EXECUTIVE INSIGHTS

Creating Opportunities and Avoiding Missteps in Biopharma Supply Chain Strategy

Supply chain challenges have emerged in a pronounced way globally and across industries during the past several years. For the biopharmaceutical industry, this can eventuate in multibillion-dollar losses if companies do not anticipate delays, changes and obstacles. To avoid this, the industry must seize the right moment and create opportunities rather than settle for being stymied by supply chain challenges. L.E.K. Consulting has developed important questions to consider within **four key areas** to help identify when to take action that mitigates potential missteps such as significant monetary and ownership losses.

1. The potential for multibillion-dollar value destruction and how to avoid it

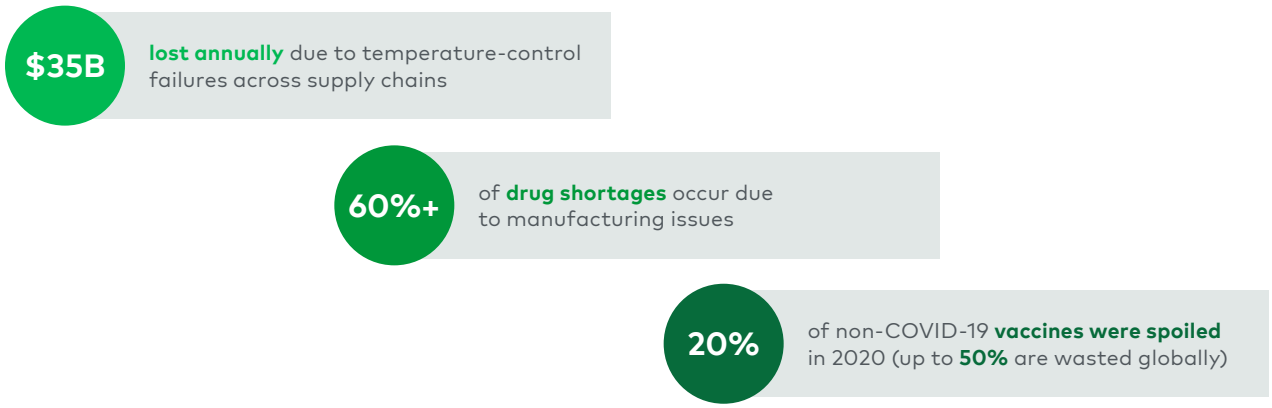
An efficient and effective supply chain is critical to the success of biopharmaceutical companies, as it plays a vital role in ensuring that drugs and medical devices are delivered to the right place at the right time. The pharmaceutical industry has experienced tremendous growth over the past decade — not only in terms of the volume of products that need to be supported (approximately $950 billion of revenue in 2012 to around $1.5 trillion in 2020) but also in terms of product complexity and just-in-time manufacturing needs (due to the growth of advanced modalities such as cell and gene therapies).

Pharmaceutical supply chains are complex networks of manufacturers, analytical testing sites, distributors, pharmacies, logistics providers, input suppliers and other players. The efficient management of these various components can optimize production costs, increase efficiency, minimize waste and improve patient outcomes with timely product delivery.

In addition, it enables companies to respond quickly to market changes, such as competitor product approvals, product recalls or natural disasters, and ensures that critical medicines and supplies are available when needed. The COVID-19 pandemic revealed the precarious nature of supply chains all around the world, with the pharma industry seeing a 350% increase in supply disruptions from 2019 to 2021 and a roughly 3x increase in lead times for some raw materials and consumables.

Beyond the impact of COVID-19, failures of pharma supply chains can carry significant consequences for pharmaceutical companies and patients. Product losses and drug shortages due to supply chain failures cost the industry tens of billions of dollars each year and can be catastrophic for individual biopharma companies (see Figure 1).

Figure 1
Industrywide losses from supply chain failures



Source: IQVIA; PharmTech; Food and Drug Administration; Informa; L.E.K. research and analysis

Case studies: Supply chain failures

Genzyme acquisition by Sanofi

- The June 2009 contamination of Genzyme's plant in Allston, Massachusetts, led to a halt in production of Cerezyme. Due to the shortage, Shire received a fast-track designation for a new experimental Gaucher's disease treatment. Cerezyme supply shortages continued in 2010, with only about 50% of demand for the drug met. As a result, Sanofi launched a hostile takeover bid and eventually completed acquisition of Genzyme in 2011.

Novo Nordisk unable to meet Wegovy demand

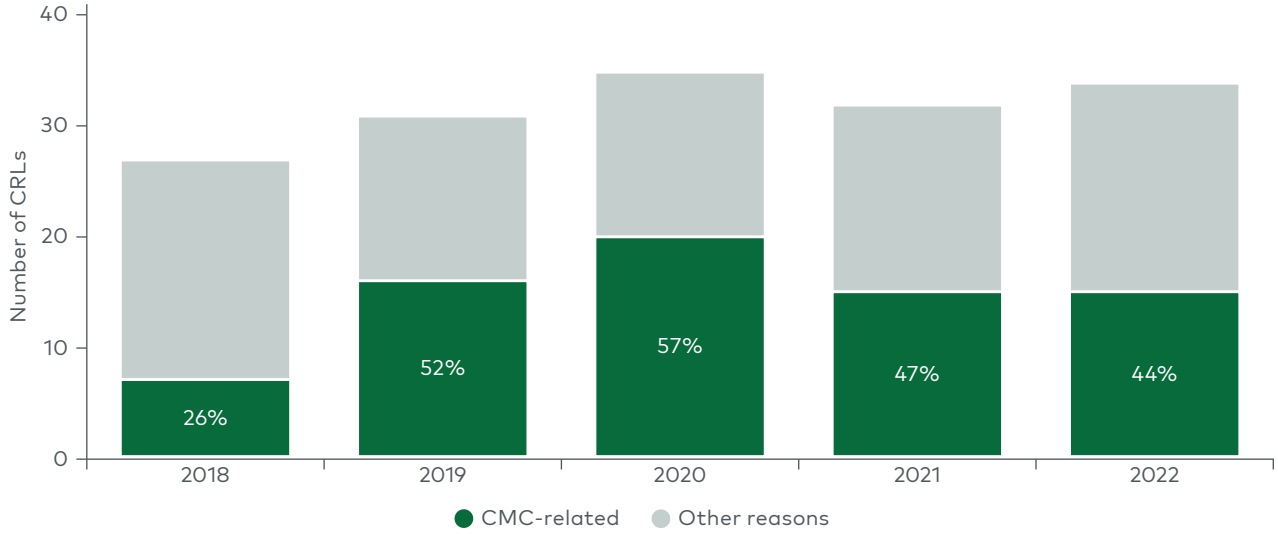
- Catalent's site in Belgium had to halt production of Wegovy, and as Novo Nordisk did not have an established backup supplier, it was not able to meet Wegovy demand in the first half of 2022. Even when supply was restored, inventory levels remained low, reducing product revenue significantly.

Emergent contamination impacted up to 400 million COVID-19 vaccines

- Persistent problems with mold, poor equipment disinfection and inadequate employee training were highlighted following inspections at Emergent's Baltimore site. Production of COVID-19 vaccines at the plant was officially paused April-July 2021, but Emergent was discarding vaccines even prior to that. Overall, up to 400 million Johnson & Johnson and AstraZeneca vaccines manufactured at the plant were discarded.

In addition, product loss or inadequate supply chain issues can impact a company's ability to get a product approved and on the market. L.E.K.'s analysis demonstrated that about 50% of complete response letters (CRLs) cite chemistry, manufacturing and controls (CMC) and supply chain deficiencies as reasons for rejections. Interestingly, these issues are not helped just by outsourcing to contract development and manufacturing organizations (CDMOs), as up to 40% of CMC CRLs are due to issues at CDMO sites. Following CMC-related CRLs, the vast majority (around 83%) of products are approved, but typically with a significant (eight-to-18-month) delay that can result in tens or hundreds of millions of dollars in lost revenues. Moreover, some of these products receive a second CRL (about 8%) or pause/permanently stop development (also about 8%) (see Figure 2).

Figure 2
CRLs per year (2018-22)



Outsourcing does not prevent CMC-related issues, as up to **40% of CMC CRLs** are due to **issues at CDMO sites**

Note: CRLs=Food and Drug Administration complete response letters; CMC=chemistry, manufacturing and controls; CDMO=contract development and manufacturing organization
Source: Biomedtracker; L.E.K. research and analysis

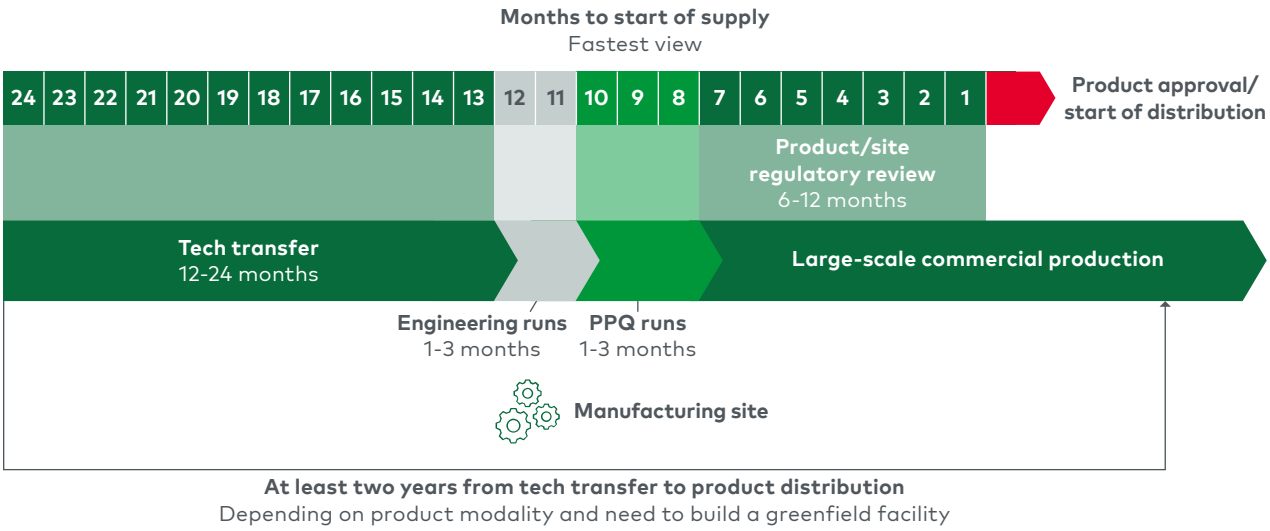
2. Key inflection points for supply chain evaluation: When may be too late?

Pharmaceutical companies need to be proactive in assessing their supply chain strategies and making adjustments to stay ahead of market trends, respond to disruptions, and meet the needs of patients and healthcare providers. The time it takes to set up a pharmaceutical supply chain can vary widely depending on the size and complexity of the supply chain, the regulatory requirements of the countries involved, and the availability of experienced staff. Key milestones include selecting and validating manufacturing sites, scaling up to commercial volumes, implementing quality control measures across the network, establishing readiness for regulatory inspections, and obtaining site regulatory approvals.

Timelines for creating a supply network depend on the design choices made — for example, building a greenfield facility instead of using a CDMO would significantly extend timelines but would provide greater control over the manufacturing process.

In practice, most biopharmas should begin thinking about supply chain strategy and design earlier than they may expect. Planning ahead will ensure that optimal decisions are made — shortcuts taken due to time or budget constraints may have drastic consequences down the line (see Figure 3).

Figure 3
Planning for supply chain strategy



Note: PPQ=process performance qualification
Source: L.E.K. research and analysis

L.E.K. identified the following six inflection points to be most relevant for supply chain strategy assessment:

1. **Start of clinical trials —** Initiating clinical trials is an appropriate inflection point to set the future supply chain strategy for a product. One CDMO may be used to manufacture product for early clinical trials, but different capabilities and scale may be necessary for late clinical development and commercial production. As setting up commercially ready supply chains likely takes at least two years, companies should begin the process when their product is just beginning phase 1.
2. **Upcoming first product launch —** Companies need to ensure that their suppliers have the right capabilities to produce the product as well as sufficient capacity to meet expected product demand. A key consideration at this stage is determining whether to outsource production or manufacture in-house. Ideally, timing for assessment of commercial-scale manufacturing capabilities is at least 24 months prior to product launch.
3. **Geographic expansion —** Entry into new global markets may require changes to the existing supply network — this may be due to existing nodes not having regulatory approval for production in the new geography or in-country testing requirements. The geographic location of supply chain nodes and efficiency of the global network constitute another key consideration — patients, especially those on time-sensitive treatments like cell therapies, cannot afford supply chain disruptions if materials are held up in customs.

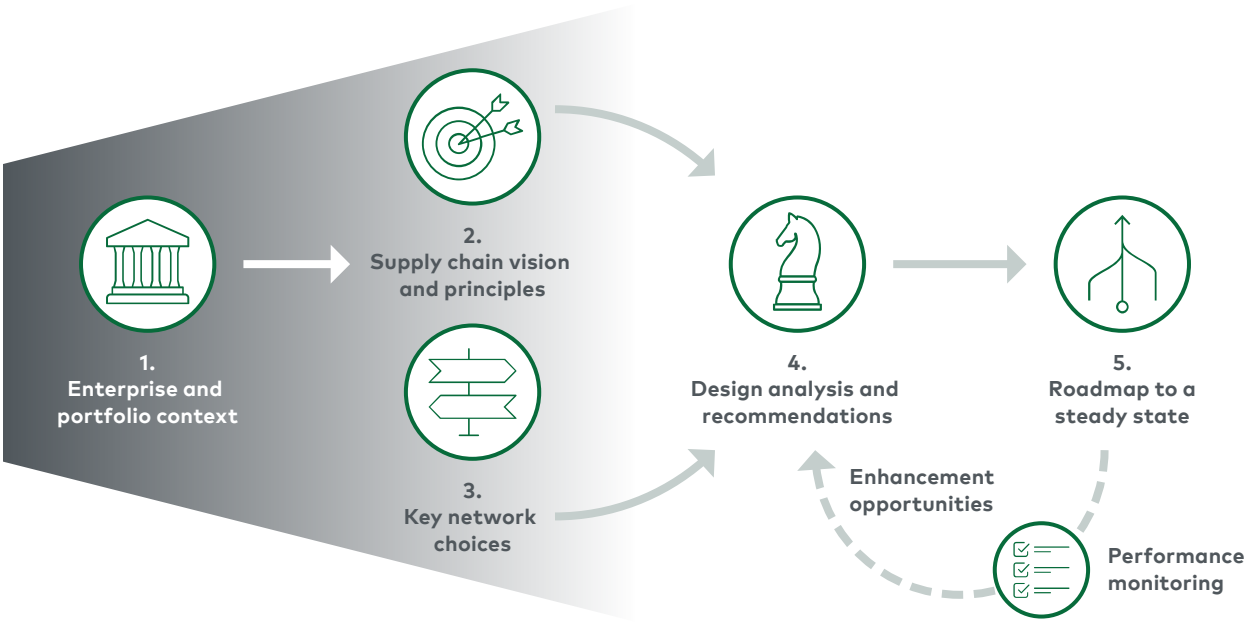
4. **Portfolio expansion —** The launch of new products may call for additional manufacturing capacity or novel capabilities (e.g., if expanding into a new modality), which can be accomplished by acquiring new supply chain nodes or contracting CDMOs.
5. **M&A —** Merging with or acquiring another company necessitates the integration of two separate supply chains, which may involve a complex process of consolidating suppliers and streamlining logistics.
6. **Cash runway extension —** The supply chain network could provide companies with substantial savings but requires well-designed strategy and execution given potentially drastic downstream implications.

Outside the situations described above, companies with established manufacturing processes should "pressure test" their supply chains on an annual basis, as part of a corporate strategy review process, and conduct quarterly operational health checks.

3. Key steps to optimize a pharma supply network strategy

Effective supply chain strategy requires an upfront vision outlined in Figure 4 below, as well as the careful assessment of the following key choices:

Figure 4
Supply chain strategy and management



Source: L.E.K. research and analysis

- **Enterprise and portfolio context** should set the tone for how a company approaches its supply chain and should be overlaid with key considerations such as expected future demand, geographic regions for product sales and desired product presentation, among others. Ultimately, each biopharma will have its own approach to supply chain management, but that approach needs to be guided by the enterprise strategy and tailored to the unique needs of the portfolio.
- At the outset of the planning process, companies should start by establishing their unique **supply chain vision and principles**. These can be defined as guardrails that guide future network design recommendations. To develop supply chain principles, company leadership should answer the following key questions:
    - **Service level —** What is our optimal service level (probability of meeting demand from current inventory) that ensures we meet the majority of product demand while mitigating over-/undersupply of portfolio products?
    - **Quality vs. cost —** What is our optimal balance of quality standards across our suppliers versus target product margins?
    - **Network redundancy —** How much redundancy should exist in our network to ensure supply continuity?
    - **Flexibility —** How much flexibility is desired for our network to account for new product types, upside capacity or new contracts?
    - **Differentiating capabilities —** Are there any unique capabilities required to maintain the company's proprietary intellectual property? Additionally, do the product characteristics require a differentiated supply chain (e.g., just-in-time therapies)?
- Careful consideration of **key network choices** and timing is necessary to ensure supply demands are met and near- and long-term goals are achieved. Network choices are upcoming decisions that must be made through the supply chain strategy process, such as extension of CDMO contracts, updating of supply management systems, establishment of a new manufacturing site and others. Some decisions must be made before others, so prioritization of network choices is an important consideration (e.g., CDMO contract renewals may be coming up next quarter versus a longer-term decision to build a new site).
- Once network choices are assessed, **network design analysis and the development of recommendations** become possible. Supply networks must be tailored to the unique needs and portfolio considerations of the company (see Figure 5).

Figure 5
Key design choices for supply networks

Internal/external capacity	Geographic distribution	Mix and vertical integration
Internally operated	**Centralized network**	**High-mix; integrated**
• Higher technical competency • Lower long-term OpEx • Higher operational control	• Lower operational burden • Easier-to-manage network	• Better operational alignment • Greater network resilience • Faster supply to clinical trial sites
VS.	**VS.**	**VS.**
Outsourced externally	**Decentralized network**	**Low-mix; specialized**
• Quicker access to new technologies • Lower short-term CapEx • Higher network flexibility	• Easier-to-reach clinical trial sites • Lower shipping costs	• Higher technical capabilities • Greater line productivity • Greater flexibility in capacity

Source: L.E.K. research and analysis

The top three key design choices for the network are most often:

1. **Outsourcing vs. internal sites —** Companies must determine the optimal balance of internally owned manufacturing sites relative to the use of CDMOs. This decision can vary based on geography (e.g., use only CDMOs for supplying a certain country) or product component (e.g., drug substance is manufactured at internal sites while labeling/packing is done at CDMOs).
2. **Geographic focus of supply chain —** Companies must also identify the optimal geographic distribution of the network. These decisions impact product shipping times/costs, regulatory efforts to secure site approval and the operational burden of the network and thus are critical to optimize.
3. **Mix and vertical integration —** Companies need to determine whether manufacturing sites are low-mix and thus produce only one component of the final product (e.g., bulk drug substance only) or are vertically integrated/high-mix and thus produce all components from the application programming interface to a ready-to-ship product. Low-mix and specialized sites usually have higher technical capabilities, while high-mix and integrated sites are usually more efficient and help streamline network operations.

Once the design of the supply chain strategy is complete, a **roadmap to a steady state** should be developed to guide execution. The roadmap should clearly outline upcoming decisions and key considerations, the impact of decision outcomes, which functions should own decisions versus provide input on them, and the timeline for making the decisions.

4. Staying ahead of biopharma supply chain issues: Readiness self-assessment

Supply chain planning is critical to biopharma companies as it helps ensure product availability, speed to market, quality/safety and cost control. Consider the questions outlined in Figure 6 below to determine whether supply chain strategy establishment or review may be appropriate for you:

Figure 6
Supply chain self-assessment

General strategy assessment	Product-specific readiness
• Have we primarily been relying on CDMOs and the product quality or has the working relationship not been up to our standards? • Did we recently complete (or are we planning to complete) an M&A transaction? • Does our company's financial situation or pressure from capital markets require a closer look at potential network cost savings? • Are we expecting an uptick in future product demand? Is our network flexible enough to support that?	• Do we have a product that is about to begin first-in-human trials? • Do we have a first product launch in the next two to three years? If so, did we establish an initial supply chain strategy? • Do we have a product that will launch in a new geography, disease area or modality? • Do we have an additional product launch in the next two to three years?

Note: CDMOs=contract development and manufacturing organizations
Source: L.E.K. research and analysis

Your answers may signal that a supply chain strategy review may be warranted for your company. If you are considering an evaluation or evolution of your supply chain model, L.E.K. can help support your decision-making process.

For more information, please contact lifesciences@lek.com.

About the Authors

TJ Bilodeau
TJ Bilodeau is a Managing Director and Partner in L.E.K. Consulting's Boston office and is a member of the Healthcare practice. TJ has more than 15 years of experience supporting clients across the healthcare industry with a focus on growth strategy for emerging and midsize biopharmas. He has extensive experience, across several therapeutic areas, in commercialization strategy, portfolio optimization, transaction support and broader strategic planning.

Peter Rosenorn
Peter Rosenorn is a Managing Director and Partner in L.E.K. Consulting's Boston office and specializes in the life sciences and pharmaceutical sector with a focus on growth strategy and organization and performance. Peter advises clients on a range of critical business issues including organizational scale-up and development, launch planning and commercialization, transaction support, forecasting and valuation, and post-merger integration.

Adam Siebert
Adam Siebert is a Managing Director and Partner in L.E.K. Consulting's New York office and a member of the Life Sciences practice. Adam has been with L.E.K. for over eight years, and has experience across diagnostics and research tools, bioprocessing, and pharma services, as well as emerging, mid-cap and large pharma. He has helped a number of clients in the life sciences industry with growth strategy, life cycle management, portfolio optimization and M&A projects.

Luba Vazhenina
Luba Vazhenina is an Engagement Manager in L.E.K. Consulting's New York office, specializing in life sciences. Luba has extensive experience advising clients on a range of topics, including growth strategy, first product launches, organizational scale-up, go-to-market strategy, supply chain strategy and PMI.

About L.E.K. Consulting
We're L.E.K. Consulting, a global strategy consultancy working with business leaders to seize competitive advantage and amplify growth. Our insights are catalysts that reshape the trajectory of our clients' businesses, uncovering opportunities and empowering them to master their moments of truth. Since 1983, our worldwide practice — spanning the Americas, Asia-Pacific and Europe — has guided leaders across all industries, from global corporations to emerging entrepreneurial businesses and private equity investors. Looking for more? Visit **www.lek.com**.