Servier's proposals for building more resilient supply chains in Europe

The pharmaceutical sector is unique in its dual role of improving the lives of patients and being a significant pillar of the European economy. In 2020, our industry invested more than €37 billion in Research and Development in Europe[1]. As a sector, we have also invested €300 billion in production activities in Europe, employing around 840,000 people[2]. In our mission to continue bringing life saving medicines to patients, we rely on a highly interlaced ecosystem of modern supply chains that operate at national, European and global levels.

Stable manufacturing and supply chains in Europe are of essential importance in our day-to-day operations that contribute to the well-being of Europeans. The COVID-19 pandemic, during which trade was heavily limited, disrupted supply chains and delayed medicine shipments to patients. This further highlighted the need for well functioning manufacturing lines and stable supply chains.

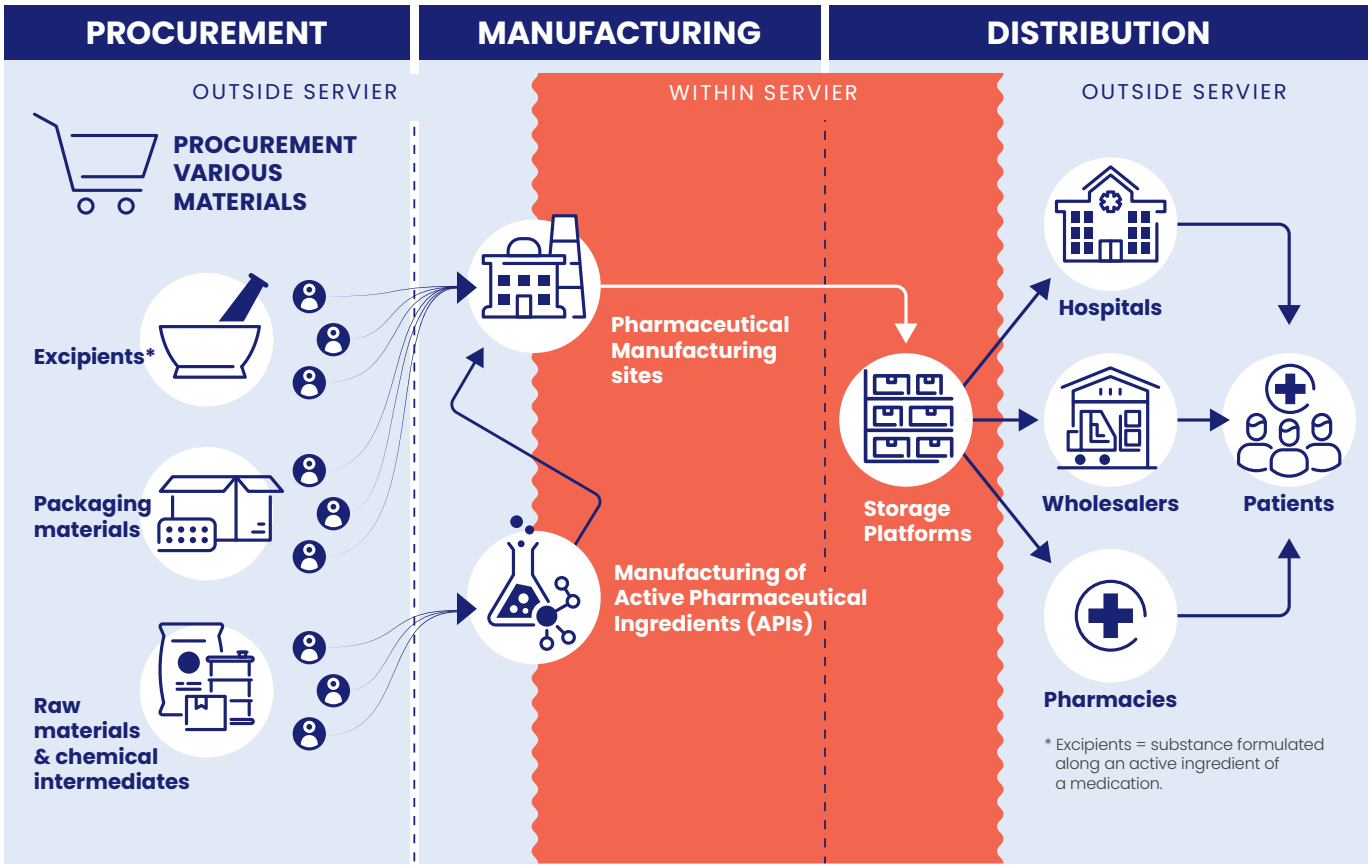
One of the key lessons learnt during the last couple of years is that supply chains need to become more resilient in the future. This is widely agreed upon, but ensuring resilience can take different routes and is therefore the subject of many debates, especially in light of the revision of the general pharmaceutical legislation at European level.

Servier is a global pharmaceutical group with a strong manufacturing footprint in Europe, which is committed to working together with all European stakeholders to build stronger and more resilient supply chains to fulfill its mission to bring to patients the medicines they need.

Functioning of the supply chain

Supply chains are complex and pharmaceutical companies only actively control a small part of the entire process. They depend on a complex set of procedures, often involving a broad range of participants spread across numerous locations around the world.

To deliver medicines on time to patients in need, success hinges on people doing the right things in the right place, at the right time.



1. EFPIA(2020). The Pharmaceutical Industry in Figures. https://www.efpia.eu/media/554521/efpia_pharmafigures_2020_web.pdf
2. EFPIA (2022). The Pharmaceutical Industry in Figures. https://www.efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf

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The need for optimisation, flexibility and dialogue

As part of the revision of the general European pharmaceutical framework, discussions are on-going on how to improve the legislative and regulatory framework to make pharmaceutical supply chains more resilient, better prevent shortages of medicines, and enhance Europe's strategic autonomy. At Servier, we strongly support these efforts and believe that newly introduced and revised measures must be seen through the perspective of: **OPTIMISATION, FLEXIBILITY,** and **DIALOGUE.**

01 Optimisation of existing processes

OPTIMISE THE PROCESS TO ALLOW FOR MORE DUAL SOURCING OF INGREDIENTS

One of the principles to ensure more security of supply is to diversify the supply chain and contract not one (mono sourcing), but at least two suppliers (dual sourcing) to provide raw or packaging materials. However, the dynamic and unique nature of modern supply chains cannot always ensure that secondary sources are available and are administratively or financially viable.

Servier has made significant efforts to maintain a European supply chain by, for example, currently producing 98% of its active ingredients of synthetised brand-name medicines in France. We see dual sourcing, where possible, as necessary risk management.

However, changing or adding suppliers to dual source ingredients and materials is very difficult in the current framework due to multiple factors:

- **Difficulty in finding suppliers with the right technological manufacturing capacity** (especially for biotechnology).
- **A time-consuming and burdensome administrative process, even when a suitable supplier has been found. The EU Variations Regulation** ((EC) No 1234/2008) requires pharmaceutical companies to change the terms of their marketing authorisation for each new supplier they procure substances from.

In addition, simply adding suppliers to procure substances for the manufacturing of medicines will not prevent shortages of medicines on its own. Situations could occur, where shortages of medicines could be caused by a shortage of one of the key materials used in the supply chain, such as, for example, the aluminium foil used for the packaging of medicines.

The difficulty of finding the right suppliers

For one of Servier's low volume but very high patient impact oncology medicines, there was only one single (external) manufacturer that had the technological capacity to produce this API not only for clinical trials, but also for full production capacity following EMA approval. It then took Servier 3 years to build the capacity to upscale its production to respond to the patient needs for this product. The delay was caused in part by difficulties of finding a manufacturer that had the capacity to upscale the production required to meet the needs of patients, but also by the administrative burden of verifying and approving the manufacturer itself.

NO ONE-SIZE FITS ALL SOLUTIONS: due to the unique and complex sourcing, manufacturing and distribution process of each medicine, there should be a case-by-case approach, with a focus on Shortage Prevention Plans (SPPs) for critical products instead of any general obligations for dual sourcing.

OPTIMISE THE DIGITAL FRAMEWORK TO ALLOW FOR A MORE TRANSPARENT SUPPLY CHAIN

Supply chains are becoming more and more digitalised, presenting immense opportunities for pharmaceutical supply chains to be made more resilient.

However, due to the speed of digitalisation, there are systematic issues that, if addressed, could unlock the true potential of the wealth of data created and collected, which would contribute to reducing drug shortages in the EU. To do so, the current legislative framework must adequately adapt to these rapidly-evolving developments.

This is apparent in the need for more transparency in the supply chain data collected by various actors in the supply chain ecosystem, which are subject to varying degrees of transparency obligations (sometimes even none). This often results in unforeseen shortages of medicines to which the pharmaceutical industry does not have sufficient time to react. In addition, there is a need for more clarity in the structure of responsibility and access to the data that is collected.

TO MAKE FULL USE OF THE ABUNDANCE OF DATA COLLECTED, WE MUST MOVE TOWARDS AN END-TO-END, TRANSPARENT MODEL OF SUPPLY CHAINS, based on a digital track and trace system (gathering information on medicines every step of the way, from the first production facility to the patient). Every participant involved in the journey of a medicine must be subject to the same transparency obligations. Such a system could be overseen by an already existing competent authority, such as the European Medicines Verification Organisation (EMVO).

DEVELOP A CLEAR FRAMEWORK ON WHO IS RESPONSIBLE AND HAS ACCESS TO THE DATA COLLECTED to help ensure that any potential issue that could cause a shortage is identified as soon as possible.

02 Flexibility in stockpiling and distribution

GRANT PHARMACEUTICAL COMPANIES THE FLEXIBILITY TO REALLOCATE PRODUCTS

The COVID-19 pandemic has made apparent the need to stockpile critical medicines to quickly respond to a public health emergency, as well as to establish different rules to ensure safety of supply during crises. To achieve this, the European Commission is considering setting up mandatory (additional) stockpiling by pharmaceutical companies of full or partially finished critical medicines to be coordinated at EU-level or nationally in member states.

However, solely introducing additional stockpiling requirements to hold stocks at national level would fall short of addressing current supply chain issues as it would continue to restrict one of the main tools we have to reduce the likeliness of shortages in the EU – the flexibility of pharmaceutical companies to reallocate products within Europe in light of a possible shortage.

Along with the establishment of a clear framework, there should be common criteria and methods for the identification of critical medicines to anticipate their shortages. With this, the introduction of state-of-the-art regulatory innovations that increase supply chain resilience such as electronic patient information (ePI) would create the flexibility needed to adapt and meet the uncertainties of modern value chains.

INTRODUCE CLEAR CRITERIA TO IDENTIFY 'CRITICAL' MEDICINES to provide clarity for which medicines additional stockpiles should be established by pharmaceutical companies.

HARMONISE STOCKPILING OF UNFINISHED PRODUCTS AT EUROPEAN LEVEL to give pharmaceutical companies the flexibility to design supply chains that can best respond to emerging needs and grant the interoperability of easily sending medicines from one country to another to prevent shortages.

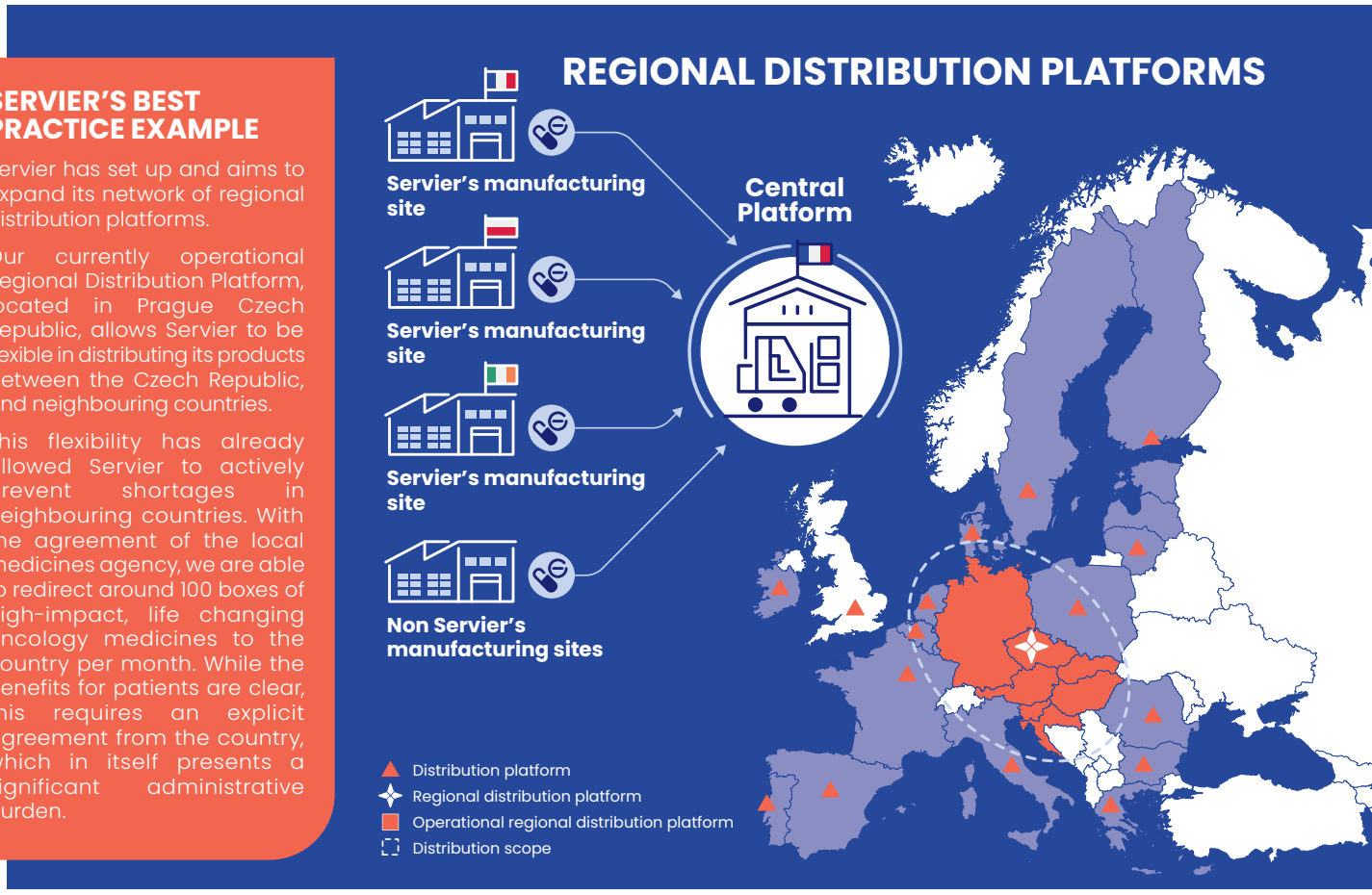
ALLOW REGULATORY INNOVATIONS such as electronic product information (ePI) to increase the flexibility of reallocating stocks across countries during shortages.

SERVIER'S BEST PRACTICE EXAMPLE

Servier has set up and aims to expand its network of regional distribution platforms.

Our currently operational Regional Distribution Platform, located in Prague Czech Republic, allows Servier to be flexible in distributing its products between the Czech Republic, and neighbouring countries.

This flexibility has already allowed Servier to actively prevent shortages in neighbouring countries. With the agreement of the local medicines agency, we are able to redirect around 100 boxes of high-impact, life changing oncology medicines to the country per month. While the benefits for patients are clear, this requires an explicit agreement from the country, which in itself presents a significant administrative burden.



03 Dialogue

ENGAGE IN A MULTISTAKEHOLDER DIALOGUE TO PREVENT MEDICINE SHORTAGES

In Europe, there has been an increasing number of shortages of medicinal products in recent years[3]. To remedy this, the European Union has given a mandate to the European Medcines Agency to monitor the risk of shortages (Regulation (EU) 2022/123) and is also considering extending the obligation for manufacturers to notify shortages of a medicine to 6 months in advance.

However, introducing this type of shortage notification obligation will not necessarily help prevent shortages, because of the inherent difficulty of pharmaceutical companies foreseeing shortages 'on time' (6 months in advance). Additionally, an obligation to notify shortages this early could create unintended consequences, such as medicine hoarding.

ALLOW FOR A CENTRALISED SHORTAGE NOTIFICATION through the harmonisation of existing national procedures of shortage notification. This would allow pharmaceutical companies to maximise their efforts to address the shortage at hand rather than spending more resources than necessary to fulfill the assymetric shortage notification requirements of each member state.

SUPPORT MORE DYNAMIC PUBLIC OVERSIGHT ON STOCK MANAGEMENT IN COLLABORATION WITH MANUFACTURERS through a competent European body such as EMVO to allow all stakeholders along the journey of a medicine to better anticipate and react to possible shortages.

ABOUT SERVIER

Servier is a global pharmaceutical group governed by a Foundation. With a strong international presence in 150 countries and a total revenue of 4.7 billion euros in 2021, Servier employs 21,800 people worldwide. Servier is an independent group that invests over 20% of its brand-name revenue in Research and Development every year. To accelerate therapeutic innovation for the benefit of patients, the Group is committed to open and collaborative innovation with academic partners, pharmaceutical groups, and biotech companies. It also integrates the patient's voice at the heart of its activities, from research to support beyond the pill.

3. Technopolis Group. 2021. Future Proofing Pharmaceutical Legislation – study on medicinal shortages.