Medicines for Europe Factsheets on
Evaluating the impact of international trade on access to medicines

Medicines for Europe is committed to improving access to medicines for all Europeans. Yet, many patients across Europe face restricted access to medicines which undermines public health. The 2019-2024 EU legislature should reshape pharmaceutical policy by prioritising **equitable access to essential medicines** for all Europeans. Equitable access is an achievable goal as the majority of essential medicines are already generic or biosimilar medicines.

As a global leader, the EU should take a strong position in defending open markets for medicines in trade agreements and lead on cooperation between regulatory bodies.

It is also necessary to coordinate on regulatory standards, thus avoiding unnecessary, and therefore unethical, clinical bridging studies. It will also eliminate the multiplication of the same bridging studies by different sponsors, support true global development, reduce development and approval timelines and thereby improve patient access and affordability for health systems overall and increase competition.

This document develops Medicines for Europe key priorities that should be reflected in the Pharmaceutical Strategy for Europe.

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1. Manufacturing and open strategic autonomy

Background Description of the issue

Europe has a strong and competitive pharmaceutical industry. Together with other public and private actors, it serves public health and acts as a driver of job creation, trade and science. . Our industry supplies close to 70% of prescription medicines in volume and employs close to 200000 highly skilled employees across over 400 factories and R&D centres in almost every country of the Union. The Pharmaceutical Strategy for Europe should build on these foundations to encourage more investment in manufacturing.

For many years, Medicines for Europe has been advocating for a more competitive framework for the manufacturing of medicines in Europe. The Commission is driven by the concern over Europe's increasing dependence on China and India for key aspects of medicines manufacturing.
The available data does confirm a considerable shift in API production from Europe, which used to be known as the pharmacy of the world, to Asia over the last 20 years. An examination of EDQM data on certificates of suitability (CEPs) shows that 62% originate from India and China. GDUFA (US law on generic medicine fees) shows that India has the most API manufacturing sites approved to supply the US but Europe (including Switzerland) is actually in second place whereas China is a smaller player. On the positive side, Europe still has a considerable manufacturing presence of both API and finished dosage forms according to EDQM and FDA data. Also, an in-house survey at Medicines for Europe related to API manufacturing showed that our members still have almost 58% of the API in house facilities located in the EU.

There is still a strong manufacturing base in Europe to boost our competitiveness with supportive policy measures, but these measures need to be seen from a global supply chain perspective. Such a global supply chain can come under pressure due to pricing policy pressures, FMD, administrative variations and costs, GMP topics included into regulatory dossier leading to drop out of suppliers/manufacturer and hence consolidation which increases the risk of shortages.

The European Commission has approved a robust funding Plan to boost the recovery after the Covid virus crisis, there could be several opportunities for our industry indirectly via plan agreed with national Governments through the Next Generation EU, but also via directly industry participation in the EU4Health program that will finance actions aimed at (1) Overcoming health inequalities, (2) Improving crisis preparedness, (3) Strengthening EU manufacturing, (4) Innovating in the off-patent sector, (5) Addressing environmental challenges, (6) Leading the digital transformation of health systems.

Policy recommendations:

1) **Regulatory optimisation and enforcement** needed to reduce the cost burden associated with the filing and maintenance of regulatory files of API and medicines production by:
   - ⇨ Taking GMP controlled information out of the regulatory dossier will increase adaptability, agility and resilience. Supply Chain Oversight maintained towards regulators via IT solutions, databases to achieve a leaner approach to the transparency of supply chain functions and actors.
   - ⇨ Reducing administrative variations to be prepared and filled= lowering the costs
   - ⇨ Including of multiple API sources into the approved dossier: Incentives or regulatory flexibility to lower fees, to bring this security into the supply chain
   - ⇨ Stricting GMP enforcement in unregulated markets which do not enforce GMP locally.

- ⇨ supporting the digital transformation of healthcare systems or development of European monitoring, reporting and notification system for shortages of medicines and medical devices.
- ⇨ strengthening the manufacturing including the production of antimicrobials and essential APIs; diversifying supply chain production of active ingredients and generics within the Union to reduce the Member States' dependence on certain third countries;
- ⇨ Supporting actions to improve the environmental-friendly production and disposal of medicinal products and medical devices and support the development of medicinal products that are less harmful to the environment;
- ⇨ supporting actions that foster the production, procurement and management of crisis relevant products within the Union, ensuring complementarity with other Union instruments, to mitigate the risk of shortages.

2) **Integrating security of supply into market policies**:
   - ⇨ Considering incentives for products where there is limited competition
   - ⇨ Incentivise API production in Europe with measures such as R&D investment tax deductions
   - ⇨ Priority review and fee waiver for the introduction of API where an EU manufacturer would intervene in a shortage.
   - ⇨ Incentives to develop value added APIs
   - ⇨ Regulatory recognition of companies that choose to invest for EU security of supply
   - ⇨ Changes to EU procurement: The Commission could introduce guidelines on medicines procurement to include security of supply criteria – provided this is objective and based on open markets.
   - ⇨ Where substantial manufacturing investments would need to be made to increase the security of supply there could be a regulatory mechanism to trigger a price review at a national level for regulated (price reference) markets.

3) Funding: EU4 Health and recovery and resilience facilities
   - ⇨ Grants may be used in combination with financing from the European Investment Bank, national promotional banks or other development and public financial institutions, as well as in combination with financing from private-sector financial institutions and public or private sector investors, including through public-public or public-private partnerships.

2. Off patent competition global development

Problem statement:

Competition in the off-patent market is a major driver of greater access to important medicines for public health. Regulatory processes and requirements directly impact competition as requirements for marketing authorisation influence both development timelines and resources involved. The off-patent industry is largely global. Regional requirements and disparities further negatively affect development timelines and the resources involved.

Global development is a cornerstone of streamlined product development. It is essential for competition, especially for complex products. Conducting multiple clinical development programs for comparison with local reference products is not only time and resource-consuming, but also unethical, as it involves superfluous experimenting in human subjects with no added benefit.

Overall, this results in higher resource investment, extended timelines and delays in broader patient access to comply with these regional requirements.

Policy Recommendations

Generic medicines aspects	Orphan biologic aspects
Ask: We call on the EU to take a leadership role in the development of strategies that may allow the use of foreign comparator products consistently across all medicines, which, together with the harmonisation of the scientific bioequivalence principles at ICH, will permit to pursue single global development for generic medicines. This will contribute to timely and efficient competition in the generic market and greater access to generic medicines. Background: Acceptability of the use of foreign comparators may be especially relevant in the cases where clinical development requires complex studies or studies in patient populations: under the current approach, for example for bioequivalence studies in patients, developers are sometimes required to prioritise development for one region over others in order not to compete in terms of recruitment. These delays access to affordable medicines to patients and decreases 1) Regulatory aspects For generic products, single global development depends on the harmonisation of scientific principles and acceptance of foreign comparator products in bioequivalence studies. International	Ask: We call on the EU to take a leadership role in designing a fit-for-purpose off-patent medicines global regulatory framework for the life-cycle of orphan and small population medicines: true global development should be enabled through acceptance of foreign reference data without bridging data, global convergence towards the scientific principles to streamline clinical comparability. This is essential to develop greater equity in access to these essential therapies. Background: By 2028, a total of 28 biologic orphan medicines will be eligible for biosimilar competition. However, the majority of orphan medicines do not have a follow-on product in clinical development. Only 11% of orphan biologic molecules have a biosimilar version in clinical development, as opposed to 23% for total biologic medicines. The development of follow-on products for these medicines certainly requires different approaches, as current biosimilar pathways did not foresee some of the challenges ahead. • Sourcing comparator product is restricted due to specific access schemes, small volumes, fewer product batches and prohibitive acquisition costs.

harmonisation of scientific principles to establish bioequivalence has already started at the International Council for Harmonisation (ICH). Generic medicine developers are generally expected to run multiple clinical development programmes that require comparison with local reference products. This means that multiple clinical studies are required, even if the reference product is the same in different regions. For biosimilar products, however, it is already acceptable to use comparator products from foreign sources. 2) Single global development in originator product development Single global development is the standard approach for the development of new originator products. As these are authorised, their clinical package is typically the same across highly regulated regions, where similar quality standards are also followed. Therefore, in many cases, it may be assumed based on certain analyses, that the reference products from different regions are actually the same product, making the repetition of the clinical development programme or other comparability exercises multiple times to compare with local references, unnecessary. 3) Acceptability of foreign comparators in other jurisdictions For the single global development of generic medicines to become a reality, acceptance of foreign comparators is required. This is not yet possible for generics in Europe although it has become very common e.g. biosimilar medicines development*. However, other highly regulated regions already accept the use of foreign comparators (including but not limited to the UK, Switzerland, Singapore, and Canada). These regions have developed methodologies that allow establishing under	• Clinical comparative studies may not be feasible. In particular, patient recruitment into studies may prove extremely slow given the low incidence of the disease, considerably slowing down the development. In addition, a recent consensus is emerging on the need for clinical comparability requirements to be waived as default requirements • The originator followed a global development pathway and was incentivised to mitigate and/or overcome the inherent hurdles to this field.

* EMA P. Richardson (2015 – Bioimilar medicines Conference) - "Global development approach – foreign comparator - proposed in 75% of the scientific advice requests for biosimilars in 2014"

which circumstances foreign comparators can be used (and from which territories), providing ideal conditions for thriving generic competition. competitiveness, given that, to optimise resources, developers may opt to develop their products only for some of the regions. This could also play an important role in the development of generic versions of orphan drugs where development resources need to be used in an especially efficient manner.	

3. WTO Supply chain agreement

Background

The pharmaceutical sector supply chain is complex and global. The covid-19 crisis has shown the importance of a well-functioning global medicine supply chains and the industry has undertaken a sustained global effort to ensure continued access to medicines for patients throughout the crisis.

As underlined in the EU Pharmaceutical Strategy published on 25 November 2020, the Commission intention is to initiate a structured dialogue with the main actors of the pharmaceutical sector and it is willing also to *"work directly with WTO members on an initiative that would aim to facilitate trade in healthcare products and contribute to an effective response to a health emergency. Such initiative would help to strengthen the resilience and robustness of supply chains in the EU and in all other WTO partners."* Moreover, the Commission is also ready to: *"Promote WTO-based actions to increase the resilience in global supply chains in essential goods."*

Recommendations

Establishing a well-coordinated dialogue between the industry and WTO partners would be beneficial as often Institutions are not up to date about the complexity of manufacturing supply chains. In addition, thanks to a structured exchange it should be easier to identify a potential lack of diversity of the certain region to the supply of essential medicines and Active Pharmaceutical Ingredients (APIs). Given the important health and trade dimensions of this exercise, the WTO and the WHO should cooperate on this initiative to promote global solidarity and international cooperation. However, by undertaking this kind of initiatives it is important to bear in mind the following key elements:

- Understanding supply chains: an important first step of any agreement should be to understand the nature of pharmaceutical manufacturing supply chains across different segments: solid oral dose production (pills/capsules), sterile/aseptic production (injectable hospital medicines) and more complex medicine forms (biologics, vaccines, drug-device combinations). **Regulatory Convergence and Good Reliance Practices in Regulatory Decision-making for Medicinal Products:**
    - Foster regulatory international collaboration which plays a key role in strengthening the efficiency and effectiveness of regulatory authority bodies
    - Reduce or eliminate regulatory and other technical barriers
    - Promote the use of good regulatory practices and streamlined regulatory review
    - Eliminate duplicate actions and other barriers to reduce the time for approvals of both facilities and pharmaceutical products
    - Build trust and expand transparency, information-sharing and cooperation with participating governments and authorities
    - Encourage the negotiation of bilateral or plurilateral Mutual Recognition Agreements (MRAs) for Good Manufacturing Practices (GMPs)
    - Promote stronger regulatory cooperation in FTA negotiations
- **Tariffs:** eliminate tariffs on imports of pharmaceutical products and APIs.
- **Prevent protectionist measures:** The threat or use of export restrictions in various guises during a health crisis exacerbates panic in pharmaceutical production and markets and undermines the global solidarity that is often needed to overcome a global crisis. This was clearly the case for therapeutics and vaccines during the Covid-19 pandemic. While it may be necessary for governments to assist manufacturers in scaling up production and to ensure appropriate allocation to patients (instead of hoarding) in a crisis,

there should be a clear proportion in interventions that re-direct production to serve home markets rather than global markets. Conversely, there should be counterweights to attempts by wealthier nations to hoard available supplies (wherever they are produced) at the direct expense of patients in less wealthy nations.

4. EU-US GPA and Single Development

Europe and the United States have a longstanding cooperative relationship with pharmaceuticals. Among other things, the two countries are part of the WTO Government Procurement Agreement (GPA), which facilitates reciprocal access to markets. Last August the US published an executive order which threatened the application of the WTO GPA agreement. On 21 April 2021, the US Government amended its policy to maintain its commitments under the WTO GPA agreement.

In addition, EU and US regulatory authorities cooperate through a Mutual Recognition Agreement on GMP inspections and have aligned a single development programme for biosimilar medicines with aligned Biosimilar Guideline/Guidance. Based on this positive experience, we strongly believe that regulatory cooperation should be extended to a single development for complex generic /hybrid medicines.

Single development is a cornerstone of streamlined product development. It is essential for competition, especially for complex products. Conducting multiple clinical development programs for the purpose of comparison with local reference products is not only time and resource-consuming, but also unethical, as it involves superfluous experimenting in human subjects with no added benefit. Overall, this results in higher resource investment, extended timelines and delays in broader patient access to comply with these regional requirements. Single development could be a stepwise process: first, there could be alignment on the use of reference product from either market; second, there could be alignment on regulatory guidelines/guidances specific to different product types – notably for scientific and clinical requirements.

Recommendations to strengthen EU-US collaboration: