Addressing Europe's Essential Medicines Exodus

Executive Summary

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Europe's strategic autonomy is waning. As a direct consequence of the COVID-19 pandemic and Russia's war on Ukraine, severe inflation – now averaging 9.8% across the EU, however reaching 16% or 17.3% in countries such as Poland and Bulgaria for example[1] - and supply chain disruptions have wreaked havoc across the continent[2,3]. People are living in uncertainty, and industries are having to take extraordinary measures to remain competitive. These problems will persist if unabated.

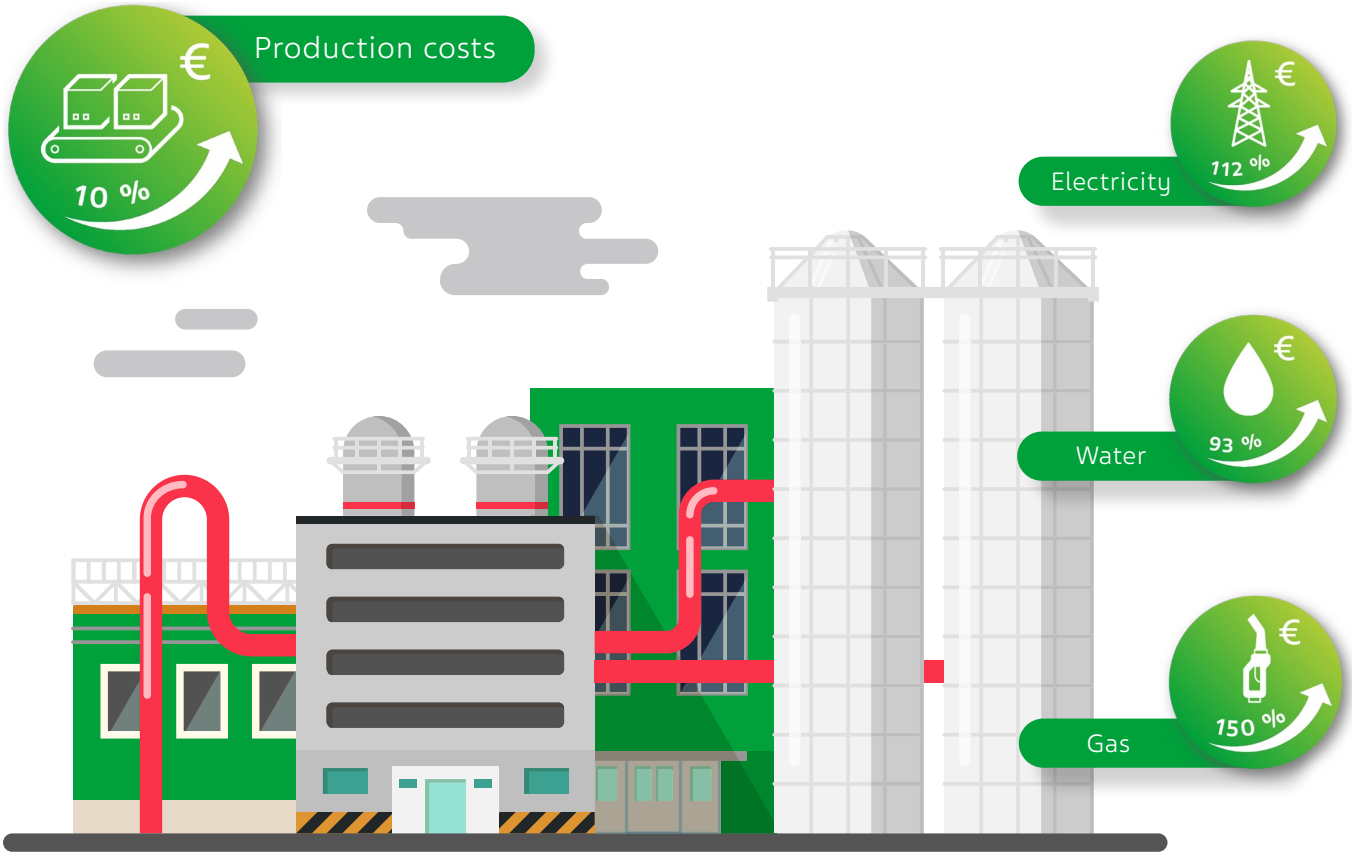
European political leaders have had to acknowledge the significant over dependency of its system and nation states on China – who the European Union (EU) relies on for over half its strategic imports including raw materials, batteries and active pharmaceutical ingredients[4] - and Russia for energy – which it imported 155 billion cubic meters of natural gas from in 2021[5]. Because of soaring inflation, and when the costs of labour, electricity and water are often already three times lower in China (and increasingly India), it is easy to see why these dependencies have ballooned.

In Spain for example, and while production costs have risen at least 10% as a result of 150%, 112% and 93% rises in the cost of gas, electricity, and water respectively, absorbing this rise in manufacturing costs immediately compromises the country competitiveness of essential medicines production[6].

"We managed to keep the same service level to our customers, but remaining competitive will be a significant challenge. The energy prices increase hit only the EU countries, which makes the competition pressure from India/China even stronger."

Romana Santar,
Site General Manager, Teva API, Croatia

1 https://tradingeconomics.com/country-list/inflation-rate?continent=europe
2 https://www.weforum.org/agenda/2022/09/5-challenges-global-supply-chains-trade/
3 https://www.imf.org/en/Blogs/Articles/2022/02/17/blog-supply-disruptions-add-to-inflation-undermine-recovery-in-europe
4 https://www.eiu.com/n/eu-unveils-strategy-to-reduce-dependency-on-china/
5 https://www.iea.org/news/how-europe-can-cut-natural-gas-imports-from-russia-significantly-within-a-year
6 AESEG medicamentos genericos: Informe: Estudio del impacto de la actual crisis de sumistros en el mercado de medicamentos genericos



Europe's essential medicines sector, which is critical for the healthcare system and has played a major role in the pandemic response, is running out of lives in its hard-fought battle with equivalent industries in China and India where governments have put in place a clear framework to attract investment and grow tomorrow's industry leading companies. Essential medicines are just that: essential. Developed healthcare systems cannot operate without them; they support people with long-term conditions to live more comfortably and they aide surgeons undertaking life-saving surgery. Too often the EU has indulged in a 'race to the bottom' on prices, alongside presiding over an onerous and archaic regulatory framework, allowing increasingly vital manufacturing assets for essential medicines to migrate from Europe eastwards.

This situation has weakened Europe's essential medicines diversity and therefore security – with antibiotics[7] and paracetamol being a case in point[8,9]. In effect, this shift has reduced Europe's capacity to provide essential medicines to patients at their time of greatest need. COVID-19 has shone a spotlight on this most uncomfortable trend. It is also threatening to debase the continent's pharmaceutical sector for good for some critical medicines. A situation exacerbated by a European-wide energy and economic crisis.
Should this continue, not only will European nations lose the ability to serve their patients in the way they have become accustomed, they will lose one of their greatest value adding sectors altogether.

7 https://asia.nikkei.com/static/vdata/infographics/chinavaccine-3/
8 https://www.outsourcing-pharma.com/Article/2009/01/06/Europe-s-last-paracetamol-plant-closes-its-doors#:~:text=As%202008%20drew%20to%20a,facility%20in%20Roussillon%2C%20southern%20France.
9 https://www.theguardian.com/world/2020/mar/04/india-limits-medicine-exports-coronavirus-paracetamol-antibiotics

Making the case for change

Teva is a global company, but that does not mean turning a blind eye to some of the pressing challenges to globalisation seen today. It is in this context, and on the eve of the development of new legislation for the pharmaceutical industry in the EU, that Teva present this paper and call-for-action.

> Asian companies now hold nearly two-thirds of the approval certificates needed to produce APIs in Europe, with the remainder held by European firms. This ratio has flipped over the last 20 years. Alarmingly, there are now 93 active ingredients for which no European company holds a certificate.

The paper provides EU policy makers with a case for enhancing pharmaceutical manufacturing resilience in Europe, urging action that goes beyond the European Commission's Pharmaceutical Strategy for Europe in 2020. The hope is that this paper supports forthcoming discussions in relation to the reopening of EU pharmaceutical legislation.
This is a once in a generation opportunity to review the policies, regulations and incentives that attract investments into Europe's pharmaceutical sector and take action that safeguards a vital sector and limit the continent's dependencies on other countries and regions.

Applying the experiences of a global company that has had to adapt to remain competitive in the most trying circumstances, Teva's goal is to offer solutions for how a policy framework can help sustain a superior pharmaceutical ecosystem in Europe and, ensure – with greater certainty – the critical and affordable supply of essential high-quality medicines to European patients for years to come.

European leaders must level the playing field.

A radical approach is needed to level the playing field for drug manufacturing in Europe. European manufacturing cannot compete on cost with markets in the Far East, but it can compete by leading on global standards development and a broad range of innovations as long as they are incentivised to do so.

With this in mind, the Member States and the European Union must shift the balance of legislation before it is too late in order to create a regulatory and an economic level playing field. Five recommendations are offered on how new EU and national legislations can elevate European pharmaceutical manufacturing from :

- **Ending a 'race to the bottom' on prices for generics**
- **Guaranteeing sustainable API & Medicines security of supply**
- **Fostering a digitalised and cost-effective regulatory environment**
- **Ensuring timely access to funding schemes notably to support the green & digital transition**
- **Ensuring clear and predictable IP incentives schemes**

With this in mind, Teva urges the EU to grasp the moment and be bold.

The time to act is now.

"I would like it if policymakers put quality, reliability and sustainability of supply on an equal footing as price when choosing pharmaceutical suppliers in a tender."

Tatjana Ilic,
Site General Manager, Haarlem, Netherlands

Contents

The value of essential medicines

The value of essential medicines

A critical starting point for this report is to reinforce the role and purpose of essential medicines in today's healthcare systems. For developed healthcare systems, essential medicines are critical and their use vast. Whether it is the anaesthetic a patient takes before an operation, the antiallergics and medicines used for anaphylaxis, or immunomodulators used to target the pathways of myelomas and cancers, they are the backbone of so many treatments. For patients, they are the difference between life and death.

Half a century of recognition as a key pillar of healthcare

The concept of 'essential medicines' was borne out of a desire to broaden and guarantee access to vital medicines. Introduced in 1977, the essential medicine list documents the medicines that developed health-care systems should be providing to patients based on the needs of a given population[10]. The intention is for essential medicines to be available in sufficient amounts, with assured quality and adequate information, at prices individuals and communities can afford.

And significant progress has been made. Nearly half a century after their creation, the concept of essential medicines has been accepted worldwide as a powerful tool to promote health equity and over time, listed medicines have proven to be increasingly cost-effective. As of September 2021, the 22nd Essential Medicines List (EML) and eighth Essential Medicines List for Children (ELMc) contained 479 and 350 medications respectively [11,12]. The WHO's list has served as a guide for the development of equivalent lists at a national level across the world, from which 155 have been created. While most medications on ELM and ELMc are available as generic products, being under patent does not preclude inclusion.

Teva's role in the essential medicines value chain

Teva is a leading supplier of medications on EML and EMLc,. In 2021, Teva's portfolio covered 60% of treatments on the lists, including:

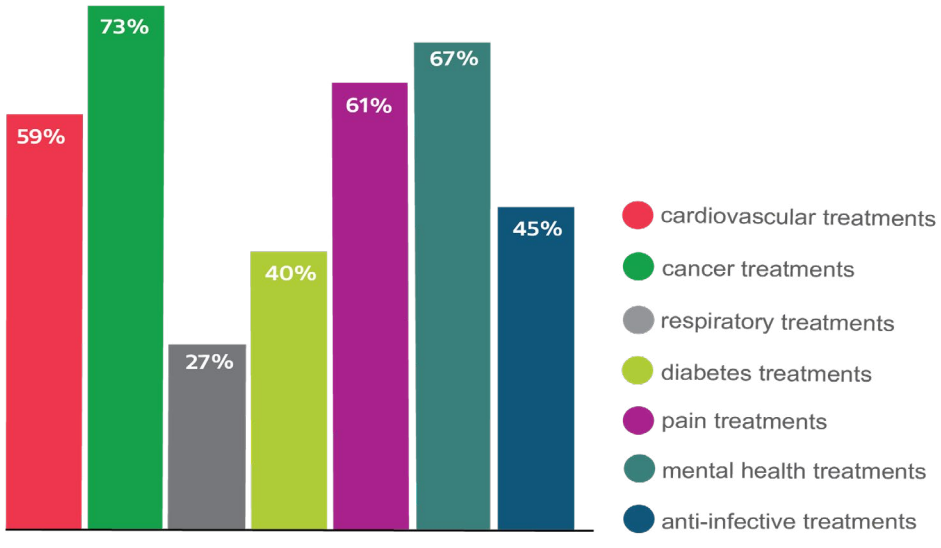


Figure 1.

10 https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists
11 WHO Model Lists of Essential Medicines
12 WHO-MHP-HPS-EML-2021.01-eng.pdf

Although Europe's essential medicines footprint is getting smaller, it is still significant. For example, Teva is still a prominent essential medicines manufacturer in Europe and serving European health systems. 65% of Teva's global portfolio is manufactured in Europe, and 96% of Teva medicines sold in Europe are manufactured at Teva's European sites. This is not to be self-congratulatory; the impact is tangible and important for Europeans. From this footprint, Teva's local purchases and payroll supports over 100,000 jobs, contributes over €25 billion to economic output, and generates €4.9 billion in labour income (a measure of aggregate worker wages) across nine European countries. In the pharmaceutical sphere, European manufacturers have to be self-confident of their value in the ecosystem.

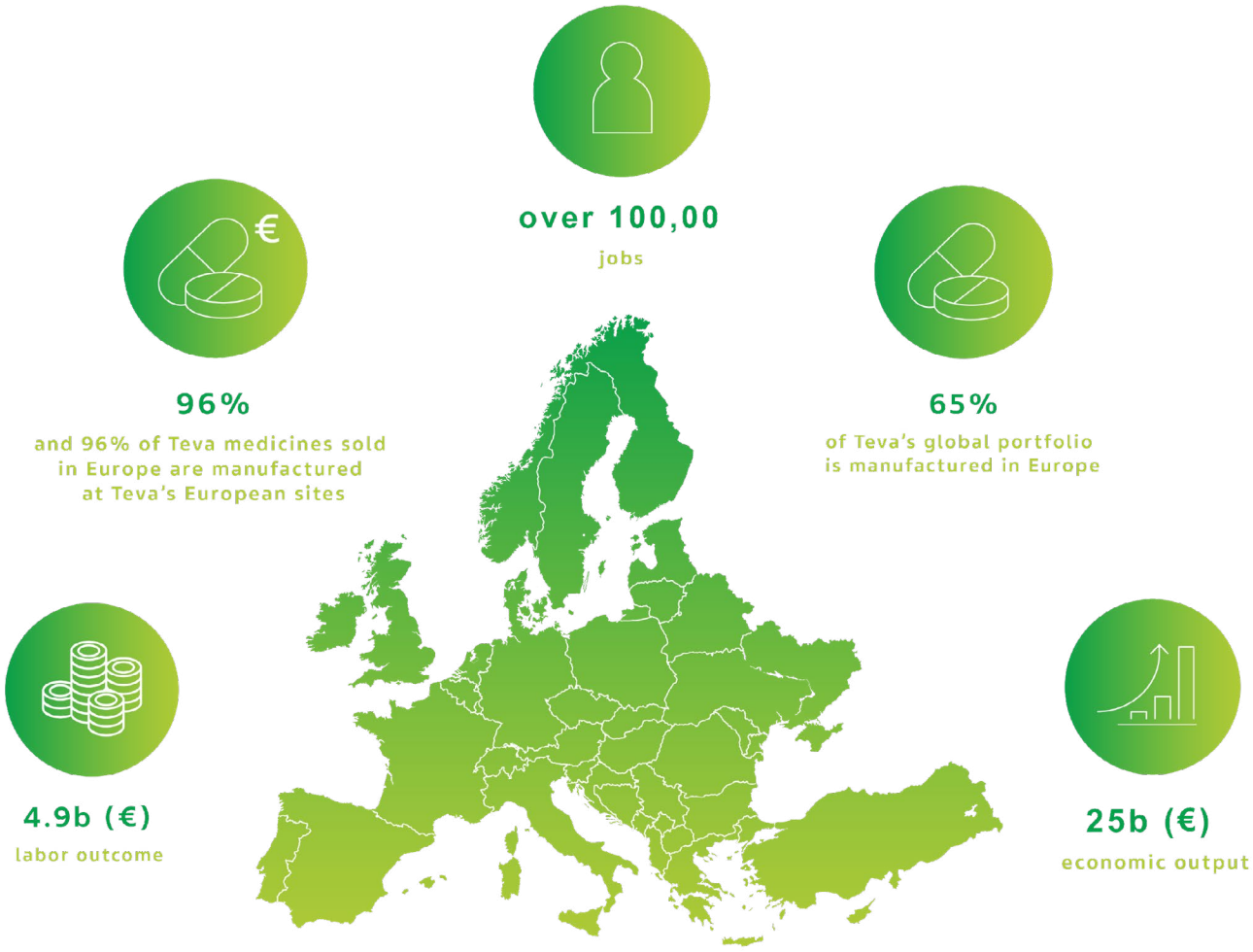


Figure 2.

Teva is making strides to connect its business ambitions to its ESG commitments. As one of the world's largest manufacturers of generic medicines, ESG is integral to the long-term strategy of our company and is part of everything we do covering 13 ambitious targets related to access to medicines, ethics, environment and responsible supply chain[13].

While Teva is growing and has proven to be an important part of the European essential medicines network and resilience today and during the pandemic, this will only continue if the right conditions are in place. Analysis of why European pharmaceutical manufacturing is less resilient than it was, and the path to a more certain future, can only begin by strengthening stakeholder understanding of the factors that determine long-term industry investment decisions which is the objective of this report.

13 Teva Publishes 2021 ESG Progress Report, Showcasing Further Integration of ESG Into Business, Robust Targets and Strengthened ESG Governance Structure (tevapharm.com)

Achieving the magic formula:

attracting essential pharmaceutical investment

Achieving the magic formula:

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Pharmaceutical companies make R&D and manufacturing investment decisions according to a combination of complementary factors

Traditionally, a combination of high-quality production potential and the ability to reduce costs over time have been significant determining factors for the off-patent industry. Over time as healthcare systems have progressively demanded lower prices for the drugs they purchase, cost competitiveness has become the strategic priority for generics manufacturers. This has been exacerbated by countries such as China and India, with significantly cheaper natural and physical resources than Europe, encouraging companies to relocate their manufacturing operations. This has created a downward cycle for European essential medicines manufacturers who have struggled to maintain a competitive cost base while investing in new technology and infrastructure required by changing regulations in Europe. Europe and the West now overly relies on China and India for many key generics, exposing them to the risks of supply disruptions due for examples to border issues or plants closures because of major events taking place outside of Europe.

In any case, pharmaceutical companies analyse an array of different factors when considering exactly where to invest and place their operations – from centralized functions and research and development (R&D) to the manufacturing of generics and essential medicines. This is a critical process to get right as the decisions that derive from it have a direct impact on the ability of patients to access the latest and most cost-effective drugs.

To ensure these decisions are based on a rational process that examines a breadth of factors, pharmaceutical companies conduct what are called feasibility assessments. This is a detailed analysis to determine the overall likelihood of manufacturing success based on associated risks and return-on-investment (ROI). To do this, Teva looks at five core areas, which align closely with industry frameworks such as Management Science for Health's Pharmaceutical Production Policy (2012) and Bain's Making a move to low-cost countries (2005)[14]. They are as follows:

1. Human capital

As a key overhead cost, being able to hire the appropriate workforce for all aspects of an operation is critical. Not only to keep costs low, but to manage the complexities of modern operations.

Access to both skilled and unskilled labour is crucial for efficient and high-quality manufacturing and R&D. A primary issue in many countries is the ability to find experienced and skilled staff, particularly scientists and engineers to manage latest manufacturing technology as well as issues of quality assurance, including regulatory compliance and meeting Good Manufacturing Practices (GMP) standards[15]. Countries and regions compete on securing these talents.

14 https://media.bain.com/Images/BB_Making_move_low-cost_countries.pdf
15 Management Science for Health 2012. Chapter 7: Pharmaceutical Production Policy

"Teva's Biotech site in the Bio Cluster South Germany around Munich attracts talents and specialists, encourages new ideas and innovation.... We have become a lighthouse for automation and digitalisation in this global industry"

Stefan Fügenschuh,
General Manager Teva Biotech at Teva Baden-Württemberg, Germany

High skilled, technical talent – particularly in biotechnology - is an area Europe excels in and must protect[16]. Doing so means keeping vital manufacturing in Europe. If manufacturing, along with the technologies and infrastructure that supports it, migrates to other parts of the world, so too will the talent and knowhow and it will be difficult to bring back. Other parts of the world are already excelling in growing significant technology workforces, mainly in Asia[17].

"Europe's talent, mindset and high standards need to be nurtured if the region is to keep its competitive R&D advantage"

Julian Blair,
VP R&D, Global Inhalations, Waterford, Ireland

16 https://www.labiotech.eu/best-biotech/countries-recruit-biotech-talents-2017/
17 https://globalpeoservices.com/top-7-countries-for-hiring-tech-talent/

2. Physical Infrastructure

In addition to human capital, physical inputs such as the raw materials and energy used for production and the quality of transportation infrastructure have a significant impact on the efficiency of operations and the ease of doing business. These are major determinants of cost, which are often offset or contributed to by government policies.

Access to raw materials

In pharmaceutical manufacturing raw materials are used to create intermediate compounds which are then synthesized to create active pharmaceutical ingredients (APIs). APIs are the active components in a drug that produce the required effect on the body to treat a condition. The availability of and proximity to the raw materials used in manufacturing enables greater certainty of supply and uninterrupted production which in turn help company's achieve economies of scale.

This can be a costly process, with API production sometimes making up to two-thirds of the total production costs (KPMG India find ref). There are often tens of intermediates that need producing at any one location to create a multitude of APIs.

Reliability and affordability of energy

Given the resource intensity of processes being carried out in manufacturing, the reliability and affordability of utilities is critical. Power supply must be economical and the availability and quality of water must be constant and of good quality.

For pharmaceutical companies, rising energy costs seen recently are affecting the entire value chain, from the cost of powering physical operations and transport infrastructure to the costs of using energy as feedstock for producing the chemicals used in API development[18]. For example, due to a power outage in China in 2021 and a subsequent rise in chemical costs, inflation of key starter materials rose by 10-30% in just one month[19]. These events and trends impact the profitability of API manufacturers, and therefore impact the production of finished medicines.

Transportation infrastructure

The quality and cost of the transportation network is also critical. An efficient transportation service is important in both API and generics manufacturing. Whether being supplied with raw materials or supplying APIs to manufacturing facilities or generics to customers, site choice has a major impact on transportation time and cost.

18 https://www.dcatvci.org/features/rising-energy-costs-and-api-supply/

19 https://www.cnbctv18.com/healthcare/how-are-high-input-costs-impacting-api-firms-profitability-margins-heres-what-experts-say-11028132.htm

3. Regulatory and legal systems

Pharmaceutical registration requirements are rules that promote the availability of quality-assured and effective medicines. In effect, this means that patients get access to medicines that have been produced in a safe and controlled environment and that have been clinically tested to deliver stated outcomes. A high-quality regulatory system will ensure that dangerous, unproven, or useless drugs are prohibited and

do not reach the market. For manufacturers, general issues related to the regulatory and registration process are the transparency, speed, fairness, and cost of the process.[20] Some of these aspects can be tackled through automation and the digitization of highly repetitive paper-based tasks.

Intellectual property

It is also critical that regulatory and legal systems provide a strong, clear and predictable intellectual property and patent protection (IP) environment. Such a system must support Europe's competitiveness. However, the European thinking on IP Incentives is very concerning. Indeed a potential overhaul of the European incentive system towards dynamic conditional incentive concepts based on access and availability criteria will have a negative effect on Europe's ability to foster investments in R&D and manufacturing. It's lack of clarity and predictability will not only impact Europe's life science innovation but it will also have an effect on access and availability of affordable medicines like generics or biosimilars. Indeed, strong, predictable, comprehensive and sufficient duration incentives are key to R&D investors. As for the generic and biosimilar industry legal clarity and predictability of these incentives is of major importance.

However some adjustments are needed in order to stimulate investments in essential medicines manufacturing. For example, for generics and biosimilar manufactures, a Bolar Exemption – which allows manufacturers to prepare products in advance of the expiration of the originators' patents – is critical because it removes the threat of patent infringements[21]. Today, the fact that EU Member States have different interpretations of its scope is making Europe a less attractive and certain place to invest for generics manufacturers. Indeed, the Bolar exemption has been transposed in EU Member States in different ways. Some national legislations have given a broader interpretation of the Directive, some others a more restrictive one. As a result, a high level of uncertainty has been created with regard to the legality of certain actions. The generic and biosimilar medicine, originator and Active Pharmaceutical Ingredient (API) industries have been directly affected. API manufacturers have been so severely impacted by these inconsistencies that they have been forced to shift their operations outside of Europe. In the long run, this is a bad outcome for Europe[22].

20 Management Science for Health 2012. Chapter 7: Pharmaceutical Production Policy
21 https://www.wipo.int/wipo_magazine/en/2014/03/article_0004.html
22 https://www.medicinesforeurope.com/wp-content/uploads/2021/03/Medicines%20for%20Europe%20Position%20Paper%20on%20Bolar%20Exemption%20-%20July%202020.pdf

Environmental and ecological regulations

In addition to drug-specific regulations, environmental & ecological regulations to mitigate soil, air, water and noise pollution also have implications for production. The European Union's ambition to achieve a net zero economy by 2050 means industrial processes have to change[23]. Teva made a series of ambitious environmental commitments in 2021 which aims to see the company reduce its Scope 1 and 2 greenhouse gas (GhG)[24] emissions by 33% versus 2017 levels, increase energy efficiency and reduce total water withdrawal from areas projected to be in water stress[25]. To facilitate companies to undertake this and achieve scale with new processes, the European Commission and nation states should provide incentives recognizing the value of companies' environment investments to create a level playing field with those failing to do so.

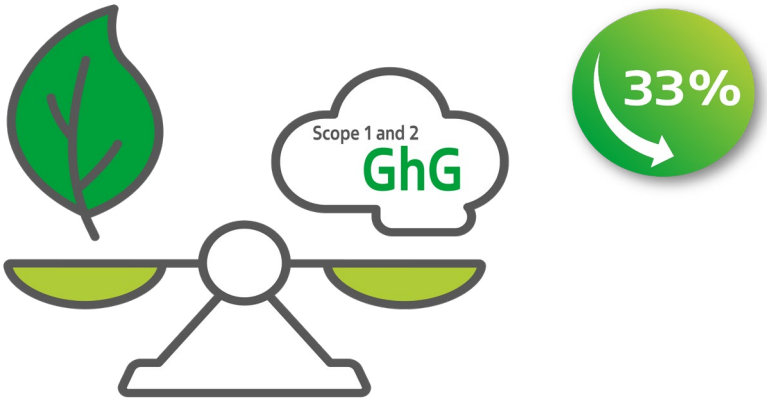


Figure 3.

Duty and import controls

Finally, duties and import controls must be considered which have an impact on manufacturing and production costs. Typically, these are the levels of taxation on and authorization processes for the importation (or domestic sourcing) of pharmaceutical materials.

Recommendation

New EU legislation must foster a digitalised and cost-effective regulatory environment and provide strong, predictable, comprehensive and sufficient duration incentives which are key for investors.

23 https://ec.europa.eu/clima/eu-action/climate-strategies-targets/2050-long-term-strategy_en#:~:text=The%20EU%20aims%20to%20be,net%2Dzero%20greenhouse%20gas%20emissions.

24 Scope 1 covers direct emissions from owned or controlled sources. Scope 2 covers indirect emissions from the generation of purchased electricity, steam, heating and cooling consumed by the reporting company. Scope 3 includes all other indirect emissions that occur in a company's value chain. https://www.carbontrust.com/resources/briefing-what-are-scope-3-emissions#:~:text=Scope%201%20covers%20direct%20emissions,in%20a%20company's%20value%20chain.

25 https://www.tevapharm.com/news-and-media/feature-stories/environmental-goals/

4. Economic Incentives

Typically, if a government makes an industry a priority area, they employ various methods to draw manufacturing firms to invest, including tax incentive, state aid, and forms of public private partnerships.

Tax incentives

Manufacturing tax incentives are a common way of enticing companies to move their manufacturing operations to a new company. For example, tax incentives for research in France had been competitive thanks to its Research Tax Credit (CIR) and the reduced rate applicable to income from industrial property rights, but France is now being outdone by more competitive schemes in Germany (CIR scheme set at 25% rate) and Italy[26].

"Essential pharmaceuticals are an anchoring industry for a country. If you want to keep it in house and support them it would help if we could benefit from the same incentives as other industries to help us digitalise faster etc. At the moment it's hard for us to apply for these incentives because we are so regulated and our lead times are longer"

Robert Kuzela,
Site General Manager, Opava, Czech Republic

R&D funding for innovative drug discovery and development can also be attractive to firms considering where to go. For example, Switzerland has R&D incentive schemes which give R&D tax deductions of up to 50% to firms if R&D is conducted in Switzerland.

It is also critical that countries offer forms of soft support which make their ecosystem a productive place to do business. Ecosystem incentives have a wide remit but include the quality of institutions, human capital, infrastructure, partnership opportunities, market sophistication and business aptitude to help an enterprise succeed.

26 https://www.leem.org/presse/la-fiscalite-des-entreprises-du-medicament-continue-d-affaiblir-l-attractivite-de-la-france

For API and generics manufacturing, the existence of infrastructure for large scale manufacturing with high quality standards is important. For innovative drugs, governments often provide sponsored large-scale innovation centers that encourage the development of novel innovations, talent and project collaboration and enterprise partnerships. In parallel, the European State Aid Framework should enable the generic medicines and API industry to participate in national recovery and resilience plans for green and digital technology investments and to enhance medicines production. As an example, Medicines for Europe, a body representing the generic, biosimilar, and value-added medicines industry in Europe, has called for Important Projects of Common European Interest (IPCEI) to include the manufacturing of essential, life-saving off-patent medicines and related APIs[27].

Public Private Partnerships

Collaborations and public-private partnerships also enable countries to gain the benefit of local production without taking on business risk[28]. This is the most common form of local production support which also helps to drive the local economy, knowledge-base and economies of scale.

"In our case when we talk about a local supply chain it is from field to the factory. We work with local farmers, taking rye that are contaminated with a fungi . There are multiple alkaloids isolated from this fungi, one of them which is used in a medicine to treat Parkinson disease"

Robert Kuzela,
Site General Manager, Opava, Czech Republic

5. Proximity to end market

The proximity of a firm's manufacturing operations to their suppliers and the end market being served is critical for a number of reasons. Cost control is made easier by improved operational flexibility and lower transportation requirements. The environment is served by reducing the carbon footprint of manufacturing and distribution. Security of medicines supply is enhanced as firms have greater control of their supply chain. Firms and patients benefit too from being closer to regulators, enabling improved engagement throughout the development phase. This can potentially mean earlier deployment of a drug.

27 https://www.medicinesforeurope.com/news/essential-medicines-must-be-included-in-eu-industrial-policy-plans/
28 Management Science for Health 2012. Chapter 7: Pharmaceutical Production Policy

The great essential medicines migration:

does East beat West?

The great essential medicines migration: does East beat West?

Over two decades, Western essential medicines manufacturing has been migrating to the East to achieve significant cost savings

Traditionally pharmaceutical companies have chosen to base the majority of their operations in the US and Europe. This was a straightforward choice: the US and Europe represented the majority of the global healthcare market and held the human capital needed to develop drugs and the processes through which they were manufactured and distributed to customers. However, due to growth in the Far East, supportive government policy, and expanding healthcare markets, many pharmaceutical companies have moved key operations eastwards[29]. The main benefactors of this shift have been China and India[30].

While innovative drug manufacturing footprint remains strong in the US and Europe[31], over the last two decades the manufacturing of APIs and generic medicines have been moving to the East. For example, the last factory in Europe producing the API for paracetamol closed in 2008, and Asia has been the primary source of production ever since[32]. To further illustrate the impact of this, there have been significant frictions in the supply of Paracetamol in Europe during the pandemic because the region did not have the leverage nor logistical capacity to scale up production in the short term[33]. This was compounded as India – a major producer of Paracetamol - temporarily banned exports of the drug to meet the needs of its internal market.

This change represents more than simply shifting the cost base of API and generic medicines production. According to a report by Pro Generika, Germany's generic drug association, **Asian companies now hold nearly two-thirds of the approval certificates needed to produce APIs in Europe**, with the remainder held by European firms. This ratio has flipped over the last 20 years. Alarmingly, there are now 93 active ingredients for which no European company holds a certificate[34]; a significant issue when major events threaten supply chains.

"We are deemed to provide essential medicines during pandemics, but during normal time this is not recognised nor encouraged. This cannot continue. We must be more prepared for the next pandemic. There needs to be wider recognition of why this is so important and create a level playing field that supports European competitiveness and investments at all time."

Antonio Cabodevilla,
Site General Manager, Zaragoza, Spain

29 https://www.efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf
30 https://www.efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf
31 https://www.efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf
32 https://www.outsourcing-pharma.com/Article/2009/01/06/Europe-s-last-paracetamol-plant-closes-its-doors#:~:text=As%202008%20drew%20to%20a,facility%20in%20Roussillon%2C%20southern%20France.
33 https://www.forbes.com/sites/forbesbusinesscouncil/2021/10/18/what-can-we-learn-from-the-pharma-manufacturers-leaving-china/
34 https://www.progenerika.de/studies/where-do-our-active-ingredients-come-from/?lang=en

What is driving this?

Many studies[35] have demonstrated that a key reason why the off-patent medicines value chain is moving to China and India is due to the 'race to the bottom' on prices for generics. **As governments and health insurance companies worldwide expanded the use of public tenders and cost containment measures to keep rising healthcare costs in check, price became the primary deciding factor**. Market participants such as generics companies were thus forced to work with the most affordable sources. This resulted in the consolidation of outsourcing to a narrow selection of manufacturers or the transfer of the companies' own API production to lower-cost countries. This opened up key areas of vulnerability due to limited supply diversity as well as the lack of a level playing field for European companies, thus challenging Europe's strategic autonomy. These trends have been exacerbated by the fact that European Regulatory regimes has become onerous[36] and do not always support operational efficiency[37].

The race to the bottom

The impact of price-based tendering has been significant on the European pharmaceutical ecosystem. **In Germany, the cost for Defined Daily Dose for generics reduced from €0.12 in 2012 to €0.06 in 2020[38]. In the Netherlands, the average generic price per counting unit attached is now between €0.07 to €0.09 per tablet/capsule. Some companies were even bidding at €0.05 cents, assumed to be non-European production[39,40].**

To put this in layman's terms, a pack of gum in Spain is now more expensive than a box of twenty 400 mg paracetamol tablets. Of course, it is easier for manufacturers of chewinggum than generic medicines manufacturers to withstand cost fluctuations in the short term; pharmaceutical production has higher quality control standards, higher regulatory compliance requirements, and regulated prices.

Figure 4.

35 Global Trade, Resilience of Pharma Supply Chains and the Impact of COVID-19 Pandemic: https://www.globaltrademag.com/resilience-of-pharma-supply-chains-and-the-impact-of-covid-19-pandemic/ 10 MundiCare on behalf of Pro Generika, Where do our active ingredients come from? https://www.progenerika.de/studies/where-do-our-active-ingredients-come-from/?lang=en

36 The great medicines migration - Nikkei Asia

37 Medicines-for-Europe-Factsheets-on-Market-and-regulatory-reforms-to-ensure-availability-and-resilience-of-the-supply-chain.pdf (medicinesforeurope.com)

38 https://www.progenerika.de/updates-en/corona-pandemic/?lang=en

39 https://asia.nikkei.com/static/vdata/infographics/chinavaccine-3/

40 https://www.progenerika.de/updates-en/corona-pandemic/?lang=en

"We are constantly battling on cost. We face strong competition from manufacturers in China supplying our customers. Production costs from China can be lower than ours from Europe by 30% or more. And that's the biggest dilemma to overcome – how to bring down costs overall to provide cost competitive API's for patients."

Kerri McCullough Wood,
Senior Vice President, Head of Commercial, Teva API & Medis

In this 'race to the bottom' on prices, manufacturers have been forced to work with the most affordable sources, most often in countries (e.g. China and India) offering lower costs and additional government incentives. **According to research conducted by Bain & Co, shifting manufacturing East has netted firms in Europe and North America cost savings of between 20% to 60%. As the author said, "When your competitors are realizing that kind of gain, whether to act is less a choice and more a matter of economic survival"**[41]. For manufacturers that have made this shift there have been some clear benefits, but the long-term outcomes are proving to be less than optimal for European competitiveness and medicines security. All other things being equal, Figure 2 illustrates why this shift has happened:

	West	East
Human Capital Costs		
Factory labour costs (2005)	$20-30 per hour	$1 per hour
Physical Infrastructure Costs		
Electricity costs (€ cost for kWh) (2021)	Germany: €0.317 Spain: €0.242 Italy: €0.214	China: €0.078 India: €0.072
Water costs (€ per cubic meter)	France (2020): €4 Italy (2020): €2	China (2016): <€0.50 China (2021): €1.26
Government Policies		
R&D funding for innovative drug development (2008-2015)	US: +7.3% Spain +27%	China: +254%

Figure 5: Global cost comparison (Sources: [42,43,44,45,46,47])

41 https://media.bain.com/Images/BB_Making_move_low-cost_countries.pdf
42 https://media.bain.com/Images/BB_Making_move_low-cost_countries.pdf
43 https://www.globalpetrolprices.com/electricity_prices/
44 https://www.weforum.org/agenda/2016/07/what-china-s-new-approach-to-water-means-for-business/
45 http://english.beijing.gov.cn/livinginbeijing/housing/202005/t20200513_1895835.html
46 https://smartwatermagazine.co m/news/locken/water-ranking-europe-2020
47 https://itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-us-industry/

Recommendation

New EU and national legislations must address the 'race to the bottom' on prices, and support essential medicines producers response to inflation by shifting procurement from cost-based to value-based economic models by implementing the concept of most economically advantageous tender as proposed by the Directive 2014/24/EU on public procurement

Another driver for the migration to the East has been the shifting government priorities. As Western governments shifted their priorities away from API and generics manufacturing, the Chinese and Indian governments moved to replace them. This has taken form in different ways in China and India, as explained below:

Europe must acknowledge its failures and learn lessons

Unlike China and India, the European Union does not offer a coherent state aid system with clear, direct support. As shown below in the *in-focus* sections below, the scale of support being provided by the governments and key agencies of China and India dwarf the EU's more selective, iterative regime. As we have already seen in Europe, efforts to reshore generics manufacturing are already stumbling due to subsidy rules that limit the ability of nation states to support essential medicines manufacturing[48]. The European Union must act with sustainable policies that enhance European strategic autonomy, including recognizing the essential medicines sector as critical in European Union and national emergency plans for energy supply, adopt measures to mitigate the impact of inflation on cost of goods and reform medicines procurement and pricing models[49]. The time to act is now.

"China and India are better at offering integrated systems – Europe is good but is not doing enough to integrate API manufacturing"

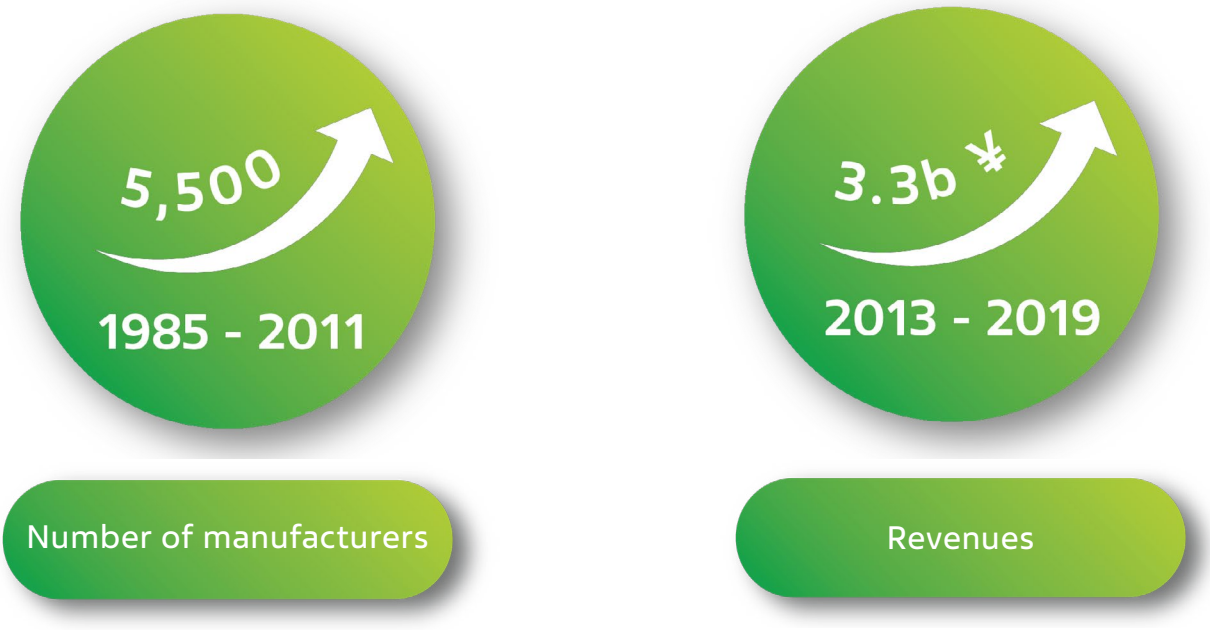
Jaroslav Chylik,
Senior Vice President, Solids manufacturing and supply operations

48 https://www.politico.eu/article/pharma-industry-drug-production-eu-subsidy-european-commission/#:~:text=EU%20regulations%20restrict%20government%20handouts%20to%20support%20drug%20production.&text=The%20EU's%20declared%20goal%20of,own%20rules%20on%20public%20investments.

49 https://www.medicinesforeurope.com/wp-content/uploads/2022/06/EPSCO-Council-_-Medicines-for-Europe-Executive-Committee-OPEN-letter-on-inflation-impacting-the-supply-of-essential-medicines.pdf

China: in focus

Since the 2000s, at the same time as the eastward migration of API factories, China implemented numerous policies, regulations and incentives that have encouraged API production[50]. This has helped grow its pharmaceutical sector. **Between 1985 and 2011 the number of pharmaceutical manufacturers grew from around 1,000 to over 5,500[51]. In turn, revenues have grown dramatically; between 2013 and 2019 revenues grew from approximately 2,100 billion yuan to more than 3.3 billion yuan[52].**



China is aiming to become a global leader in pharmaceuticals. Made in China 2025 – the country's national strategic plan and industrial policy – has aimed to transition China from a low-cost factory to the world to a technology-intensive powerhouse. The plan targets a breadth of sectors, including life sciences, and sets an ambition for China to become a major global biopharma competitor, particularly by developing a world-class generics industry.

As McKinsey notes, by 2025 China wants to achieve drug quality standards and systems that are in line with international standards, among which at least 100 pharmaceutical enterprises obtain US, EU, Japanese and WHO authentication and become successful exporters. It is also seeking to industrialise 20 to 30 innovative drugs, 5 to 10 with indigenous property rights with the Food and Drug Administration (FDA) or European Medicines Authority (EMA) and enter the international market. Achieving this would make China a strong global competitor across the value chain[53].

50 https://www.ft.com/content/10ffe24b-9637-462b-9f91-2c85fa03cf5f
51 https://link.springer.com/chapter/10.1007/978-981-13-8102-7_10/tables/1
52 http://www.cpema.org/uploadfile/2022/0406/20220406031714956.pdf
53 www.mckinsey.com/industries/life-sciences/our-insights/the-dawn-of-china-biopharma-innovation

"China has launched initiatives to support their innovative as well as generics industries. Just from their size, we should expect competition, even though very few finished drugs come from China now. That could change in the next 20 years. We need to decide now how much dependence we want to have on other parts of the world."

Edith Koller Dette,
Senior Vice President, Global Quality and EHS&S

The economic incentives powering the Made in China 2025 plan illustrate their determination to transition their economy from lower paid, lower skilled to higher paid, higher skilled, and in turn taking a larger portion of the value chain. China has reduced some corporate income taxes by up to 15%, set a 150% pre-tax 'super-deduction' on specific R&D activity in China, and permitted full taxation exemptions for all export products. The Chinese government has also supported pharmaceutical firms through R&D funding at a national and local level, support for venture capital and regulatory changes. As an example, between 2009-2013 Chinese government funding for medical research through the National Natural Sciences Foundation of China increased by a factor of four to $710 million[54]. The annual growth rate in pharmaceutical R&D expenditure has been higher in China than in the US and Europe for over 15 years now[55]. This combination of incentives has enabled Chinese generics firms, which make up the majority of Chinese biopharmaceutical firms, to begin making significant profits over the last decade[56].

Finally, China is actively facilitating wider ecosystems that will power the innovation of tomorrow. Zhaofeng Zhang, director of MOST's Science and Technology for Social Development programme, reported in 2020 that China will spend around $1.45 billion to support 20 biomedicine science parks. This is in addition to the 100+ national level and biotechnology industry parks and more than 400 provincial level parks. To indicate the level of impact this has already had, Shanghai's "Pharma Valley" holds more than 500 biotechnology companies[57].

The scale and pace of reforms – supported by significant funding to improve the business environment and reduce corporate costs, an abundance of unskilled and skilled talent together with the increasing size of the total addressable market for healthcare – are galvanizing a new era of innovation in China.

54 www.itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-us-industry
55 https://www.efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf
56 www.itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-us-industry
57 www.itif.org/publications/2020/09/08/impact-chinas-policies-global-biopharmaceutical-industry-innovation

India: in focus

India is also ambitious to redefine its position in the global pharmaceutical value chain. Currently third in the world in terms of volume, it is valued at $41 billion[58]. Yet, although its pharmaceutical industry grew at a compound annual growth rate (CAGR) of 13% over the last two decades, much of this growth came at the start of the period. For example, CAGR in the last decade was 8.5% and only 6.2% during the second half of this period[59]. As a result, India is refreshing its efforts to become a more competitive location for pharmaceutical manufacturing

To incentivize global and domestic pharmaceutical companies to invest in and grow production across key product categories – and also incentivize local production - the Department of Pharmaceuticals has launched three core schemes.

"India used to produce a lot of key starter materials (KSM) and raw materials. Many years ago, this production shifted to China due to competitiveness. Now, due to the pandemic, India has acknowledged the risk and is bringing back manufacturing of these KSMs and raw materials through incentives in local production. India is now de-risking in other areas and incentivizing areas of local production. This is happening right now. These actions are being expedited to ensure they have those products for their patient populations."

Kerri McCullough Wood,
Senior Vice President, Head of Commercial, Teva API & Medis

Firstly, a production linked incentive scheme for bulk drugs. The scheme, valued at almost $1 billion over six years, intends to boost domestic manufacturing of identified key starting materials (KSMs), drug intermediates (DIs) and APIs by attracting large investments in the sector and thereby reducing their import dependence for critical APIs. Under the scheme, financial incentives are being given based on sales made by selected manufacturers for 41 products covering the list of 53 APIs for which India currently has import dependence. Producers of fermentation-based and chemical systhesis-based products will receive between 5% and 20% bonuses on sales revenue achieved[60].

Secondly, a production linked incentive scheme for pharmaceuticals. The scheme, valued at almost $2 billion over five years, intends to enhance India's manufacturing capabilities by increasing investment and production in higher value goods in the pharmaceutical sector. Further, India intends to use the scheme to create champion brands that have the potential to scale and penetrate global value chains. The scheme covers three categories. The first category covers bio-pharmaceuticals, complex generic drugs, and cell based

58 https://www.investindia.gov.in/schemes-for-pharmaceuticals-manufacturing
59 https://assets.ey.com/content/dam/ey-sites/ey-com/en_in/topics/health/2021/ey-ficci-indian-pharma-report-2021.pdf?download
60 https://static.investindia.gov.in/s3fs-public/2020-08/PLI%20bulk%20drug%20schemes.pdf

and gene therapy drugs among others. The second category covers key starter ingredients (KSMs), drug intermediates (DIs), and APIs. The third category includes any drugs not coverered by categories 1 and 2 such as repurposed drugs, auto immune drugs, and in-vitro diagnostic devices. Under the scheme, rates of incentives start in FY2022-23 at between 5% and 10% depending on the category and taper off to between 3% and 6% in FY 2027-28.

And thirdly, a bulk drug parks scheme. The scheme, valued at over $350 million and running over a four year period, intends to promote the setting up of bulk drug parks that provide easy access to world class common infrastructure facilities, enabling greater optimization of resources and e conomies of scale. It also aims to use the scale of such parks to meet environmental standards through innovation and combined waste management systems[61]. Among other things, the common facilities will include central effluent treatment plants, solvent recovery and distillation plants, steam generation and distribution systems, common cooling system and distribution networks, and common logistics facilities. Depending on the region, the financial assistance will cover between 70% and 90% of the project costs of creating common infrastructure facilities.

Together, the ambition is to make India's pharmaceutical industry more resilient to external shocks, enable greater drug security and boost the capacity for domestic production for critical bulk drugs and high-value products alike. As with China, these ambitions are built upon not only bolstering their production capacity for bulk drugs (generics), but towards establishing market strength in higher-value pharmaceuticals too[62].

Recommendation

Political ambitions to strengthen EU supply chain resilience should integrate the impact of the financial crisis on the industry manufacturing global competitiveness. Systemic economic and regulatory reforms are needed to enhance Europe's strategic autonomy and provisions should be made to facilitate access to funds for the manufacturing of essential medicines - the ultimate goal being to create a level playing in a fair and open way.

61 https://static.investindia.gov.in/s3fs-public/2020-08/Gazettee%20notification%20of%20bulk%20drug%20schemes-pages-deleted.pdf
62 https://www.investindia.gov.in/schemes-for-pharmaceuticals-manufacturing

A world in flux: turbulent times, soaring inflation and a widening of the EU manufacturing competitive gap

A world in flux: turbulent times, soaring inflation and a widening of the EU manufacturing competitive gap

Soaring inflation has been a direct consequence of the pandemic and Russia's invasion of Ukraine has had direct consequences on the production costs of already low-priced generic medicines.

Events of the last three years have had a profound impact on many of the things that the public, companies and governments have taken for granted for so long. **As Professor Edward Anderson, Professor of Analytics and Operations Management at Imperial College Business School said: "We have become so used to global supply chains that we barely think about them. But almost every product we consume arrives on our doorstep courtesy of a global network of firms each feeding their components into the finished product. And it is when things go wrong that we sit up and take notice."[63]**

For hundreds of millions of people in the West, the COVID-19 pandemic was the first time in generations that members of the public have had to endure significant disruptions to their living situations alongside widescale uncertainty about their livelihoods. These challenges were added to in February 2022 when Russia invaded Ukraine, leading to a major armed conflict in Europe and the most comprehensive set of economic sanctions imposed on a single country. These sanctions would include cutting structural energy dependence on Russia.[64] The difficult consequences for society have been direct and quickly realized as dramatically increasing general inflation, and raw material and transportation costs have spread[65,66].

The crisis has revealed uncomfortable realities for much of the West, which had become over-reliant on manufacturing output of China and the energy resources of Russia. In the case of manufacturing, 52% of the EU's strategic imports, including raw materials, batteries, active pharmaceutical ingredients, semiconductors, and other key technologies, come from China[67]. In the case of energy, despite warnings from Poland and Baltic states to consider other options, Germany chose Russian gas in favour of nuclear as it attempts to transition away from coal to support its industries[68]. However, Germany was not alone; in 2021 the European Union imported 155 billion cubic meters of natural gas from Russia[69]. Equally concerning is Ukraine's position as one of the world's leading grain exporters, supplying more than 45 million tons of grain annually to the global market[70]. As a result of the war and the Black Sea Blockade, energy prices are rising rapidly and global food security is at risk.

As with the severe impact of inflation being experienced by households in all corners of the globe, there have significant impacts on the cost base and competitiveness of industries in Europe too.

63 https://www.imperial.ac.uk/stories/global-supply-chain-crisis/
64 https://www.eeas.europa.eu/eeas/sanctions-against-russia-are-working_en
65 https://www.medicinesforeurope.com/wp-content/uploads/2022/06/EPSCO-Council-_-Medicines-for-Europe-Executive-Committee-OPEN-letter-on-inflation-impacting-the-supply-of-essential-medicines.pdf
66 https://www.imf.org/en/Publications/WEO/Issues/2022/07/26/world-economic-outlook-update-july-2022
67 https://www.eiu.com/n/eu-unveils-strategy-to-reduce-dependency-on-china/
68 https://www.theguardian.com/world/2022/jun/02/germany-dependence-russian-energy-gas-oil-nord-stream
69 https://www.iea.org/news/how-europe-can-cut-natural-gas-imports-from-russia-significantly-within-a-year
70 https://www.fao.org/newsroom/detail/ukraine-fao-scales-up-efforts-to-save-upcoming-harvest-ensure-export-of-vital-grains/en

For the pharmaceutical sector, inflationary pressure on the cost of raw materials, active ingredients, and intermediates is driving pharmaceutical price growth worldwide. With numerous essential off-patent medicines subject to strict price regulation for many years, mounting inflation is significantly adding to the costs of production and transport of medicines, and thus the vulnerability of the supply chain.

But how are these damaging trends in Europe impacting some of the key determining factors mentioned previously for pharmaceutical manufacturing success?

Overall Production Costs

Increased Costs of Physical Infrastructure

Spain is a good example of how these global issues are contributing to inflation and are affecting industry. The Spanish Agency for Medicines and Health Products (AEMPS) revealed that pharmaceutical firm margins were being squeezed by the supply chain crisis. Production costs have risen 10% as a result of 150%, 112% and 93% rises in the cost of gas, electricity, and water respectively. Absorbing this rise in manufacturing costs immediately compromises the production of generic medicines[71].

Increased costs of transportation

The rise in the costs of shipping container freights from China to Europe since the pandemic has been staggering. Between November 2020 and May 2022, the container freight rate index has gone from approximately 1,200 to over 5,000 points, a rise of more than 400%[72].

71 AESEG medicamentos genericos: Informe: Estudio del impacto de la actual crisis de sumistros en el mercado de medicamentos genericos
72 https://www.statista.com/statistics/1266631/china-eastern-asia-to-northern-europe-container-freight-rates/

Building resilience: a sink or swim moment for European Essential pharmaceutical manufacturing

Building resilience: a sink or swim moment for European Essential pharmaceutical manufacturing

The pandemic, Russia's war on Ukraine and the resulting towering inflation has told many home truths about the relative dependency, strength and resilience of European pharmaceutical manufacturing and essential medicines supply security. Changing course now can still yield success.

Although the critical importance of the pharmaceutical industry has been proven in its response to COVID-19, the pandemic also exposed some weaknesses and caused challenges to industry operations and norms. As countries across the world entered lockdowns, transport and logistics between countries across the world grew more difficult. This had a significant impact on the pharmaceutical industry, restricting the manufacturing, supply and distribution of medicines[73]. Despite these strong logistical headwinds the industry has shown its resilience to meet a unique and unprecedented spike in demand for some essential medicines needed to care for COVID19 affected patients.

These challenges were compounded by surging demand for some medicines used in the treatment of patients with COVID-19. As referenced previously, paracetamol, an essential painkiller faced supply tensions after India announced an export ban at the start of the pandemic[74]. These situations have resulted the UK[75], France[76] and Ireland[77] among others announcing protocols to manage the supply of paracetamol.

However, today's inflation crisis is putting additional pressure on costs, further undermining existing producers of essential medicines in Europe. Policy reforms must strengthen Europe's ability to diversify supply.

Market failure in Europe

Beyond the pandemic and more recently, other medicines have been affected too, showcasing the state of essential medicines scarcity. **In Germany, delivery bottlenecks for tamoxifen, an active ingredient used as an effective hormone therapy to treat hormone receptor-positive breast cancer, caused shortages[78].** The only European API manufacturer of tamoxifen stopped producing because it had become uneconomical for them to do so, which caught European finished drug producers by surprise and left them without any European supply source, and only a few non European suppliers. Such instances pose difficult questions to pharmaceutical companies and policy makers for how they can best support patients at their time of greatest need.

More than two years into the pandemic these pressures remain and have been exacerbated by the current inflation spike; decreased manufacturing capacity, logistical and transport challenges, and increased purchasing costs are causing countries and regions to rethink their approach to protecting and enhancing key industries. In the case of essential pharmaceuticals, it is causing governments to reevaluate how they can guarantee the public and patients with medicines security and timely access to treatments.

73 https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/availability-medicines-during-covid-19-pandemic
74 https://www.theguardian.com/world/2020/mar/04/india-limits-medicine-exports-coronavirus-paracetamol-antibiotics
75 https://www.pharmacymagazine.co.uk/news/government-issues-shortage-protocol-for-paracetamol-suppositories
76 https://www.connexionfrance.com/article/French-news/French-health-body-takes-action-to-prevent-Paracetamol-shortage
77 https://www.irishtimes.com/business/health-pharma/paracetamol-supplies-to-irish-pharmacies-experiencing-shortages-1.4865826
78 https://www.progenerika.de/presse/tamoxifen/

A solution is needed in Europe

In Europe, this has meant more radical thinking on how its pharmaceutical manufacturing base can become more resilient to ensure efficiency and uninterrupted supply chains[79]. This process has taken several forms including 2020's Pharmaceutical Strategy for Europe, the launch of the European Health Emergency Preparedness and Response Authority (HERA), and an updated New Industrial Strategy.

"We adapted to keep the business continuity, but did not adapt to keep the same level of competitiveness, site expenses are significantly increased. In this respect, aggressive and urgent action is needed to prioritize pharmaceutical industry, agree on common incentives and measures to keep the production competitive until the situation calms down, so we secure EU operating sites long term presence."

Romana Santa,
Site General Manager, Teva API, Croatia

At its inception, the European Commission outlined two key **challenges and needs** that **it** would attempt to address via its COVID19 lessons learned and the Pharmaceutical Strategy for Europe. Firstly, that Europe needs to have a crisis-resistant system to ensure that patients have access to medicines under all circumstances. Secondly, tEurope needs to be more competitive, resilient and less dependent on non-EU countries for the medicines.

The Pharmaceutical Strategy is based on four pillars, requiring a combination of legislative and non-legislative action. Firstly, to ensuring access to affordable medicines for all patients. Secondly, to support the competitiveness, innovation and sustainability of the sector, including the development of greener medicines. Thirdly, enhancing crisis preparedness and response mechanisms, diversified supply chains, and address medicines shortages. And finally, ensuring a strong EU voice in the world through a high level of quality, efficacy and safety standards. The strategy should also align with the Industrial Strategy, European Green Deal, Europe's Beating Cancer Plan, and European Digital Strategy (ibid).

79 Global Data: State of the Biopharmaceutical Industry, 2022]

Crisis preparedness and response

A critical part of building this resilience was the launch of the European Health Emergency Preparedness and Response Authority (HERA) in 2021. Capitalising on the COVID19 lessons learned from the early stage of the pandemic, HERA is a direct response to the relative failure of the European Union to respond in a timely and effective manner in the early stages of the pandemic[80]. A key pillar of President von der Leyen's State of the Union address in 2021, HERA's mission is to prevent, detect and rapidly respond to health emergencies[81],ensuring the development, manufacturing, procurement, and equitable distribution of key medical countermeasures. During future health emergencies, HERA will manage the development, production and distribution of medicines, vaccines and other medical measures that promote public health and safety.

Although interactions with industry have started, it has to be seen how concretely HERA will support the development and manufacturing of essential medicines in Europe, particularly to best face future crisis.
Additionally, the European Medicines Agency (EMA) has been given strengthened powers in crisis preparedness and management of medicinal products and medical devices[82]. These powers have enabled the EMA to appoint a medicines shortages steering group to prepare a critical medicines list to ensure a level of preparedness for a public health emergency or major event. At a minimum this list, for which a shortage monitoring system will be set up, will cover medical devices and medicines necessary for emergency care, surgery and intensive care. However, it is unclear how a two-way dialogue between the EMA and industry will take place. Such a dialogue must facilitate maximum transparency of supply levels for essential medicines to help manufacturers adjust production or ease the movement of products across the European Union. Greater regulatory flexibility is needed to achieve this goal.

Dealing with dependencies

The European Commission is also determined that new approaches to supporting the pharmaceutical sector and essential medicine security in Europe are compatible with the aims of both : its 2020 Pharmaceutical strategy and Industrial Strategy, which pledged to support a twin transition towards climate neutrality and digital leadership while supporting Europe's manufacturing competitiveness.

This goal remains, but there has been a recognition that Europe must learn from the pandemic to plan and execute its strategy more effectively, aligned to industry and society's most pressing challenges. In this context, the European Commission issued an update to its industrial strategy with the goal of strengthening the resilience of the single market, supporting Europe's Open Strategic Autonomy by dealing with dependencies, and further supporting the business case for twin transitions[83] and will propose a reform of its Pharmaceutical legislative framework. However no concrete tangible outcomes have emerged yet that stop pharmaceutical companies moving to the Far East.

In order to grasp the opportunity to make the region a world leader in life sciences, and essential medicines, several gaps have been identified by both Medicines for Europe[84] and EFPIA[85]. Both trade organisations recognized that more needs to be done across the various policy levers available to improve the strategic autonomy and growing dependencies of Europe.

80 https://www.bmj.com/content/378/bmj.o2237
81 https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_en
82 Publications Office (europa.eu)
83 https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy_en
84 Essential medicines must be included in EU industrial policy plans | Medicines for Europe
85 EFPIA response to the publication of the updated EU Industrial Strategy

The European Commission also set up a Structured Dialogue in early 2021 to further investigate and address aspects that were impacting the resilience of the whole pharmaceutical manufacturing value chain, from raw materials, intermediates, active pharmaceutical ingredients to finished drugs. The exercise was unique in that it brought together all relevant supply chain stakeholders and policy makers to discuss solutions to the most pressing issues concerning the security of Europe's pharmaceutical supply chain.

Will Europe rise to the challenge ?

The rationalisation of the essential medicines value chain and an increased reliance of European pharmaceuticals on China and India was proven during the pandemic. As reflected on earlier, not only has India shown its intent to serve the needs of its population first during times of crisis, China has taken a markedly different approach to handling the pandemic with its zero-Covid policy. These factors, among others, have had serious implications on the reliability of previously trusted supply chains and which are now exacerbating by the inflation crisis. It has become clear that if Europe wants to have essential medicines security and maintain a competitive pharmaceutical sector, it must make cogent efforts to address its weaknesses.

The reshoring of some key pharmaceutical manufacturing to Europe has had only modest success and won't address the root cause of the current migration that we see[86]. Policy reform to address Europe's loss of competiveness should be the way forward to redirect investments in essential medicines production in Europe. This is seen as an important step to reducing the chances of future market failure, and for the public this means direct action to ensure patients do not go without necessary and timely treatments. Speaking at a gathering of executives from Europe's off-patent medicines industry in Athens last year (October 2021), European Commission Vice President Margaritis Schinas called the pandemic a "wake-up call" for Europe to strengthen its pharmaceutical sector. "Being able to produce and supply medicines ... is a matter of great strategic and geopolitical importance for our union,"[87].

Attracting investments would add resilience to Europe's medicine security. According to The Buck Consultants International survey, European industrial companies are mainly looking at Central and Eastern Europe as possible production destinations. These nearshore destinations currently have higher labor costs than in the East, but in the shadow of the pandemic, maneuverability and flexibility have become more important than low labor costs[88].

Europe is not alone in its efforts to refocus priorities on securing its supply chain and reshoring key manufacturing activities. In other parts of the world, similar initiatives are taking place to ensure the same outcome. The US is prioritising and funding making its pharmaceutical supply chains more self-sufficient. Reshoring is key part of this, so too is enticing manufacturing from higher cost areas into the US. For example, in June 2021 the Biden-Harris Administration signed an executive order for a 100-Day Review of Pharmaceuticals and API, announcing a set of actions to ensure the US has access to the pharmaceuticals necessary for economic security, health security, and national defence[89]. Critical to this is the implementation of a strategy to create a robust and resilient pharmaceutical and active pharmaceutical ingredients

86 https://www.europarl.europa.eu/RegData/etudes/STUD/2021/653626/EXPO_STU(2021)653626_EN.pdf
87 https://www.politico.eu/article/pharma-industry-drug-production-eu-subsidy-european-commission/
88 https://www.consultancy.eu/news/amp/7430/european-companies-increasingly-moving-to-reshore-asia-production
89 https://www.fda.gov/about-fda/reports/executive-order-14017-americas-supply-chains#:~:text=100%2DDay%20Review%20of%20Pharmaceuticals%20and%20API%20(June%208%2C,health%20security%2C%20and%20national%20defense.

(API) supply chain that reduces US reliance on key starting materials (KSMs) and APIs from overseas. Further, as noted in the previous section, India has set up production-linked incentive schemes for the promotion of domestic manufacturing of critical KSMs, drug intermediates and APIs within which companies are being heavily incentivized to take or build manufacturing capabilities there.

Creating a level playing field: recommendations for a strengthened essential pharmaceutical ecosystem in Europe

Creating a level playing field: recommendations for a strengthened essential pharmaceutical ecosystem in Europe

The European Union and Member States must take swift action to build resilience into the European pharmaceutical ecosystem and introduce new policy reforms that ends a 'race to the bottom' on prices. Not only is action critical to protect patients, it is critical to protect high skilled jobs in Europe.

With the reopening of pharmaceutical legislation in Europe, there is an opportunity to create an ambitious policy platform that supports European pharmaceutical companies while building lasting resilience into the system. The purpose of the legislation should be to make these ambitions mutually reinforcing.

The availability of essential medicines and generics in Europe have been taken for granted for several decades, but the upheaval of the past three years has exposed Europe's recent overreliance on China and India for KSMs, and APIs. In a world now defined by volatility and complexity, clinging to the status quo presents an unacceptable risk.

Underpinning the policymaking process should be a clear ambition to ensure patients in Europe have timely access to medicines when they need them. To achieve this, European legislators must do more to support pharmaceutical companies and initiate policy that puts an end to the 'race to the bottom' on prices. In a context of rising inflation this is a difficult debate to have, but it is necessary. Affordability of essential medicines and generics is of critical importance, but this needs to be balanced against the risk of low or now supply.

Applying the findings of this research and wider consultation across the business, Teva has drawn up four recommendations for European policymakers to consider in the months to come. These recommendations reflect on the lessons learned from COVID-19, supporting timely access to affordable medicines while driving an open and competitive European pharmaceutical ecosystem that attracts investments in R&D and manufacturing. They are as follows:

1. Healthcare reforms must eliminate the 'race to the bottom' on prices, notably by shifting procurement from cost-based to value-based economic models

Teva strongly believes there should be a shift from cost-based economic models to value-based economic models to avoid a 'race to the bottom' which may negatively impact access to both on- and off-patent medicines.

Market access and regulatory barriers and their root causes that delay access or limit availability to innovative medicines (as shown by EFPIA WAIT Indicator Report[90]) or generics or biosimilars should be clearly identified and addressed.

90 EFPIA WAIT Indicator Report : https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/access-to-medicines-inequalities-persist-but-solutions-must-be-found-in-partnership/

As highlighted in the report many studies have demonstrated that a key reason why the off-patent medicines value chain is moving East is due to the 'race to the bottom' on prices for generics[91]. As a result, Teva believes procurement should be drastically reformed to ensure tenders systematically introduce multi-winner, multicriteria models that reward supply diversity, resilience, environmental performance and sustainability. Via the reopening of the pharma legislation and a connection with the public procurement directive 2014/24/EU, Teva believes that tender regimes could be adapted to address the above trends by introducing measures to ensure sustainable tender practices.

Another mechanism that should be very carefully considered is Joint Procurement. Teva remains extremely concerned about the use of such a mechanism which has been used to procure ICU Medicines during the COVID pandemic. Based on Teva's experience so far, joint procurement has not delivered any positive outcomes to boost the availability of medicines, while wasting significant resources. For example, lack of proper consultation, lengthy timelines, no clear volume commitments are among the short comings identified a Joint procurement of ICU medicines launched by the Commission in June 2020[92]. Teva believes advance purchasing of specific critical medicines should be considered instead.

"Tenders should look at the flexibility and reliability of supply as well as the green legislation."

Jaroslav Chylik,
Senior Vice President, Solids manufacturing and supply operations

However, if deployed, it should be limited in scope for crisis situations, and be carried out in a transparent, timely and effective way to prevent market disruption. Doing so will ensure the manufacturers deliver production and authorities purchase their agreed reserved volumes.

91 Global Trade, Resilience of Pharma Supply Chains and the Impact of COVID-19 Pandemic: https://www.globaltrademag.com/resilience-of-pharma-supply-chains-and-the-impact-of-covid-19-pandemic/ 10 MundiCare on behalf of Pro Generika, Where do our active ingredients come from? https://www.progenerika.de/studies/where-do-our-active-ingredients-come-from/?lang=en

92 https://www.medicinesforeurope.com/wp-content/uploads/2022/05/Factsheet_Joint-procurement.pdf

2. Rather than pursuing a broad revision of existing incentives, new legislation must provide clarity and predictability on the European incentives regime to avoid jeopardising investments in innovation and manufacturing.

An overhaul of the European incentive system towards dynamic incentive concepts based on access, availability or affordability criteria will have a negative effect on Europe's ability to foster innovation and stimulate access and availability of more affordable medicines like generics or biosimilars.

Indeed, strong, predictable, comprehensive and sufficient duration incentives are key to R&D investors. As for the generic and biosimilar industry legal clarity and predictability of these incentives is of major importance. Therefore, Teva does not support a broad revision of existing incentive regimes that will jeopardise innovation and the current established balance between on- and off-patent medicines.

3. New EU legislation must foster a digitalised and cost-effective regulatory environment.

Europe's regulatory framework is based on strong quality, safety and efficacy standards that should not be diluted by the reopening of the pharmaceutical legislation. However, there is scope to improve the operational effectiveness of the regulatory system. Teva strongly believes that there is a need for a more cost-effective and digitalised regulatory system. The current interactions between industry and regulators are heavily paper-based and not aligned with Europe's digital and green priority agenda. Such digital transformation is critical to Europe's pharmaceutical competitiveness, providing significant opportunity to achieve efficiencies while providing improved regulatory standards and allowing regulatory authorities to focus on higher value tasks. Priorities should include timely implementation of e-Patient Information Leaflet, streamlining API assessments, and ensuring better GMP/Manufacturing management and resources.

With regards to the environment, a sciencebased approach and self-regulated initiatives should be favoured over new regulations and requirements. Some of the industry's initiatives have proven to be very ambitious, such as the AMR alliance, which could serve as an appropriate benchmark for any new initiative. Also, it is crucial that coherence and alignment are ensured among various existing environmental, health and industrial policies.

4. Healthcare reforms must guarantee sustainable security of supply

For Teva, every patient should have access to the drugs they need when they need them. Unfortunately, medicines shortages in Europe is a real problem and their root causes need to be better assessed and addressed.

Teva believes it is incumbent on the European Union and industry to address these shortages to prevent future issues. Open trade, supply diversity, transparency about shortages and where medicines are available, and flexibility to move products quickly across nation states are key hurdles that needed to be overcome.

As mentioned in the recent Technopolis report of the European Commission about future-proofing pharmaceutical legislation —"Study on Medicine Shortages"[93], it is typically where medicines are, rather than total volume that determines availability of supply. Inevitably, if fewer suppliers exist, these challenges grow.

This is based on three critical principles:

1. To ensure diversity of supply: The 'race to the bottom' on price for generics, combined with an onerous European regulatory framework, have forced the generic supply value chain to consolidate, often outside Europe, in order to survive. It is essential to address those regulatory and economic root causes weakening the industry's ability to supply and impacting European manufacturing strategic resilience.

3. To ensure transparency: A pan-European shortages reporting system, integrated with existing data systems, should be launched, alongside a two-way formal dialogue between industry and authorities, to enable companies to respond to needs in a timely manner.

5. To enable fast movement of goods across Europe: digital tools that reduce the time for translation and repackaging are critical. Also greater use of the "repeat use procedure" is needed to allow products to be authorised and placed on the market more quickly.

Critically, these recommendations enable better business operations and improved patient outcomes in Europe. Teva believes that any additional burdensome regulatory requirements risk fragmenting the single market and jeopardise its integrity by shifting shortages from one country to another. This would threaten the economic sustainability of products and lead to further shortages.

The State Aid EU and national framework should enable the generic medicines and API industry to participate in national recovery and resilience plans for green and digital technology investments in order to enhance medicines production competitiveness.

Notably, for the so-called Important Projects of Common European Interest (IPCEI) set up to support the political commitment to deliver on Europe's vision for increased open strategic autonomy and build industrial capacity to deliver for European industry and on access to medicines for patients, they must:

- Encourage access to manufacturing incentives such as funds to support investments in new technology and innovation by including the API and off-patent industry in the health IPCEI project
- Make EU funds and recovery funds available to support green and digital production and technology transformation to reinforce our strong European manufacturing footprint vs. competing geographies

93 European Commission Report from Technopolis : Future-proofing pharmaceutical legislation - Publications Office of the EU (europa.eu)

A resilient manufacturing system requires long term investments to ensure it can withstand minimum production losses during major disruptions. The European Union has the ability to foster manufacturing resilience and reinforce the sector's global competitiveness

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