

Pharma supply
chains of the
future



Introduction

Since its worldwide emergence in 2020, COVID-19 has impacted global supply chains with effects that are still being witnessed today. Each day comes news of choked ports, out-of-place shipping containers, record freight rates, and other problems that cause disruption and defy easy answer, the World Economic Forum acknowledged in January 2022.¹

Air transportation routes, as well as shipping, have suffered from the effects of the pandemic, with global air traffic falling by more than 90% in April 2020. With armed conflicts leading to airspace closures in early 2022, the effects of the pandemic and other disruptive global events seem set to continue for the foreseeable future.

Like other sectors, the pharmaceutical industry (hereafter, pharma) has had to absorb the impact of recent events on its supply chain operations. Throughout the pandemic, pharma has stood on the front line of the public health battle to develop and deliver vaccines and antivirals against COVID-19, working closely with governments and regulators. To their credit, these stakeholders have recognized the need for an unusual degree of regulatory flexibility during the pandemic, embracing a level of close collaboration with the pharma industry which will hopefully continue into the future. But while acknowledging the industry's achievements during the crisis and the potential longer-term benefits it may yield in terms of improved

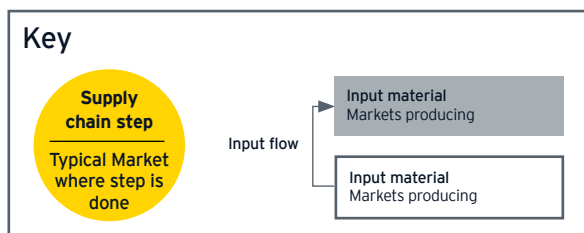
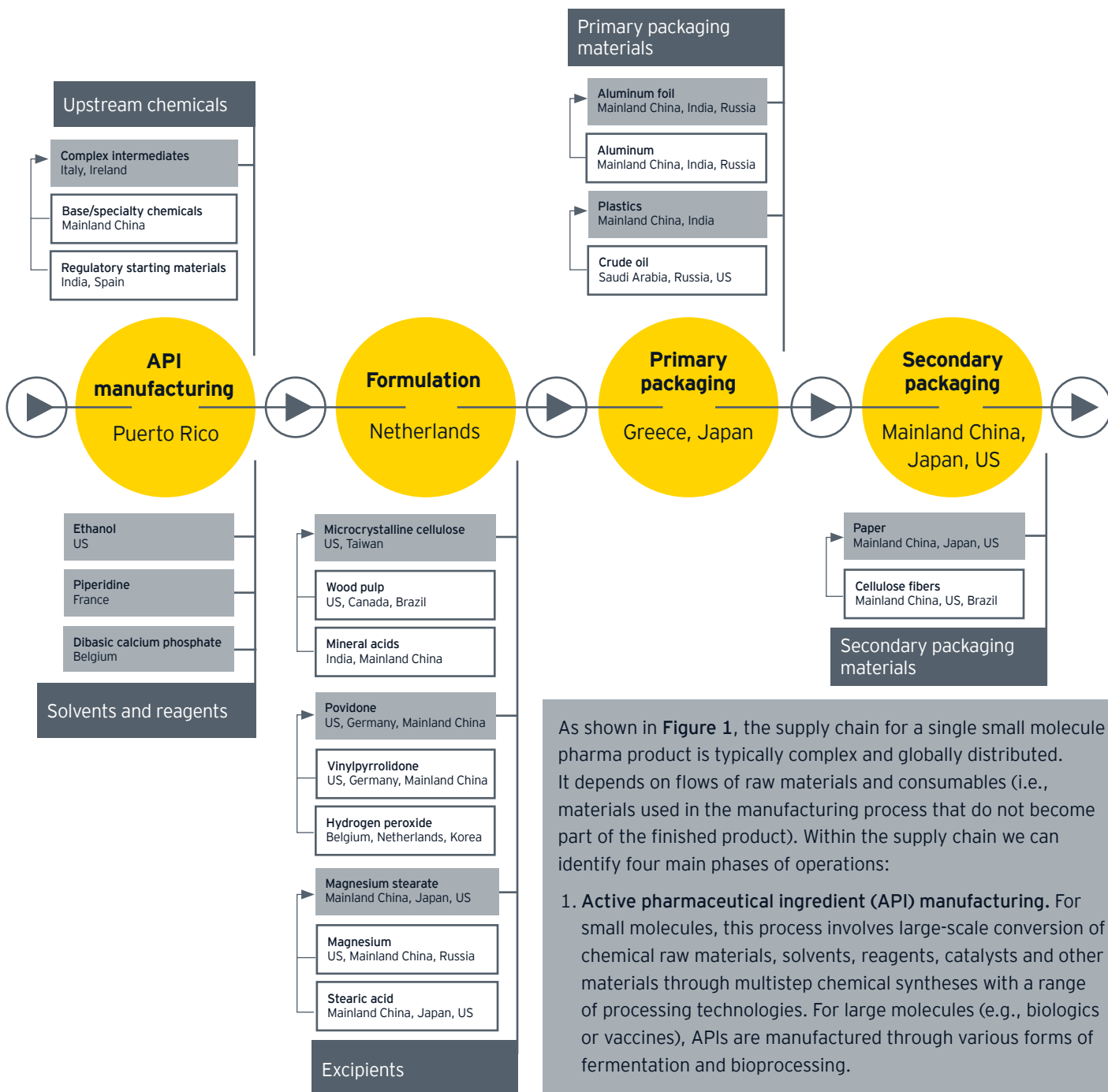
collaboration, we must also recognize that COVID-19 was a serious challenge for the industry's supply chains. Leading pharma executives told us in the early months of the outbreak that their operations had already faced a "stress test" of unprecedented dimensions.²

Now, more than two years after COVID-19's emergence, it is time to evaluate how pharma has coped with this stress test and what learnings for the future can be taken from its performance. To this end, we have held discussions with 17 global heads of manufacturing and supply chain operations at companies that are members of the Pharmaceutical Manufacturing Forum (PMF). The group comprises technical operations and supply leaders of global research and development based pharmaceutical companies. The goal of our discussions and the subsequent analysis presented in this paper was to understand what the future for pharma supply chains may look like and what measures the industry can take to build greater resilience into supply chains.

¹ Tarek Sultan Al Essa, "5 ways the COVID-19 pandemic has changed the supply chain," *wef.org*, 14 January 2022, ©2022 World Economic Forum.

² "How can unprecedented times now create unprecedented opportunities for what's next? Executive summary of 22 July roundtable reassessing life sciences supply chains to increase pandemic resilience and governmental actions." *ey.com* website, September 2020, ©Ernst & Young Global Limited.

Figure 1. Example supply chain for a small molecule pharmaceutical product



As shown in Figure 1, the supply chain for a single small molecule pharma product is typically complex and globally distributed. It depends on flows of raw materials and consumables (i.e., materials used in the manufacturing process that do not become part of the finished product). Within the supply chain we can identify four main phases of operations:

- 1. Active pharmaceutical ingredient (API) manufacturing.** For small molecules, this process involves large-scale conversion of chemical raw materials, solvents, reagents, catalysts and other materials through multistep chemical syntheses with a range of processing technologies. For large molecules (e.g., biologics or vaccines), APIs are manufactured through various forms of fermentation and bioprocessing.
- 2. Formulation.** Manufacturing the product in the correct form and dosage for administration to a patient involves the mixing of APIs with all necessary inactive product ingredients (i.e., excipients). It also covers additional steps, such as tableting or sterile filling.
- 3. Primary packaging.** This term denotes materials that are in direct contact with the finished pharmaceutical product. These may include tablet blisters, ampoules, vials or prefilled syringes, among others. The process of primary packaging refers to the insertion of the finished product into these materials.
- 4. Secondary packaging.** This involves the placing of the primary package into the required outer packaging that contains the required printed data and branding, as well as the package insert.



How pharma coped with COVID-19

Pharmaceutical supply chains are essential for the national and health security and economic prosperity of the United States, stated Janet Woodcock, the then-acting FDA Commissioner, in June 2021. She added, The COVID-19 pandemic revealed just how vulnerable the supply chain is in this country.³

This comment from the then-acting head of pharma's chief US regulatory body captured the fact that pharma industry's supply chains are suddenly in the spotlight. The heightened level of attention to pharma supply chains is by no means confined to the US. Anxieties over pharma's ability to supply key products have surfaced worldwide and major tensions, such as the disputes over resource priority for COVID-19 vaccines, have received significant media coverage. To take one prominent example, consider the European Commission's January 2021 litigation over vaccine access.⁴

Beyond the headlines, how vulnerable have pharma's supply chains proven to be? In practice, the absolute number of shortages is relatively small when placed in context. In the US, for example, in 2020 and 2021, supply issues have been reported for under 1.5% of the 20,000+ prescription drug products registered with the FDA.⁵ While shortages are reported by the manufacturers, stocks of products are typically kept by wholesalers, hospitals and pharmacies; hence, a reported shortage does not necessarily mean that patients are missing treatments.

Focusing on innovative pharma companies (i.e., the segment of the industry engaged in the research and development of new drugs), our interviews with PMF members revealed that this

segment of the industry has confronted a number of challenges during the pandemic. In our discussions, senior executives at the industry's leading companies described difficulties acquiring sufficient levels of certain raw materials and consumables. These included ethanol, toluene, acetonitrile, magnesium and neodymium, as well as specific single-use items such as biobags and other consumables required to maintain production output. For example, in 2021 there was a limited supply of the sterile filters used in biological drug manufacturing. Since vaccine manufacturers were depending on the same filters, the prioritization of mass vaccination programs resulted in a global shortfall that year. One respondent commented that "it has been even more challenging for small biotechnology companies to buy filters." With filter shortages expected to last for up to two more years, delays to development programs are likely to continue.

Yet despite these issues, our data suggests that, to date, PMF member companies succeeded in solving or mitigating the challenges they faced during the pandemic. Our analysis, presented on the left of **Figure 2**, shows that there is no significant trend indicating increased shortages of innovative pharma products in the 2019-2021 period.

³ "Biden Administration Recommends Policy Changes to Secure U.S. Pharmaceutical Supply Chain," *U.S. Department of Health and Human Services website*, 8 June 2021.

⁴ "Midday press briefing from 22/04/2021," *European Commission website*, <https://audiovisual.ec.europa.eu/en/video/I-204771>, accessed 26 April 2022.

⁵ "Drug Shortages for Calendar Year 2020," *U.S. Food and Drug Administration website*, www.fda.gov/media/150409/download, accessed 26 April 2022; "Drug Shortage Statistics, January 2001 to December 31, 2021," *American Society of Health System Pharmacists website*, www.ashp.org/Drug-Shortages/Shortage-Resources/Drug-Shortages-Statistics, accessed 26 April 2022.

This is confirmed by the overall assessment of the PMF members we spoke to (presented on the right of **Figure 2**). Companies maintained pre-pandemic service levels throughout. Where companies did face shortages, these affected only specific products experiencing demand surges due to COVID-19. Indeed, some companies told us that supply chains had performed better than in “normal” times. With a reduction in reporting demands (including a lower level of internal and external auditing) and a heightened focus on productivity, some companies paradoxically found themselves operating more efficiently and with better service levels. As one interviewee said, “sites could focus on what they are supposed to do – manufacturing and releasing the product.”

Though the pandemic continues to impact global health care provision, innovative pharma does not, at this stage, appear to be among the industries most vulnerable to supply chain disruption. It has not yet, for example, experienced anything comparable with the challenges faced by the automotive, high-tech and consumer electronics industries in 2022 as a result of the global semiconductor shortage.⁶ Moreover, while wrestling with emerging supply issues, the global pharma industry simultaneously succeeded in developing and manufacturing nearly 17.8 billion doses of 35 different COVID-19 vaccines by March 2022.⁷ The vaccines’ speed to market was

unprecedented: the first draft of the virus’ genome sequence was published by a consortium led by the Shanghai Public Health Clinical Center and School of Public Health on 10 January 2020 and the first novel mRNA-based vaccine against COVID-19 was approved in the UK on 2 December the same year.^{8,9} The vaccines are high-complexity products, with one requiring 270 constituent materials sourced across 70 suppliers.¹⁰ In a bold step, the manufacturing and delivery network for this vaccine was constructed at risk as the product progressed through clinical trials. Overall, with the qualifications and caveats noted above, the innovative pharma industry showed evidence of significant resilience during the crisis.

⁶ Aaron Aboagye, Ondrej Burkacky, Abhijit Mahindroo, Bill Wiseman, “When the chips are down: How the semiconductor industry is dealing with a worldwide shortage,” *wef.org*, 9 February 2022, ©2022 World Economic Forum.

⁷ “COVID-19 Vaccine Market Dashboard,” *Unicef website*, www.unicef.org/supply/covid-19-vaccine-market-dashboard, accessed 26 April 2022.

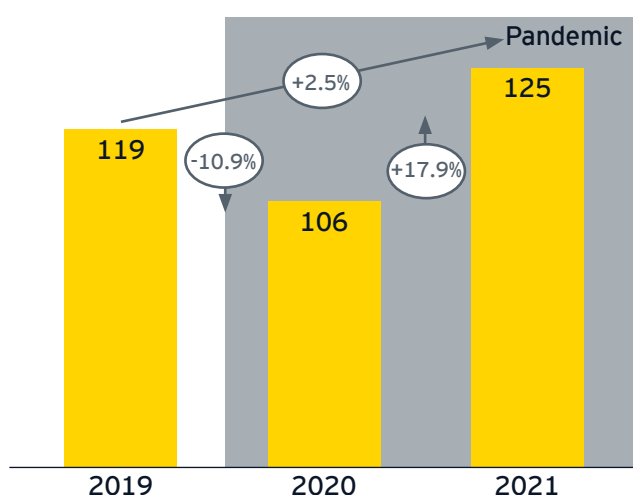
⁸ “Novel 2019 coronavirus genome” *Virological website*, <https://virological.org/t/novel-2019-coronavirus-genome/319>, accessed 26 April 2022.

⁹ Heidi Ledford, David Cyranoski, Richard Van Noorden, “The UK has approved a COVID vaccine – here’s what scientists now want to know,” *nature.com*, 3 December 2020, ©2020 Springer Nature Limited.

¹⁰ “Risk-based investment for rapid scale-up and mass manufacturing of the COVID-19 vaccine,” *EY virtual forum*, 15 June 2021, ©Ernst & Young Global Limited.

Figure 2. Performance of innovative pharma industry’s supply chain during the pandemic

Total shortage reports for innovative products¹ in the US and EU4 (Germany, France, Italy, Spain)

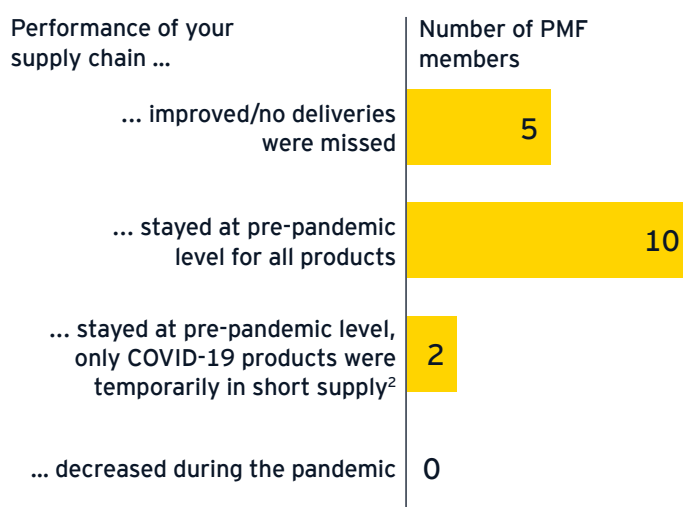


¹ Patent protected products

² Due to multifold increase of demand

Source: FDA; Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM); Agenzia Italiana del Farmaco (AIFA); Agence nationale de sécurité du médicament et des produits de santé (ANSM); Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

Innovative supply chains’ service levels during the pandemic





Protecting public health: supply chain policy interventions in the pandemic

For pharma, as well as for the policymakers, providers, payers and patients that constitute its major stakeholders, the ultimate aim is the same: to allow patients to access the right drug at the right time.

Industry supply chains largely succeeded in that goal in 2020–2021. Nevertheless, governments and regulators demonstrated during the pandemic that they are willing to intervene to help ensure the security of pharma supply. The three main economic and political global centers and trading blocs, i.e., the US, the EU and China have all implemented wide-ranging measures since early 2020 aimed at securing supply of medical and pharmaceutical products:

- ▶ In the US, recent policy trends have revealed a bipartisan focus on rebuilding domestic pharma manufacturing capabilities to address concerns over national security and public health and safety. Both the Trump and Biden administrations targeted accelerated vaccine and antiviral drug production and increased stockpiles (via, e.g., Operation Warp Speed and the Defense Production Act), including the use of rated orders to prioritize supply for vaccine development and manufacturing. A year-long review of the US' public health supply chains, published in February 2022, reaffirms the Biden administration's ongoing efforts to encourage domestic production and innovation, develop redundancies and ensure that diversification within drug supply chains will continue.¹¹

- ▶ The pharmaceutical strategy for Europe, adopted at the end of 2020, highlights the EU's aim to “develop the EU open strategic autonomy and ensure robust supply chains.”¹² Among other moves, the EU has imposed temporary vaccine export restrictions, signaling its willingness to directly intervene in the market in order to secure the supply of vital medicines for its citizenry.¹³ It has also undertaken to monitor supply chains, assess stockpiles and build regional capacity via its Health Emergency Preparedness and Response Authority (HERA).
- ▶ China applied export restrictions to multiple medical products in 2020 and has moved to strengthen the role of local innovative companies via the Made in China 2025 initiative.¹⁴ The Chinese government has also pursued vaccine diplomacy initiatives, expanding local vaccine production, pushing for vaccine distribution within developing countries and exporting Chinese vaccines to over 100 countries.^{15,16}

In recent decades, we have witnessed increasing globalization of pharma supply chains. The policies in the three major trading blocs as detailed above suggest that we are seeing the start of a counter-trend toward increased localization of supply chains and greater emphasis on regional or national self-reliance.

¹¹ “Public Health Supply Chain and Industrial Base One-Year Report,” *U.S. Department of Health and Human Services website*, <https://aspr.hhs.gov/MCM/IBx/2022Report/Pages/default.aspx>, accessed 26 April 2022.

¹² “A pharmaceutical strategy for Europe,” *EC website*, https://ec.europa.eu/health/medicinal-products/pharmaceutical-strategy-europe_en, accessed 26 April 2022.

¹³ “Commission Implementing Regulation (EU) 2021/111 of 29 January 2021 making the exportation of certain products subject to the production of an export authorization,” *EU website*, <https://op.europa.eu/en/publication-detail/-/publication/b8f9621d-62eb-11eb-aeb5-01aa75ed71a1>, accessed 26 April 2022.

¹⁴ “Export Controls and Export Bans over the Course of the Covid-19 Pandemic,” *WTO website*, www.wto.org/english/tratop_e/covid19_e/bdi_covid19_e.pdf, accessed 26 April 2022.

¹⁵ “Strengthening Vaccine Cooperation to Build a Great Wall Against COVID-19,” *China Embassy website*, www.china-embassy.org/eng/zgyw/202108/t20210806_9015424.htm, accessed 26 April 2022.

¹⁶ “China's COVID-19 Vaccine Diplomacy Reaches 100-Plus Countries” *VOA News website*, www.voanews.com/a/china-s-covid-19-vaccine-diplomacy-reaches-100-plus-countries/6233766.html, accessed 26 April 2022.

This change is part of a far broader ongoing shift in national strategic thinking, which may have been accelerated by COVID-19 but is driven by deeper underlying factors that pre-date the pandemic. Among these factors:

- ▶ The globalization model is changing, with major trade regions increasingly seeking autonomy, resulting in sector supply mandates, including changes to trade, regulatory and tax policy.
- ▶ Global trade agreements have declined in relevance as regionalized trade and bilateral agreements assume greater importance; the diminished role of the World Trade Organization (WTO) underlines this shift.¹⁷
- ▶ All stakeholders increasingly acknowledge the importance of sustainability and the need to measure the impact of companies' environmental, social and governance commitments, supported by the increased ease of tracking metrics such as carbon footprints and other externalities.

Moreover, it hardly needs stating that COVID-19 will not be the last major crisis that must be confronted in the 21st century. Recent developments in Europe emphasize the dangerous tensions present at geopolitical fault lines. The long-term impacts of the present military turbulence for the pharmaceutical sector specifically remain unclear for now, but supply chain operations across all industries will inevitably be

affected by an increase in logistical complexity and cost. We can also anticipate that trade with regions at the center of ongoing military disruption will be negatively affected by difficulties in exchanging currency and/or executing bank transfers, as well as a lack of trusted institutions to serve as contract guarantors. Moreover, pharma companies may confront increased IP and cyber challenges if warring nations decide to breach norms on patent protection or block key external data connections. Beyond these immediate impacts, the larger consequences of the military conflict – from sanctions and escalating inflation to the broader human and economic dislocation – will be felt across the global macroeconomic landscape. This will have ongoing and potentially significant consequences for industry supply chains.

Beyond the current crises, moreover, the world will inevitably also face other, less predictable shocks in the future. From new pandemic outbreaks to cyber attacks (or even cyber war) to the effects of climate change, developments are all likely to aggravate geopolitical tensions further. As a result, we expect states to continue pursuing self-reliance through supply chain localization over the coming decade.

¹⁷ Kent Jones, "Is This the End of the WTO as We Know It?" *barrons.com*, 29 January 2019, ©2022 Dow Jones & Company, Inc.



Securing a strategic sector: the next steps for policymakers

There is reason to believe that pharma will have an enlarged role in these national strategic calculations. In the wake of the national public health crises unleashed by the pandemic, governments are beginning to acknowledge pharma as a “strategic sector” vital to economic and national security. The raft of policy measures to secure pharma supply chains taken in the US, the EU and China in 2020-2021 are evidence of this growing recognition. Ensuring supply of sufficient numbers of pharma products to support public health objectives is becoming an increasing priority worldwide.

We can therefore expect to see policymakers explore a broader range of interventions in the industry’s operations. **Figure 3**, below, sets out the range of possible measures policymakers may choose to implement in the future.

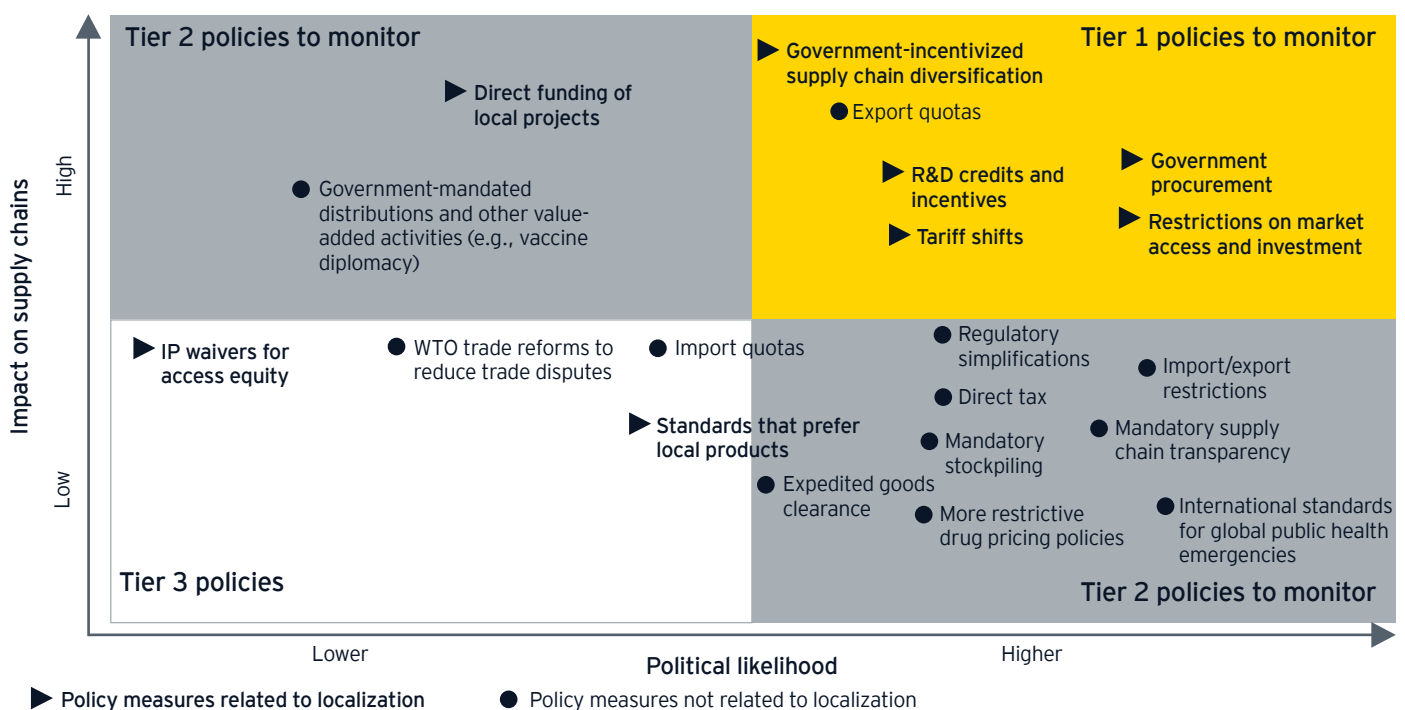
Our analysis, shown in **Figure 3**, estimates the political likelihood of each of the possible measures governments may implement (plotted on the x-axis across the bottom) and their potential impact on supply chain operations (shown on the y-axis). The measures were obtained and evaluated based on EY research into recently-passed laws, bills and statements from policymakers and competent authorities. Based on this assessment, six of the measures identified have the highest potential impact on the industry. These “Tier 1 policies to monitor” appear in the upper right quadrant of **Figure 3**. The

majority of these measures would encourage greater national or regional “localization” of supply chains:

- ▶ R&D credits and incentives are proactive measures deliberately designed to encourage the local development and manufacturing of pharma products. These levers have longer lead times and could influence long-term manufacturing footprint decisions.
- ▶ Four of the other “Tier 1 measures” place restrictive conditions on pharma supply chains, either by constraining local competition (through limiting market access and investment or imposing export quotas) or by imposing certain conditions on local companies (via procurement mandates or government-incentivized supply chain diversification). When employed, these policy levers could rapidly create constraints on supply chains.
- ▶ Lastly, changes to tariff levels can act as both enabling or restricting measures to a pharma supply chain, depending on how the changes are erected and whether any exclusions are made available.

While policies such as these may drive the industry toward greater supply chain localization, there are additional measures companies can take to attempt to build resilience. In some cases, companies are already exploring these possibilities. The next step is to evaluate what measure or combination of measures can deliver the results the industry and its stakeholders want to see.

Figure 3. Overview of potential policy measures across three trading blocs (the US, the EU and China) and their impact on pharma supply chains



What measures will best secure future supply chain resilience?

As companies assess their supply chain strategies for the future, which levers they choose to pull will depend, among other things, on their portfolio, strategy, commercial operations and manufacturing footprint in a specific geography. Any potential strategy will involve costs and benefits – the challenge will be to find the optimal balance in each regional context.

While the industry can expect to see some moves toward localization, these moves are likely to be combined with other new approaches. Ultimately, some combination of localization and other strategies may provide the most satisfactory answer for all stakeholders.

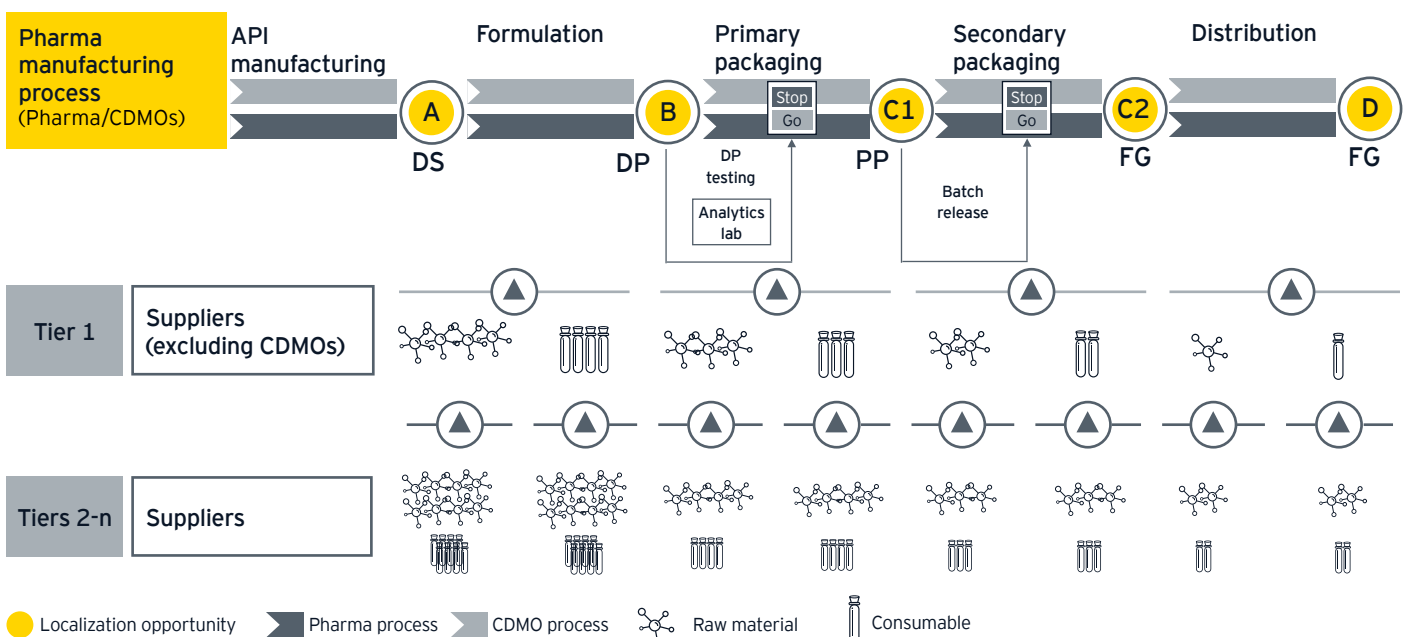
The practical implications of localization depend on what steps of the supply chain are considered. At the simplest level, localization could just denote companies ensuring local stockpiles of finished goods inventory. More ambitiously, the entire end-to-end manufacturing process could be brought inside a single national or supranational region. **Figure 4** below shows a simplified pharma value chain, with the letters A to D indicating the value chain steps that could be localized.

The different steps of the manufacturing process would entail different levels of investment to localize. For example, a pharma company could, relatively easily, localize secondary

packaging (C2). This would entail building a local GMP-approved and licensed site, or outsourcing the same to a local contract development and manufacturing organization (CDMO), which would require infrastructure to receive and store the primary packaged product from the previous stages of the supply chain. Carrying out the on-site secondary packaging would need basic additional raw materials, such as cardboard, adhesives and printer cartridges; plus manual labor, which should be easily supplied locally, and the presence of a local (or regional) quality organization and maintenance team.

If companies seek to localize the earlier stages of the manufacturing process (C1 and potentially B, in addition to C2), the complexity would rise correspondingly, with increased needs for complex raw materials, skilled labor and higher capital outlay to build sites for higher-technology manufacturing.

Figure 4. Localization opportunities in the pharma supply chain



Active pharmaceutical ingredient (API), drug substance (DS), drug product (DP), primary packaged product (PP), finished good (FG) and contract development and manufacturing organization (CDMO)

Localizing API manufacturing (stage A) would be the most significant challenge, both in terms of the scale of capital investment and the levels of technical and quality competency required. EY analysis of industry data suggests that upgrading or expanding end-to-end manufacturing capabilities (stages A to C2 on the chart) for small molecules and biologics within all of the three major trading blocs would incur significant costs – both one-time costs, e.g., capital expenditure (CapEx), and incremental recurring costs, e.g., operating expenses (OPEX) and remnant costs. It should be noted that if this expansion of end-to-end manufacturing and supply capability were to be extended to multiple individual countries outside the major trading blocs, the one-time and recurring cost would rapidly escalate and inefficiencies from volume disaggregation would grow exponentially. Moreover, at the time of writing, the apparent shift toward a higher-inflation financial environment suggests that the cost of capital is likely to become a more significant concern than it has been in recent years.

Still, if this investment were undertaken, what would it achieve? In **Figure 5**, we have assessed resilience as a composite of five distinct metrics: reliability, time to innovate, agility, risk exposure and efficiency (see sidebar to right).

As **Figure 5** suggests, focusing on the lower-cost, lower-complexity option of localizing finished goods rather than the manufacturing process itself would likely improve the reliability of product supply because more of the product would be locally stockpiled for distribution. Yet this process would be unlikely to significantly enhance any of the other aspects of resilience.

In our analysis, we defined supply chain resilience as a combination of the following five criteria:

- 1. Reliability:** the degree to which a supply chain yields consistent performance and quality
- 2. Time to innovate:** the time it takes to bring a new product to market factoring in the complexity of chemistry, manufacturing and controls (CMC) development and regulatory approvals for the manufacturing system
- 3. Agility:** the supply chain's reaction speed to changes in the market, in demand mix or in regulation
- 4. Risk exposure:** the degree to which a supply chain is exposed to existing or new risks
- 5. Efficiency:** the financial impact considering CapEx, OPEX and remnant cost

Figure 5. Supply chain localization and stockpiling impact on supply resilience

Resilience evaluation						
Evaluation vs. status quo from global perspective*						
Localization scenario		Reliability	Time to innovate	Agility	Risk exposure	Efficiency
Local stock	D Finished goods stockpiling	⊕ ⊕ ⊕	⊕	⊖	⊖	⊖
E2E localization	A — C2 API manufacturing to secondary packaging	⊖	⊖ ⊖	⊕ ⊕ ⊕	⊖ ⊖	⊖ ⊖ ⊖

⊕ ⊕ ⊕ High positive impact ⊕ No impact ⊖ ⊖ ⊖ High negative impact

*Impact on overall resilience of a globally set up supply chain.

The comprehensive localization of manufacturing would significantly boost supply chain agility within the region in question; a localized supply operation would have significant capability to respond rapidly to local conditions. However, this agility would be purchased at the cost of a considerable loss of efficiency given the need to build and maintain infrastructure, services and talent at local sites. The heavy reliance on local sites entailed by localizing the entire manufacturing process is also likely to heighten risk exposure and increase timescales for bringing innovations to local markets. Overall, this shift will reduce reliability as a result of the separation of operations from established centers of excellence in quality, process engineering, regulatory and IT operations.

Aside from its direct positive effects on agility, localization also offers significant political benefits to states that implement these measures. As geopolitical tensions continue, states are increasingly likely to see advantages in reducing their dependence on potential rivals and claiming the security of end-to-end control of production capabilities.

It must be recognized that even end-to-end localized manufacturing cannot remove all dependence on externalities, such as internationally sourced or supplied raw materials and consumables. This approach cannot entirely resolve all vulnerabilities (consider again the illustrative small molecule global supply chain shown in Figure 1).

In practice, localization's implications need to be considered not in isolation, but relative to the alternative options that exist for bolstering pharma supply resilience. As shown in Figure 6, multiple plausible approaches exist. Initiatives can be led by an individual pharma company, by the broader industry working collaboratively or by the policymakers and regulatory bodies that interact with pharma and have a stake in the future of its supply chain operations.

Pharma companies are already embracing several of these initiatives; among others, companies have implemented multisourcing and leveraged local CDMOs. These relatively simple measures can deliver benefits for supply chain resilience. Certain other approaches will need a longer-term investment and commitment to realize. Seven of the prospective alternative approaches to strengthening supply resilience are briefly detailed in the sidebar detailed below. This overview of potential measures is by no means exhaustive; the industry could also consider, for example, working with nation-states to build strategic inventories or to collaborate and partially fund public-private partnerships.

Figure 6. Potential alternatives to localization for improving resilience

	Raw materials/consumables	Manufacturing (including outsourced services)	Business processes, IT systems, quality and regulatory
Individual pharma company	<ul style="list-style-type: none"> ▶ Multisource raw materials/consumables ▶ Increase/rebalance inventories (internally or at Tier 1 supplier/CDMO) ▶ Procure for CDMOs/Tier 1 suppliers ▶ Increase planning security 	<ul style="list-style-type: none"> ▶ Implement smart localization strategies (hub-and-spoke) ▶ Cross-register sites ▶ Provide equipment to CDMOs with prioritized access 	<ul style="list-style-type: none"> ▶ Improve E2E supply chain visibility and transparency (including digital twins) ▶ Modify regulatory file <ul style="list-style-type: none"> ▶ Take out nonmandatory specifications ▶ Qualify multiple suppliers
Pharma industry ¹	<ul style="list-style-type: none"> ▶ Set up a procurement clearinghouse ▶ Set up a physical joint warehouse ▶ Pool procurement 	<ul style="list-style-type: none"> ▶ Set up joint manufacturing <ul style="list-style-type: none"> ▶ Companies take shifts in using infrastructure/facility ▶ Companies share infrastructure/facility 	
Government/regulator	<ul style="list-style-type: none"> ▶ Maintain safety stocks for widely used raw materials and consumables to maintain operations in the industry (including pharma) 	<ul style="list-style-type: none"> ▶ Subsidize equipment to industry with prioritized access in crisis times 	<ul style="list-style-type: none"> ▶ Introduce regulatory notification principle ▶ Optimize regulatory requirements ▶ Shorten regulatory processing timelines² ▶ Ensure sustainable reimbursement

¹ Discussions around these measures would need to be held within the frame of the antitrust regulations, including the European Competition Network (ECN) guidance.

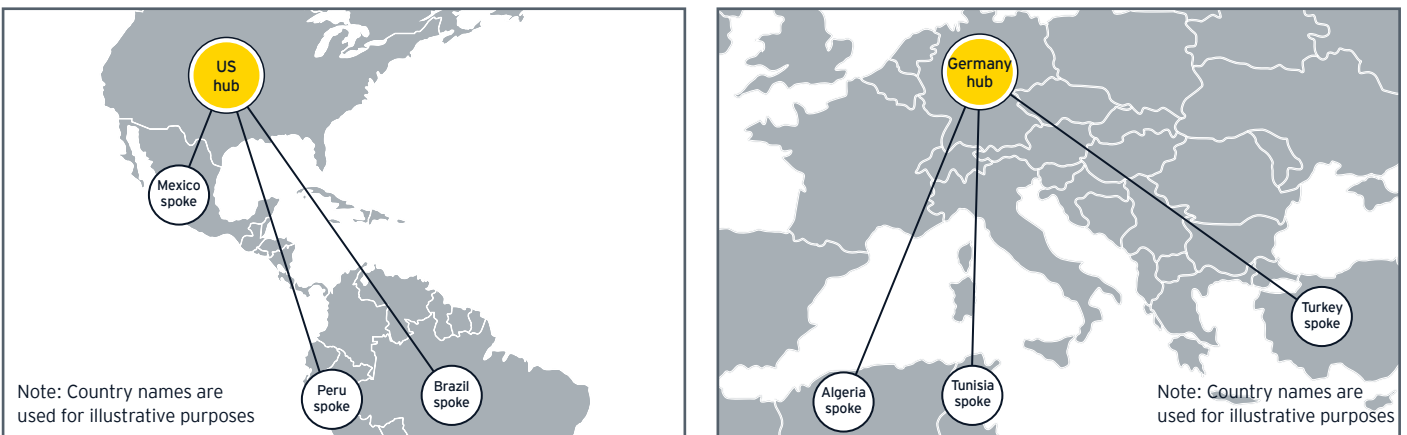
² E.g., rolling reviews, parallelization of clinical trials/at risk capital investment by pharma companies.

Alternatives highlighted in bold font are further detailed below.

The “hub-and-spoke” concept is a cost-efficient model for localizing manufacturing (either end-to-end or in part) in a specific country. While the global hub is a full-scale manufacturing site, the spokes offer a small-scale operation, allowing limited supply chain operations to be executed locally. The approach offers sufficient locally based production capacity to meet the volume needed in a domestic market. This is achieved by shifting indirect services (such as planning, procurement, raw materials and consumables staging, quality control and others) from the local “spokes” to the global “hub.”

The hub-and-spoke approach increases supply chain agility without incurring the level of expenditure needed for a full-scale local site. The equipment needed at the spoke sites can be kept to a minimum: biological drugs, for example, can be locally manufactured in single-use biobags rather than the steel bioreactors potentially used at the global hub. Developing a hub-and-spoke model may increase a company’s risk exposure and extend their time to innovate in the local market. However, the model ultimately offers some of the benefits of localization strategies while mitigating some of the risks and costs of these strategies. See Figure 7.

Figure 7. Smart localization (hub-and-spoke)

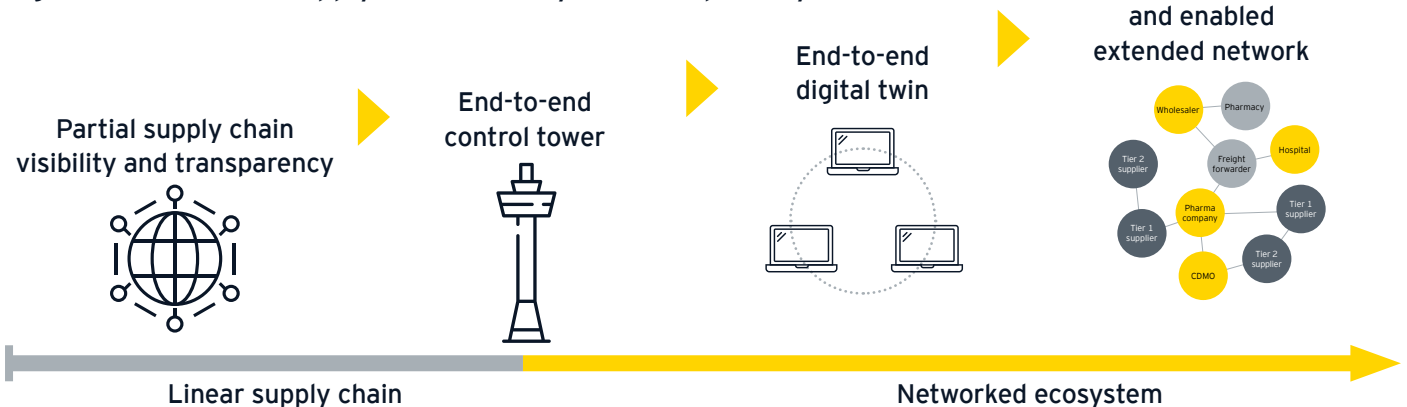


Improvement in end-to-end supply chain visibility is another potential approach to increase resilience through the development of integrated digital platforms. These platforms would link up manufacturers, suppliers and ultimately wholesalers, connecting them to a collaboration hub enabling them to mutually share and access data. As a result, the industry and its stakeholders would have greatly enhanced (and, to a certain extent, reciprocal) insight into the real-time supply chain situation, enabling more efficient management and intervention.

would give companies greatly enhanced visibility. By enabling companies to better predict and respond to challenges, this approach could significantly mitigate supply chain risk. However, pursuing this approach also involves challenges. Pharma companies and other players in the ecosystem are already addressing challenges around data privacy and cybersecurity and resolving these issues will be key to enabling end-to-end visibility. Moreover, building and scaling the digital infrastructure needed for this approach would require a significant commitment of time and money. See Figure 8.

The possible benefits of integrating supply chain oversight in this way are obvious: end-to-end supply chain monitoring

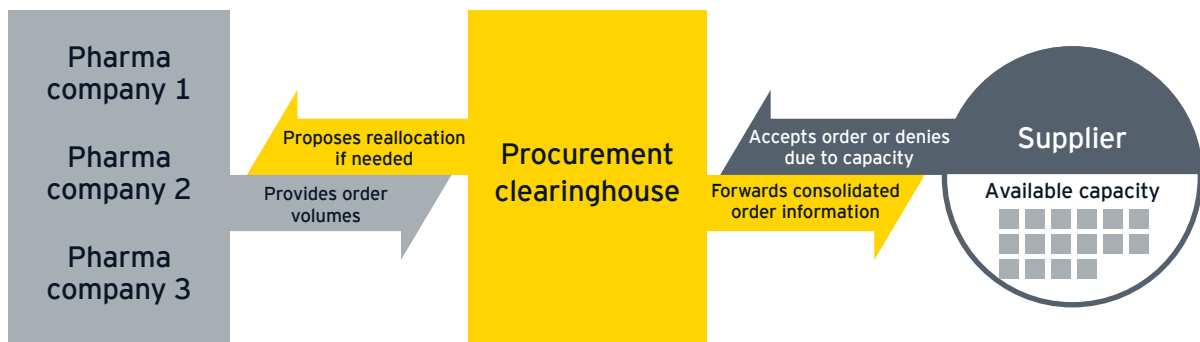
Figure 8. End-to-end supply chain visibility and transparency



A procurement clearinghouse is a virtual, potentially AI-supported entity that balances the supply of raw materials and consumables with the pharma industry's demand for these goods. It would provide pharma companies with an order management vehicle that could consolidate and forward their various orders for common raw materials and consumables to suppliers. If a supplier proved unable to meet the total demand, the system could propose reallocations between companies, balancing excess stock in one area with shortages in another.

By fulfilling this role, the procurement clearinghouse would mitigate the risk of stockpiling and distorting the balance of supply-and-demand in the event of a crisis-driven "bank run" on these goods. Ultimately, its operations could be extended to incorporate customers (such as wholesalers), as well as suppliers, thereby providing a greater level of transparency and integration across industry supply chains. For individual companies, this approach would slightly increase risk exposure simply because it would add another intermediary into supply chain operations. See **Figure 9**.

Figure 9. Procurement clearinghouse

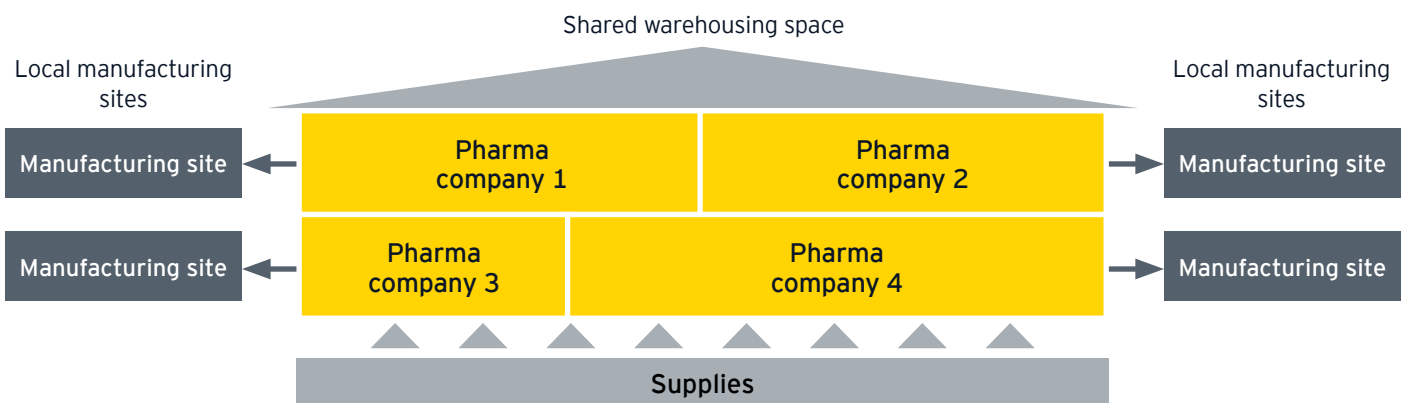


Joint warehousing entails pharma companies sharing warehousing capacity, with dedicated areas for each company's own raw materials and consumables. The operation could potentially also incorporate additional on-site services, such as quality control and material staging. Potentially of relevance in smaller countries, the joint warehouse can be seen as playing the "hub" role in a "hub-and-spoke" network (with the "spokes" potentially operating additional small warehouses at the

pharma company's local manufacturing site) or as the physical component of a procurement clearinghouse.

The advantages of joint warehousing lie in the fact that the co-location of supplies would enable easier sharing of materials between companies where necessary, thereby improving collective agility in the face of disruptions. Against this, the need to set up additional warehousing facilities would involve more expenditure for a company. See **Figure 10**.

Figure 10. Physical joint warehouse



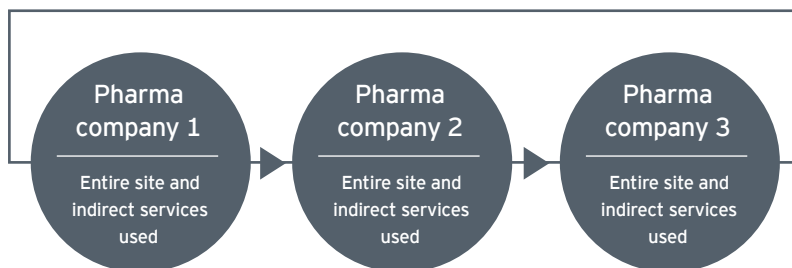


Joint manufacturing facilities would entail pharma companies working together to operate a single large-scale facility with capabilities comparable with current global sites. By sharing the costs of setting up and running the joint facility, pharma companies would reduce their own expenditure. The allocation of the facilities between companies could be done on a shift basis, with companies agreeing to a schedule giving them access to the entire site at specific times. Alternatively, the facilities could include dedicated manufacturing suites for each company, with certain indirect services (e.g., analytics lab or staff facilities) shared between the companies.

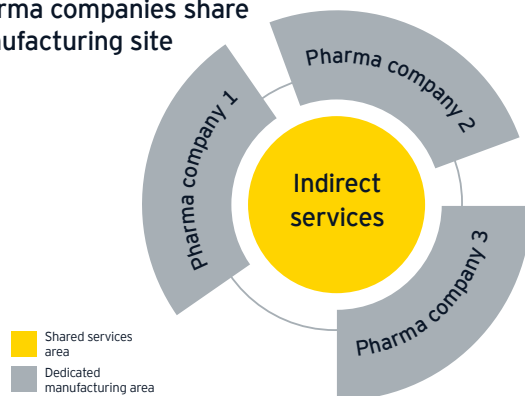
This approach would obviously affect strategic planning and potentially necessitate negotiations and mutual compromises between companies over access. Investment in the facilities would also represent an ongoing commitment for the companies involved, with investment difficult to unwind if a company shifts strategic focus. However, the joint manufacturing approach would increase agility by allowing pharma companies access to a full-scale local site. Alternatively, companies could build up and jointly own a CDMO facility in geographies where CDMO access is currently difficult. See **Figure 11**.

Figure 11. Joint manufacturing

Pharma companies take shifts



Pharma companies share manufacturing site



Additionally, two potential regulatory adjustments offer alternative approaches to increasing resilience.

The regulatory notification principle would simplify the process of making changes to, for example, the manufacturing process for a specific drug. Pharma companies recognized as trusted and competent would be able to expedite the process of updating information. These companies would be considered compliant as soon as they provide the necessary change notification information to regulators. Though companies would commit to providing full change documentation and stability data as soon as possible, they would be able to implement

changes in the meantime. Without the need for subsequent prior approval inspection or data review and approval, companies could increase agility and reduce their time to innovate.

Regulatory requirements could also be streamlined by, for example, making regulatory filing specifications supplier-agnostic; in this instance, a specific raw material or consumable could be delivered from a substitute source with equivalent specifications if the primary supplier was unable to meet the order.

The full implications of each of these alternative approaches are wide-ranging and their multiple ramifications for supply chain resilience are complex to predict (see **Figure 12** for an initial evaluation).

Considered alongside end-to-end localization, which offers a way to increase agility but at considerable financial cost, these measures require comparatively low investment to realize. Each of the seven alternative measures considered here is

inexpensive relative to localization and some would even enable companies to reduce their expenditure. The seven measures also offer a range of possible benefits to resilience, though each has its limitations. A combination of these approaches with localization of certain supply chain functions or value chain steps may therefore offer the best approach to improve resilience in future.

Figure 12. Alternative measures: Impact on supply resilience

Resilience evaluation					
Evaluation vs. status quo from global perspective*					
	Reliability	Time to innovate	Agility	Risk exposure	Efficiency
1. Implement smart localization strategies (hub-and-spoke) ●	⊖ ⊖	⊖ (⊖)	⊕ ⊕	⊖ ⊖	⊖
2. Improve E2E supply chain visibility and transparency (including digital twins) ●	⊕	⊕	⊕ ⊕	⊕ ⊕	⊖
3. Set up a procurement clearinghouse ●	⊕	n/a	⊕ ⊕	⊖	n/a
4. Set up a joint physical warehouse ●	⊕	n/a	⊕ ⊕ ⊕	⊕	⊖
5. Set up joint manufacturing ●	⊖	⊖ ⊖ (⊖)	⊕ ⊕ ⊕	⊖ ⊖ (⊖)	⊖
6. Introduce regulatory notification principle ●	⊖	⊕ ⊕ ⊕	⊕ ⊕ ⊕	⊖ ⊖	⊕
7. Optimize regulatory requirements ●	⊕ ⊕	⊖ ⊖	⊕ ⊕ ⊕	⊕	⊕
Local finished goods stock (D, finished goods stockpiling) ●	⊕ ⊕ ⊕	⊕	⊖	⊖	⊖
E2E localization (A-C2, API manufacturing to secondary packaging) ●	⊖	⊖ ⊖	⊕ ⊕ (⊕)	⊖ ⊖	⊖ ⊖ ⊖

● Pharma ● Industry ● Government/regulatory

⊕ ⊕ ⊕ High positive impact ⊕ No impact ⊖ ⊖ ⊖ High negative impact

*Impact on overall resilience of a globally set up supply chain.



Conclusion and outlook

Greater collaboration and cooperation between pharma and its stakeholders will be key to successfully building resilient and sustainable supply chains for the future — and delivering the outcomes sought by patients and by all parties in the ecosystem that serve them. In this paper, we have provided an initial assessment of the various possibilities for rethinking pharma supply chains that the industry and the stakeholders it serves may consider in the future. *It is important to emphasize that there will not be a single or simple path forward from this point.*

Governments in different trade regions will have different supply priorities, and different biopharmaceutical companies have different starting points leading to different supply chain strategies. The pharma industry and its stakeholders in fact have a range of viable options for increasing supply chain resilience. These options include varying degrees of localization in addition to other alternatives, some of which have been explored in this paper. While we expect different combinations of these approaches to be implemented in different regions, we can nevertheless predict a few specific general trends.

Most significantly, the fully globalized supply model will be transformed to a hybrid model balanced more strategically across global, regional and local sites. This hybrid model will aim to enhance supply resilience through building redundant capabilities with multiple suppliers, working with CDMOs, developing internal sites and holding more inventory. Collaboration between companies – whether in the form of joint warehousing, manufacturing, or other shared functions – is also likely to play an enlarged role in the future, where antitrust regulations permit.

With the implementation of the hybrid model and other resilience-boosting measures, the supply chains of the future will become increasingly expensive to operate, at least until the introduction of newer enabling technologies. Digital capabilities – including automation, AI, and end-to-end supply chain systems and process integration – will be necessary to support these increasingly complex supply chains in the long term.

Deciding on how to target investment into these new supply chain models will require a dialogue for mutual education between pharma and politicians. With pharma increasingly recognized as a sector of critical importance to global strategic thinking, it is imperative that all parties commit to a deeper and more effective conversation at national and supranational levels.

At the most basic level, the industry needs to understand their partners' intentions: will governments focus primarily on securing supplies of essential drugs (as well as stocks of personal protective equipment and other key equipment) or will their planning consider a broader range of products? Working in collaboration with pharma, governments can set the parameters and priorities for future discussion. Governments in turn need to recognize the level of complexity and specialist expertise integral to pharma supply chains and the industry's need for a commitment to a sustainable reimbursement model that can support its future operations. This level of reciprocal, structured and ongoing engagement between pharma and its stakeholders has not existed in the past; but if all parties commit to it now, it can form the basis for a strategic approach to future pharma supply chains that can work to the benefit of all partners in the ecosystem.

In this initial publication, we have set out some of the key possible directions for the evolution of pharma supply chains. In the future, we will seek to explore the different possible strategic approaches outlined in this paper in greater depth, in dialogue with all the industry stakeholders.

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