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Future-proofing manufacturing and supply chains

Today's headwinds, and the uncertainty that is expected to continue, will require life sciences companies to have agile manufacturing processes and resilent supply chains. This includes retooling technology and transforming environments.[1]

Scaling smart factory transformation

In 2022, more life science organizations are scaling smart factory capabilities to boost agility. Biopharma and medtech companies are investing in fully digitizing and integrating information technology (IT) and operational technology (OT) capabilities in manufacturing.[2] As smart factories scale, manufacturing organizations are looking for ways to:

- Improve performance
- Make data integration sustainable
- Upskill workers' digital and data skills
- Transform infrastructure and culture
- Minimize cyber risk

Deloitte believes there are four drivers of performance for life sciences companies looking to get the most out of smart factory investments:

1. Human performance, reducing error rates on the production floor
2. Process performance, getting that extra yield, extra gram of product from the current processes
3. Asset performance, getting more up time from manufacturing assets
4. Network performance, optimizing the performance that you need across the entire manufacturing network[3]

A high-performing smart factory empowers shop floor personnel with predictive analytics to take productivity and quality to the next level. As they analyze reams of data, asset performance issues can be revealed, allowing for more proactive and corrective optimization. The optimized processes, in turn, result in cost-effective production.[4]

Making data integration sustainable

Smart factories employ data-driven technologies—like artificial intelligence (AI), machine learning (ML), and the Internet of Things (IOT). (see figure 1). By seamlessly connecting and integrating disparate manufacturing systems and processes, companies increase visibility and performance capabilities. Figure 1 shows the level of business case-based opportunities for various medtech capabilities.

For example, on a digitized shop floor, machine intelligence is able to monitor processes and provide actionable insights for floor staff to reduce errors, deviations, and production losses.[7] For biopharma, AI can predict asset maintenance requirements based on operational and maintenance history data stored in the cloud to prevent disruptions and loss of expensive APIs (Active Pharmaceutical Ingredients).[8]

Estimating the net value of a smart factory investment

After a rapid assessment and identification of where digital capabilities could be scaled more effectively, a leading biotech/pharmaceutical manufacturer put numbers against a smart factory's expected benefits. The company combined top-down financial analyses with bottom-up evaluations of the impact of the proposed use cases on operational key performance indicators (KPIs) at two pilot sites. The company then scaled the opportunities across the network at full potential to determine which benefits were recurring and which were one-offs. Finally, the company validated the scaling and clustering approach and confirmed business case input parameters such as duration, rate of return, and cost of capital.[5]

The net value of the smart factory platform was projected to be at $50 million to $75 million year-over-year in operational expense reduction on a baseline of $700 million—a direct bottom-line impact. This approach also created additional capacity that effectively negated the need for $500 million in capital expenditures over a five-year period.[6]

Figure 1: Smart factory digital transformation

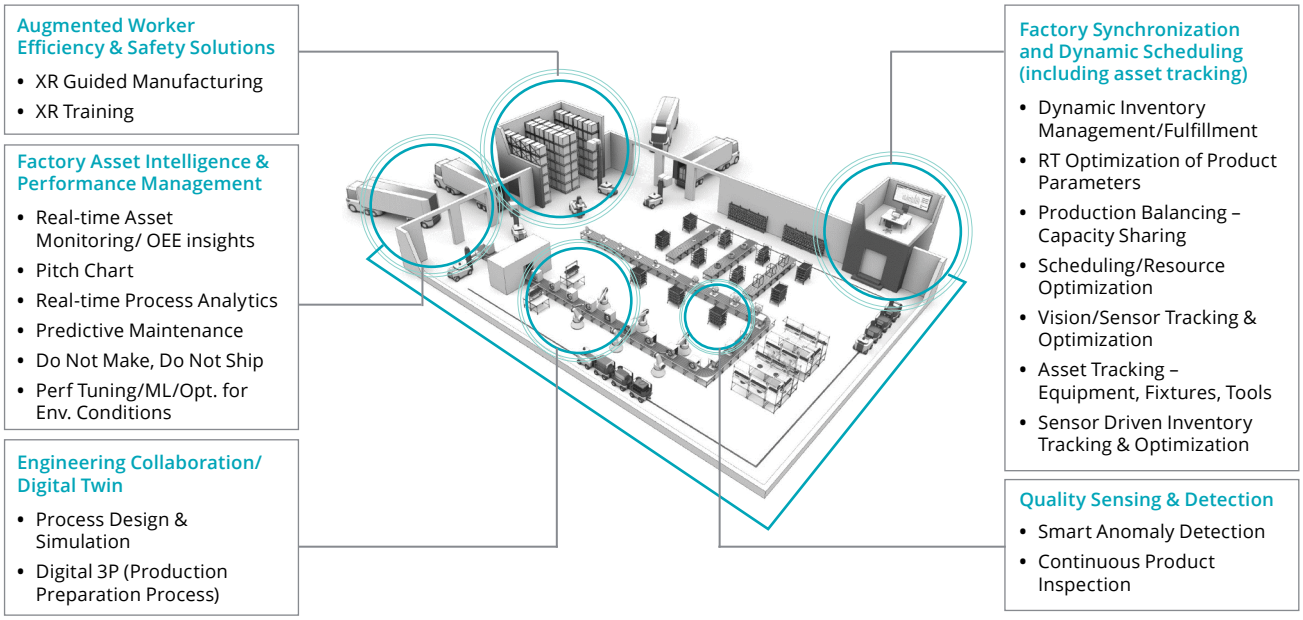
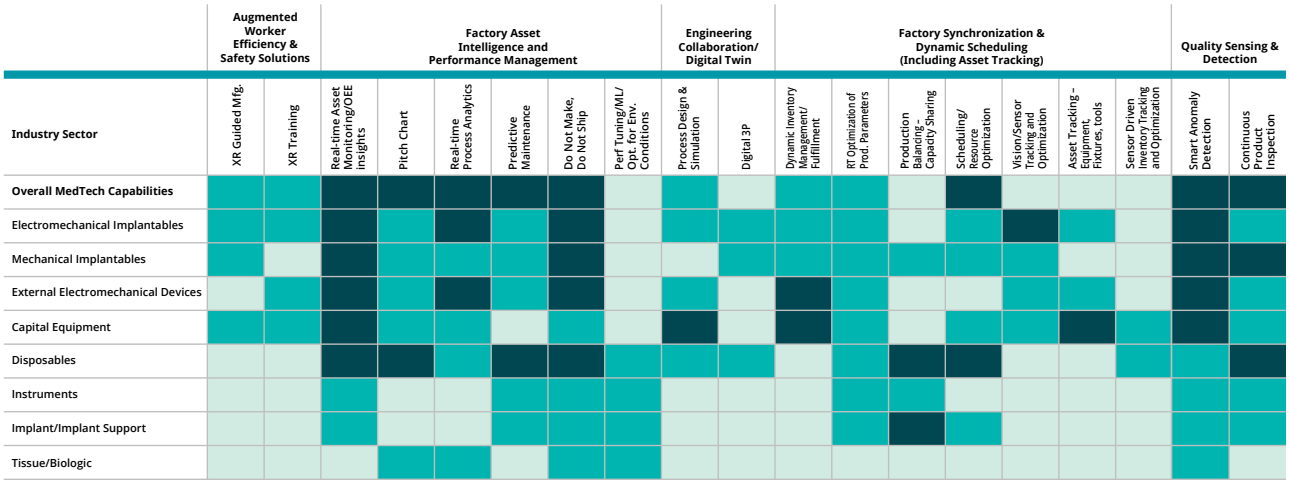


Figure 2: Business case-based oppportunities for medtech capabilities



Source: Deloitte analysis

LEGEND: Business Case-based Opportunity

High	Medium	Low

> Legacy biopharmaceutical companies have grown and proliferated sources of data by establishing different systems across their operations. One of the fundamental challenges for a smart factory transformation is integrating those data sets from different sources—and making sense of them—with the least possible effort and investment.
>
> *Laks Pernenkil, Principal, Life Sciences Operations, Deloitte.*[9]

Data integrity, a global issue for regulators

While investments already made represent huge opportunities, too often, they are impeded by manual and disconnected processes and documentation, especially if paper-based. Data integrity issues are a risk for life sciences companies,[10] and a global issue for regulators. Poor documentation is a top data integrity concern covered in the US FDA's Compliance Program 7356.002M implemented 1 October 2021.[11]

Regulatory intelligence platform REDICA Systems analyzed US FDA warning letters to manufacturing sites for 23 countries over a five-year period (see figure 3).[12] Their research identified letters that included data integrity issues, and they were surprised to find that Canada led the list by percentage of issues.

Figure 3: Country comparison: Manufacturers with US FDA warning letters (WL) and letters identifying data integrity (DI) issues, 2014-2019.

Country	Number WLs with DI n-grams	Total Number of WLs	Percent with DI Issues
Canada	10	11	97
India	40	51	78
Japan	5	7	71
USA	9	13	69
China	40	62	65
South Korea	7	14	50

n-gram: Natural Language Processing (NLP) identifies a series of n items in text, in this case, data integrity issues.

Source: "What can regulatory data tell us about data integrity trends?" REDICA Systems, 31 August 2021.

Automated processes still require upskilling workers' digital and data skills

Solutions that automate batch records and other documentation processes are designed to prevent incorrect, missing, or out-of-date entries, but automation tools can be deployed with greater speed by less-technical people and that may pose a risk.[14] As companies pursue automation capabilities, they should develop a flexible, mature validation strategy to implement controls that support regulatory compliance and product safety.[15]

Insufficient training and awareness is one of the factors that has made data integrity challenging for a while. Staff members are expected to fully understand all the requirements and standards relating to data integrity, and today's environment requires upskilling workers' digital and data capabilities.[16]

If work is outsourced, life sciences companies maintain responsibility for the integrity of all data involved.[17] Two clinical research organizations in India were recently told by regulators that studies would need to be redone due to data integrity issues—affecting an untold number of drug makers.[18]

Transforming infrastructure and culture

In 2022, as life sciences companies look to change the innovation-averse DNA in some manufacturing organizations, they are also looking at ways to transform their infrastructure and culture. Companies might adopt a think-digital-to-be-digital mindset—considering how digital technologies augment human capabilities and change execution of processes. Shifting away from siloed manufacturing systems and processes requires building connectivity for the flow of information, data, and actionable insights.[19]

Minimizing cyber risk

As connectivity expands, cyber risk increases. In 2020, manufacturing moved up the list of most targeted industries from 8th to 2nd—a rise of 300% globally, according to the 2021 Global Threat Intelligence Report.[20] Over the year, attacks against manufacturing increased from 7% to 22%; health care increased from 7% to 17%.[21]

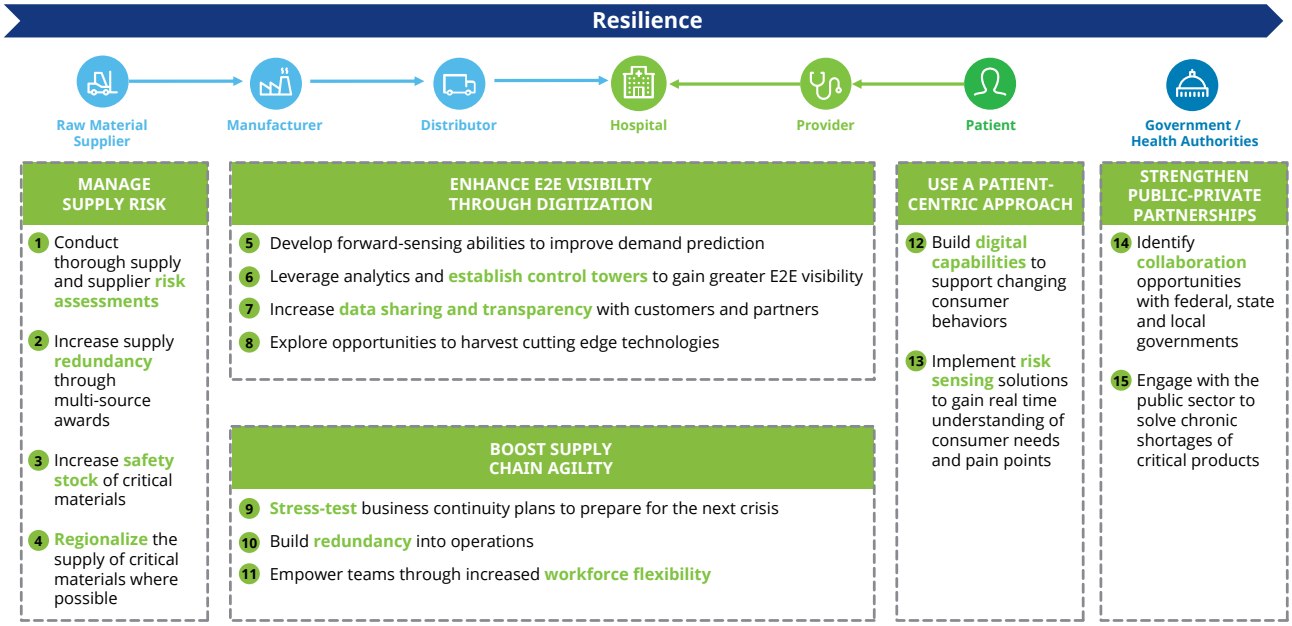
Organizations should have clear agreement on which data is most critical, who has access to that data, and an understanding about the potential impact if it is compromised. While no amount of money can make the risk completely disappear—and the long-term costs associated with data breaches can be difficult to quantify—brand reputation, supply chain, patient safety, and consumer trust may all be affected.[22]

Building supply chain resilience

Starting with a global suppply chain strategy

As disruptions to logistics and transportation impacted the timely delivery of products during the pandemic, life sciences companies rapidly digitalized their supply-chain operations. IoT solutions tracked and traced product shipments in real time and plugged gaps in supply-chain visibility.[23] The ability to anticipate and react to disruptions and shifts quickly requires a resilient global supply chain strategy (see figure 4).[24]

Figure 4: Building a resilient global supply chain strategy



Source: "The Semiconductor Chip Shortage Hits MedTech: Strategies to Build Resilient Supply Chains," AdvaMed/Deloitte, 2021.

Regionalizing supply and continuous manufacturing

The pandemic created new urgency to reduce dependence on bulk active ingredients and generic drugs sourced from India and China. Manufacturers in Europe and the United States are building new in-country API development and manufacturing capabilities.[25] In addition to reshoring and regionalizing the supply of critical materials, companies are using innovative, continuous manufacturing to mitigate supply chain risks.[26]

Continuous manufacturing is a way for drug manufacturers to more easily adapt supply to demand

Fully end-to-end systems, like **CONTINUUS**' Integrated Continuous Manufacturing (ICM) platform, seek to encompass both API and final dosage form manufacturing in one integrated system. More cost-effective manufacturing for small molecules can be performed at CONTINUUS sites or even clients' facilities through a Mobile Pharmaceutical (MoP) offering.

GlaxoSmithKline says its agile, continuous flow chemistry manufacturing has smaller operations that are more efficient and environmentally friendly. In Singapore, the company's commercial continuous API manufacturing process requires a facility approximately one-ninth the size (100 m2) of a facility required for a batch process (900 m2).[27]

Continuity Pharma, a start-up out of Purdue University, is using flow chemistry to develop a system for continuously manufacturing multiple APIs with shorter turnaround times and higher volume. Innovative, streamlined, and automated systems are needed to compete with offshore API manufacturing.[28]

In 2022, as life sciences companies conduct risk assessments, data analytics tools can be leveraged for deeper insights across the supply chain. These tools are designed to improve demand prediction and support data sharing with customers and partners.[29] Other digital innovations, like AI, can predict or forecast supply chain-related events (e.g., logistics challenges, geopolitical issues, and supply disruptions), either executing actions autonomously or recommending actions stakeholders should take—ultimately, helping life sciences companies build resilience and gain competitive advantage (see figure 5).[30]

Figure 5: Sample innovations driving predictive and autonomous supply chain management

Digital innovations	Description
Control towers (data lakes)	• By building control towers or data hubs, organizations can merge internal data (such as production and inventory data) with data from intermediaries and partners to provide real-time longitudinal visibility into material and product flow.
Machine-assisted business response (AI)	• As part of day-to-day operations, self-healing AI solutions analyze supply chain, manufacturing, and market data to highlight potential issues (e.g., stockout of a raw material), analyze their root causes (inability of a vendor to make a delivery due to logistics issues) and suggest next steps to supply chain operators (ordering from an alternative supplier or changing production schedules).
Machine-driven resilience management (AI)	• AI predicts or forecasts events (such as logistics challenges, geopolitical issues, and supply disruptions) to execute actions either autonomously or recommend actions to stakeholders to respond to long-term risk/disruptions.
Market and product tracking (AI, IoT, blockchain)	• Companies track and analyze nontraditional data such as consumer sentiment, competitor, product user, and experience data along with traditional data (such as order patterns, demand signals) to optimize supply chain planning. • As more next generation therapies enter the market, IoT, and blockchain are increasingly applied to track and trace product movement and temperature and coordinate timely delivery of such therapies to treatment centers.

Addressing external forces disrupting supply chains

Research shows that the life sciences sector expects to experience continued disruption in 2022 to its supply chains from external factors, including inflation and labor shortages.[31] We see the pandemic, global volatility,[32] and the semiconductor shortage (affecting two-thirds of the medtech industry)[33] continuing to be major supply chain issues.[34]

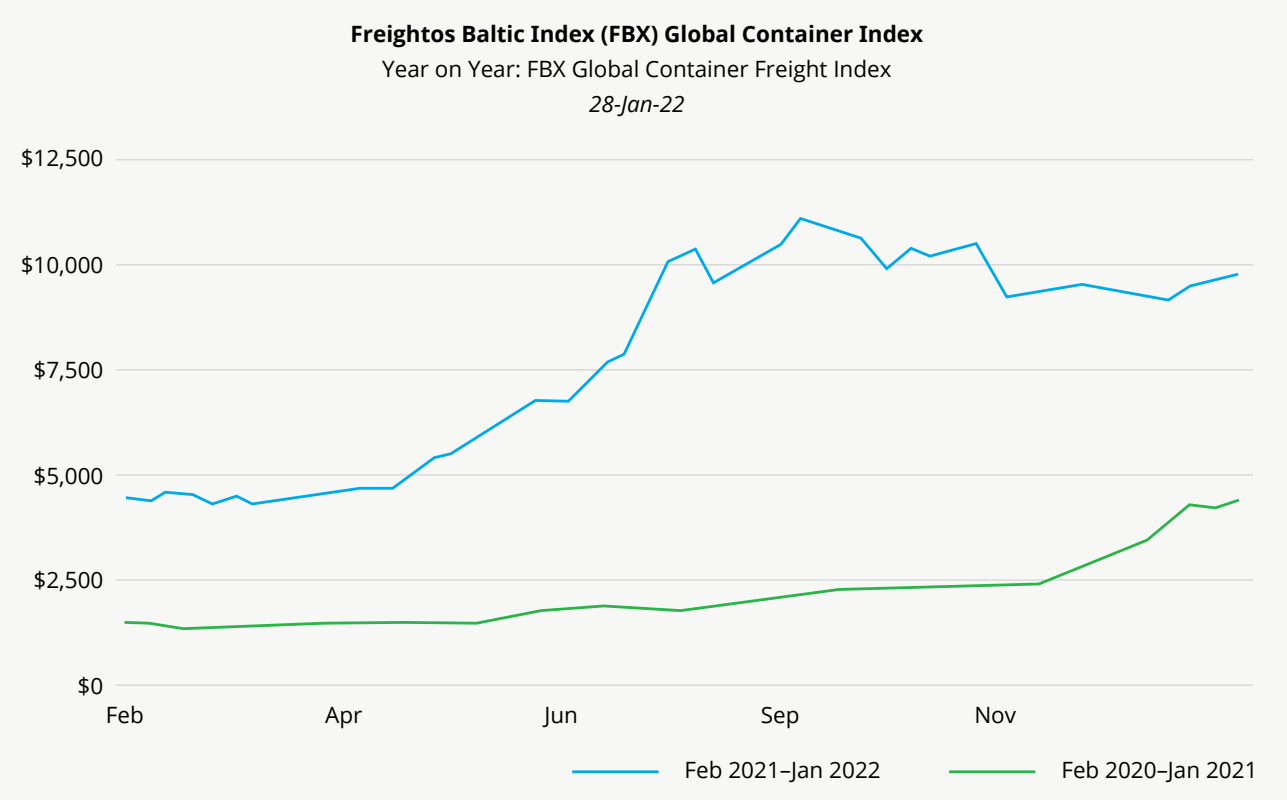
Pandemic-era inflation linked to supply chain constraints

Today's economic climate and inflationary pressures present challenges not seen since 2008.[35] But pandemic-era inflation is different[36]—attributed mostly to constraints connected to transportation and supply chain bottlenecks.[37]

Access to raw materials is a factor.[38] Global ocean freight rates increased substantially in 2021 (see figure 6),[39] and trucking spot rates increased by 20%.[40] Air freight rates in January 2022 were ahead of last year.[41] According to Abbott CFO Bob Funck, inflation and the supply chain are really linked together.[42]

> "The global supply chain has not been able to keep up with strong demand out there. So, like others, we're seeing some increased input costs across areas of our business. We're experiencing some higher shipping costs and, in some cases, higher commodity costs."
>
> *Bob Funck, CFO, Abbott.*[43]

Figure 6: Year-on-year global container freight rates, Feb 2020 – January 2022



Source: Freightos, 28 January 2022.

Today's market headwinds are different; inflation is higher, but also more volatile,[44] and inflation is not likely to go back to pre-pandemic levels.[45] While price increases did not significantly impact the financial results of many sector companies in 2021, change could come when Q4 2021 reports are released in early 2022.[46] Going forward, companies will need to look holistically across a range of levers—analyzing people, financial, and operational data—for effective inflation margin management.[47]

Addressing volatility

Increasing global trade friction, on top of the global pandemic, have, in places, led to disruption in tariffs, regulatory changes, diminished access to suppliers/vendors, limitations on cargo capacity, and shortages of products.[48]

Some life sciences companies are looking to minimize trade uncertainties and reduce customs taxes by rethinking operations and diversifying supply chains. Diversification or business model changes can lead to unintended tax costs or presence. Tax leaders should be engaged early to analyze potential impacts.[49]

Semiconductor chip shortage

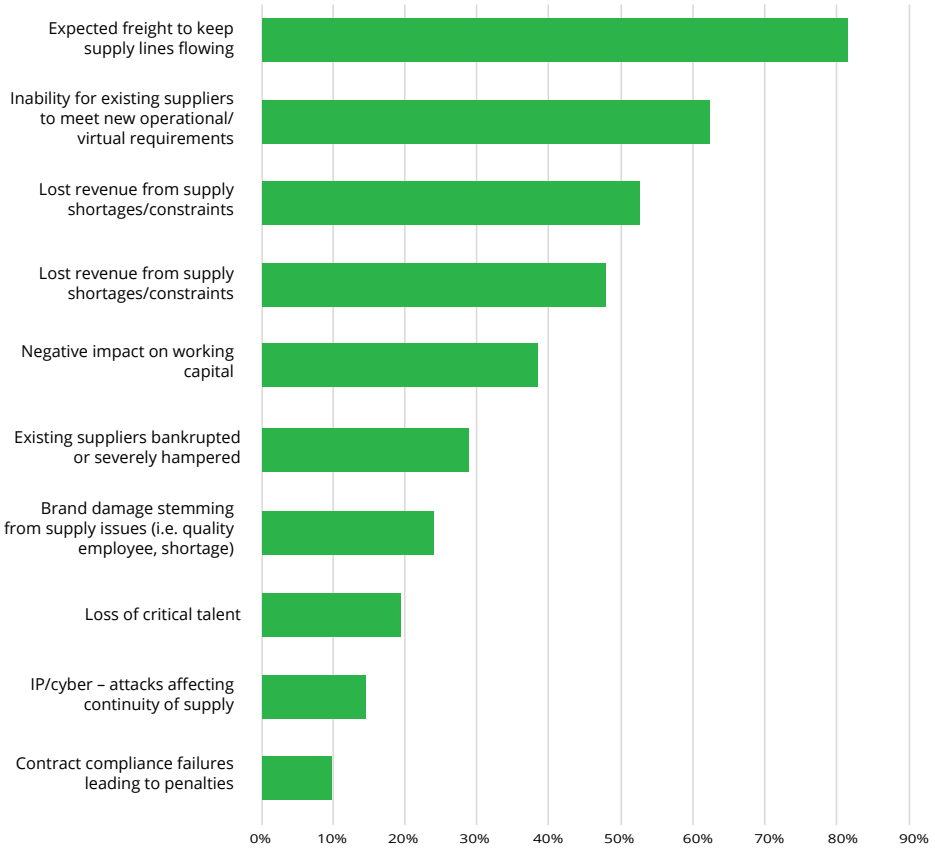
It took the chip shortages of 2020 and 2021 for semiconductors to cement their "critical" status. In 2022, Deloitte expects the global semiconductor chip industry to grow 10% to over US$600 billion for the first time ever. Shortages and supply chain issues are likely to remain front and center for the first half of the year, hopefully easing by the back half, but with longer lead times for some components stretching into 2023, possibly well into 2023.[50]

Whether explicitly or inadvertently, it is unknown which sectors could be prioritized if chip shortages persist. Many medical devices are chip-dependent, including ventilators and defibrillators; imaging machines; glucose, ECG, EEG, and blood pressure monitors; implantable pacemakers; and more. Patients who rely on these technologies for lifesaving and life enhancing care may be at risk.[51]

The issue is industry-wide for the hundreds of diagnostics, therapeutics, and capital equipment companies that produce essential medical technologies. An Advanced Medical Technology Association (AdvaMed) study conducted by Deloitte found that two-thirds of medical technology companies surveyed say semiconductors, firmware, and/or embedded software are required for at least half of the medical devices they produce for patients.[52]

Deloitte found that half of semiconductors for the majority of those surveyed (mostly with over US$1 billion in revenues) are single source—raising the stakes for supply chain disruption. All experienced chip supply chain disruption ranging from two weeks to more than a year, mostly from delays, order cancellations, and short orders.[53] Disruptions were all across the supply chain, many affecting the bottom line—e.g, increased shipping costs, decreased revenue from shortages, or negative impacts on working capital (see figure 7).[54]

Figure 7: Have you experienced any of the following disruptions to your overall supply chain in the last 12 months?



Source: "The Semiconductor Chip Shortage Hits MedTech: Strategies to Build Resilient Supply Chains," AdvaMed/Deloitte, 2021.

Medtech's primary needs are 2nd or 3rd generation chips,[55] and the use of chips in life sciences and health care will likely grow. Regulators are approving new connected home health care devices such as wearables and smart patches whose use may span hundreds of millions of units, especially given the rise in virtual visits and decentralized clinical trials.[56]

The United States is looking for companies to onshore larger portions of the semiconductor supply chain.[57] In October 2021, the US Department of Commerce established the Microelectronics Early Alert System to coordinate government resources and help companies resolve supply chain bottlenecks due to the chip shortage.[58] Intel is spending $20 billion on a cutting-edge, 1000-acre chip manufacturing campus in Ohio which would make it one of the largest chip manufacturing facilities in the world. Production is scheduled to start in 2025.[59]

In addition to the chip shortage there is a growing demand for software skills required to program and integrate chips—and an overall labor shortage—that will likely exacerbate the situation for the near future.[60]

Growing popularity of RNA therapies and short-term plasmid shortage

Increased demand has led to an industry shortage of plasmid starting material, prompting a growing number of viral vector facilities to consider manufacturing plasmid in-house to avoid potential supply-chain issues. The shortage may continue for the next couple of years.[61]

Demand increased with the rise of viral vector and gene therapy facilities, and is further complicated by increased interest in mRNA manufacturing. Plasmids are the raw material for both viral vector and in vitro-transcribed (IVT) mRNA manufacturing.[62]

Expanding the supply chain ecosystem in 2022

A business is only as strong as its chain of suppliers,[63] and the pandemic highlighted the need to transform traditional supply chain models.[64] According to a recent Fortune/Deloitte survey, the majority of LSHC CEOs say that supply chain disruption has resulted in higher costs of doing business and margin impacts,[65] and continued challenges will influence and disrupt business strategy over the next 12 months (see figure 8).[66]

Figure 8: Winter 2022 Fortune/Deloitte CEO Survey, LSHC CEO responses

What supply chain challenges has your organization experienced?

Challenge	% of LSHC CEOs
Input/raw material shortages	33%
Labor shortages	92%
Maintaining quality standards	8%
Production and/or logistics issues	50%
Reduced logistics capacity (any mode)	33%
Reduced manufacturing capacity	0%
Other	8%

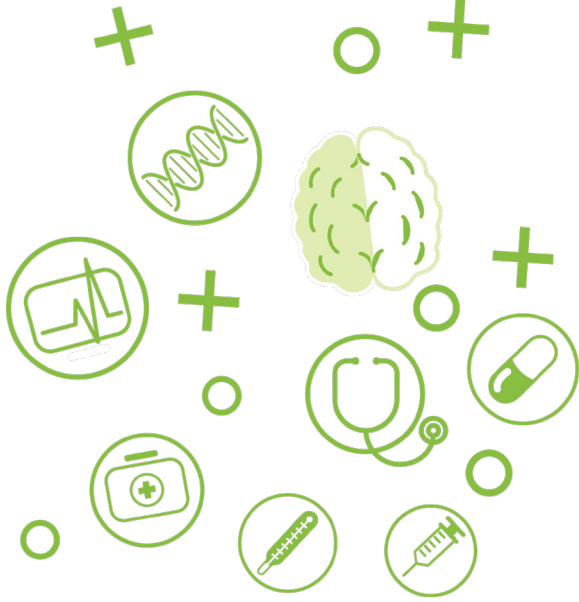
What supply chain actions do you expect to take in the next 12 months?

Action	% of LSHC CEOs
Change product portfolio and roadmap	25%
Change profit/pricing model (e.g., higher prices)	67%
Expand sustainability/climate change initiatives	17%
Expand the supply chain ecosystem with more partners	50%
Update/change the logistics network and modes	33%
Vertical integration acquisitions	25%
Other	8%

Source: Winter 2022 Fortune/Deloitte CEO survey, Deloitte, 2022.

According to the survey, half of LSHC CEOs plan to expand their supply chain ecosystem with more partners in 2022, with a majority planning changes to profit/pricing models (see figure 8).[67] The research further shows that a new normal appears to be setting in, wherein leaders expect new challenges to arise continuously, but are confident they can manage through them to achieve positive business results.[68]

Contacts



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