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Your views and contributions will not be published directly as received; they will be published in the form of an aggregated summary report, or included in a wider policy document.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.

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
Safeguard public health		X				
Provide an attractive and robust authorisation system for medicines			X			
Provide resources and expertise to ensure timely assessment and authorisation of medicines at all times			X			
Enable timely access to medicines for patients and health systems			X			
Enable access to affordable medicines for patients and health systems			X			
Minimise inefficiencies and administrative burden of regulatory procedures					X	
Provide harmonised measures for improved functioning of internal market for medicines			X			
Ensure quality of medicines including through manufacturing rules and oversight of manufacturing and supply chain		X				
Enhance the security of supply of medicines and address shortages			X			
Provide clear and appropriate responsibilities to all actors throughout the lifecycle of medicines, including post-marketing obligations and oversight		X				
Ensure a competitive EU market for medicines			X			
Improve competitiveness of EU pharmaceutical industry on the global market				X		
Facilitate generic/biosimilar product entry to markets			X			
Enable progress in science, technology and digitisation for the development of high quality, safe and effective medicines			X			
Accommodate innovation for the development of complex and combination medicinal products			X			
Accommodate innovation for medicine manufacturing			X			
Reduce the environmental footprint of medicines				X		

Consideration shall be made regarding the detachment between regulatory decisions and actual access to market of new medicinal products – including equal access to medicines across MS.

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]

The current legislation, along with the common Guidance supported by the European Committees /Coordination Group has ensured a good cooperation among MSs in assessing and authorising medicinal products based on a coordinated approach also through drafting and releasing updated guidance and Q&As.

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]

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]

Definitions in the EU legislation may need to be revised. e.g. the definition of medicinal product pursuant to Art.1(2) a) of Dir. 2001/83, the so-called 'by presentation' approach - see below - may need a revision taking into consideration that also medical devices may have treatment and prevention claims, even though through a different mechanism of action. This has been object of Court's rulings on borderline cases.

Medicinal product:

(a)Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(b)..."

As for concerns on medical devices and in-vitro diagnostics legislation, an integrated approach to assessment/authorisation procedures would be needed, in cooperation between medicines and medical devices authorities, in particular for combined products (drug-device combination products) and borderline products.

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]

Sharing national experiences with MSs has been demonstrated to be always fruitful.

Moreover, every single national Application could become a European one via Mutual Recognition procedures. As a consequence, adopting the same principles during the assessment of national authorization procedures as the European ones is necessary.

Examples are:

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 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.

F7. Please provide an estimate of the **total additional annual costs** your organisation incurred in the financial year 2019 due to the implementation of the revised EU general pharmaceutical legislation (e.g. additional monitoring of compliance, enforcement of compliance and/or (more) reporting obligations due to the legislation).

Estimate of additional annual 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 cost savings were made possible by the legislative changes. [Open]

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F8. Please provide an estimate of **one-off adjustment costs** your organisation incurred due to the implementation of the revised EU general pharmaceutical legislation.

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

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

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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

Pro It is appealing for the industry as it may potentially offer an innovative new incentive that could provide the needed financial scale to attract new antibiotic R&D investment. It does not require upfront government funding and is not dependent on a country's current economic situation. It could be delinked from sales volumes, target appropriate use, as well as new and forgotten antibiotics, and include environment considerations.
Cons It should be designed carefully so that SMEs and small innovative R&D companies may benefit from it with only one product.
Comment It could be based on a list of eligible priority pathogens.

Additional market protection period
Pro This option could help incentive novel antimicrobial development by allowing longer development and drugs marketing periods so to earn profits with less direct competition, such as from generics.
Cons It is necessary to address the current low ROI and avoid keeping prices high for new antimicrobials.

Introduction of a 'play or pay' model
Pro In theory, the investment charge on antibiotics could encourage investment in R&D
Cons Significant drawbacks in its design, its added value and its impact on supporting novel antimicrobials development, including compared to other market incentive options.
Comment It needs to be designed carefully so it does not penalise the industry and investors while ensuring transparency at all stages.

Comple(i)mentary Advisory Role (Scientific Advice, Rolling Review, CMC assistance, lifecycle management plan support)
Pro The Network became experienced in offering these services during pandemic
Appreciation from industry
Shorter timeframe for approval
Cons Impactful on financial and human resources for the Network

Comment Develop eligibility criteria to access to CSS

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						X

coordination with other concerned authorities in particular related to medical devices and/or blood, tissue and cells (BTC) legislations						
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]

While agreeing to simplify the regulatory requirements for the authorisation of less complex cell-based medicinal products by NCAs, harmonisation is desirable to avoid less stringent countries and patients traveling as for the HE.

Exclusion of less complex cell-based medicinal products from the scope of pharmaceutical legislation is not supported and should be assessed carefully because even less complex products cannot bring benefits and expose patients to harmful products and procedures.

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

through emergencies, would better support MSs decisions in case of difficult decisions (EG the withdrawal of some COVID vaccines batches in 2021).

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]

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.

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]

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]

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]

Avoiding duplicate work by the EU assessors through the implementation of WS procedures (or single procedures) is necessary. Moreover, having the possibility to close a procedure at an earlier stage in case of incomplete MAA is also important, so not to waste EU assessors time and work . Furthermore, deleting renewals is useful, at least in case of generics.

Streamline procedures to avoid duplicative processes could contribute to enhance the efficacy of pharmacovigilance measures decreasing the used resources.

Considering the medicinal products subject to additional monitoring, the inclusion criteria, as defined "to be included in the list", could be further restricted by limiting it to medicines derived from new technologies.

Well-defined centrally criteria for the use of RWE in the pharmacovigilance process could optimize the utility of real-world evidence. Improving data reliability and quality and harmonize principles for regulatory use of RWE is needed.

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]

NN

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] **direttoregenerale@aifa.gov.it**

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'.