PRACTICAL MEASURES ARE PARAMOUNT FOR ROBUST MEDICINES MANUFACTURING

By Adrian van den Hoven - Medicines for Europe Director General

COVID-19 has heightened existing debates on global supply chains, but informed and practical policy making is needed to strengthen medicines supply chains.

TAKING STOCK OF THE GLOBALISATION OF MEDICINES SUPPLY CHAINS: WHERE DO WE STAND?

Over the last 15 years, China and India have become highly competitive manufacturers in the global pharmaceutical chain. This has raised political concerns about dependence on foreign suppliers and the competitiveness of European pharmaceutical manufacturing is once again in the spotlight. The highly regulated nature of pharmaceutical manufacturing from finished products (FDF), active pharmaceutical ingredients (API), to excipients and intermediates makes scale and technology critical competitiveness factors at all stages of the supply chain. Can Europe develop a industrial policy to boost the competitiveness of pharmaceutical manufacturing on the old continent?

For a long period, Europe was the leader in medicines manufacturing with a large portion of the global production located on the continent. In the 1960s and 1970s, with the economic and health system development of India and China, governments adopted measures to decrease dependency of the domestic pharmaceutical market from third countries - mostly the EU and US. The pharmaceutical manufacturing in India and Chinas was heavily subsidized to respond to growing domestics needs. In 1990s and 2000s, the Indian industry capitalised on its production surplus to develop a successful export industry. Over time, Indian manufacturers strengthened their competitiveness relative to European manufacturers.

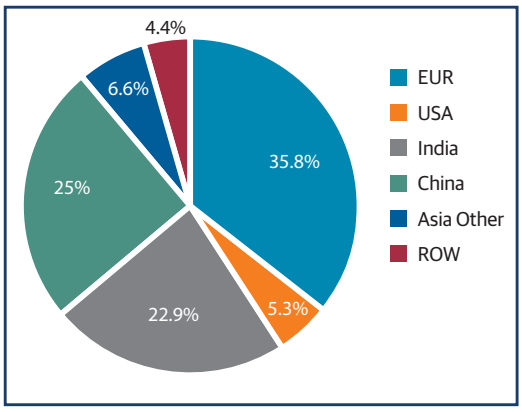
This phenomenon was accelerated for generic medicines production by the financial crisis of 2009, which drove EU countries to adopt widespread cost containment measures in medicines purchasing. The intense price pressure on manufacturers combined with the continuous update of regulatory frameworks for the benefit of patients but at great cost to the industry drove investment in manufacturing to countries like India or China for cost competitiveness reasons.

Despite the rapid growth of Indian and Chinese manufacturing, the EU remains a strong contender when it comes to global pharmaceutical manufacturing leadership. This is particularly relevant when it comes to highly specialized and complex products where the EU is still a global leader such is the case of biologic medicines and complex generics, namely sterile formulations. The US GDUFA data support this, showing that 31% of finished product sites for generics are in Europe. When it comes to API production, according to EDQM data, 35.8% of API manufacturing sites are in Europe which again shows that Europe can compete.

COVID-19 OUTBREAK SHOWS RESILIENCE OF MEDICINES SUPPLY

The COVID-19 crisis clearly showed the resilience of the European supply, with the industry being able to massively scale-up production to face unprecedented levels of demand for medicines needed to ventilate infected

REPARTITION OF MANUFACTURERS APRIL 2019*



Source: MEDICINES FOR EUROPE
**Certification of Substances Department - EDQM (Feb 2020)*

patients in intensive care units (ICU) - mostly sterile products of complex manufacturing nature. The pandemic showcased the essential role that off-patent medicines play in a large public health crisis, as the majority of medicine needs were covered by the generic industry. For example, in Germany, 97% of the medicines needed to treat patients infected with COVID-19 had a generic medicine option available on the market.

However, at the onset of the pandemic, the Indian government imposed export restrictions on several API and medicines under strong demand , in an attempt to guarantee sufficient supply for its own population. Critically, we should underline very few of those products used in hospitalized ICU patients were banned for export by the Indian government, highlighting that EU (and to a large extent US) demand was being fulfilled by both EU medicine and API producers.

This brings us to the discussion about reshoring medicines manufacturing to Europe to strengthen supply security. The European generic industry has advocated for the EU to strengthen its manufacturing leadership, highlighting the public health value of a resilient and strong European generic, biosimilar and value added medicines manufacturing industry.

In a global supply chain, it is not reasonable to expect that all production is localised in Europe. However, it is possible to build on the European manufacturing footprint of over 400 sites and 190 000 direct jobs by encouraging investment in technological leadership. This will deliver a cost-effective solution aligned with public health needs. The EU should set an ambitious goal to restore Europe to its former position as the leading global manufacturing region for finished product (medicines) and active pharmaceutical ingredients for both the EU and the global market.

PRACTICAL POLICY MAKING NEEDED

Europe is committed to achieving multiple policy objectives for medicines: make them economically sustainable for patients and healthcare systems, reduce their environmental impact, increase manufacturing competitiveness and supply chain resilience and adapt to the digital era. Restoring Europe as the world leading manufacturing site for pharmaceuticals, from innovative to generic and biosimilar medicines will require some European funding (Recovery fund, Green deal, EU4health) and updated state-aid criteria (to enable national tax deductions, API and medicines development incentives or other facilities) to kick start development, manufacturing and supply chain investments. **Sustainability will also need to be restored in market policies** to encourage more manufacturing investment. Better global **regulatory oversight and enforcement will also enabl**e European manufacturers to compete on a level playing field.

Manufacturers will need clear signals and initiatives to encourage the expansion of the European manufacturing footprint. Investments in telematics to digitalise regulatory submissions and oversight; newer or greener or more efficient technologies to develop and manufacture API and medicine formulations; securing existing sites, construction or renovation of manufacturing facilities or production lines for competitiveness and new manufacturing processes like flow chemistry for API; information technology deployment across the manufacturing and logistics chain and; environmental studies are some of the measures that would incentivize manufacturers to invest more in Europe.

Financial support needs to be combined with market incentives (value added

medicines, green or multi-winner procurement market options that consider long-term volume and price certainty) to ensure that these investments are ultimately financed by competitive markets. Currently, the European market for prescription medicine is dominated by government (direct or indirect) purchasing focused on obtaining the lowest price possible for most off-patent medicines. This jeopardises the existing manufacturing footprint in Europe, disincentivises future investments in European manufacturing and in supply chain resilience measures and generates market or manufacturing chain consolidation.

The EU needs to rebalance the market toward investment by rewarding resilience and security of supply or other relevant most economically advantageous tender (MEAT) criteria into the implementation Public Procurement and the Transparency Directives. Shorter and proximate supply chains can be an important factor of increased security of supply and resilience, allowing for better regulatory oversight and mitigating dependence on third countries. In addition, factors such as geographic diversification of manufacturing and supply can also improve supply security. There are also other features such as the number of active manufacturing sites for any individual API, secondary back up options and the ability to scale up production rapidly which requires changes in pharmaceutical regulation.

Purchasing policies will have to be readjusted to balance between cost and supply chain reliability including the investment in supply chain resilience, mature quality systems and environmental, health and safety standards. New pricing models for off-patent medicines that reflect increases in costs of goods or regulation are needed for the supply of essential, lower cost medicines. The development of innovative off-patent regulatory pathways for biosimilar medicines, which increased the production of and access to biopharmaceuticals in Europe, could be replicated for other technically complex off-patent medicines (value added medicines) with positive results for healthcare and spin-off benefits for manufacturing.

In parallel, European regulators must move towards better regulatory oversight. Currently, all medicines marketed in the EU must comply with high regulatory, scientific and quality standards and are extensively monitored by industry and regulatory (medicine) agencies. For imported medicines or ingredients, manufacturers conduct a wide array of good practice audits for manufacturing, laboratories and testing (GMP, GCP, GLP) as well as testing procedures for imports to ensure compliance. To enhance this effort and for a level playing field on enforcement, regulatory agencies will need to devote more resources to GMP inspections in less regulated countries, especially for API. Regulatory oversight can be improved by reducing maintenance costs for older medicines (variations), giving a legal role for API producers to submit variations in the regulatory dossier, conducting GMP inspections of foreign API and finished product (medicine) sites and introducing quality metrics and risk assessment systems.

This three-pronged approach of financing, market sustainability and regulatory oversight will strengthen manufacturing in Europe without resorting to a protectionist agenda. This could even propel open markets by developing a new medicines trade agenda, that includes measures for security of supply (reciprocal commitments to avoid export restrictions and cooperation on enforcement of GMP rules), equitable access (enable global development of APIs and generic, biosimilar and value added medicines to lower development costs) and mutual open trade (removing barriers to EU exports - including in procurement).

Ultimately, if Europe wishes to strengthen manufacturing of medicines and affirm its leadership, it will need to shift the focus from achieving the lowest-price possible for off-patent medicines to ensure supply security and diversity in a functioning competitive internal market. Simultaneously, it will need to stimulate investment the development of manufacturing base, embrace its specialization in complex forms and improve regulatory oversight in third countries to secure a level playing field with European manufacturing. With these policy reforms, Europe can regain its global leadership in pharmaceutical manufacturing. ■

About the author

Adrian van den Hoven
Director General, Medicines for Europe.

Adrian van den Hoven joined Medicines for Europe as a Director General in September 2013. His priorities at Medicines for Europe are to stimulate competition in off-patent medicine markets, to foster market access for generic, biosimilar and value added medicines, to support policy measures for sustainable pricing, to promote high regulatory standards while ensuring that the associated costs can be integrated into market dynamics and to develop a coherent EU industrial strategy to support the long-term viability of the generic, biosimilar and value added medicines industries.