genetic variations, absence of diagnostic mechanisms or patients with the disease in the country.

Administrative burdens

Increasing the administrative burden and freedom to operate of the biotechnology industry, will disincentivise launches of innovative medicines in the EU and potentially favour priority launches in other regions with less burdensome regulation. For SME biotechnology companies, preparing the relevant dossiers for multiple HTA and payer bodies with varying requirements across several Member States represents a significant and challenging administrative and financial burden. In most cases, national P&R requirements or other criteria will hinder the market accessibility, as such an obligation to launch will not improve or speed up the accessibility of medicines. In many instances, simultaneous market launches are simply not feasible. For example, Bulgaria requires that a company obtain a pricing and reimbursement status in at least three other Member States before it will engage in negotiations. This inevitably leads to a launch delay of years – an issue that mandatory launches would not fix. Similarly, an obligation to conduct rolling reviews, for example, will not lead to more rapid access for patients. Rolling reviews should be available where appropriate based on the specific product and assessment processes, complementary of best-evidence-generation practices. Misalignment of processes indirectly forces some companies to prioritise certain markets, based on their own resource capacities.

Multi-country packs

Further facilitation of the use of 'multi-country packs' should be encouraged, particularly where supplemented by electronic patient leaflets. For example, where a single presentation can be

used across neighbouring countries to avoid shortages/write-offs, or for rare disease products to allow the use of single presentation in multiple countries with few patients.

Simplified and accelerated regulatory pathways

Increasing the attractiveness of the EU as a region to launch should be made a priority focus. Rather than implementing hurdles and obligations, the process of making biotechnology products available in each EU Member State should be improved. It requires accelerated and streamlined regulatory pathways for innovation, with better use of digital and emerging technologies in the EU and more effective pricing and reimbursement systems in the countries. Where possible the EU should facilitate convergence between HTA and payer requirements, and ensure that required evidence at the EMA level is also accepted in health technology assessments.

Future policy measures: Enhance the competitive functioning of the market

The European Commission aims to increase the availability of alternative treatment options for patients by stimulating competition of medicines for the same condition. This section explores specific policy measures related to off-patent competition.

K1. Please rate the expected impact of each of the following policy measures **on supporting early market entry for off-patent medicines**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Introduce new simpler regulatory pathway for generics and biosimilars to reduce assessment time by authorities				X		
Certification procedures to include outcomes that can be used for multiple products to avoid duplicative assessment e.g. active substance master file (ASMF), bioequivalence studies, core summary of product characteristics		X				
Establish legal basis for EMA committee to provide advice on interchangeability of specific biologics			X			
Broaden the scope of 'Bolar exemption' by allowing additional beneficiaries (companies, producers of active pharmaceutical ingredients [APIs]) and non-industry actors) to conduct studies/trials without infringing ongoing patent rights				X		
Broaden the scope of 'Bolar exemption' beyond generics by allowing repurposing studies/comparative trials without infringing patent rights				X		
Introduce specific incentives for a limited number of first biosimilars for a shared market protection				X		
Restrict duplicate marketing authorisations to cases of intellectual property protection or co-marketing				X		

Retain the current regime for duplicate marketing authorisations but exclude auto-biologicals						X
Other (please specify):						

You may provide further comments regarding your responses above. [Open]

EuropaBio is not supportive of simpler regulatory pathways for biosimilars or generics. The rules should be that the same standards and requirements should be applied to all medicines. Introducing looser regulatory requirements for biosimilars could undermine the quality and safety of the whole therapeutical offer.

The "Bolar" exemption was introduced in the EU law in 2004 by Article 10(6) of Directive 2004/27 amending Directive 2001/83 on the Community code relating to medicinal products for human use. Access to medicines (to both new and older products) is a complex situation that involves many different factors such as health system infrastructure, health financing, distribution and regulatory capacity. Within this equation the protection of IP plays a relatively small role. For example, the vast majority of medicines viewed as essential are off-patent. Yet even many patients in the EU have difficulties to access medicines.

For the biotechnology industry, the pharmaceutical legislation revision should focus its efforts in fostering innovation originating from SMEs in the EU, this vital biopharmaceutical innovation relies totally on the availability of strong IP incentives.

Strong predictable IP incentives have been historically a key driver for innovation but also for incremental improvements in some of the most heavily prescribed medicines that over time have resulted in radically improved and effective products that are safer and easier to use for patients. For instance Orphan drug laws and their provision of market exclusivity incentives have led to significant new research, clinical trials and the development of new drugs for rare diseases.

In the case of COVID-19 vaccines or treatments, IP incentives have shown to be an effective mechanisms in stimulating biopharmaceutical innovation; any measures undermining these strong EU incentives would have a detrimental effect on developing a strong life sciences and biotechnology sector in the EU.

Future policy measures: Ensure quality, manufacturing and environmental challenges

It is important that pharmaceutical production and distribution is of the highest quality and has low environmental impact. Currently, environmental risk assessment of pharmaceuticals is not considered decisive in the marketing authorisation process. This section explores proposed policy measures to meet the quality, manufacturing and environmental challenges of the future.

L1. Please rate the expected impact of each of the following policy measures **on ensuring the highest quality of medicinal products and good manufacturing practices**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don't know
Introduce a harmonised system of sanctions related to good manufacturing practice (GMP) and good distribution practice (GDP), thereby strengthening the enforcement of MAHs responsibilities regarding quality of medicinal products			X			
Reinforce Member States GMP/GDP inspections capacity by setting up a joint audit scheme		X				
Extend the scope of mandatory inspections to encompass MAHs supply chains (including distributors and active pharmaceutical ingredient [API] manufacturing/importing sites)				X		
Increase the responsibilities of MAH vis a vis the quality of the supply of APIs and raw materials and clarify responsibilities of business operators over the entire supply chain			X			
Strengthen the role of the EMA in supporting the robust oversight of manufacturing sites, through adapted IT tools and enhanced coordinating role of multinational inspection teams		X				
Strengthen the role of the EMA in the coordination of all inspections, including setting up multinational inspection teams*		X				
Adapt the terms of the legislation to accommodate new and emerging manufacturing methods (digitisation, decentralised manufacturing, continuous manufacturing etc.).		X				
Other (please specify)						

You may provide further comments regarding your responses above. [Open]

The EU can lead in the manufacturing of innovative therapies by ensuring an effective regulatory framework adaptable to the newest technology and by fostering global collaboration on medicines supply, rather than through localisation measures. When reimbursement schemes or inspection requirements favour national production, this often results in delays for patients. An EU strategy for security of supply should not only focus on bringing back production but also on fostering production still present in Europe, such as anti-infectives, biologics, CAR-T therapies, etc. A manufacturing-friendly EU environment, including favourable trade policies and sustainable market conditions, will be paramount to ensure the continued supply of quality medicines. The EU regulatory framework should be modernised and adaptive to latest technologies, such as CAR-T or other advanced therapies to ensure rapid uptake and approval of production upgrades in bio-pharma manufacturing sites.

The Pharmaceutical Strategy should truly become a building block for an ambitious industrial policy that makes the EU an attractive investment destination for innovative biotech and bio-pharma companies. There is great regional, societal and economic potential for advanced biotechnology manufacturing. Creating regional manufacturing hubs for advanced biotechnology manufacturing can go some way in mitigating the economic disparities within and between European countries.

The current measures to ensure quality manufacturing are in general appropriate and have proven successful, only minor changes are needed. In terms of competitiveness, implementation of the same quality standards for all players in the global market are in this regard paramount.

L2. Please rate the expected impact of each of the following policy measures **on addressing environmental challenges**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Strengthen the environmental risk assessment (ERA) requirements and conditions of use for medicines			X			
Introduce a requirement to include information on the environmental risk of manufacturing medicines, including supply chain actors (manufacturers of APIs and raw materials) in ERA / application dossiers			X			
Adapt GMP procedures so that MAHs are required to plan for and report on their management of the environmental challenges relating to the release of antimicrobials to the environment			X			
Establish an advisory role for EMA with regard to ERA and green manufacturing aspects and quality of medicines		X				

You may provide further comments regarding your responses above. [Open]

The EU should recognise "bio-production" as a strategic sector to produce advanced therapy and biological products establishing the EU as a global leader for breakthrough technologies that can compete at a global level. In general, current manufacturing and oversight are appropriate but it is critical that those rules continue to converge with international regulations. New manufacturing methodologies and requirements on environmental risk assessments should ensure predictability and fair competition of the EU with other regions and never lead to additional barriers for biotechnology SMEs to compete and produce in the EU. Advanced biological therapies and manufacturing bring significant advantages to advance the EU's digital and green agenda, create high-skilled jobs and establish greater security of supply.

EuropaBio supports the development of a common database system for medicinal products, i.e. hazard and environmental fate data, as well as environmental monitoring data, to assess environmental impacts.

Patients' access to innovative medicines should remain the priority, the rules should remain pragmatic and not create additional bureaucracy in the process.

Future policy measures: Security of Supply of Medicines

Medicine shortages compromise patient health and burden healthcare systems. This section explores possible policy measures for ensuring robust supply chains of medicines, particularly those related to enhanced transparency of stocks and shortage monitoring.

M1. Please rate the expected impact of each of the following policy measures **on ensuring security of supply of medicines**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don't know
Require MAHs to notify authorities of impending/anticipated shortages at least two months in advance			X			
Require MAHs to notify authorities of impending/anticipated shortages 6 months in advance, through a common template, including details of root causes, alternative medicines and impact				X		
Require MAHs to provide increased transparency of their supply chain to public authorities, including of active supply sites and volumes supplied			X			
Introduce an EU shortage monitoring system for all medicines		X				
Establish a mechanism for information exchange on supply chains between Member States to identify bottlenecks and vulnerabilities		X				
Introduce an EU information exchange on critical shortages based on national supply-demand monitoring data		X				
Use the Falsified Medicines Directive (FMD) system to monitor shortages			X			
Other (please specify):						

You may provide further comments regarding your responses above. [Open]

During the COVID-19 crisis our industry has been operating under pressure to avoid shortages "in the dark" with governments sharing limited information to companies on global country needs and spiking demands.

In order to avoid the repetition of such situations, there are three critical areas for policy support 1) the need to build strong resilient supply chains (through international cooperation on regulatory approaches and oversight); 2) the creation of adequate demand forecasts for critical medicines supplies (supported with transparent supply and demand information from authorities and supply chain stakeholders), and 3) the implementation of quick supply response/preplanning processes based on true patient needs, the ability to move stocks to respond to needs and to identify stockpiling requirements not justified and not coordinated across countries in Europe

EuropaBio is very concerned that most of the above mentioned measures could have a negative impact on biotechnology companies with additional reporting on supplies activities that could generate additional costs without real added value for the supply chain security. For instance reporting shortages 6 months in advance is totally unrealistic given the multitude of factors which impact supply chains, and could be considered as an additional barrier to market entry for smaller companies.

EuropaBio believes that the right approach is to create a clear information process for critical medicines only based on national forecasts and consolidated at EU level to better alert of potential bottleneck situations.

Biotechnology companies have shown during the crisis their capacity to adjust to emergency situations and to build over years the resilient supply chains they need to serve patients best. Providing detailed information over their supply chains will in no manner strengthen the supply security but will inevitably add administrative burden to their business model.

Future policy measures: Streamlining and simplification of the legislation

The EU pharmaceutical system aims to ensure safe and high-quality treatments are available to patients, while remaining attractive to the pharmaceutical industry and sustainable for the regulators. To be competitive in a global environment, future policy proposals consider streamlining and simplification of the EU general pharmaceutical legislations.

N1. Please rate the expected impact of each of the following policy measures **on ensuring streamlining and simplification of legislative procedures**. Where you have no relevant knowledge, please choose 'don't know'.

	Strongly positive impact	Positive impact	Little or no impact	Negative impact	Strongly negative impact	Don' t know
Streamline procedures to avoid duplicative processes, e.g., GMO requirements, prioritisation of applications, pharmacovigilance requirements, risk management plan (RMPs) for generics and low volume products		X				
Streamline procedures to facilitate efficient interaction and synergies between different but related regulatory frameworks, e.g. medical device and health technology assessments		X				
Abolish the requirement for the 5-year renewal of marketing authorisation		X				
Abolish the "black symbol" for identifying medicinal products that are subject to additional monitoring			X			
Allow medicines regulators to reject marketing authorisation applications without conducting a full assessment when data is insufficient to support a decision			X			
Establish structured exchanges to ensure that advice provided at each step of the product lifecycle is known and taken into account by all relevant bodies (e.g. EMA's		X				

scientific advice is aligned with the authorisation processes of the relevant clinical trials)						
Formalise the structure of the European Medicines Regulatory Network* including the role and tasks of Heads of Medicines Agencies**		X				
Establish a legal basis for the European Medicines Regulatory Network to analyse real world evidence, create computing capacity, store and manage large data sets		X				
Regulators to adapt the product information in the summary of product characteristics (SmPC) without full consent of the marketing authorisation holder based on evidence on safety and efficacy				X		
Reduction of legislative requirements for packaging, e.g. electronic package leaflet to replace paper leaflet and paper to be available only upon demand in outlets	X					
Mandatory electronic submission for applications or registrations by companies including for the centralised procedure, decentralised procedure and mutual recognition procedure		X				

* Closely-coordinated regulatory network of over 50 national competent authorities (NCAs) from EEA Member States, EMA and the European Commission. By working closely together, this network ensures that safe, effective and high-quality medicines are authorised throughout the European Union (EU), and that patients, healthcare professionals and citizens are provided with adequate and consistent information about medicines

** The Heads of Medicines Agencies (HMA) is a network of the heads of the NCAs whose organisations are responsible for the regulation of medicinal products for human and veterinary use in the EEA

You may provide further comments regarding your responses above. [Open]

The EU needs a strong collaborative network involving EMA, national agencies and other involved bodies (e.g. GMO authorities, Notified Bodies) with sufficient resources and the right expertise to anticipate increasing complexities linked with breakthrough innovation.

Timely access to standardised data sets and streamlined GDPR implementation will enhance data use for cross-border scientific collaboration.

High-quality RWD and AI must be harnessed as part of the planned EU Health Data Space. RWE should be supported by EU-wide measures and the acceptance of this RWE should be encouraged among all stakeholders as they will transform how clinical trials will be conducted in the future.

Lessons learned from the response to COVID-19 (rapid scientific advice, rolling reviews, labelling, etc.) should be scaled to other treatments addressing unmet needs where possible.

We need to work together to build a more agile regulatory framework based on EMA and EU network leading expertise; efficient assessment processes and appropriate resourcing to address the increasing complexities of regulatory undertakings.

EuropaBio fully supports all streamlining initiatives that result in reduction of administrative burden or avoid duplication of efforts along the regulatory processes. This is particularly valuable for SMEs.

There is also value in abolishing the black triangle symbol which is imposed based on regulatory reasons rather than effective risk.

Any decision by regulators to reject MAAs without conducting a full assessment when data is insufficient should follow clear and transparent criteria and should be discussed prior to the decision between the applicant and the regulator as there could be scientific basis for not including certain items in the MAA submission. There should not be any rejection from the regulator without prior interaction with the applicant.

EuropaBio is obviously supportive of the establishment of structured exchanges of advice that can be obtained throughout the product lifecycle. But in the case of clinical trials authorisation is in the remit of the Member States and the requirements may sometimes diverge from the EMA scientific advice. EuropaBio believes that beyond the structured exchanges a clear mandate for the role of the HMA over individual Member States would contribute to better convergence and general efficiency.

On the possibility to establish a legal basis for the EMA to analyse RWE and create computing capacity, storage and management of large data sets that is today in the remit of Member States, EuropaBio would recommend to define under which conditions companies could participate, contribute to the set up of such data sets and access to them.

EuropaBio believes that for innovative products the SmPC should never be changed without prior exchange with the MAH.

All other initiatives consisting in reducing requirements for packaging, for e.g. facilitating the introduction of multi-country packs, or electronic package leaflets to replace paper leaflets, are welcome.

Conclusion

O1. What in your view will be the greatest impact of any changes to the legislation on the economy, society and environment? Please provide examples and supporting data or evidence e.g. through weblink if necessary. [Open]

EuropaBio firmly believes capturing the full potential of biotechnology is fundamental to finding new solutions to the challenges that Europe is facing, from health, ageing, through climate change, to sustainable economic, environmental and societal development. We outline eight key pillars for how biotechnology will help achieve a healthier and more sustainable Europe that attracts innovation and clinical development and delivers to its citizens: Capital and financing for fostering cutting-edge innovation by start-ups and SMEs; Skills and labor for a knowledge-based economy; R&D incentives for competitive innovation; Intellectual Property for sustainable biotech business model; Advanced manufacturing for sustainable production; Digitalisation to accelerate research and innovation; Regional development for jobs & growth creation; Global competitiveness for recovery and sustainability.

EuropaBio Life Science and Biotechnology Strategy - https://tinyurl.com/2p89k53u

EuropaBio/WifOR study measuring the economic footprint of the Biotechnology Industry in Europe - https://tinyurl.com/52fvtrzd

The Pharmaceutical legislation revision has the potential for the EU to reclaim its position as a leader in life sciences, to respond efficiently to future health threats and to contribute to a healthy society for the long term.

Medicines are at an important crossroads: more innovation needs to originate from the EU through a leading life science and biotechnology ecosystem

The COVID-19 crisis has shown that only science-based research embedded in a thriving life science industrial ecosystem, strong manufacturing capacities and well-functioning regulatory and health systems can bring effective solutions to the health challenges our society faces. The EU needs to regain its global leadership position as a primary source of health research, development and innovation and as a strong cutting-edge industry hold, in order to maintain high quality care at affordable levels for all European citizens.

Innovation for unmet needs can be achieved through digital and emerging technologies

Healthcare is experiencing a major paradigm shift, from traditional one-size-fits-all medical care to personalised medicine tailored to the genomic, molecular, and lifestyle characteristics of individual patients. Unlocking the power of health care data to fuel innovation in medical research is at the heart of today's health care revolution, where medicine is increasingly a collaboration between data science and clinical science realms. Harnessing data offers biopharmaceutical companies deeper understanding of disease pathways and ultimately helps develop targeted treatments with improved efficacy and safety. As a result, cellular therapies, gene therapies and genome editing are a reality today. The pipeline of biopharmaceutical innovation is rich in these transformative therapies that would not exist were it not for this remarkable convergence of modern biotechnology and the digital sciences.

- Consideration should be given to continued use of non-legislative approaches to emerging technology which have proven effective in responding to COVID-19.
- The EU needs a strong collaborative network involving EMA and national agencies with sufficient resources and the right expertise to anticipate increasing complexities linked with breakthrough innovation.
- Timely access to standardised data sets and streamlined GDPR implementation will enhance data use for cross-border scientific collaboration.
- High-quality RWD and AI must be harnessed as part of the planned EU Health Data Space. RWE should be supported by EU-wide measures and the acceptance of this RWE should be encouraged among all stakeholders

Unequal access should be addressed through the right means and not create new uncertainties or new hurdles for investors ready to take risks to innovate in the EU.

The complexity of unequal access to innovation cannot be addressed by reducing Intellectual Property Rights for innovators or creating unpredictability in the innovation value chain. EuropaBio shares the ambition of better and faster access to innovative medicines in the EU, but it is not through EU legislation that the solution should be targeted as most of it depends on factors in Member States. Only a continuous dialogue with all stakeholders involved in this process will contribute to concrete solutions tailored to national specificities.

EuropaBio looks to engage in a concerted effort to achieve better regulatory efficiency, in particular in the area of gene and cell therapies, successfully establishing HERA, creating a fit for purpose European Health Data Space, and sharpening the EU's competitive edge with strong incentives for innovation. The number one lesson learnt from the COVID-19 pandemic is that public health and the economy are strongly interlinked. A successful Pharmaceutical Strategy will be measured on its capacity for the next generations to strengthen the preparedness of EU health systems, to improve the well-being of citizens and to contribute to better functioning of our economy and society.

Close

Thank you for your response, we appreciate your input. If you are willing to be contacted in case of follow-up questions, please provide your contact details below.

Email: [open text]

Please be assured that your personal data will be handled according to our privacy statement.

Please click 'Done' once you have completed the survey and you are content with your answers. Note that you will not be able to return to your survey and change your answers once you have clicked 'Done'.