26 April 2021

# Revision of the EU general pharmaceuticals legislation

# EFCG analysis and proposals

## INTRODUCTION

**EFCG, the European Fine Chemicals Group, represents European manufacturers of APIs, excipients and fine chemicals. As producers of the essential building blocks used to make medicines, we welcome the Commission's initiative to ensure a future-proof and crisis-resistant medicines regulatory system that will allow all EU citizens full and equal access to safe, state-of-the-art therapies**.

The European Commission's Pharmaceutical Strategy aims to ensure the availability and affordability of medicines and medical technologies for citizens as well as fostering innovation, adapting to new scientific and technological developments. It highlights the need to build a holistic, forward-looking EU pharmaceutical strategy that covers the whole lifecycle of pharmaceutical products.

We salute and support the Commission's intention to achieve this goal whilst ensuring the highest possible quality, environmental and safety standards and maintaining the competitiveness at global level of the European-based industries.

To guarantee European patients **Accessible, Affordable and Available medicines**, we need to rely on a robust and resilient supply chain. Over recent years, structural shortages of medicines have been building up, as a consequence of weaknesses in the supply chain. The recent Covid-19 pandemic only exacerbated this existing problem, highlighting the urgent need to significantly improve the robustness of the pharmaceutical supply chain and allowing the identification of its vulnerabilities.

Whilst APIs for innovative drugs are mainly sourced from Europe, more than two-thirds of APIs for generic drugs are sourced from Asia. Moreover, for both innovative and generic drugs, three-quarters of starting materials or critical process chemicals are sourced from Asia.

Our European companies already produce the essential building blocks for innovative and generic medicines, operating within the strictest and highest quality, security and environmental standards. They can adapt to variations in demand, whilst maintaining these high standards. We firmly believe that in order to attain its ambitious pharmaceutical strategy goals, Europe should rely on its existing manufacturing capabilities and rely on its its innovation capability and its highly skilled workforce to reduce its dependency on imports from third countries, especially in times of crisis, where short reaction times are needed to cope with peaks of demand.

We therefore propose an approach that leverages EU manufacturing capabilities and relies on processes that are sustainable, innovative and up to EU environmental, safety and quality standards.

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Our proposal aims to:

1. **Support the existing European manufacturers of APIs and intermediates** in the on-shoring of essential technologies that will guarantee the supply of essential medicines.

2. **Level the playing field** with other world regions to ensure that criteria as important as the security of supply, process safety and respect for the environment are also considered for the purchase of products. Linking the supply of critical supplies to the sole criteria of price cannot be a sustainable supply strategy. Therefore, for EU joint procurement and public tenders, the implementation of sustainable supply practices that comply with European standards in terms of quality, safety and respect for the environment should be imposed.

3. **Implement a long-term EU industrial policy** that can accelerate sustainable Research, Development and industrialization of innovative and green technologies, as well as manufacturing capacities within the EU territory.

# EFCG DETAILED PROPOSALS

## 1 – BUILDING ROBUST SUPPLY CHAINS

A robust and reliable supply chain is one that reduces the EU's dependence on third countries and is built on resilient, responsive, competitive and sustainable manufacturing capabilities in Europe.
This should allow the fulfilment of patients' needs and allow them uninterrupted access to the supply of essential medicines. Even in case of unforeseen events, the adjusted demand should be met within a short period of time.
An essential part of the pharmaceutical strategy should be to promote and enforce a level playing field, whereby companies exporting APIs to Europe are subject to equivalent/mutually recognised regulations for quality, process safety and protection of the environment.

**Analysis of the situation:**

- **Robust** supply chains must rely on robust, reliable, competitive and sustainable manufacturing capabilities that can deliver at any time and over the long-term

- **Reliability** entails that the supply of API and excipients can be ensured without interruption despite unforeseen events.
  In order to meet this criterion, supply chains should be built to allow demand to be fulfilled from multiple independent points of supply in different geographic regions including, where possible, a minimum European requirement.

- **Responsiveness:** Changes in demand can be addressed on short notice by ramping up production.

  In order to meet this criterion, a multipurpose industrial infrastructure is necessary, with the ability to respond quickly to changes in the nature of demand, i.e. different APIs can be manufactured flexibly on multipurpose plants in a seamless way.

Access to a broad portfolio of essential chemical technologies is a prerequisite – these technologies act as platforms for multiple key precursors required in modern API chemical synthesis.

- **Sustainability** also entails the **long-term profitability** of the supply chains, with sufficient margins and investments to maintain in Europe the manufacturing capabilities over the long term and to develop new technologies with lower environmental impacts.

- **Product quality:** the quality of API and excipients should meet global standards, regardless of their origin.

- **Operational efficiency:** This is the basis for fast, cost efficient and environmentally sound manufacturing processes.

**Recommendations for a robust and reliable supply chain**:

- **Regulatory standards:** A **level playing field** should be achieved whereby regulatory requirements such as environmental, safety, security of supply and quality standards should be comparable worldwide.
  These regulatory standards should have built in flexibility, allowing any shortages or surges in demand to be swiftly addressed.

- **Security and integrity:** Supply chains should be built to allow demand to be fulfilled from multiple independent supply nodes, preferably geographically diverse.

- **Innovation:** Innovation and the industrialisation of breakthrough technologies are indispensable to re-establish critical manufacturing technologies that are needed for the manufacture of essential medicines. These technologies and manufacturing processes should combine competitiveness, sustainability, quality and meet the highest environmental standards

- **Transparency** of the supply chain of medicines should be guaranteed all the way up to the registered starting materials of the API and excipient, as this will help to identify potential vulnerabilities.

- **Financial sustainability:** API and excipient production have to be economically sound to ensure business continuity and willingness to invest in robust supply chains.

## 2 – IDENTIFYING AND OVERCOMING VULNERABILITIES AND DEPENDENCIES OF SUPPLY CHAINS

European medicines supply chain depends for more than 74% on supplies sourced from Asia. Europe's strong dependence on other world regions poses an unacceptable risk for the European healthcare system with increased occurrences of shortages of essential medicines in Europe.

**Analysis of the situation:**

- A significant number of raw materials produced in Asia enter in a multiplicity of APIs and medicines. As a result, the technologies used to produce some of these raw materials were divested and are no longer mastered in Europe.

- **Vulnerability is a direct consequence of our dependency** from China & India where there is no guaranty of sustainability of supply due to e.g.:
    - Raw material, intermediates and APIs producers operating under high EHS risk that can lead to production outages or plant closures,
    - Increasing risk of a political decision from the powers in place to secure or favour their own local pharmaceutical market, resulting in import limitations.

- As a consequence, most of the other regions (US, Japan and even China and India) have taken specific measures to drastically reduce their dependence on other regions.

**Recommendations:**

- **Reduce the dependency** of EU supply chains on Asian suppliers.

- **Reinforce the requirements of health authorities in terms of security of supply of essential medicines** and reduce to the strict minimum sourcing from producers who cannot guarantee reliability of supplies.

- Develop an economic framework that **promotes European-based manufacturers** by ensuring that the EU demand of essential medicines is partially covered by medicines, active ingredients and precursors manufactured in the EU.

- **For public tenders**, impose wherever possible at least one EU producer to be retained for each public tender and/or demand a commitment on security of supplies for each chosen supplier.

- **Impose the implementation of sustainable supply practices** that comply with European standards in terms of quality, safety and respect for the environment. Suppliers from other world regions should be made to comply with the same rules as European manufacturers, in terms of quality of products, safety of processes and workers, environmental standards and social responsibility.

- EU authorities will have to impose **stricter controls for the entrance of medicinal products** on EU territory and **reinforce controls and inspections** on non-EU manufacturing sites.

- Introduce wherever possible procedures to **reduce red tape**, always in full respect of the strictest EU quality and safety standards. Long procedures discourage change and increase vulnerability.

All these actions should be supported by EU regulators in order to give priority to safe sources and be accompanied by appropriate communication to patients.
Customs should put in place the appropriate import standards based on EHS criteria.
Health regulators should implement or apply qualification processes that foster relocation actions linked to strategic medicines.

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## 3 - IDENTIFY MEDICINES CRITICAL TO PUBLIC HEALTH AND LINK TO MANUFACTURING CAPABILITIES

### 3.1 IDENTIFICATION OF CRITICAL MEDICINES

Europe needs to define, validate and regularly update a list of essential medicines, for which long-term supply must be guaranteed. This list in turn has to be linked to the respective manufacturing capacities and technologies.

**Analysis of the situation:**

- Building resilient supply chains for essential molecules is key for the European Health industry
- A special focus on essential molecules is key to ensure their long-term supply
- Such essential molecules must not be limited to "critical" or" life-saving" drugs for the following reasons:
  - The consequences of the shortages are not only limited to life-saving drugs
  - Needs evolve and some drugs may become lifesaving drugs in the future.
  - The capability to produce strategic molecules is key to maintaining the competences and skills to manufacture drugs in Europe.

**Recommendations:**

- **A centralised coordination** at EU-level of the list of medicinal drugs critical for public health.

- **Objective criteria** for establishing the list, such as:

  - **Level of therapeutic interest**: identify therapeutic areas that are critical or require urgent development (as was the case for medicines to treat COVID and its consequences), taking into account both the therapeutic criticality of the drug for the patient, the existence of alternatives on the market that are equivalent in terms of efficacy and cost and also the number of patients using it.
    Ideally, the focus should go **beyond the current pandemic** in order to future-proof Europe against any future crises. The therapeutic areas proposed below can serve as an example and thought-starter.

  - **Existence of shortages**: identify molecules for which the supply suffers from structural irregularities, in particular for production or quality reasons that may result from failures throughout the value chain.

  - Create a European registry for "Medicines Shortages" and secure a **centralised coordination** for the European medicine shortages

  - **Lack of sufficient production in Europe**: determine the molecules that place the EU in a position of strong dependence on non-European countries, either because of the absence of European producers or because of a strong concentration on a small number of non-European producers. For this, the CEP database, kept by EMA and referencing the valid CEPs per API, can be used.

- **Category of technologies used**: the analysis of technologies used in production makes it possible to assess the risk of supply disruption in the short or medium term.

- **Continuous monitoring** and assessment of any risks of supply disruptions over the value chain in the short to medium term should be ensured.

**Thought starter: a possible list of critical therapeutic areas**

- Treatments for chronic illnesses, including antidepressants, antipsychotics, antiepileptics, treatments for asthma, metabolic diseases (Diabetes, NASH), Parkinson's, hypertension and cardiovascular diseases,
- Anticancer drugs and, more generally, all the molecules used in cancer treatment protocols;
- Antivirals, whether they are mature antiviral molecules or new candidates for the treatment of viruses,
- Antibiotics,
- Antifungals,
- Anaesthetics and more generally all the molecules used in resuscitation or anaesthesia,
- Analgesics, whatever their mode of action,
- Antibacterial and antiparasitic agents,
- Anticoagulants,
- Gastrointestinal and metabolic agents,
- Nervous system,
- Respiratory system,
- Anti-inflammatory,
- Orphan drugs,

### 3.2 METHODOLOGY TO TRACE EU MANUFACTURING CAPACITY FOR CRITICAL PRODUCTION

Existing European intermediates and APIs manufacturers, with their hundreds of existing manufacturing sites across Europe, are the ultimate guarantees of Europe's health autonomy. They provide critical molecules along the value chain of essential medicines and adapt their production to the needs of the Healthcare Industry, especially during medical crises.
Some critical technologies and industrial capabilities have left EU and must be on-shored where possible.

**Analysis of the situation:**

- This list aims to guarantee Europe's resilience in terms of health safety on these essential active ingredients and their synthetic intermediates.

- **Not all supply chains can be relocated**. Priority must therefore be given to tackling the most critical technologies to ensure the capability to produce essential APIs at any needed time.

- We must therefore **build on the existing EU industrial facilities**, developing their capabilities to manufacture the essential APIs identified and ensuring their resilience and sustainable manufacturing. This entails the identification of the relevant technologies that are needed to manufacture these essential APIs and ensure their maintenance and development.

**Recommendations:**

- Maintain and encourage the existing **dynamic and decentralised industrial base** to secure manufacturing capabilities in Europe as well as innovation capacities

- Target the **onshoring of key technologies** on existing facilities linked to the essential molecules all over the value chain

- Target the **onshoring of essential medicines supply chains** to facilities that are deemed to be compliant with the strictest standards in terms of safety, quality and respect for the environment.

- **Critical molecules need to be correlated with technology gaps in Europe**. We strongly recommend that this exercise is done on a few therapeutic families, as different families need different approaches.

- **Determine the upgrade and expansion investment needs** for each of these.

## 4 - IDENTIFY THE MODERNISATION NEEDS AND PRIORITY R&D AND INNOVATION AREAS

Europe should implement a long-term EU industrial policy that can accelerate sustainable Research, Development and Industrialisation of innovative and green technologies, as well as develop manufacturing capacities within the EU territory.

**Analysis of the situation:**

- **Innovation in the pharma supply chain** is key for the resilience of our industry over the long term.

- Innovation must be supported along all steps of the value chain:
  - Innovation to **develop new treatments and drugs**
  - Innovation to **improve the bioavailability** of existing drugs
  - Innovation in the **manufacturing processes** of the APIs and their precursors

- Innovation in manufacturing processes must be accelerated with a strong focus on **improving the performance and the respect for the environment of new processes**, in order to ensure a resilient European pharmaceutical industry.

- We need to **anticipate and take the necessary measures to be ready for future crises**: identify the critical technologies that are missing and the reasons they are no longer made in the EU and determine how they can be innovated in view of reshoring in full respect of EU standards.

- **Support to innovation is needed** to improve the competitiveness of European manufacturers while achieving the best safety, quality and environmental standards but it is not sufficient to address the other issues that they face: lack of level playing field and unfair competition from other regions.

**Recommendations:**

- Support innovation and industrialisation of **breakthrough technologies** that combine competitiveness, sustainability, quality and respect for the environment.

- Rationalise and **focus incentives on a few strategic areas,** for instance the reshoring of Key Technologies needed to ensure resilience of Supply Chain, EHS benefits and bioavailability-improvement technologies.

- **Improve the support system for research and innovation** and simplify its access, opening it to small innovative companies.

- **Reinforce European excellence in the field of pharmaceutical synthesis** (chemistry and biotechnology) while **supporting research and education** in this field at EU level.

- Take actions to **improve the speed of mechanisms for assigning funds**, incentivising the creation of spin-off and innovative start-ups, to accelerate the transformation, in connection with Industry.

- **Support Digitalization, AI and Automation** (Industry 4.0) in development & manufacturing to improve European competitiveness.

- **Policies to be introduced**:
    - Promote and enforce a **level playing field**, where companies exporting APIs to Europe are subject to equivalent/mutually recognized regulations in the area of quality, process safety and environmental protection (e.g. Reinforce European Quality & HSE Inspections for any precursors, API and Excipients imported in Europe)

    - Introduce policies **incentivising Resilient and Sustainable pharmaceutical supply chains** (compliant with the Green Deal), including economical mechanism to promote its adoption in the longer term.

    - Introduce a “Fast Track” policy to facilitate procedures for Capacity Expansion and Key Technology re-shoring (e.g. permission, quality, regulatory, other permits).

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