Drug Availability: Considerations for the Hospital Pharmacist

Andrew Mica, MBA[1] and Larry Green, PharmD[2]

[1]Global Supply Chain and [2]Global Scientific Affairs, Amgen Inc., Thousand Oaks, CA, USA

INTRODUCTION

- Drug shortages are a growing global concern.[1-5] In the US, drug shortages are routinely tracked.[6,7] European countries, including Germany, Hungary, and UK have reported shortages;[1] however, data on drug shortages across Europe are not available.
- Faced with shortages, hospital pharmacists need to find alternative drug suppliers.[3] Additionally, healthcare providers (HCPs) may need to consider rationing drugs, delaying critical treatments, and utilizing less efficacious or more expensive medications.[2-5]
- Regulatory agencies are striving to develop processes to address drug shortages; these include inventory reporting and rapid market notifications.[5-7]
- Drug manufacturers including biotechnology (Biotech), large pharmaceutical (Pharma), and generic manufacturers face operational challenges, placing stable supply to patients at risk.
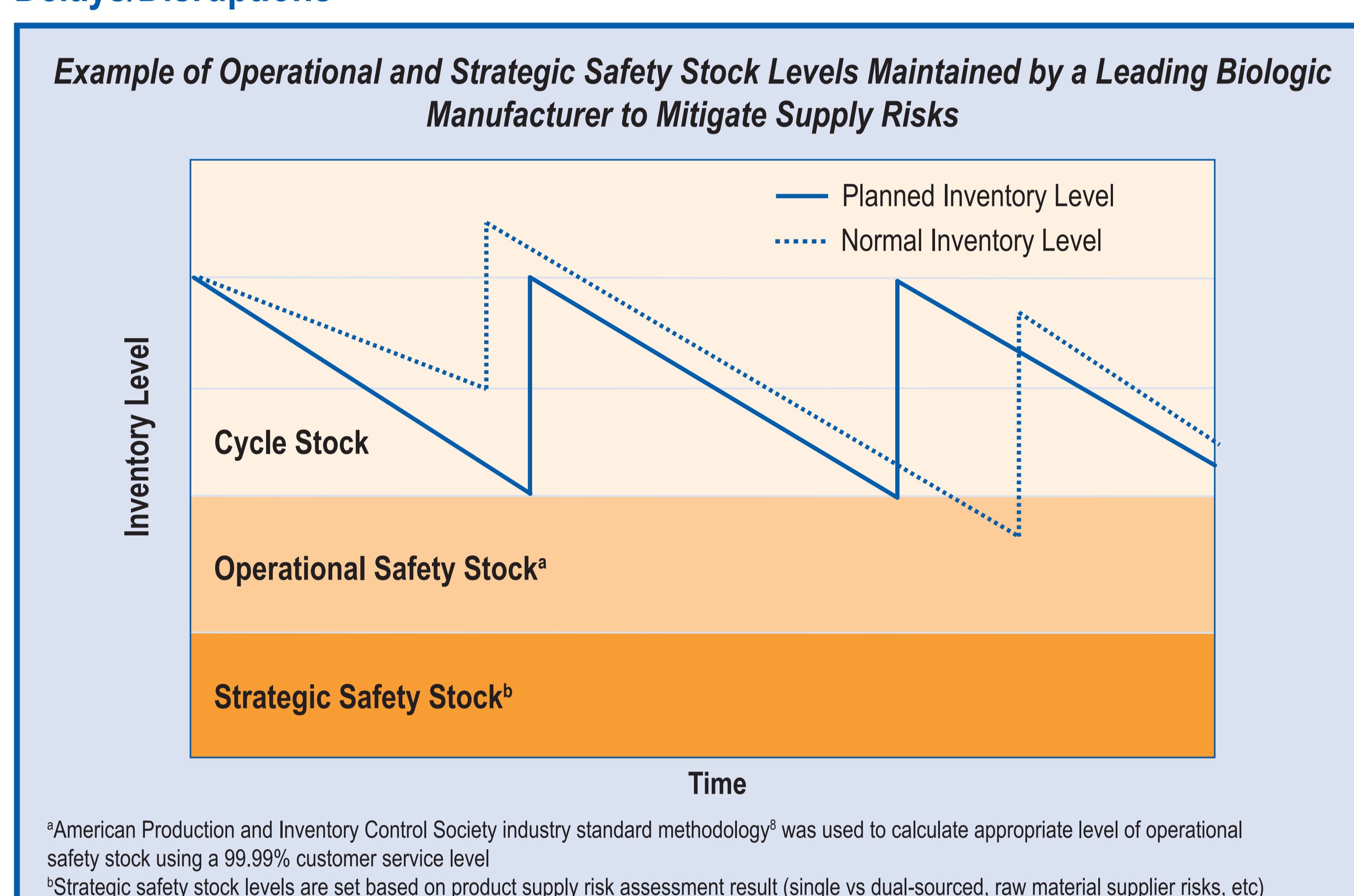
OBJECTIVE

- To highlight critical supply chain parameters that pharmacists should consider when evaluating a manufacturer's ability to maintain and deliver a continuous supply of medications
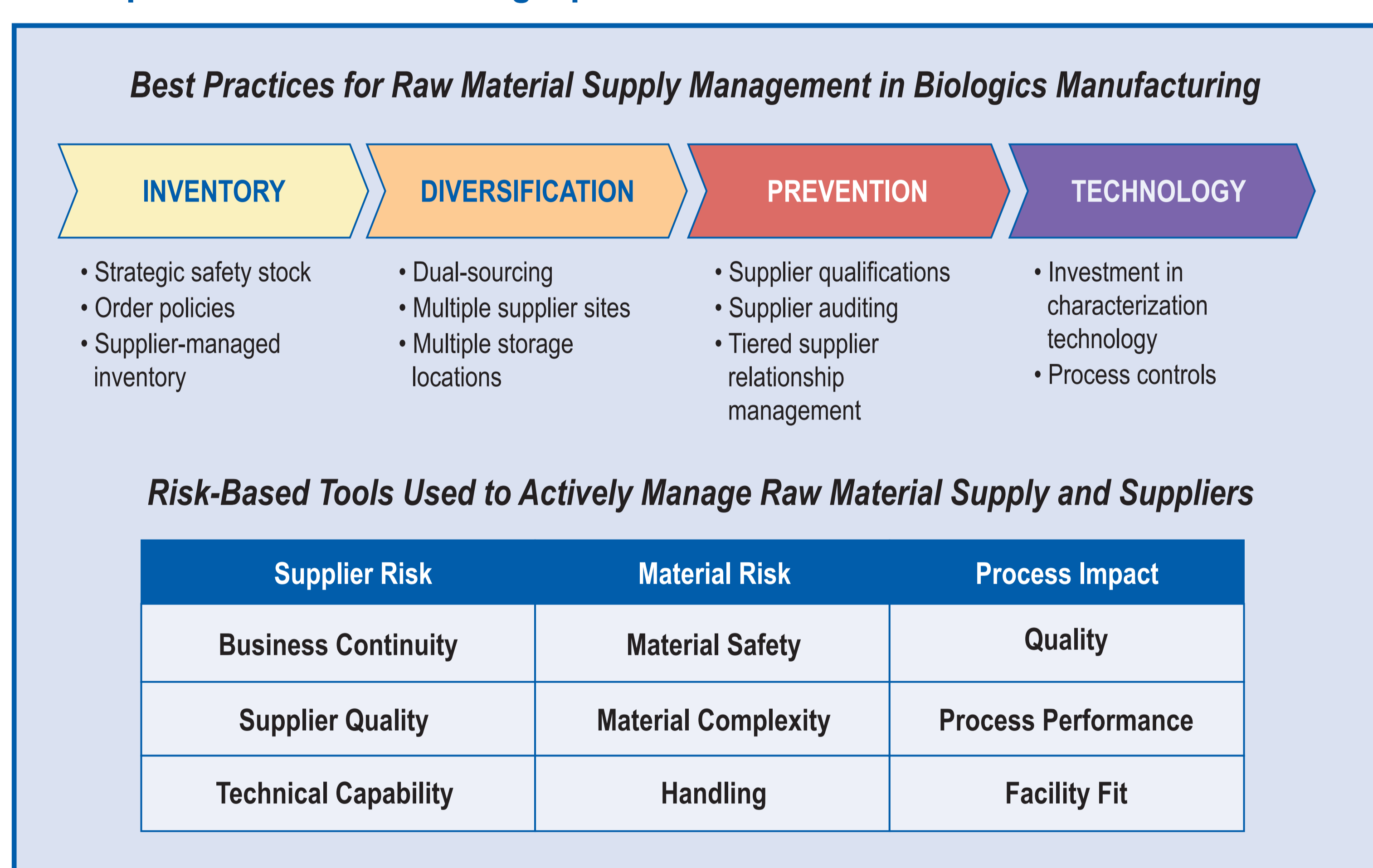
METHODS

- This assessment focused on key practices employed by biologic manufacturers to mitigate the risk of drug shortages.
- Parameters assessed include:
  - Number of drug shortages for seven selected major drug manufacturers as reported by the American Society of Health-System Pharmacists (ASHP)[7]
  - Inventory management: measured as inventory turnover (turn), which is the number of times inventory cycles or turns over in a year; this was calculated as cost of sales divided by total inventory
  - Raw material management
  - Manufacturing capabilities
  - Demand and supply management
  - Distribution network management
- Presented assessments were generated from publicly available data sources including ASHP, FDA and manufacturers' corporate websites and financial reporting statements (eg, 10-K filings).

RESULTS

Reported Drug Shortages and Inventory Turns for Major Drug Manufacturers

Drug Shortages (Jan 2011–Jan 2012)[7]

Inventory Turns (2006-2010)[b]

[a]Includes reported shortages of small molecule and biologic drugs as tracked by ASHP[7]
[b]Data source: Annual 10-K filings from 2006–2010 as reported on corporate websites
[c]Minimum, average, and maximum turns calculated as **Cost of Sales** divided by **Total Inventory**
Note: 1 inventory turn per year is equivalent to 12 months of average inventory on-hand cumulative across all stages of manufacturing

- Low inventory turn generally implies a large amount of stock on hand at any given time.
- Typically for non-pharmaceutical industries, a high inventory turn indicates greater sales efficiency and a low risk of loss through unsold inventory. For drug manufacturers however, a high inventory turn can increase the risk of drug shortage.

BEST PRACTICES BY LEADING BIOLOGICS MANUFACTURERS

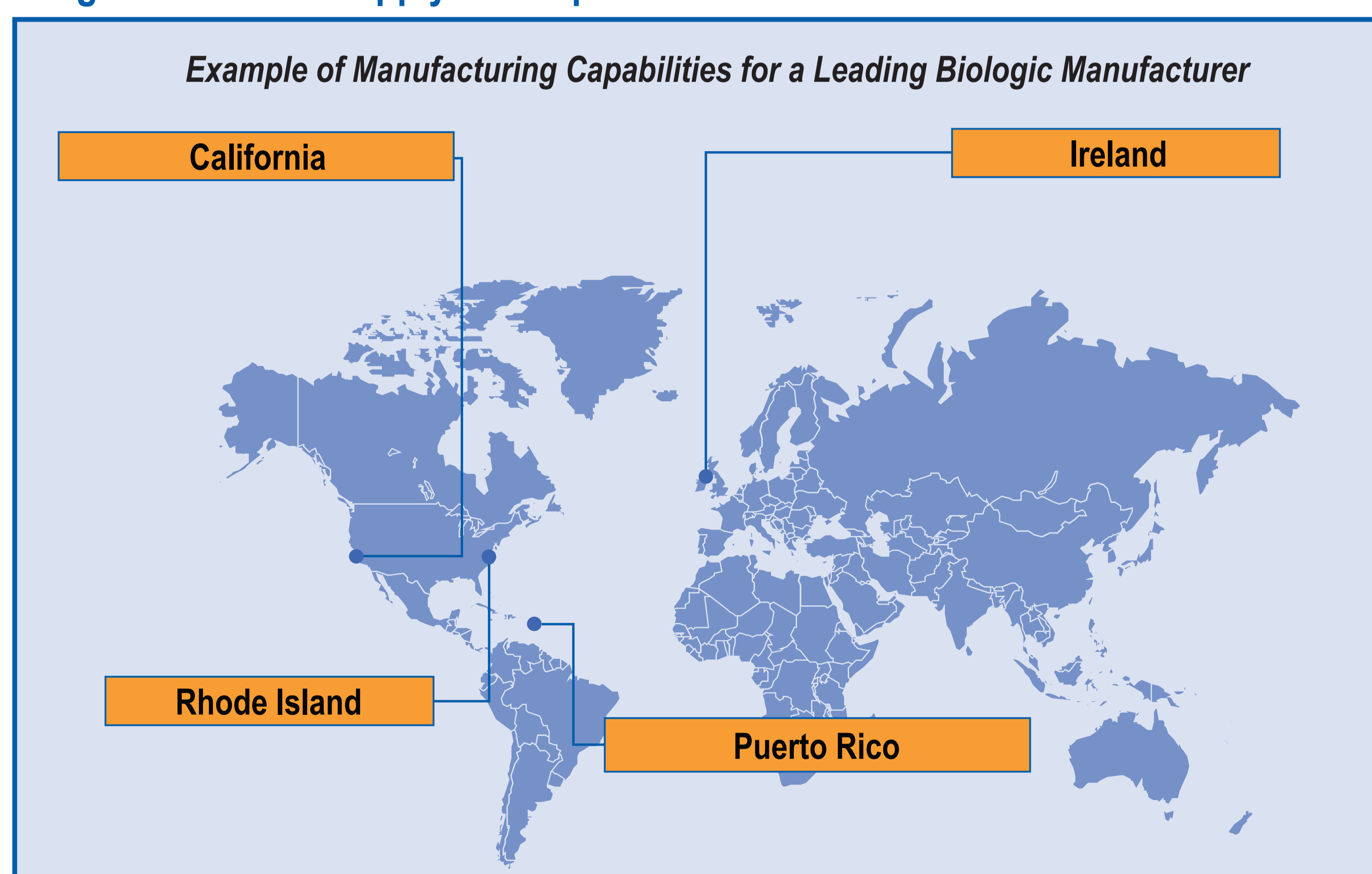## Maintenance of Strategic Safety Stocks Minimizes the Impact of Manufacturing Delays/Disruptions

Example of Operational and Strategic Safety Stock Levels Maintained by a Leading Biologic Manufacturer to Mitigate Supply Risks

[a]American Production and Inventory Control Society industry standard methodology[8] was used to calculate appropriate level of operational safety stock using a 99.99% customer service level
[b]Strategic safety stock levels are set based on product supply risk assessment result (single vs dual-sourced, raw material supplier risks, etc)

- Approaches to inventory management include:
  - Maintenance of cycle and operational safety stock to cover normal manufacturing cycle times and variability in demand and supply.
  - Maintenance of strategic safety stock to cover disruptions to supply; eg, caused by natural disasters. This represents additional investment to ensure continuous drug supply.

Active Management of Raw Material Supply Reduces the Likelihood of Interruptions to Manufacturing Operations

Best Practices for Raw Material Supply Management in Biologics Manufacturing

INVENTORY	DIVERSIFICATION	PREVENTION	TECHNOLOGY
• Strategic safety stock • Order policies • Supplier-managed inventory	• Dual-sourcing • Multiple supplier sites • Multiple storage locations	• Supplier qualifications • Supplier auditing • Tiered supplier relationship management	• Investment in characterization technology • Process controls

Risk-Based Tools Used to Actively Manage Raw Material Supply and Suppliers

Supplier Risk	Material Risk	Process Impact
Business Continuity	Material Safety	Quality
Supplier Quality	Material Complexity	Process Performance
Technical Capability	Handling	Facility Fit

- Ensuring continuous supply of high quality raw materials is critical to manufacturing operations.

Multi-Site Manufacturing Capabilities and Strategic Capacity Management Mitigate Extended Supply Interruptions

Example of Manufacturing Capabilities for a Leading Biologic Manufacturer

California   Ireland   Rhode Island   Puerto Rico

- Back-up manufacturing capabilities ensure continuous and reliable drug supply in the event of unexpected disruptions at the primary site; eg, caused by a natural disaster.

Systematic Demand and Supply Management Coupled With Supply Continuity Planning Allow for Rapid Response When Drug Supply May Be Limited

Integration of Demand and Supply Systems at the Enterprise Level Facilitate Monitoring and Response to Changing Supply Conditions

Procedural Supply Impact Assessments Ensure Information Flows Quickly, Facilitating Supply Stabilization Efforts

- Robust supply management programs may not mitigate all risks to uninterrupted drug supply. Seamless transmission of demand and supply information across global manufacturing and distribution networks is critical and can be achieved by:
  - Enterprise Resource Management systems that couple customer ordering information with upstream supply plans to ensure that production and shipping plans match customer needs
  - Manual procedural-based supply continuity plans, which facilitate the flow of information and supply prioritization in the event of a supply disruption; eg, caused by a natural disaster

Active Management of Robust and Secure Distribution Networks Ensures That Manufactured Products Reach Patients

Distribution Risk Management Programs Help Biologic Manufacturers Manage Extended Supply Chains

PREVENTION	TECHNOLOGY	INVESTIGATION	ENFORCEMENT
• Facility audits • Risk assessments • Training	• Security features • Diversion data analysis • Pallet tracking • Serialization	• Market surveillance • Internet monitoring • Test purchases	• Engage key trade boards • Terminate benefits to diverting practices

Manufacturers Use a Combination of Distribution Models to Serve Patients

MANUFACTURER — LOGISTIC SERVICE PROVIDERS — WHOLESALE DISTRIBUTORS — PHARMACIES + HOSPITALS — HCPs + PATIENTS

Pharmacy

Hospital

Manufacturers Implement Product Security Programs to Ensure Supply to Patients

1 Product Authentication   2 Warehouse Security   3 Cargo Security   4 Market Surveillance

- Forensic security technologies
- Security systems and procedures
- Cargo security at pallet, truck, and carrier level
- Counterfeit signal detection
- Product diversion monitoring

- Drug manufacturers rely on extensive and complex distribution networks to deliver drugs to patients. Delay, diversion, or theft increases the risk of supply shortages.
- Biologic manufacturers need to establish controlled temperature ("cold chain") distribution channels to maintain product quality.
- Biologic manufacturers use multiple approaches to mitigate distribution-related risks to supply, including:
  - Controlled shipping lanes using validated shipping containers to maintain chain of custody
  - Anti-theft and anti-counterfeiting measures to prevent or mitigate the risk of diversion and adulteration
  - Risk management programs to systematically address risks as they develop
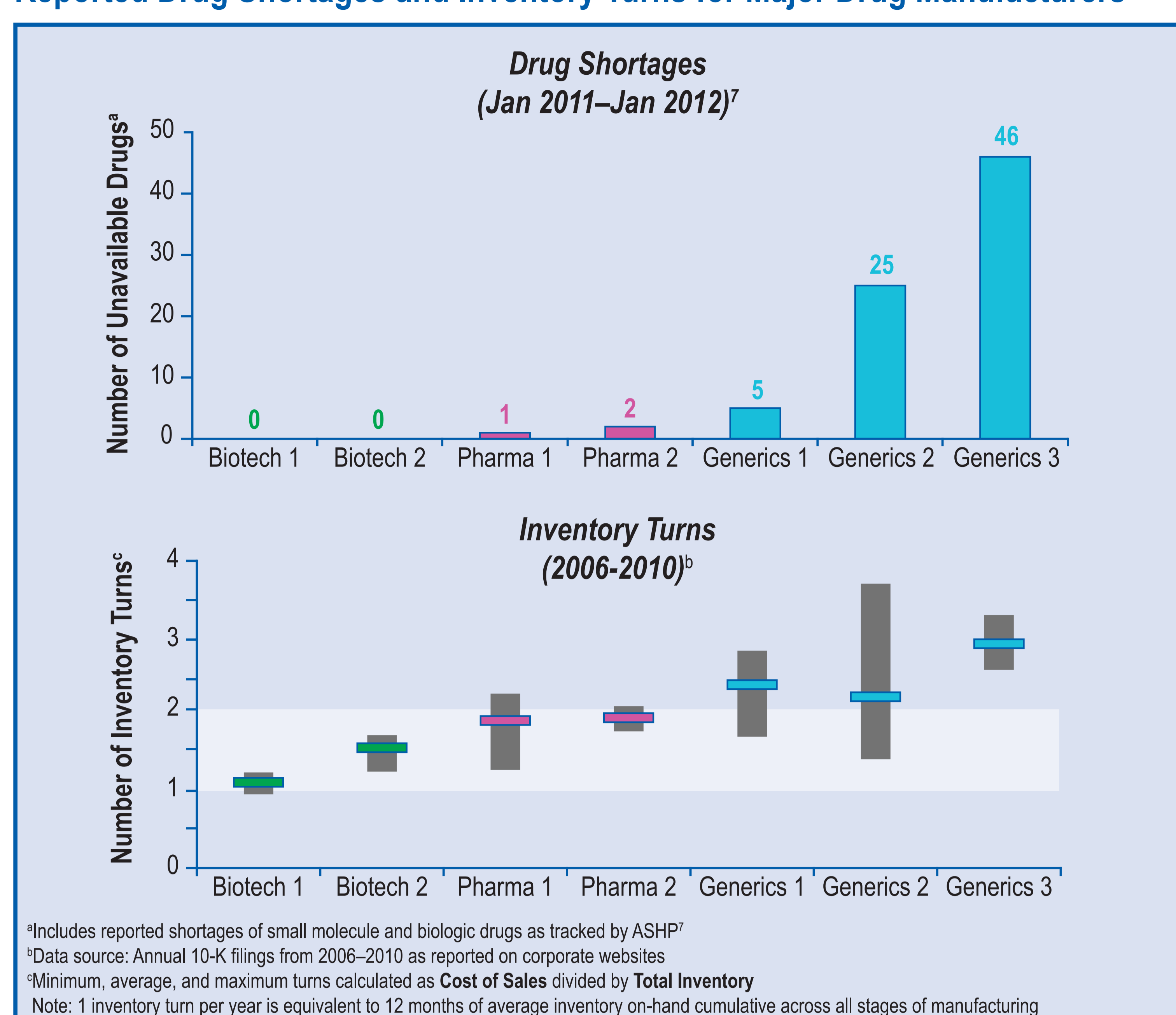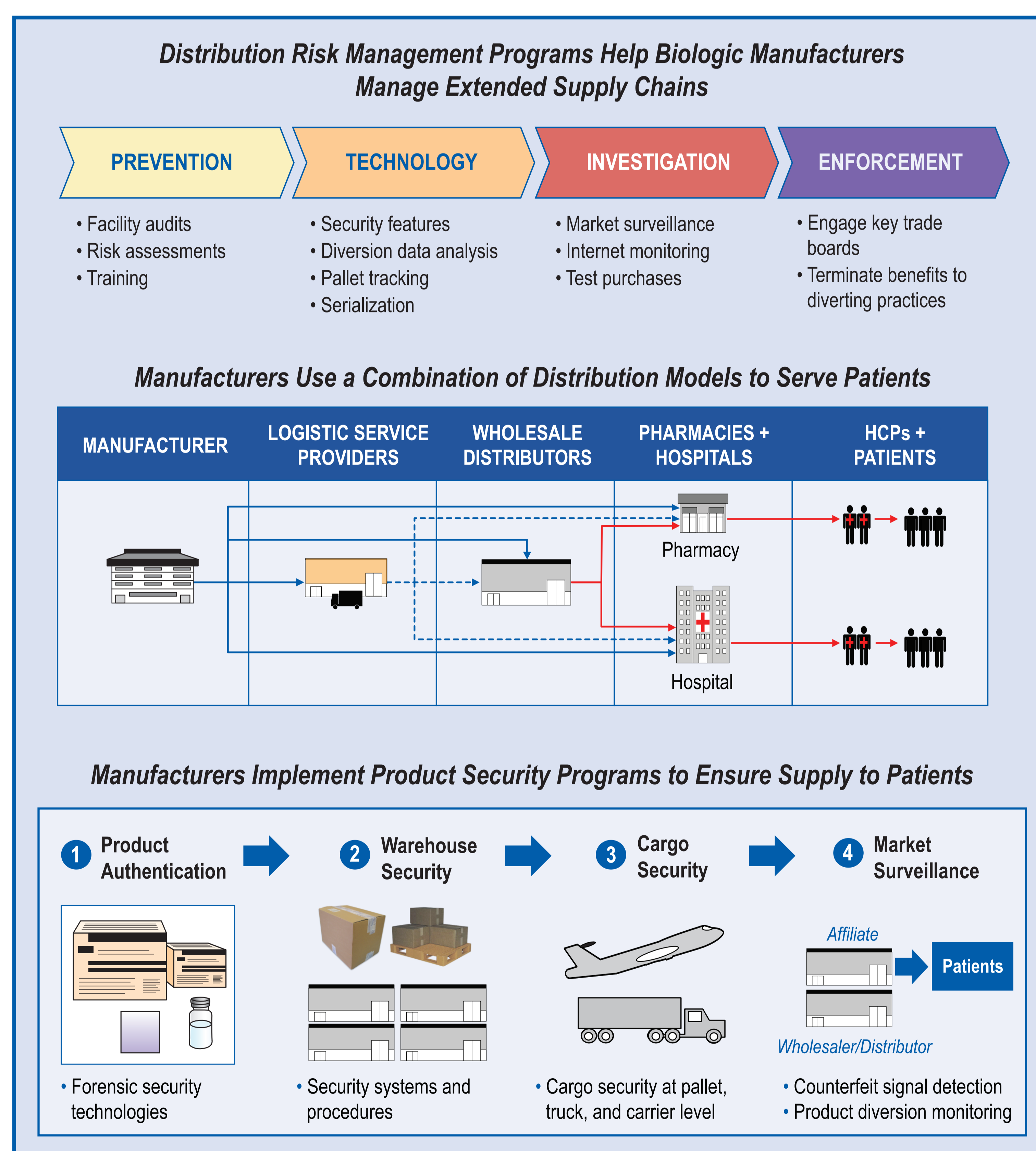
CONSIDERATIONS FOR THE PHARMACIST

- Inventory turns for most manufacturers can be found on corporate financial reporting statements or can be obtained from investment firm websites; eg, Forbes.com.[9]
- Raw material supply risks are reported through various mechanisms; eg, Rx-360.[10]
- Distribution channel security information should be available through wholesaler networks.
- Sales or customer service representatives should be able to access information related to:
  - Supply continuity plans
  - Product security features
  - Policies and practices regarding distribution management

SUMMARY

- Key practices that can enable biologic manufacturers to ensure continuous supply of high quality products to patients require leveraging resources, both financial and human, to ensure that approved drugs are available through normal operations, and during periods of supply shortages.
  - Proactive drug manufacturers heavily invest in inventory and supply chain infrastructure to reduce the risk of drug shortages and to shorten recovery times in the event of a drug shortage.

CONCLUSION

- When weighing formulary decisions, it should become an integral part of the hospital pharmacist's role to understand and consider key supply chain parameters that can impact a manufacturer's ability to manage drug supply.

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