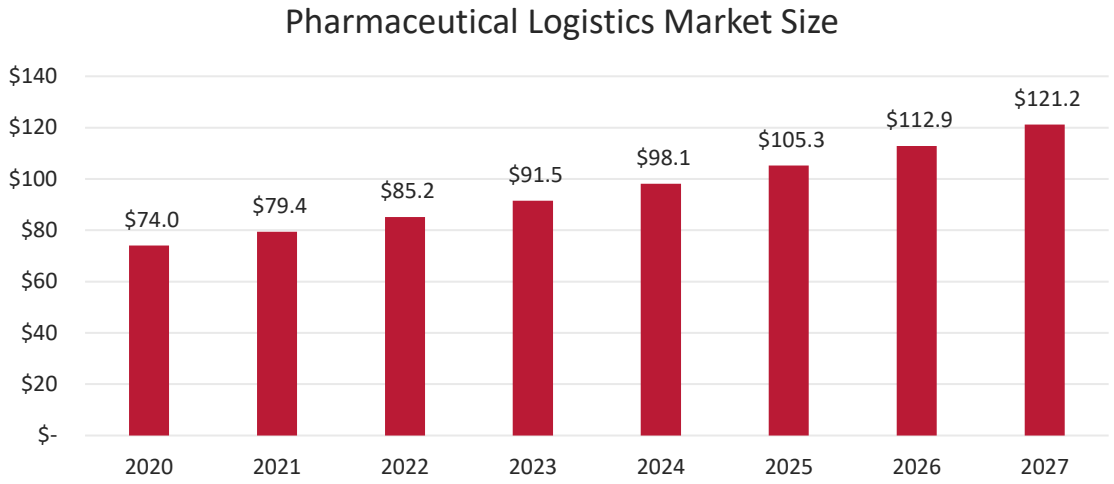
DRUG SUPPLY CHAIN MARKET PRIMER

October 2020

Table of Contents

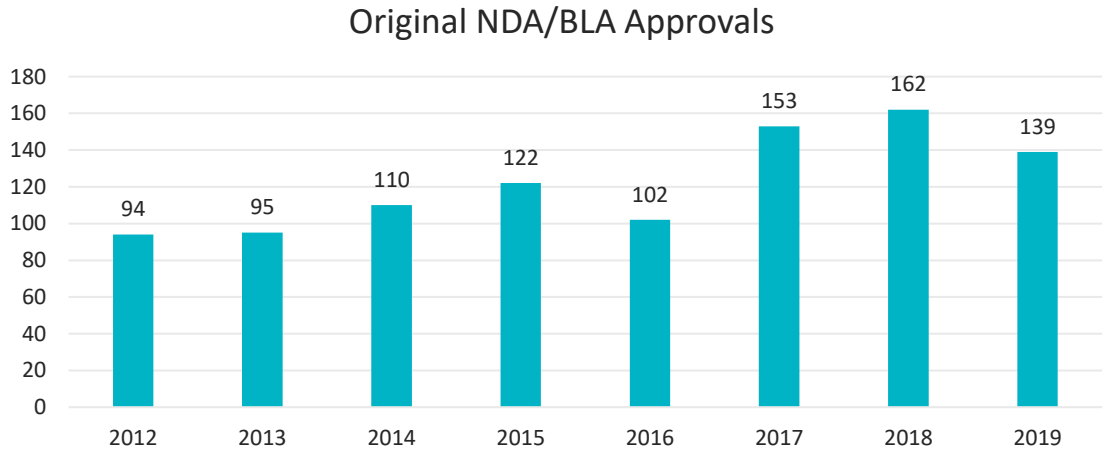
MARKET OVERVIEW

The drug supply chain logistics market is large and getting larger. While the drug supply chain includes pharmaceutical manufacturers, wholesaler distributors, and pharmacies, the drug supply chain logistics market focuses on those companies that help transport drug substances and drug products from one place to another — from wherever the drug was manufactured and to all of the places it passes through before it reaches the patient. The market is projected to grow at a compound annual growth rate (CAGR) of 7.3% from 2020 through 2027 and its market size is projected to surpass $100 billion by 2025.[1]



Source: "Pharmaceutical Logistics Market Size, Share & Trends Analysis Report by Type, by Component, by Region, and Segment Forecasts, 2020-2027," (Grand View Research — May 2020)

This projected growth in the supply chain market is driven in large part by the long-term growth in drug approvals over the past two decades.[2] Over the past decade, the number of original NDA/BLA approvals increased from the mid-90s in 2012-2013 to exceeding 150 in both 2017 and 2018.



Source: FDA.gov

SUPPLY CHAIN COMPANIES

There are many companies that offer supply chain/logistics services. Here are some of them. Note: This is not an exhaustive list.

DDS companies that offer drug supply chain logistics services

CardinalHealth™ | fisher clinical services by Thermo Fisher Scientific | McKESSON

Drug supply chain logistics companies

LifeConEx CONNECTING PEOPLE WITH LIFE | MARKEN a UPS Company | QuickSTAT A Kuehne + Nagel Company Global Life Science Logistics

World Courier AmerisourceBergen | YOURWAY THE BIOPHARMA SERVICES COMPANY

Specialty drug supply chain logistics companies

BE THE MATCH BioTherapies | cryoport SCIENCE. LOGISTICS. CERTAINTY.

Freight companies that offer drug supply chain logistics services

Agility | AIT WORLDWIDE LOGISTICS | DHL EXCELLENCE. SIMPLY DELIVERED.

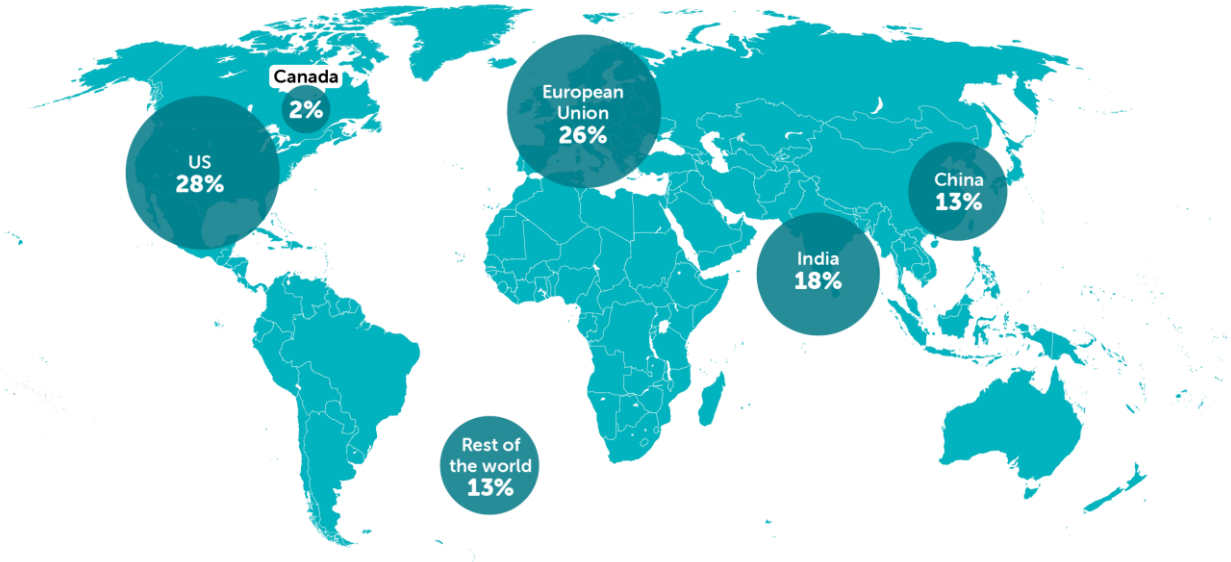
DSV Global Transport and Logistics | FedEx

KENCO | UPS Healthcare Quality Focused. Patient Driven.

VARIABILITY IN SOURCING AND RAW MATERIALS

Janet Woodcock, director of the Center for Drug Evaluation and Research (CDER), stated in her congressional testimony on October 31, 2019, that, "Historically, the production of medicines for the U.S. population has been domestically based. However, in recent decades, drug manufacturing has gradually moved out of the United States."[3] According to the FDA, the majority (72%) of manufacturing plants that are registered with the U.S. to supply active pharmaceutical ingredients are outside of the U.S.[4] Almost one-third are in India or China.

Plants that are registered with the U.S. to supply active pharmaceutical ingredients can be found all over the world.



Source: "COVID-19 Is Reshaping the Pharmaceutical Supply Chain," (Chemical & Engineering News — 4/27/20)
Source: U.S. Food and Drug Administration, August 2019.

It should also be noted that bioprocessing materials themselves are a serious threat to the drug supply chain. While there have been advances in testing of bioprocessing materials,[5] improved testing can also increase the number of documented cases of contamination.[6] Still, accurate testing can catch the presence of trace impurities that are either toxic or can react with the desired compound in a way that is detrimental to the drug manufacturing process. Ed Gump, vice president of small molecules at U.S. Pharmacopeia, noted, "As manufacturers adjust or adapt materials and processes to continue manufacturing supply, each change opens another door for poor quality or allows harmful contaminants to enter the system. Using standards to test products for identity, purity, strength, and performance, manufacturers can ensure consistency and quality of medicines in the supply chain."[7]

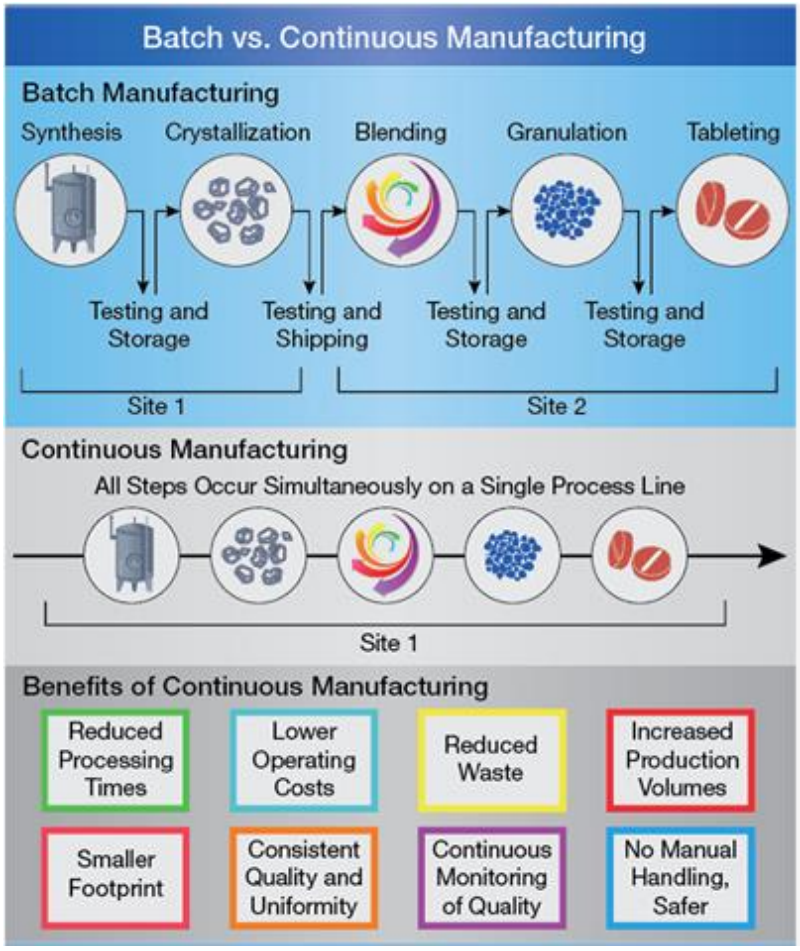
Another problem is the lack of consumables needed to make APIs, including "filter media and cell cultures, single-use plastics, bags, vessels, and other components."[8] Shortages of any of these consumables result in delays in drug manufacture or drug packaging.

GROWING COMPLEXITY

Continuous Manufacturing

Drug manufacturing is becoming increasingly complex. As stated on the previous page, greater variability in sourcing and raw materials makes for a more complex supply chain.

- The utility of highly potent API (HPAPI) drugs in cancer treatments has resulted in their becoming a larger part of the small molecule drug market.[9]
- The FDA encouraging the adoption of advanced manufacturing technologies such as continuous manufacturing and 3-D printing also increases system complexity.[10]



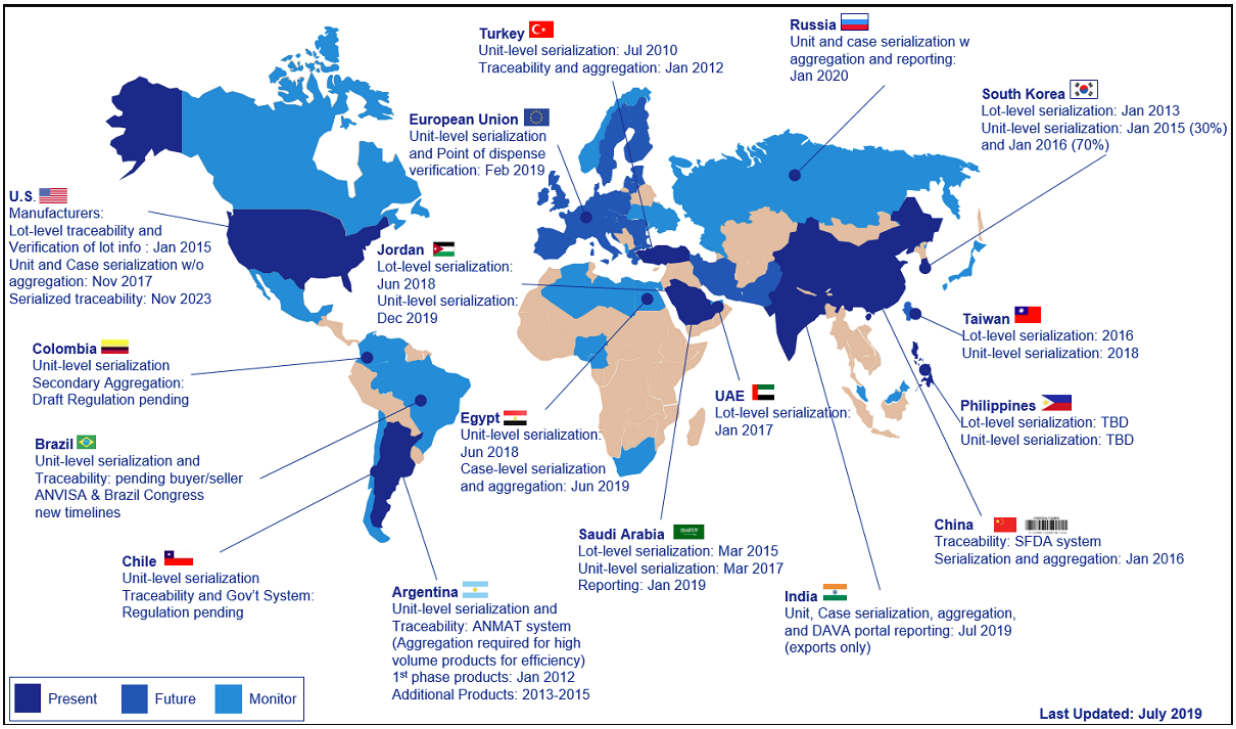
Source: "Pharmaceutical Manufacturing: Current Trends and What's Next," (AIChE — December 2018)

When applied in isolation and under ideal circumstances, each of these processes can save time and lower costs. But when raw-material shortages occur, the resulting bottlenecks overwhelm any time and cost savings that would have occurred as a result of these processes being implemented.

Safety

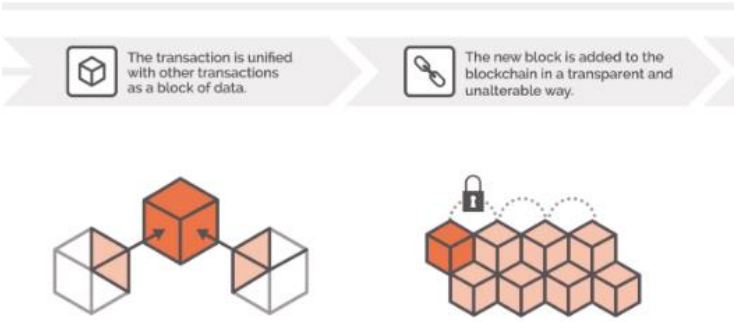
The driving force behind serialization is to help protect patients from drugs that are "counterfeit, stolen, contaminated, or otherwise harmful."[11] The serialization process, by assigning "a unique serial number to each salable unit of each prescription product," allows for improved traceability of a drug by connecting it to information about the drug's origin, batch number, and expiration date.[12] Theoretically, this makes it more difficult to produce counterfeit drugs or to steal and resell drugs.

The 2013 Drug Supply Chain Security Act instituted timelines for all participants in the supply chain — manufacturers, repackagers, wholesalers, and dispensers — to comply in the incorporation of increased efforts at serialization and traceability.[13]



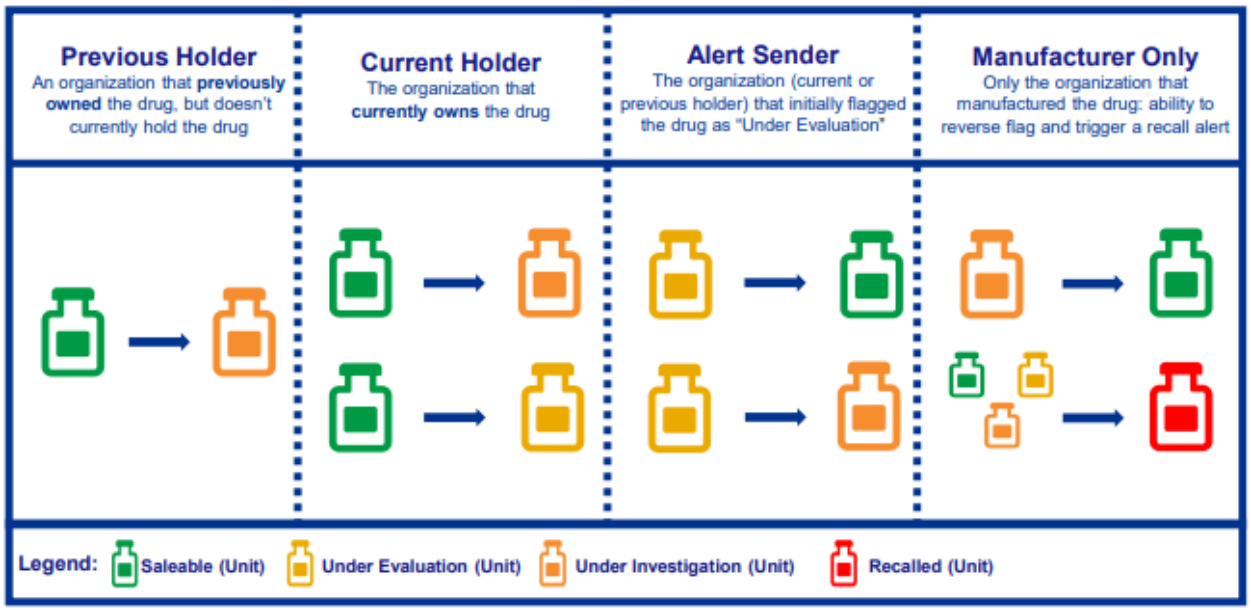
Source: "Next Steps for Serialization in the Pharma Supply Chain," (Pharmaceutical Online — 7/22/19)

Blockchain is another example of a technological innovation that can be applied to help make drugs safer. Blockchain technology is a "digital ledger of transactions"[14] that is difficult to change or hack.



Source: "Blockchain Could Solve Many Challenges Facing the Clinical Trials Process: Analyst," (Outsourcing-Pharma — 11/20/18)

Pharmaceutical companies are utilizing blockchain technology to share sensitive information on a common platform without compromising the privacy or security of the information.[15] And the FDA has started a pilot program using blockchain to help track and trace prescription drugs and vaccines.[16] The graphic below illustrates how the application of blockchain could allow only specific users to send alerts depending on the stage of the drug manufacturing process.

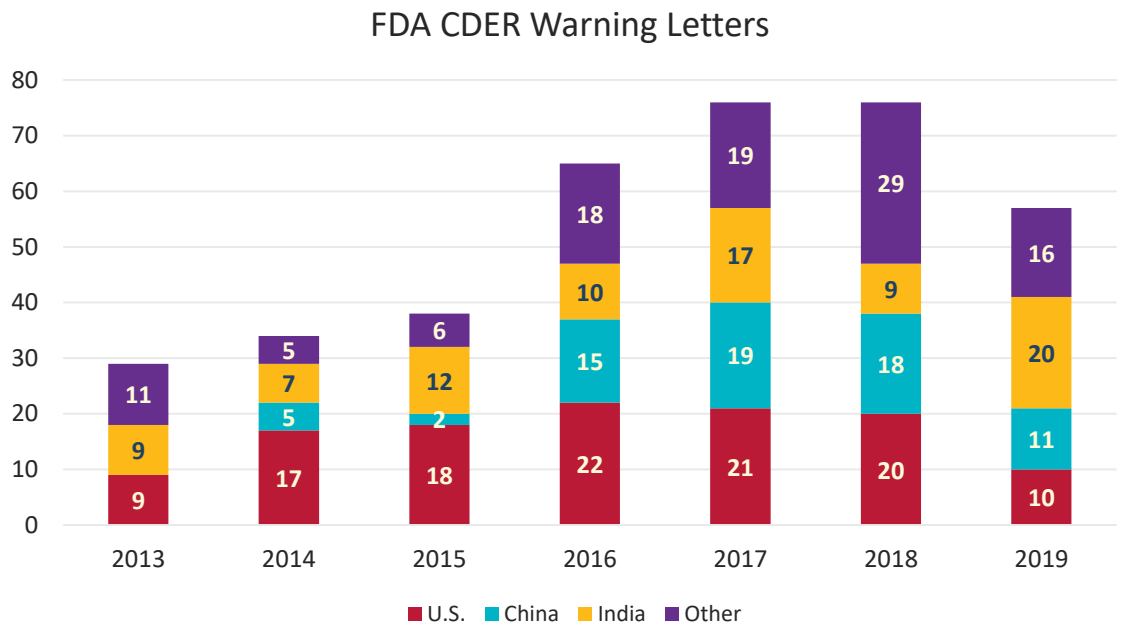


Source: "FDA DSCSA: Blockchain Interoperability Pilot Project Report (IBM — February 2020)

In the long run, serialization and blockchain should make the supply chain more efficient and safer by making it easier to trace where drugs go between the time they are manufactured and when they are eventually delivered to patients.

INCREASED REGULATION

Over the past decade, the FDA has issued more warning letters to drug manufacturing facilities. The increase has been due primarily to greater issuance of warning letters to manufacturing facilities outside of the United States,[17] especially in China and India.

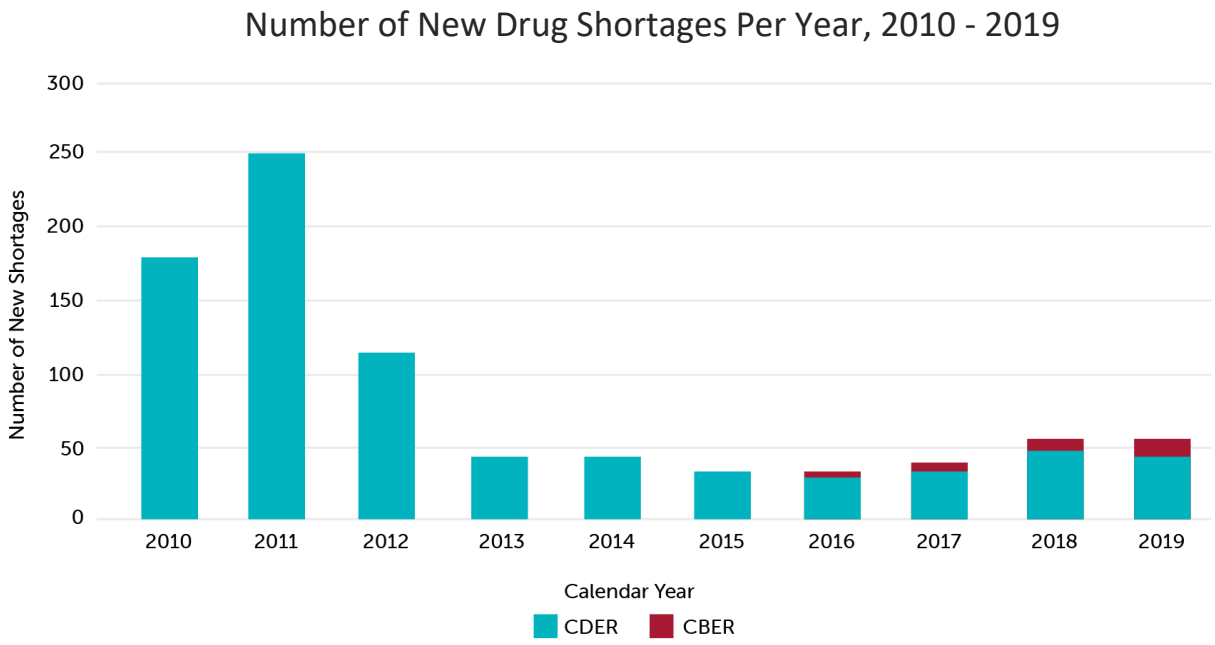


Source: FDA.gov

And with COVID-19, earlier this year the Securing America's Medicine Cabinet Act was introduced in the U.S. Senate to encourage the production of active pharmaceutical ingredients in the United States. In addition to working with existing FDA programs to prioritize issues related to national security or drug shortages, the bill also authorizes $100 million to develop centers of excellence where universities and the industry can collaborate to develop new drug manufacturing technology and processes.[18] The act also proposed tax credits for drug manufacturers who close overseas plants and open or expand plants in the United States.[19]

DRUG SUPPLY SHORTAGES

Drug supply shortages, defined by the FDA as "shortages of human drug and biological products,"[20] are not a new phenomenon. As tracked by the FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), there were significant drug shortages in 2010 and 2011 before hitting a relative low in 2015. Since 2016, the number of new drug shortages has increased each year to about 60 in 2019.[21]



Source: "Report on Drug Shortages for Calendar Year 2019," (U.S. FDA — 4/23/20)

Each of the factors discussed in previous sections — growing complexity of drug manufacturing, greater raw material variability, and increased regulation — has exerted slight upward pressure on the number of drug shortages.

THE IMPACT OF COVID-19

While drug shortages and the conditions that led to them existed pre-COVID-19, the arrival of COVID-19 further exacerbated the weaknesses in the drug supply chain and caused the number of drug shortages to substantially increase.

As Heather Sugrue of Recro Gainesville said, "Every entity that is part of the supply chain in the drug development process can be a factor in triggering a domino effect in shortages, from raw materials for manufacturing the APIs to PPE needed for manufacturing a drug product to shipping materials needed for delivery to its final destination."[22]

First and foremost, we have seen COVID-19-related drug shortages. More than half of 2020's drug shortages were directly or indirectly caused by events brought on by COVID-19.[23]

As of this writing (on 10/6/20), there are 173 drugs listed as "currently in shortage" on the FDA's Drug Shortages webpage.[24]

We have also witnessed the following:

- A shortage of APIs: COVID-19 initially caused plant closures and lockdowns in both China and India that adversely affected the production of active pharmaceutical ingredients needed by drug manufacturers.[25]
- A shortage of packaging materials: This includes, but is not limited to, labels, cartons, and blister film.[26]
- A glass vial shortage: This affects the packaging and distribution of both non-COVID-19 and potential COVID-19 vaccines.[27]
- Higher costs: "'COVID inflation' [means] every aspect of running a pharmaceutical business has increased at least six to 12 percent."[28]

FUTURE IMPLICATIONS

The COVID-19 pandemic has forced both drug manufacturers and logistics companies to reexamine how they conduct their businesses. But is this the first step toward longer-term change or will processes revert to how they were pre-COVID-19? The industry participants and observers reviewed here believe that longer-term change is likely.

Regarding drug manufacturing, the common beliefs are that there must be greater geographic diversity of sources and there must be additional options for supplies or manufacturing:

- Heather Sugrue, senior VP, sales and marketing of Recro Gainesville: "We, as an industry, often rely on just-in-time or on-demand delivery for many of our resources from all over the globe. Our focus needs to shift toward more of a stockpiling approach… For the near term, 12-18 months, industry should continue to build larger amounts of inventory of materials needed to support current commercial projects. Companies could also begin to vet second (or third) source CDMOs for manufacturing their drug substances and drug products in order to diversify their vendor bases and spread out the risk of running into shortages."[29]
- Anthony Lakavage, senior VP, global external affairs of U.S. Pharmacopeia: "Vulnerabilities can be addressed by increasing the geographic diversity of production around the world,including more, but not exclusively, domestic manufacturing, investing in advanced manufacturing, strengthening international regulatory cooperation, and creating additional transparency in the supply chain."[30]
- J.P. Duffy, partner of Reed Smith: "Over the long term, businesses across several markets are going to be looking at whether it makes sense to have lots of factories in any one market or if they should be attempting to diversify by building factories elsewhere."[31]
- Ferdi Steimann, global industry strategist, life sciences at OpenText: "COVID-19 has demonstrated just how real these supply chain risks are, and the need for pharma companies to, wherever possible, have multiple sources of supply spread across different geographies so they can quickly switch production from highly impacted to lesserimpacted territories… Some companies have already begun the process of complexifying their supply chains by recruiting two or three alternate suppliers."[32]

Regarding supply chain logistics, one of the common threads that ties forecasts together is the need to be agile in utilization of direct-to-patient offerings:

- Jason Mieding and Michelle Freidman, Fisher Clinical Services: "Preventing acts of nature, people, or politics from unravelling the supply chain requires contingency planning … Effective contingency planning involves a thoughtful three-step process of [identifying, assessing , and responding to] risk."[33]
- Jim Kilpatrick, global supply chain & network operations leader of Deloitte: "New supply chain technologies are emerging that can dramatically improve visibility across the end-to-end supply chain and support much more supply chain agility and resiliency, without traditional 'overhead' associated with risk management techniques."[34]
- Ariette Van Strien, president of Marken: "After Amazon took one or two days to deliver goods to homes, we strongly believed this would happen with clinical trials. One of the first things we did was to develop a direct-to-patient service. We worked in many countries, if they would allow us, to deliver the drug product to patients at home. Once COVID-19 started to hit us, we went from 57 to 80 countries and are looking to further expand to other countries."[35]
- Andrew Thress, project group manager for supply chain management at Almac: "Moving into the future of clinical supply, we expect to see patient centricity continue as the prevailing factor of what makes a clinical trial solution successful. Since the start of the pandemic, Almac has seen a rise in decentralized trials and direct-to-patient solutions, both of which have provided sponsors the ability to be agile and maintain continuity during uncertain times."[36]
- Amy Malkani, Clinical Trials Arena: "COVID-19 has completely reshaped the clinical supply chain. Firstly, the crisis has propelled direct-to-patient (DtP) drug distribution as a leader in clinical trial logistics. DtP was already emerging as progressive strategy for delivering drugs to patients directly to create patient-centric trials with fewer site visits and less burden on the participant; yet for pharmaceutical companies now facing the perplexing challenge of distributing clinical products to home-based patients who cannot access the clinical site, offering a DtP service may be the only solution to keep their study going."[37]

SUMMARY

The drug supply chain is and has been in a constant state of change. But COVID-19 has resulted in some rethinking, which can, in turn, result in greater longer-term change.

- **Market Overview** – The drug supply chain logistics market is growing and will continue to grow. More drugs are being developed, more drug manufacturing processes are being employed, and more patients are receiving drugs directly.

- **Growing Globalization + Complexity = Periodic Drug Shortages** – The increase in the number and greater variety of drugs means more raw materials and consumables are needed to make the drugs. This, along with cost considerations, has led to a gradual move away from drug manufacturing in the United States and toward manufacturing in China and India. Furthermore, processes such as continuous manufacturing and requirements such as serialization are causing drug manufacturing to become more efficient, yet more complex. Both the increased variability of sourcing and the increased complexity have contributed to some drug shortages.

- **The Impact of COVID-19** – Weaknesses in the drug supply chain that led to some drug shortages have become more pronounced because of COVID-19. This has resulted in more drug shortages and greater innovation in finding ways to both manufacture drugs and to get them in patients' hands.

- **The Future of Drug Supply Chain Logistics** – While the impact of COVID-19 will at some point recede, the effects of how it accelerated change in the drug supply chain are likely to remain long after. Post-COVID-19, we are likely to see a reemphasis on increasing drug manufacturing capacity in the United States while reducing its concentration in China and India. We are also likely to see greater agility in supply chain logistics featuring increased focus on direct-to-patient (DtP) solutions.

REFERENCES

[1] "Pharmaceutical Logistics Market Size, Share & Trends Analysis Report by Type, by Component, by Region, and Segment Forecasts, 2020-2027," Grand View Research, May 2020, https://www.grandviewresearch.com/industry-analysis/pharmaceutical-logistics-market

[2] "Trends in FDA Drug Approvals Over Last 2 Decades: An Observational Study," Journal of Family Medicine and Primary Care, January 9, 2020, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7014862/

[3] "Drug Supply Chains and US-Based Manufacturing," DCAT Value Chain Insights, March 18, 2020, https://www.dcatvci.org/6400-drug-supply-chains-and-us-based-manufacturing

[4] "COVID-19 Is Reshaping the Pharmaceutical Supply Chain," Chemical & Engineering News, April 27, 2020, https://cen.acs.org/business/outsourcing/COVID-19-reshaping-pharmaceutical-supply/98/i16

[5] "Raw Material Supply: Many Issues to Manage," Pharma's Almanac, December 4, 2016, https://www.pharmasalmanac.com/articles/new-post-raw-material-supply-many-issues-to-manage

[6] "Study Analyzes Contamination in Drug Manufacturing Plants," MIT News, April 27, 2020, https://news.mit.edu/2020/contamination-drug-manufacturing-plants-0427

[7] Correspondence with Ed Gump, vice president of small molecules at U.S. Pharmacopeia, September 29, 2020.

[8] "The Real Threat to Biopharma Supply Chains: Bioprocessing Materials," Bioprocess Online, May 12, 2020, https://www.bioprocessonline.com/doc/the-real-threat-to-biologics-supply-chains-bioprocessing-materials-0001

[9] "HPAPI Drug Manufacturing Trends," Contract Pharma, May 5, 2020, https://www.contractpharma.com/issues/2020-05-01/view_features/hpapi-drug-manufacturing-trends/53332

[10] "Drug Supply Chains and US-Based Manufacturing," DCAT Value Chain Insights, March 18, 2020, https://www.dcatvci.org/6400-drug-supply-chains-and-us-based-manufacturing

[11] "Pharmaceutical Serialization: What Do Industry Leaders Think?," Pharmaceutical Processing World, September 14, 2017, https://www.pharmaceuticalprocessingworld.com/pharmaceutical-serialization-what-do-industry-leaders-think/

[12] "Serialization: What It Means for Pharmaceutical Manufacturing," WellSpring blog, December 28, 2016, https://www.aniglobalsource.com/blog/serialization-what-it-means-for-pharmaceutical-manufacturing#:~:text=Serialization%20is%20the%20assigning%20of,batch%20number%20and%20expiration%20date.

[13] "Timeline for the Drug Supply Chain Security Act," Pew, April 30, 2014, https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2014/timeline-for-the-drug-supply-chain-and-security-act

[14] "What Is Blockchain?," Euromoney Learning, undated, https://www.euromoney.com/learning/blockchain-explained/what-is-blockchain

[15] "Why Big Pharma Is Betting on Blockchain," Harvard Business Review, May 29, 2020, https://hbr.org/2020/05/why-big-pharma-is-betting-on-blockchain

[16] "How the FDA Is Piloting Blockchain for the Pharmaceutical Supply Chain," IBM Blockchain Blog, May 4, 2020, https://www.ibm.com/blogs/blockchain/2020/05/how-the-fda-is-piloting-blockchain-for-the-pharmaceutical-supply-chain/

[17] "Top Challenges Facing Drug Supply Chains," BioPharma Dive, April 23, 2018, https://www.biopharmadive.com/news/top-challenges-facing-drug-supply-chains/521876/

[18] "Senator Blackburn?: Shoring Up Our Healthcare System Via Supply-Chain Security (SAM-C Act)," Forbes, March 21, 2020, https://www.forbes.com/sites/steveforbes/2020/03/21/shoring-up-our-healthcare-system-via-supply-chain-security-sam-c-act/#1664caad4025

[19] "To Help the US Economy Bounce Back From the Pandemic, We Need to Make Sure Businesses Aren't Buried by Red Tape," Business Insider, May 7, 2020, https://www.businessinsider.com/blackburn-deregulation-helps-us-business-economy-coronavirus-pandemic-recovery-2020-5

[20] "Report on Drug Shortages for Calendar Year 2019," U.S. FDA, April 23, 2020, https://www.fda.gov/media/139613/download

[21] "Experts Say COVID-19 Will Likely Lead to US Drug Shortages," CIDRAP, March 27, 2020, https://www.cidrap.umn.edu/news-perspective/2020/03/experts-say-covid-19-will-likely-lead-us-drug-shortages

[22] "Drug Shortages and CDMOs: A Conversation With Recro Gainesville's Heather Sugrue," SCORR OnPoint Blog, June 30, 2020, https://www.scorrmarketing.com/onpoint/drug-shortages-and-cdmos-a-conversation-with-recro-gainesvilles-heather-sugrue/

[23] "FDA Data Shows Numerous Drugs in Shortage, Including a Leading Antidepressant," USA Today, June 12, 2020, https://www.usatoday.com/story/news/2020/06/10/coronavirus-and-fda-drug-shortage-list/5330491002/

[24] "FDA Drug Shortages," U.S. FDA, undated, https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm

[25] "COVID-19 Update: Coronavirus and the Pharmaceutical Supply Chain," European Pharmaceutical Review, April 1, 2020, https://www.europeanpharmaceuticalreview.com/article/116145/covid-19-update-coronavirus-and-the-pharmaceutical-supply-chain/

[26] "Shortage of Packing Materials Hits Drug Industry," Pharmabiz, April 13, 2020, http://www.pharmabiz.com/NewsDetails.aspx?aid=122395&sid=1

[27] "Strained Supply Chain for Glass Vials Could Delay Coronavirus Update," ABC News, June 21, 2020,https://abcnews.go.com/Health/strained-supply-chain-glass-vials-delay-coronavirus-vaccine/story?id=71349287

[28] "Responding to COVID-19 in Pharmaceutical Supply Chains," Pharma Logistics IQ, July 2, 2020, https://www.pharmalogisticsiq.com/clinical-supply/whitepapers/responding-covid-19-pharmaceutical-supply-chains?ty-ur

[29] "Drug Shortages and CDMOs: A Conversation With Recro Gainesville's Heather Sugrue," SCORR OnPoint blog, June 30, 2020, https://www.scorrmarketing.com/onpoint/drug-shortages-and-cdmos-a-conversation-with-recro-gainesvilles-heather-sugrue/

[30] "COVID-19 Has Exposed Cracks in the Global Medicines Supply Chain. We Need to Fix Them," STAT News, June 2, 2020, https://www.statnews.com/2020/06/02/covid-19-exposed-cracks-global-medicines-supply-chain/

[31] "COVID-19 Update: Coronavirus and the Pharmaceutical Supply Chain," European Pharmaceutical Review, April 1, 2020, https://www.europeanpharmaceuticalreview.com/article/116145/covid-19-update-coronavirus-and-the-pharmaceutical-supply-chain/

[32] "4 Lessons for the Pharma Supply Chain After COVID-19," OpenText IoT & Supply Chain blog, May 29, 2020, https://blogs.opentext.com/4-lessons-for-the-pharma-supply-chain-after-covid-19/

[33] "Is Your Supply Chain Bulletproof?," Fisher Clinical Services, July 16, 2020, https://www.fisherclinicalservices.com/en/learning-center/insights-blog-overview/is-your-supply-chain-bulletproof-.html

[34] "COVID-19: Managing Supply Chain Risk and Disruption," Deloitte, undated, https://www2.deloitte.com/global/en/pages/risk/articles/covid-19-managing-supply-chain-risk-and-disruption.html

[35] BeTheComeback testimonial from Ariette Van Strien, president of Marken, June 17, 2020.

[36] "Almac: How to Build a Solid Clinical Trial Supply Chain," Outsourcing-Pharma, July 22, 2020, https://www.outsourcing-pharma.com/Article/2020/07/22/Almac-offers-clinical-trial-supply-chain-advice

[37] "The Impact of COVID-19 on the Global Clinical Supply Chain," Clinical Trials Arena, July 2, 2020, https://www.clinicaltrialsarena.com/analysis/covid-19-clinical-supply-chain/

About SCORR Marketing

SCORR Marketing is the leading full-service marketing and communications firm in the health science industry. We are a global partner for organizations around the world involved in research, development, and commercialization of biopharmaceutical and device products and the delivery of health care products and services. At SCORR, we provide integrated programs that help our clients achieve their goals and improve health and well-being worldwide. For more information, visit www.scorrmarketing.com.