European Commission

COMBINED EVALUATION ROADMAP/INCEPTION IMPACT ASSESSMENT

This combined evaluation roadmap/Inception Impact Assessment is to inform citizens and stakeholders about the Commission's work to allow them to provide feedback on the planned initiative and to participate effectively in future consultation activities. Citizens and stakeholders are, in particular, invited to provide views on the Commission's understanding of the current situation, problem and possible solutions and to make available any relevant information that they may have, including on possible impacts of the different options.

TITLE OF THE INITIATIVE	*Evaluation and revision of the general pharmaceutical legislation.*
LEAD DG – RESPONSIBLE UNIT – AP NUMBER	Directorate-General Health and Food Safety, Medicines: policy, authorisation and monitoring (Unit B5)
LIKELY TYPE OF INITIATIVE	Legislative proposal
INDICATIVE PLANNING	Q4 2022
ADDITIONAL INFORMATION	https://ec.europa.eu/health/human-use/strategy_en

This combined roadmap/Inception Impact Assessment is provided for information purposes only. It does not prejudge the final decision of the Commission on whether this initiative will be pursued or on its final content. All elements of the initiative described by this document, including its timing, are subject to change.

A. Context, Evaluation, Problem definition and Subsidiarity Check

Context

The European Commission is building a stronger European Health Union, in which all EU countries prepare and respond together to health crises, innovative, safe and effective medicines are available at an affordable cost, and countries work together to improve prevention, treatment and aftercare for diseases such as cancer. On 25 November 2020, the Commission published a Communication on a Pharmaceutical Strategy for Europe. The unprecedented COVID-19 pandemic has clearly demonstrated the criticality of ensuring timely access to safe, high quality and affordable medicines at all times. The strategy is an ambitious, long-term project in the area of health. It is intended to make the European pharmaceutical system patient-centred, future-proof and crisis-resistant. The development and supply of medicines is a global operation. The EU pharmaceuticals system should ensure the quality and safety of medicines, while boosting the sector's global competitiveness and creating a regulatory environment, which is attractive for innovation and investment and supported by international harmonised standards and, where possible, regulatory convergence. As such, the strategy is a key pillar of the Commission's vision to build a stronger European Health Union.

The revision of the general pharmaceutical legislation is complementary to other ongoing initiatives in this context, such as the European Health Data Space (EHDS), which aims to provide high-quality healthcare while making the most of digital health and the work on the EU Health Emergency Preparedness and Response Authority (HERA). It also relates to the European Green Deal, notably through the impact of pharmaceutical substances on the environment. The Pharmaceutical Strategy is in line with the objectives of the Industrial Strategy, with a pharmaceutical related focus, such as the provision of an investment friendly environment for research and innovation, enabling key technologies, supporting industry and SMEs especially, creation of European Industrial ecosystems in areas of strategic importance, diversification of supply in the provision of starting and raw materials for the manufacturing of medicines. Other links include the adoption of the Health Technology Assessment Regulation (planned for 2021) which is expected to improve access by facilitating national decisions and creating a more predictable assessment process throughout the EU.

The Pharmaceutical Strategy proposes flagship initiatives and other actions to ensure the delivery of tangible results. As a part of the implementation of the strategy, the Commission is evaluating the current general pharmaceutical legislation and assessing the impacts of any changes intended to address the objectives outlined in this document.

Evaluation

In line with the 'evaluate first' principle, the initiative and the accompanying impact assessment will be based on

the findings of an evaluation which will assess to which extent the general pharmaceutical legislation (namely Directive 2001/83/EC[1] and Regulation (EC) No 726/2004[2]) has delivered against its initial objectives. Using the effectiveness, efficiency, relevance, coherence and added value criteria, the evaluation will particularly assess:

- the extent to which existing measures can still effectively reply to the problems identified within the pharmaceutical strategy, also taking into account the international context and regulatory developments globally;
- the coherence and complementarity with other related pieces of legislation, including those on medical devices, medicines for children and rare diseases, the proposal for the European Health Data Space, the EU blood, tissues and cells legislation;
- the mechanisms for the continuous and timely adaptation of technical requirements in light of emerging science and technologies; potential administrative burden and complexity linked to the implementation of this legislation.

The evaluation will cover the period from 2005 to present (date covering the last fundamental amendments to the Directive and Regulation). The geographical scope will be the EU Member States. The evaluation will not cover all the provisions of the legislations and focus on those that relate to the objectives of the Pharmaceutical Strategy for Europe and presented in this roadmap. The preliminary results of the evaluation will be used to establish the baseline situation for the impact assessment, refine the problem definition and the policy options and feed into their analysis.

Problem the initiative aims to tackle

The Commission is launching a revision of the pharmaceutical legislation to further improve its measures and address its potential weaknesses as they will emerge from the evaluation, and consider, amongst others, the following issues:

- **Unmet medical needs and market failures for non-orphan and paediatric medicines**
  There is a need to stimulate innovation and breakthrough therapies, especially in areas of unmet needs that are not covered by the rare disease and medicines for children legislation. This includes addressing antimicrobial resistance (AMR), as well as preventing excessive and inappropriate use of antimicrobials. It also includes finding the right synergies with the activities under HERA to address this problem.
- **Unequal access to affordable medicines for patients across the EU**
  Innovative and promising therapies do not always reach the patient. Due to various factors, companies market medicines differently across Europe and access can therefore vary considerably across Member States. Competition in the medicines market is at times lacking. This affects access to generic and biosimilar medicines, which in turn can have negative results on affordability for patients and health systems budgetary sustainability.
- **The legislative framework may not be fully equipped to respond quickly to innovation**
  Pharmaceutical legislation was developed at a time when certain technologies, such as genomic sequencing, genome editing technologies or artificial intelligence did not exist or were in their infancy. Likewise, technological progress is leading to the development of complex combination products. The current legislation should be fully adapted to cover new scientific and technological developments and models. In addition, for medicines that contain or consist of genetically modified organisms (GMOs), the assessment of environmental impacts should be adapted to the specific characteristics of these products.
- **Inefficiency and administrative burden of regulatory procedures**
  There may be room for simplification and streamlining of procedures and internal processes to reduce timelines and regulatory burden. The EU pharmaceuticals system needs to remain attractive in a competitive global environment, which demands regulatory attractiveness and agility while upholding the fundamental principles of safety, efficacy, quality and making sure that innovation reaches those who need it. There is also room to optimise interplay with other frameworks (such as medical devices and substances of human origin). Full use should be made of digital tools. There is a need to further strengthen the regulators' power to adapt the terms of marketing authorisations on the basis of scientific evidence.
- **Vulnerability of supply of medicines, quality, environmental challenges and sustainability**
  Shortages of medicines compromise patient health and severely burden healthcare systems and

[1] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67)

[2] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1)

healthcare professionals. The current provisions ensuring the supply of medicines can be enhanced including to ensure transparency of stocks, early notification and stronger obligation of supply so as to manage the problem. Pharmaceutical residues and pharmaceutical waste products enter the environment. Some pharmaceuticals, such as antimicrobials, are used improperly which contributes to antimicrobial resistance and environmental issues. The current legislation needs to be improved in terms of its environmental risk assessment provisions in combination with measures in advertising, prescription and packaging of medicines. The provisions relevant for manufacturing and quality control should be assessed in light of the developments of production technologies. Finally, the oversight of the supply chain and responsibility of actors could be improved to increase transparency, ensure the quality of medicines and strengthen security of supply.

- Any other issues, which might emerge from the evaluation.

Basis for EU intervention (legal basis and subsidiarity check)

Legislation regulating medicinal products is based on Articles 114 and 168(4)(c) of the Treaty on the Functioning of the European Union (TFEU). As a shared competence with Members States and in line with the principle of subsidiarity, Article 168(4)(c) of the Treaty allows the Union to set measures establishing high standards of quality and safety for medicinal products. The authorisation of medicinal products is fully harmonised at EU level. EU action takes advantage of the single market (Article 114) to achieve a stronger impact as regards access to safe, effective and affordable medicines, as well as the security of supply across the EU. Uncoordinated measures by the Member States may result in distortions of competition, barriers to intra-Union trade and shortages. A Union approach also provides greater potential for incentives for development in the area of unmet needs. EU-level measures are best placed to address such issues effectively. These could bring significant efficiencies for Member States, avoiding the need for multiple exercises in risk, benefit and cost analysis.

B. Objectives and Policy options

As part of the Pharmaceutical Strategy for Europe and the European Health Union and in line with EU's industrial, green and digital ambitions, this initiative will be driven by the following **objectives**:

- Ensure access to affordable medicines for patients, and address unmet medical needs;
- Enable innovation for the development of high quality, safe, effective medicines, harnessing the benefits of digital and emerging science and technology while reducing the environmental footprint;
- Enhance the security of supply of medicines and address shortages;
- Reduce regulatory burden and provide a flexible regulatory framework.

The policy options on the following elements will be developed on the basis of the evaluation findings and analysed in the impact assessment. In order to address the policy problems identified, the Commission will consider different sets of measures, which will contribute to supporting the international competitiveness and innovative capacity of the European pharmaceutical industry.

Baseline scenario: No changes to the current regulatory framework - The established system of incentives remains in effect and is only affected by possible changes in related policy areas such as the intellectual property regime. The existing provisions on generics and biosimilars access remain in effect. Future medicinal products will continue to be assessed on the basis of established rules and pathways relying on guidance and interpretation of existing provisions. The existing challenges in terms of adapting promptly to possible scientific advances and novel products will remain, as the system will have to rely on current rules. Obligations on marketing authorisation holders in terms of making authorised products available on the market and securing supplies remain unchanged, as guidance cannot change legal obligations. The identified problems will continue and may even exacerbate. Achieving the above objectives on the basis of the current legislation can prove challenging.

Elements to be covered by policy options:

a) Reach a common understanding (either criteria based or through a definition) on the notion of '**unmet medical needs'** building on the relevant discussion taking place in the field of medicines for children and rare diseases and discussions with public authorities responsible for health technology assessment, pricing and reimbursement;

b) **Simplify legislation and create regulatory attractiveness** with the aim to reduce, where possible, regulatory approval times and regulatory costs while keeping the high standards of robust assessment of quality, safety and efficacy. Provide regulatory authorities the possibility to adapt on their own initiative the terms of marketing authorisations on the basis of scientific evidence will also be considered. Improvements can be considered both in terms of administrative process and scientific assessment. Potential synergies with downstream decisions will be considered. Possible measures will seek to leverage digital technology and the use of electronic product information;

c) Revise the **system of incentives** aiming to ensure options that attract and promote innovation, especially in

areas of highest medical need, and establish a tailored system of incentives that links rewards with possible obligations, including the placing on the market of the products in most/all Member States, or more transparency on R&D costs. Options shall explore novel incentives that complement or replace or adjust the market protection (or a combination thereof) taking into account the relationship with intellectual property rights;

d) Consider the creation of specific incentives to promote the development of new classes of **antimicrobials** in combination with rules aiming to promote their prudent use and measures aligning use to patient needs, such as reduction of package sizes;
e) Examine ways to increase the **support and accelerate product development and authorisation in areas of unmet need** through the incorporation of the European Medicines Agency's (EMA) priority medicines scheme (PRIME) or similar mechanisms in the regulatory framework and consider measures supporting academic research and SME involvement;
f) Introduce elements of flexibility that allow **future proofing of the legislation** through adaptability to the new innovative ways medicines are developed and evidence is generated. This should take into account new possibilities in areas such as digital and personalised medicine and the interplay of medicines and medical devices. Options shall consider adaptations to the current system of authorisations, the possibility of new regulatory pathways, the possibility to change the scope of the centralised application procedure for innovative products, as well as other adaptations of the regulatory requirements including for medicines containing GMOs;
g) Improve the provisions relevant to **competition considerations** especially as regards aspects that impact the **generic/biosimilar** competition, faster market entry of competitor products and eventually affordability. Options shall include provisions on conducting clinical trials on patented products to support generic and biosimilar marketing authorisation applications, the so-called 'Bolar' exemption. In this context it shall also cover options on revising the provision on duplicate marketing authorisations;
h) Provide for a single assessment process across Member States for active substances used for different generic medicines (**active substance master files**) to facilitate their authorisation and life-cycle management;
i) Enhance **security of supply** through stronger obligations for supply and transparency, earlier notification of shortages and withdrawals of medicines, enhanced transparency of stocks and stronger EU coordination and mechanisms to monitor, manage and avoid shortages;
j) Improve the transparency and **oversight of the supply chain** in particular as regards international supply chain aspects, by revising the **manufacturing and distribution** provisions in the pharmaceutical legislation and clarify responsibilities to safeguard the quality of medicines. Ensure preparedness for new manufacturing technologies;
k) Enhance **environmental** sustainability of the production, use, disposal of medicines and strengthen the environmental risk assessment requirements to ensure the support for greener manufacturing. Assess how environmental considerations are taken into account in the advertising and prescription of medicinal products and improve the responsibility of actors to ensure the quality of medicines, to also address the transparency of the environmental information;
l) Addressing where needed any structural challenges for an efficient **crisis management** complementing the reinforced role of the European Medicines Agency (EMA) in times of crisis, in particular in case of pandemics;
m) Review the role of EMA in relation to related bodies and authorities and the governance provisions of the Agency where necessary;
n) Non-legislative instruments aiming at improving implementation of existing EU legislation through guidance and soft law, which will be applied on a voluntary basis.

The policy options will be developed on the basis of the above elements and the evaluation findings.

C. Preliminary Assessment of Expected Impacts

Likely economic impacts

The impact on the European economy as a whole is expected to be a positive one. Elements such as regulatory flexibility to accommodate swiftly emerging scientific and technological developments, the ability to use new evidence generation tools and simplification will make the EU more attractive for investment and marketing of innovative medicinal products. A more tailored system of incentives to increase access and innovation for unmet needs will promote private engagement in areas where the market does not attract investment. Furthermore, adapting incentives in areas where the market attracts investment and return of investment is ensured will allow for earlier competition by competing products, which is expected to reduce pharmaceutical costs. The measures promoting market launch of medicines are conducive to the achievement of the Single Market in the area of medicines and take full advantage of the possibilities given by the central marketing authorisation. The long-term positive economic effects to the global pharmaceuticals market are likely to counterbalance the initial one-off negative economic impact created by additional obligations to operators.

A faster generic/biosimilar competition is expected to have a positive economic impact on the financial and fiscal sustainability of EU Member State health systems and a positive impact on household medicines budgets, as they are likely to decrease the overall financial burden for medicines procured by national health systems in the medium-term. This positive effect is likely to be reinforced by the simplification of legislation, as it will allow for reduction of administrative burden for companies and regulatory authorities in the long-term. Elements relating to security of supply are likely to have a positive effect on indirect economic costs relating to cost of no treatment due to shortages of medicines, but may increase the fixed costs of the pharmaceutical sector due to increased operating costs, which can eventually spill over in prices.

The economic benefits to the European pharmaceutical sector in terms of reduction of administrative burden will be further enhanced through the future-proofing of the legislation and new possibilities for accelerated product development. Regulatory flexibility to use improved evidence generation techniques throughout the lifecycle of a medicine through the possibility to use real word data and artificial intelligence (AI) applications for evidence generation with the possibility to adjust decisions based on new evidence. **SMEs** stand to gain most from a simplified regulatory system and flexibilities related to modern developments. Start-ups and small companies are often responsible for basic R&D and are expected to benefit from a simpler regulatory environment.

Likely social impacts

The targeted introduction of public service obligations (such as an obligation to make products accessible when an enhanced incentive is used) and tailored incentives would be expected to have a positive effect on the availability and accessibility of therapies for patients across the EU. These effects would be combined with competition gains, which, as explained above, would help reduce the cost of medicines and have a positive impact on health expenditure. The provisions enhancing the security of supply would enhance social protection and assist health systems to provide society a stable supply of critical medicines. Elements relevant to flexibilities related to future-proofing legislation would allow the EU pharmaceutical system to be up-to-date and ready to deal with modern solutions that would in turn be made available and placed to the service of society.

The above is likely to contribute to societal spill over effects in terms of healthy life years, opportunities of employment, social inclusion and benefits for patients and their caregivers.

Likely environmental impacts

Implementing policy options as regards the manufacturing and supply provisions in the pharmaceutical legislation to reinforce oversight of the supply chain, transparency of the environmental information and clarifying responsibilities to ensure environmental sustainability, in combination with a revision of the rules on environmental risk assessment requirements and conditions of use of medicines, would lead to environmentally safer production, use and disposal of medicines. This would have a positive effect on the environment itself, as it would contribute to a reduced presence of pharmaceutical residues and waste residues in the natural environment and protect biodiversity and ultimately human health via the environment. Options aiming at the reduction of use and prudent use of antimicrobials would contribute to the fight on antimicrobial resistance as well as address the AMR challenges in the environment. These outcomes would contribute to the European Green Deal, the Chemicals Strategy, Zero Pollution Ambition and Industrial strategy.

Likely impacts on fundamental rights

This initiative aims to improve access to and availability of medicines as well as the environmental protection. As such, it is expected to have a positive impact on access to medical treatment and contribute to the improvement of health protection and environmental protection as described in Articles 35 and 37 respectively of the Charter of fundamental rights of the EU.

Likely impacts on simplification and/or administrative burden

The impact on administrative burden will be assessed as part of the policy options considered. Specifically, the reduction of administrative burden through simplification of legislation and the possibility to use digital technology in medicines regulation and information to patients and healthcare professionals will be a part of the basic scenario for any option considered.

D. Evidence base, Data collection and Better Regulation Instruments

Impact assessment

The impact assessment will build on the preliminary results of the evaluation to assess the economic, environmental and social impacts of the proposed measures under each of the policy options considered to provide a patient-centred, future-proof and crisis-resistant regulatory framework. It will support the preparation of

this initiative and will provide a robust evidence base for the content of the legal proposal(s). The options considered in the impact assessment should be consistent with the outcome of the evaluation findings. The impact assessment will quantify, as far as possible, the costs and benefits of the changes described in the options considered. It is expected to run until Q1 2022. In undertaking the analysis of impacts for all the involved stakeholder groups (e.g. stakeholders, national and local competent authorities, EU citizens etc.) the impact assessment will make best use of all available Better Regulation tools.

Evidence base and data collection

A study will be commissioned to support the evaluation and impact assessment process. It will be used to source additional evidence on the costs and benefits of the different policy options outlined. It will provide data on expected impacts.

The analysis will take into account qualitative and quantitative data obtained through a stakeholders' consultation, desk research and literature review as well as data collected in existing studies and reports, an indicative list includes:

- Study on shortages of medicines (forthcoming)
- Studies on performance of pharmaceutical acquis, complementing data gathering activities supporting policy development and related initiatives to the pharmaceutical framework (planned)
- Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe
- Study to support the evaluation of the EU Regulation on orphan medicinal products
- Study on experience acquired as a result of procedures for authorisation and monitoring of medicinal products for human use (forthcoming)
- Study on market sales data (forthcoming)
- Study "Options for a strategic approach to pharmaceuticals in the environment" 2016
- Studies on the package leaflets and the summaries of product characteristics, on the feasibility and value of a possible "key information section" in patient information leaflets and summaries of product characteristics of medicinal products of human use and related Commission report.

The Commission will also use several analyses and reports from EMA and other regulators on the performance of the system.

Additional studies may need to be conducted to further inform the evaluation of the current pharmaceutical legislation and to establish the baseline upon which policy options have to be assessed. The methodology used in the evaluation/impact assessment will follow the guidance provided in the Better Regulation Guidelines and Toolbox. The most significant environmental, social and economic impacts of the options under consideration will be assessed and compared.

Consultation strategy

A thorough stakeholder consultation process will underpin the policymaking process. Interested parties will be consulted through a mix of public and targeted consultations. Targeted stakeholders will include the EMA, national competent authorities, pharmaceutical industry (including SMEs), civil society representatives (e.g. patients, public health organisations) and healthcare providers (e.g. professional associations). The Commission will make use of its consultative committees and expert groups and will organise meetings, which will include policy makers and representatives of the parties concerned.

A public consultation for citizens and all stakeholders will be launched during the second half of 2021 and will run for a period of 12 weeks. The questionnaire will be available in all official EU languages and replies can be submitted in any EU official language. The consultation will be accessible from the Commission's 'Have Your Say' portal.

A synopsis report on all consultation activities will be published on the consultation webpage together with the result of the assessment of impacts.

Will an Implementation plan be established?

The revision concerns a Regulation and a Directive. The final form of the legislative instrument(s) is yet to be decided. The development of an implementation plan will depend on the final decision.