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OPEN STRATEGIC AUTONOMY FOR THE PHARMACEUTICAL SUPPLY CHAIN IN EUROPE
The position of the API and fine chemicals industry

Our goal is to achieve a robust, sustainable and competitive EU API manufacturing industry that contributes to building a resilient pharmaceutical supply chain and open strategic autonomy for the EU, guaranteeing access to medicines for all EU Citizens.

How to reach this goal:

- Foster a legislative and policy framework that encourages the development of a robust, sustainable and competitive industrial capacity for the EU manufacturers of Active Pharmaceutical Ingredients (APIs) and their precursors.
- Foster strong R&D and industrial capabilities enabling reshoring of industrial processes previously offshored to other world regions in a socially responsible and environmentally compliant way.
- Continue investing in R&D, technologies and industrial capabilities to produce locally and sustainably innovative APIs for new drugs.

Promoting Sustainability and Environmental Stewardship

European Active Pharmaceutical Ingredients (API) manufacturers adhere to the highest safety and environmental standards and strive to reduce their carbon footprint, even beyond current legislative requirements. European API manufacturers further excel in quality track-record and supply reliability.

We welcome the EU Commission's proposal for revision of the pharmaceutical legislation with a strong focus on sustainability and environmental stewardship of the pharmaceutical industry.

Backbone of the pharmaceutical supply chain

Active Pharmaceutical Ingredients (APIs) are the active components of a medicine that produce the effects required in the body to treat a disease. **API manufacturers are therefore the backbone of the pharmaceutical supply chain, providing its** essential building blocks and key components.

The European API industry requires state-of-the-art infrastructure, advanced technologies, specialised equipment and a highly skilled workforce to continue operating to the highest quality, environmental, safety and social standards.

Exodus of API manufacturers out of the EU

The European API Production is currently in a worrying decline. From a global production share of 53% in 2000, the 2020 share tumbled to a mere 25%. Europe has become dependent on other regions for APIs (56% currently originate from India and China).[1] With many critical APIs no longer being produced in Europe.

> This can be illustrated with the striking example of Metoprolol, used for high blood pressure. Formerly produced in the EU, it is currently mainly produced in China and India, as 16 sites in the EU have stopped producing it. Similarly, Gabapentin, a treatment for epilepsy, now mainly originates from India after 10 EU manufacturers have seized its production. These are just two of the many molecules which can help illustrate Europe's dependence on other regions, creating a risk for the security of supply.

Currently 80% of APIs are imported into Europe from just five countries, with China supplying 45%. There are currently 93 essential active ingredients for which no European company holds a CEP certificate.

The main factor that has driven the delocalisation to other world regions is the need to manufacture APIs at extremely low costs, mainly due to the cost-containment measures imposed by the EU member states, which lead to extremely low prices for mature medicines. Additionally, the following factors have contributed to the current decline:

- Social, safety and environmental standards are very high in Europe as compared to other regions (Asia, America) and the additional manufacturing costs of such high but essential standards, are not valued at all in the case of mature medicines where price is the only determining factor.
- Manufacturers in Asian countries benefit from lower production costs (notably due to different social and environmental standards), economies of scale and, in recent years, from incentives from local governments to support their production. Utility and raw material prices also put EU producers at a disadvantage compared to other world regions.
- Comprehensive investment support schemes to local API manufacturing, R&D and production in among others China, India and US. The EU lacks support and incentives to stimulate API production and innovation in greener manufacturing processes.
- Public procurement practices are currently based on price as the sole criterion, disadvantaging the European API industry that adheres to the highest environmental standards.
- Hurdles caused by an archaic paper-based regulatory framework.

Supply Chain Security and Medicine Shortages

These factors help explain the reliance on other world regions for pharmaceutical products, contributing to the medicine shortages and disruptions to the pharmaceutical supply chain facing European citizens and Producers today. This was brought to the forefront during the

[1] Source: APIs facts & figures infographic, https: Infographics - EFCG (cefic.org)

COVID-19 pandemic further highlighting the need for local API production capabilities. This need is even more evident with the current war in Ukraine and other geopolitical tensions.

Crisis preparedness

The last three years have also underlined the need for an agile industry and regulatory framework, capable of responding quickly and effectively to crises - whether health, geopolitical or economic - and the resulting unexpected shifts in demand for medicines.

A steady demand for EU produced APIs is vital for maintaining the readiness of industrial infrastructure in case of a crisis. It enables ongoing equipment operation, supports workforce preparedness, ensures supply chain stability, facilitates inventory management, and contributes to the financial viability of industries. All these factors are necessary to ensure the ability of the industrial infrastructure to respond effectively and efficiently to crisis.

Vital role to be played by European API manufacturers

European API manufacturers can play a vital role in ensuring the resilience and security of supply of the European pharmaceutical supply chain and in responding to fluctuations in demand. By producing APIs in the EU, the European pharmaceutical industry reduces its dependence on producers located in distant geographic regions and thus mitigates the risks of supply chain disruptions, thereby enhancing crisis preparedness.

Measures needed to reverse the trend

1. **Support mechanisms**: One way in which the EU could enable EU API manufacturers to play this role is by supporting investments that stimulate the decarbonation of the industry, breakthrough technologies and the construction or modernisation of production facilities. A financial framework for API investments would encourage the relocation of production and halt the collapse of existing manufacturing operations.

   Various scenarios can be envisaged:
   - Public/private cooperations, with a commitment from industry to supply the needed quantities of medicines in case of shortage of supply.
   - Financial incentives for supply chains entirely based in Europe.
   - Support from the authorities to limit severe fluctuations in the price of utilities in cases where they would severely jeopardise the competitiveness of EU companies and lead to the offshoring of production outside the EU.
   - Facilitating access to EU funding schemes to enable investment of EU companies in sustainable process innovation. The current schemes are too complex for the scale of API producing companies and only a handful of the larger companies can currently benefit from them.
   - An incentive system (either direct or through fiscal incentives) should be set up to support companies investing own funds in R&D. This will encourage the development in the EU of new sustainable processes and new medicines.

- Fiscal advantages for companies buying European APIs based on innovative and sustainable processes

A current successful example of such measures can be found in France where the government announced an ambitious financial investment plan to reshore between 50 and 80 pharmaceutical production chains, linked to critical and essential medicines. [2]

> Example: To enable the reshoring of the production of paracetamol - completely off-shored from the EU in 2008- the French authorities supported a €100m investment which enables the implementation at industrial scale of a new process with breakthrough environmental performances. Thanks to this support, the project became financially viable and the construction of a 15,000 t/y unit is in construction to provide half of the EU's needs.

2. Overhaul of public procurement policies – levelling the global playing field:

The current market reality is not compatible with the need to achieve open strategic autonomy. To align them, public procurement policies need to be revised to achieve their initially intended targets.

Public procurement contracts are awarded according to "most economically advantageous tenders" (MEAT)[3], this allows for use of both price and non-price related criteria. However, the opportunity to use non-price related criteria regarding pharmaceuticals is currently not being taken advantage of. By ensuring their use to their full potential, non-price criteria such as process innovations/ improvements and social and environmental factors could reward those API producers that follow good environmental and social practices.

Measures to be taken could include:

- Criteria for public tenders should not solely be determined by the price of the final medicines but should encompass health, safety and environmental (HSE) considerations as well as social standards used in their production, irrespective of the region of origin.
- Preference should be granted to medicines with APIs, excipients and manufacturing processes that are compliant with quality, environmental and social standards set by the EU. A lower price should not be a justification for compromising fundamental EU values.
- It is essential to promote the procurement of medicines and APIs from EU-based companies consistently, beyond periods of crisis and scarcity. This objective can be achieved by incorporating a minimum percentage of "Made In Europe" ingredients. This approach enhances crisis preparedness and empowers EU producers to efficiently address surges in demand, especially for critical medicines.

[2] https://sante.gouv.fr/actualites/presse/dossiers-de-presse/article/relocalisations-de-medicaments-essentiels
[3] Directive 2014/24/EU on public procurement and most economically advantageous tender (MEAT) criteria

- Ensuring that whenever possible, a tender is granted to multiple producers, which ensures a steady demand for multiple producers who can subsequently more readily scale up production in case of crisis.
  Establishing stringent border controls and prioritising the training of EU inspectors are crucial measures to identify and prevent any violations of EU regulations. This proactive approach aims to prevent imports from producers who, due to social or environmental concerns, would not be permitted to operate within the EU.

3. **Environmental protection:** The EU should provide financial incentives and rewards for investments in environmentally friendly manufacturing. Such incentives would stimulate industries to increase their investments in Europe, speed up the Green Transition, and establish a fair competitive environment with regions that do not adhere to stringent standards. Additionally, Market Authorisations should be withheld when alternatives with lower environmental or health impacts are available.

4. **Efficient regulatory framework:** The EU must prioritise the digitalisation of regulatory processes, aiming for fast-track approval of innovative, sustainable, cost-effective and environmentally friendly processing technologies, for new APIs as well as for already approved APIs for which the production process can be improved or optimised. The outdated paper-based regulatory framework[4] imposes unnecessary burdens on API manufacturers, fostering inefficiencies that hinder swift responses in times of crisis.

   > Under Commission Regulation 1234/2008, a slow paper-based notification is needed for various "variations" described in Annex II of the regulation. For example, to make changes to the produced quantity or to the packaging material not in contact with the finished product.

To address these issues, it is imperative to transition to digital, nimble, and cost-effective systems. This shift will foster more efficient and agile interactions between the industry and regulators, ensuring a streamlined and responsive regulatory environment.

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[4] In particular Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products