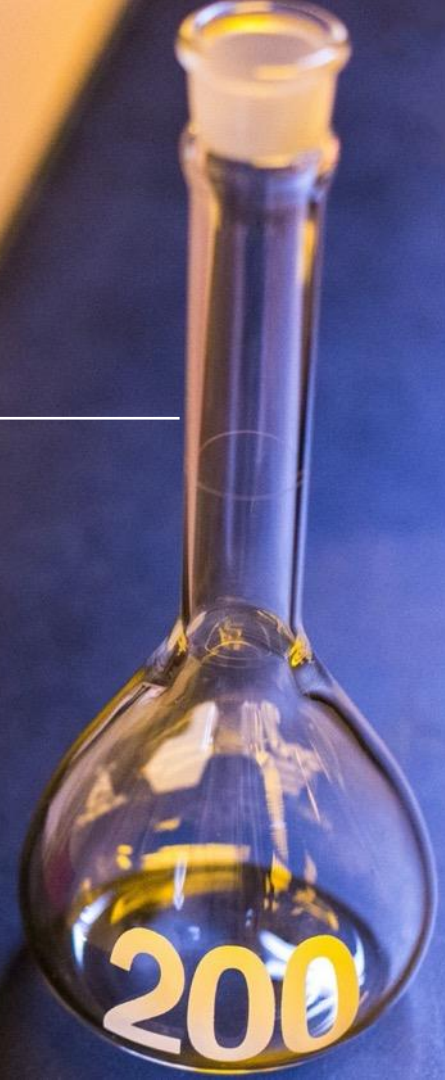


Increasing Transparency In The Medicines Supply Chain

Anthony Tann

General Manager and Senior Director, USP APAC



- **Who is USP?**
- **Global pharmaceutical supply chain**
 1. **Overview of the supply chain**
 2. **Vulnerabilities**
 3. **Key actions : Supply chain transparency**



Who is USP?

Need for medicine quality standards

- **11 Founding members with a vision**
- **Legal recognition**
- **Official compendium**



To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.”



USP standards are utilized in over **150** countries



Documentary standards

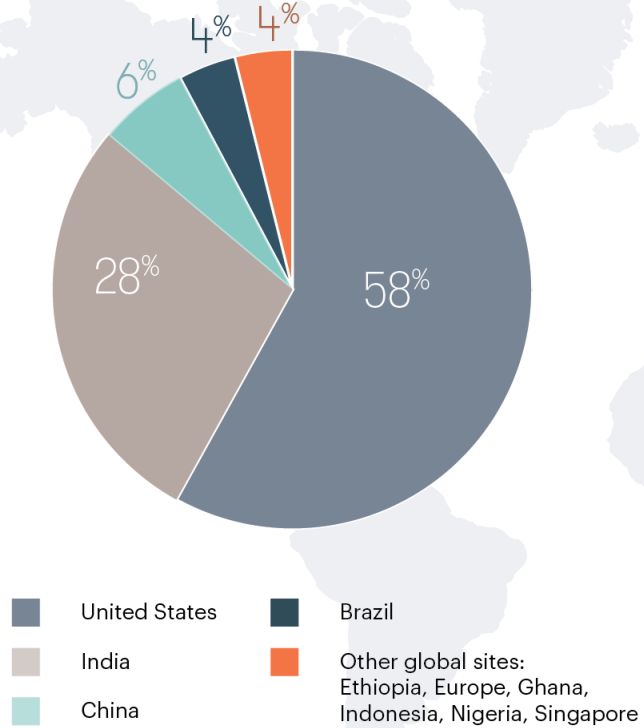
Provides information and methods needed to assess quality

Reference standards

A benchmark against which to compare tested material

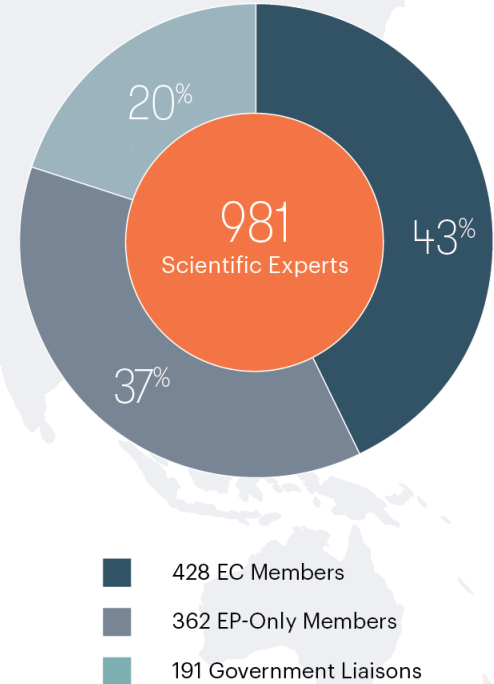
Our people – USP’s global staff and volunteers

1200+ Staff



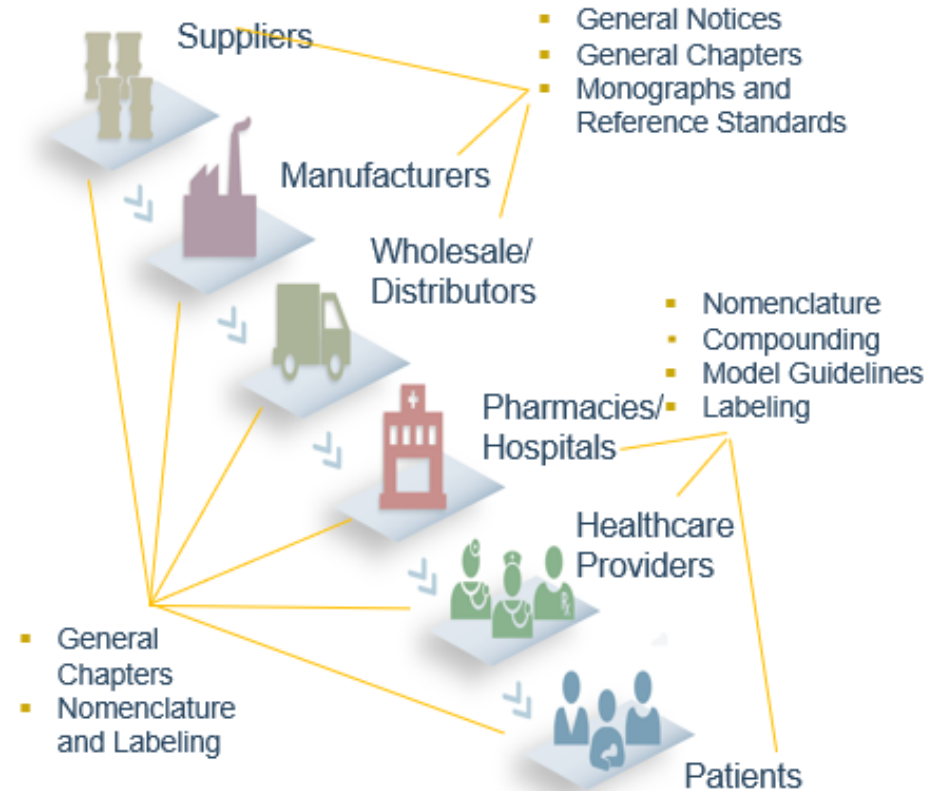
981 Scientific Experts –

Volunteers and Government Liaisons



More than 9,000 USP Standards provide quality benchmarks across the supply chain

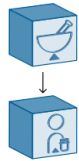
- ▶ **Standards for medicines, excipients, and APIs in *USP-NF***
 - 350 General Chapters
 - 4,900 product-specific monographs
 - 3,500 physical reference standards
- ▶ **More than 1,200 standards for dietary supplements in the *Dietary Supplements Compendium (DSC)***
- ▶ **Nearly 1300 standards for Food Ingredients in *Food Chemicals Codex (FCC)***
- ▶ **More than 500 standards for biologics**
- ▶ **About 300 Healthcare Quality & Safety Standards, including compounding, nomenclature and labeling, safety, etc.**



1

Overview of the supply chain

Increasing complexity of supply chain of medical products



1820s-1860s

Botanicals and herbal medicines

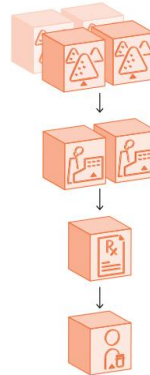
Local apothecaries with knowledge of botanicals, prepare remedies for patients.



1870s-1950s

Rise of manufacturing

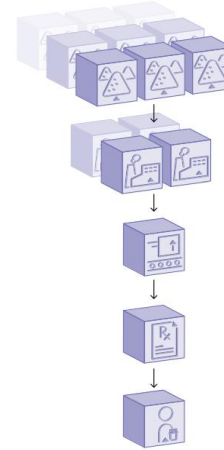
Analytical chemistry and pharmacology along with advances in automation give rise to large-scale manufacturing.



1960s-1970s

Global expansion

Pharmaceutical companies continue expanding manufacturing plants to other countries to increase their markets and reduce operating costs. As a result medicines are produced and packaged at a greater distance.



1980s-2020s

Growth, distribution, consolidation

Rise of generics in the early 80s extends the supply chain as more companies manufacture medicines outside the U.S. Today, many intermediaries play a role in medicine's production, distribution, and delivery.

Participants in the modern pharmaceutical supply chain

Raw Material Suppliers

- Pharmaceuticals typically contain active ingredients (API) and excipient(s)
- Production of starting material, reagents, catalysts, and solvents to make API/excipients is usually outsourced
- Packaging, labeling and containers are often procured from different suppliers

Pharmaceutical Manufacturers

- Contract manufacturing orgs (CMOs) are often turned for their specific expertise
- Relabelers and repackagers are often involved

Wholesalers or Distributors

- There may be several intermediaries and procurement channels (publicly-funded, privately-funded, donor-funded)
- Buying groups or warehouses

Providers

- This could include hospitals, online, mail order, community or retail pharmacies, etc.
- Physician or veterinary offices can also administer or supply medicine

Patients

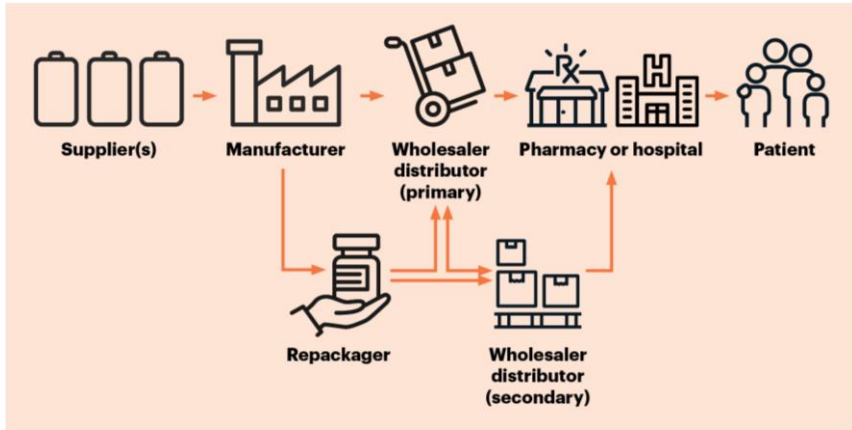
- Ultimately, patients trust that a medicine is of high quality because they cannot perform tests to ensure quality themselves

Upstream

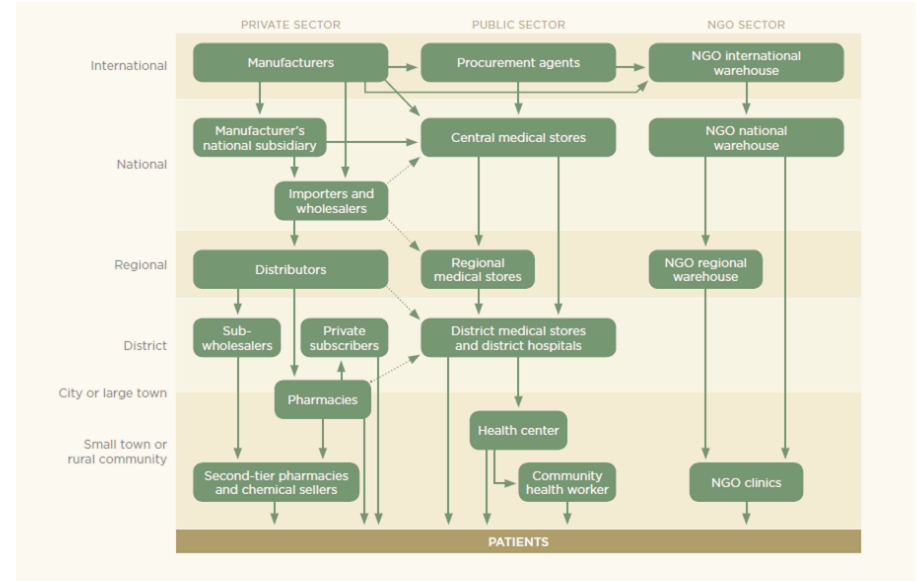
Downstream

The downstream supply chain differs by country and can involve many intermediaries

Country A



Country B

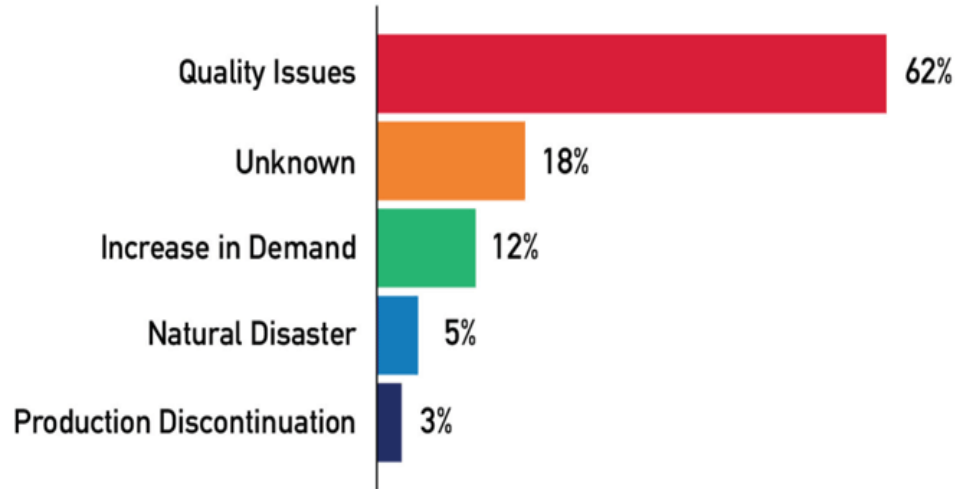


Sources: ¹Institute of Medicine (IoM) (Feb. 2013); ²Onyango (Mar. 2019); Munson et al. (Sep. 2013)

2 Vulnerabilities

Drug shortages overwhelmingly have quality issues as root cause

Percentage of Drugs Newly in Shortage by Reason, Calendar Years 2013-2017



Most drugs in shortage were experiencing supply disruptions, specifically quality issues.

Sources: FDA. "Drug Shortages: Root Causes and Potential Solutions." Oct. 2019

The European Association of Hospital Pharmacists (EAHP) reported that 43.7% of shortages were related to quality issues.

Source: FIP. "Report of the International Summit on Medicines Shortage June 2013

Vulnerabilities are driven by greater complexity of the upstream supply chain...leading to drug shortages

Root causes

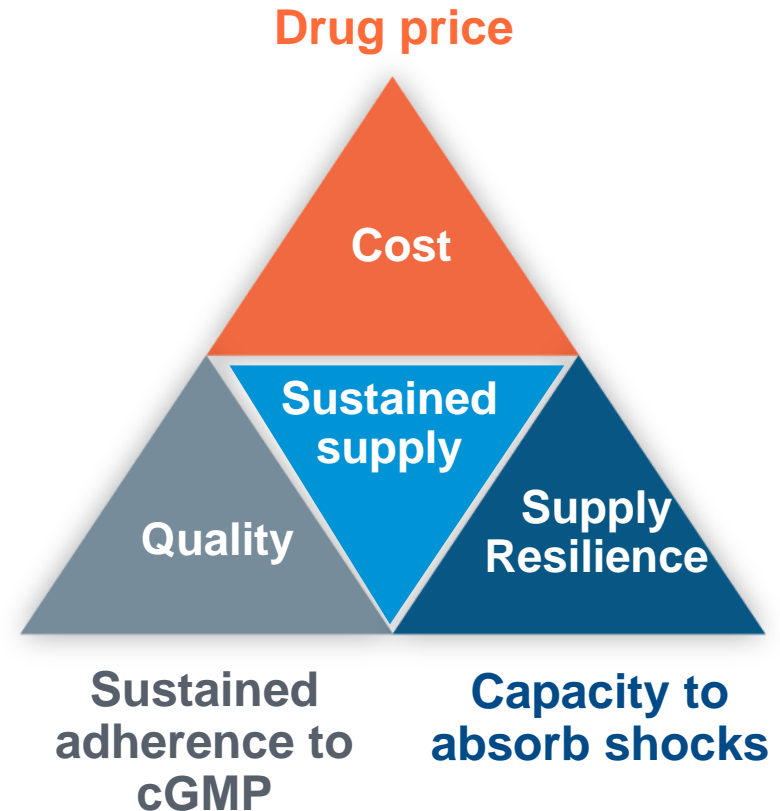
- ▶ Increased pressure on margins, particularly for generics
- ▶ Insufficient incentives for quality
- ▶ Regulatory and logistical hurdles that prevent agile responsiveness to market events

Leading to....

- ▶ “Just-in-time” manufacturing with little redundancy to absorb demand or supply shocks
- ▶ Increased outsourcing of ingredients and even final product manufacturing
- ▶ Lack of transparency limiting the ability of stakeholders to take mitigative action before its too late

A sustained supply of quality medicines relies on stakeholders balancing cost, quality and supply chain resilience

- ▶ Tension arises because the only reliable information often available is cost
- ▶ Supply resilience and quality can also require a tradeoff because investing in supply resilience through multiple suppliers may introduce variability, which increases quality risk
- ▶ Increasing transparency on quality and supply resilience can rebalance negotiations to mitigate supply disruptions



USP has identified key actions to secure a more resilient supply chain

- ▶ Foster more, not less, supply chain diversity
- ▶ Invest in more manufacturing capacity for critical medicines
- ▶ **Enable more transparency and data sharing**
- ▶ Conduct crisis contingency planning and action
- ▶ Strengthen regulatory systems and quality assurance globally

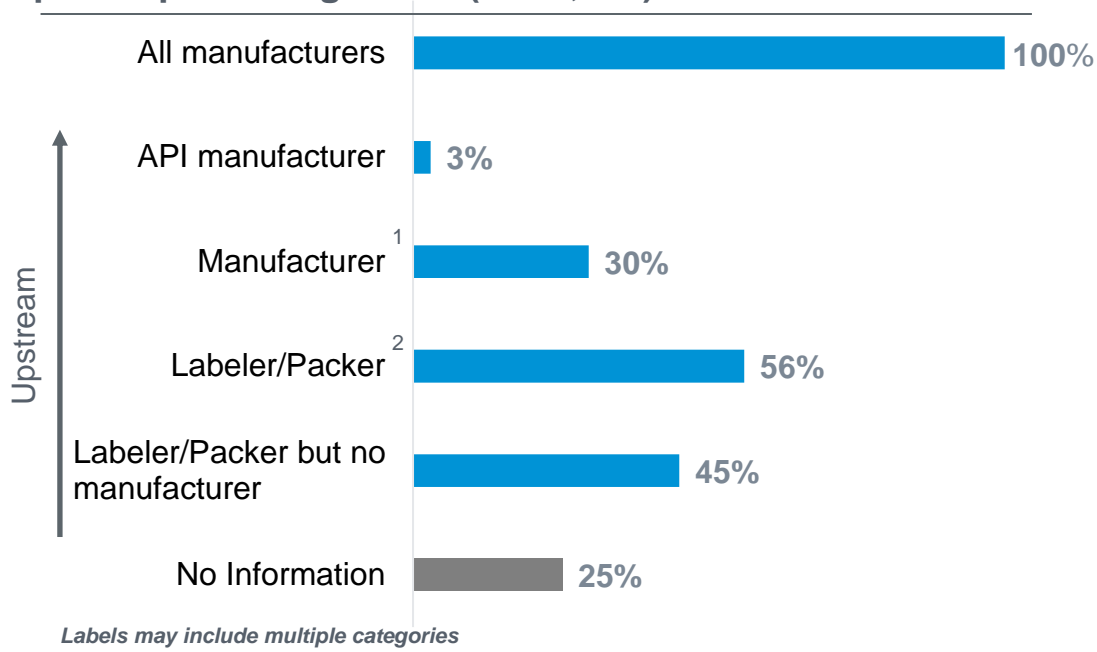


3 **Key actions:** _____

Supply chain transparency

Need for greater upstream supply chain transparency

Information listed on US approved human prescription drug labels (N=40,178)



- ▶ All labels specify ANDA filer, an entity responsible for the drug's quality. However, manufacturing is often done by a different entity than the filer
- ▶ While manufacturers are required and do report suppliers to US FDA, also sharing supply chain information publicly could help providers proactively safeguard patient health. (e.g., when a safety issue is identified with an API manufacturer, providers will have on-hand information about impacted brands)

Source: USP analysis of DailyMed

¹ Includes 'Analysis', 'FDF Manufacturer', 'Manufacturer', 'Particle size reduction', 'Positron Emission Tomography Drug Production', 'Recovery', 'Sterilize', 'Transfill'

² 'Label, Relabel, Pack, Repack'

U.S. case example: dexamethasone

Context:

- Widely available generic
- As a steroid, has many substitutes
- WHO Working Group meta-analysis of 7 randomized trials with 1703 patients showed 28-day all-cause mortality was lower among patients who received corticosteroids

What is known about its supply chain

- 24 approved manufacturers
- 9 registered API manufacturers
- FDA is informed of all qualified suppliers during drug registration, although this information is not public

What is NOT known about its supply chain

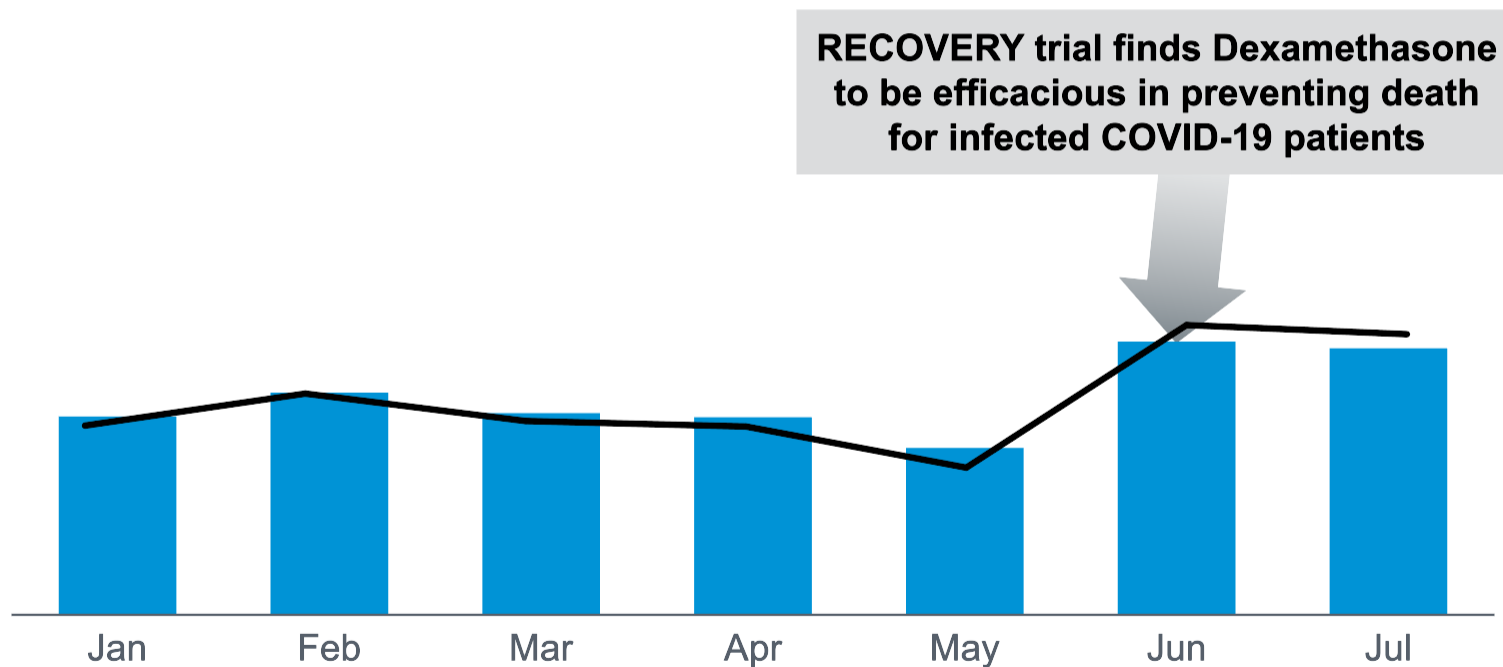
- While approval information is known, we don't know how many are manufacturing the medicine/API
- How much volume is each manufacturer responsible for? *Available via proprietary sources*
- What API supplier does each FD manufacturer use at any point in time? *If most are using the same source, then the supply chain has a vulnerable node!*
- What is global capacity for production?

Driving supply chain transparency through the **USP Pharmaceutical Supply Chain Center**

- ▶ Helps stakeholders to identify, characterize, and quantify risk in the upstream pharmaceutical supply chain so that stakeholders can proactively help protect patient access to quality medicines
- ▶ New asset: Medicine Supply Map
 - Data model that links across 10+ datasets and dozens of data elements, including USP's proprietary reference standards demand data
 - “In-the-field” data gathering, including through USP's subject matter expert network



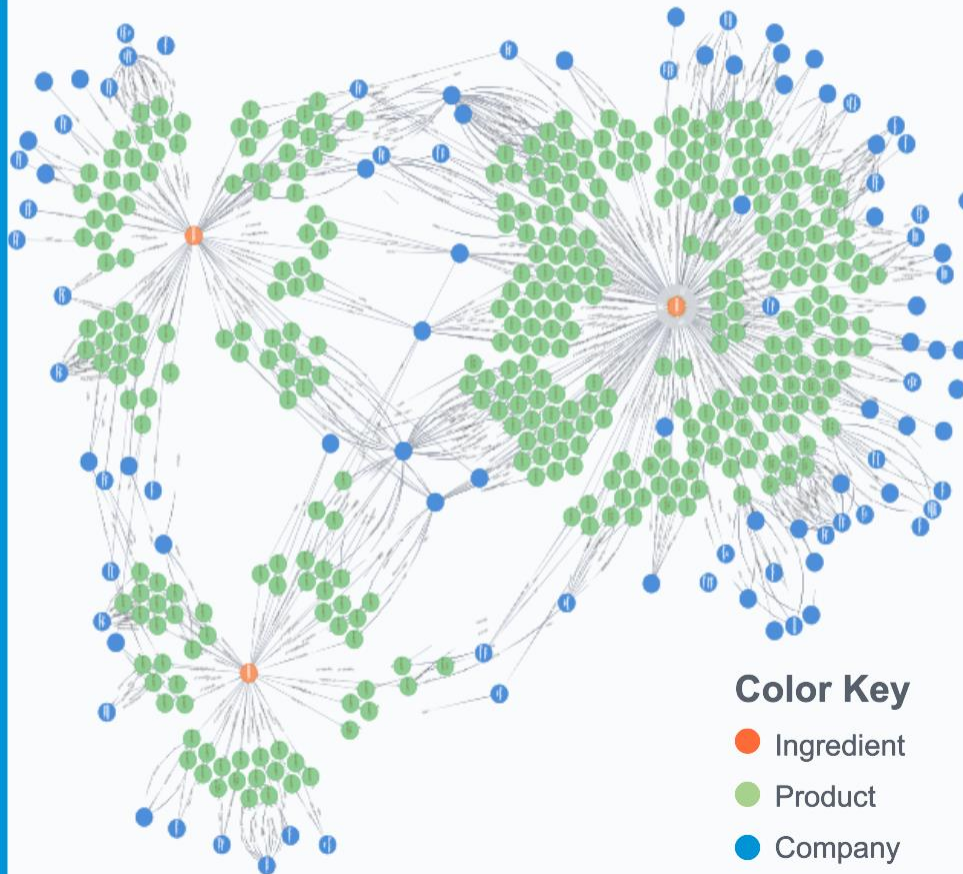
Monthly unit demand for the Dexamethasone USP Standard (Jan-Jun 2020)



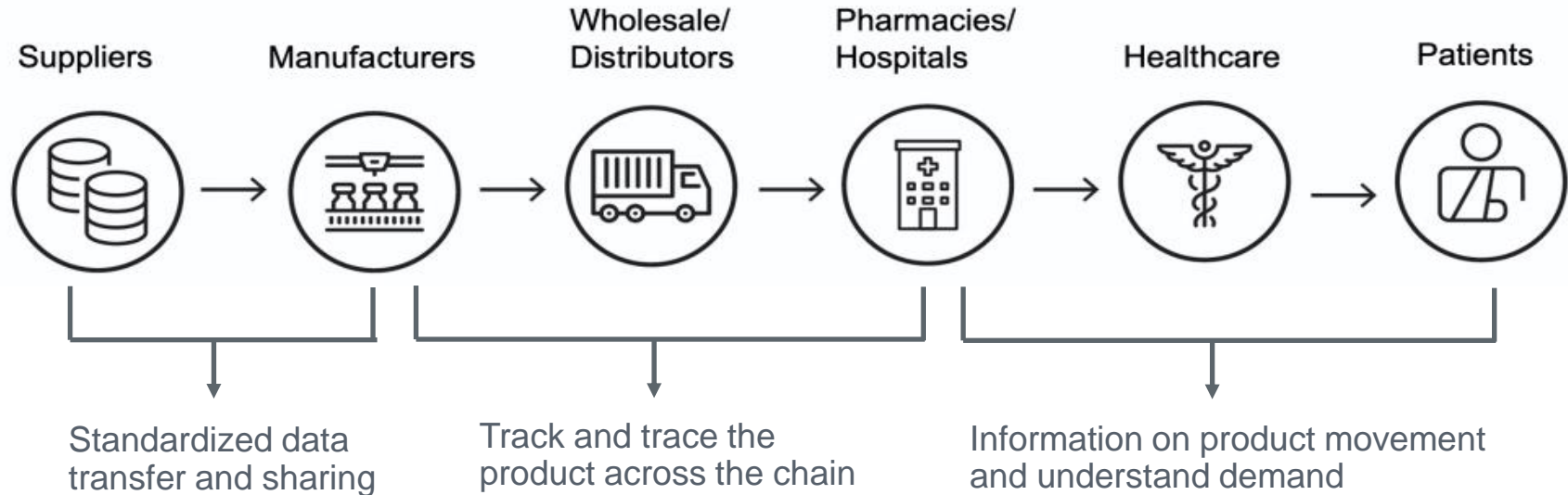
Graph-based data model enables tracing of quality

Example illustrates the case of Bumetanide, Furosemide and Chlorthalidone

Graph-based data model can identify manufacturers that make some or all products, and discern spillover implications – e.g., company A gets warning letter for one drug, what are potential implications on quality for other products made by company A, and what are some alternate supplier options for the basket of products?



Increased transparency is meaningful only if data is standardized and shared



Upstream

Downstream

Increased transparency is meaningful only if data is standardized and shared

Transparency across the supply chain

Manufacturers should track and share information about:

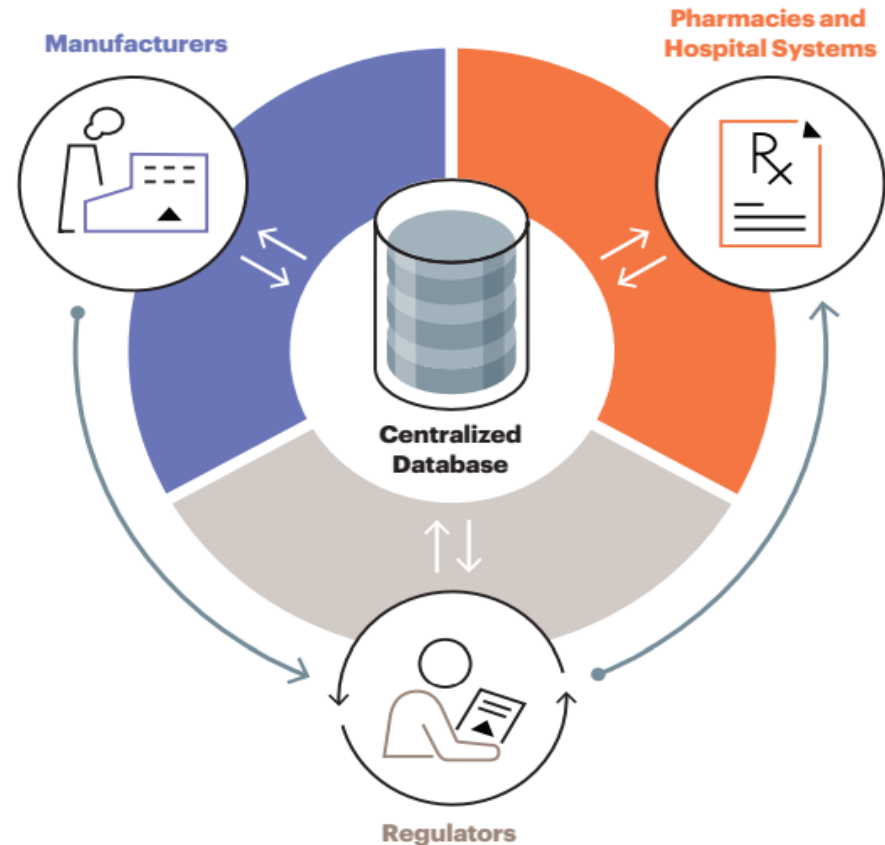
- ▶ Types of medical products and at what volume they are produced
- ▶ Sources of raw ingredients and other essential materials (such as for packaging)
- ▶ Information about distributors and distribution channels

Regulators should:

- ▶ Have access to insights about manufacturers' sites, products, volume, and capacity
- ▶ Be able to share with other regulatory authorities

Pharmacies and hospital systems should track and share information about:

- ▶ Prescription data from electronic health records (EHRs)
- ▶ Granular details about the medications dispensed and drug shortages encountered





4 Further reading

Further reading on supply chain policies



USP Global Public Policy Position

Key Elements to Building a More Resilient Supply Chain



Increasing transparency in the medicines supply chain

Harnessing information to inform effective action
to reduce vulnerabilities and prevent or mitigate
disruptions in the global supply of quality medicines

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