



Safeguarding the biomanufacturing supply chain: practical steps to manage raw material and process risks

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CY15173-13Jul20-PT



Safeguarding the biomanufacturing supply chain: practical steps to manage raw material and process risks

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Abstract

Biomanufacturing supply chains are growing quickly to service a rapidly expanding industry delivering critical medical products. The increasing demand for often complex raw materials and a limited ability to change approved processes challenge the entire industry to focus on strategies that manage raw material variability and its impact on process performance.

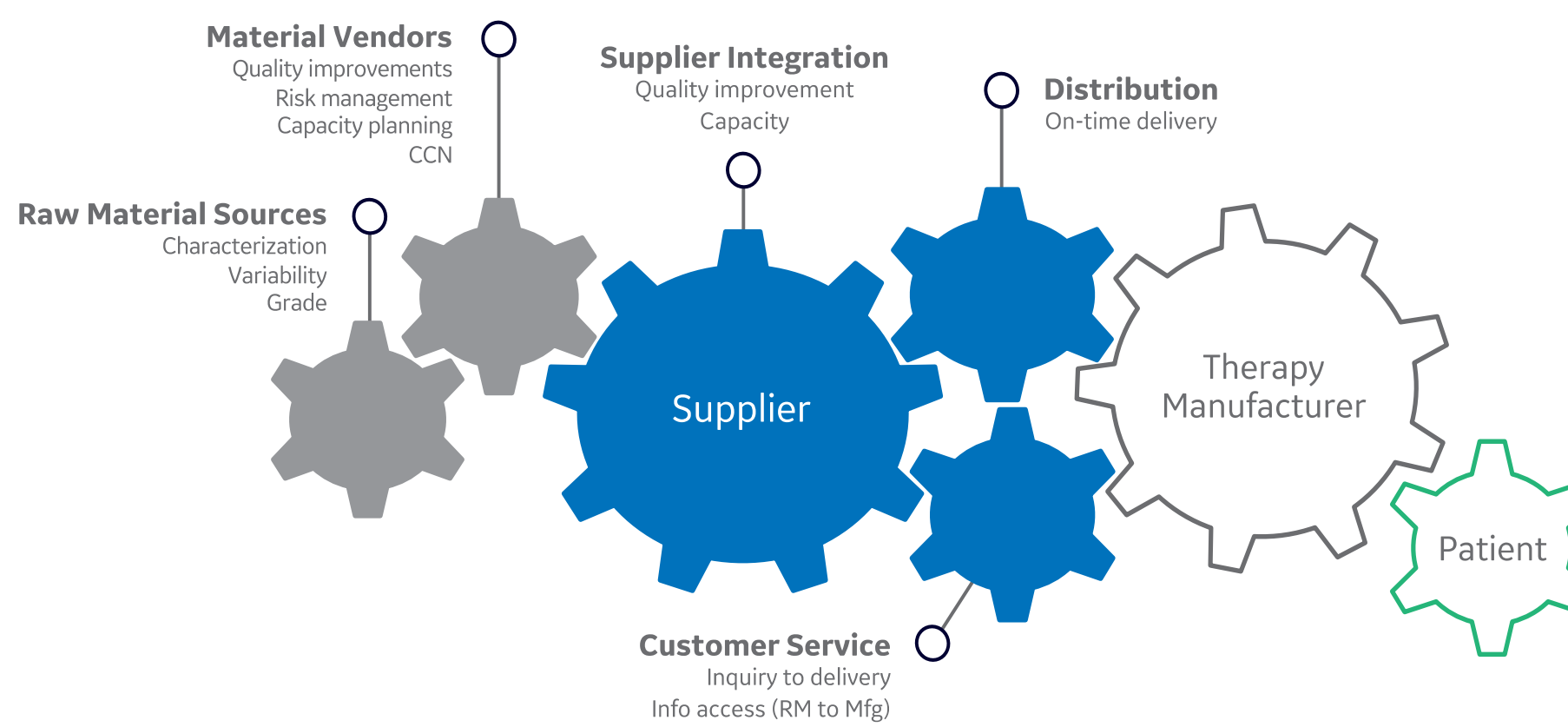
This poster demonstrates how suppliers can secure long-term process robustness for the biopharma industry. In the near term, this is driven by increased focus on supply chain transparency and management, as shown in examples of expanding manufacturing capacity and introducing multiple sources, transferring and modernizing manufacture. In addition, raw material and process analytics are expected, as well as a robust implementation of Quality by Design by both suppliers and drug manufacturers.

Longer term, we foresee increasing ability to use raw material and process analytical data to better understand how raw materials impact efficiency and quality in biopharmaceutical manufacturing.

Introduction

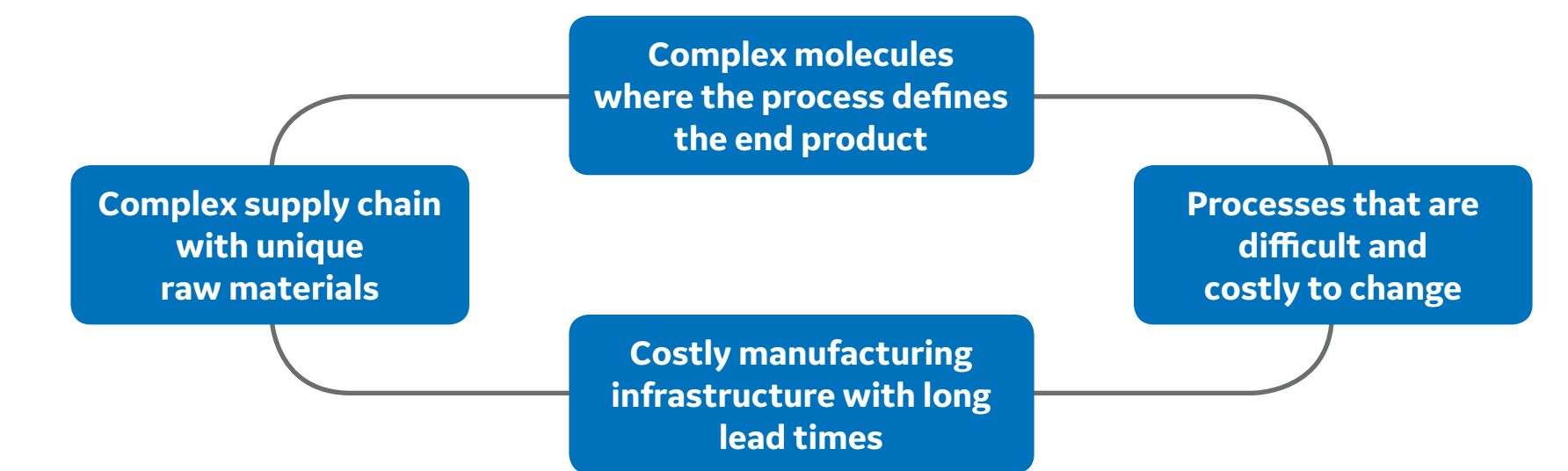
This poster will focus on the management of the quality of critical and complex raw materials and the challenges of securing their supply, which may require multiple sources.

Interrelationships and interdependencies from raw materials to patients

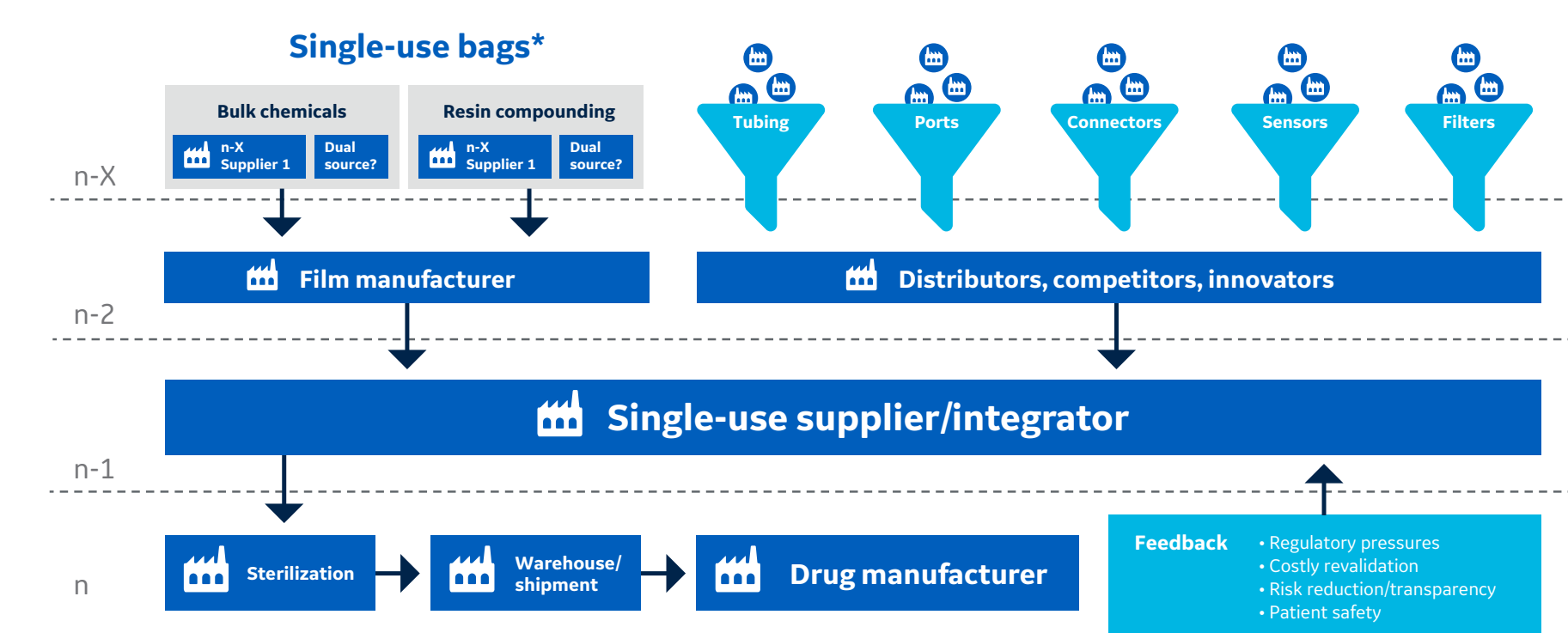


Manage raw materials

Raw material risks



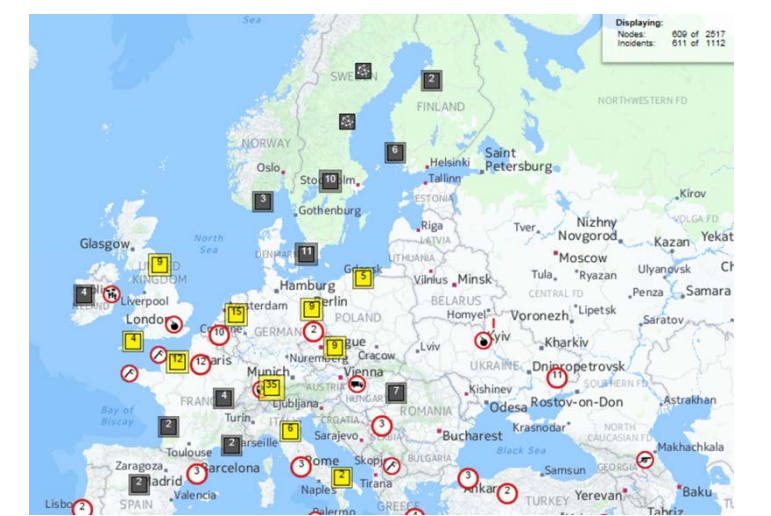
Complex supply ecosystems



Key elements of raw material supply

Global monitoring of supply chain status is increasingly possible.

- Supply chain mapping
- Raw material characterization
- Raw material control
- Raw material risk management



Securing supply of complex raw materials

Three major projects with \$10s of millions invested 2014 to 2018 to manage our own raw material challenges.

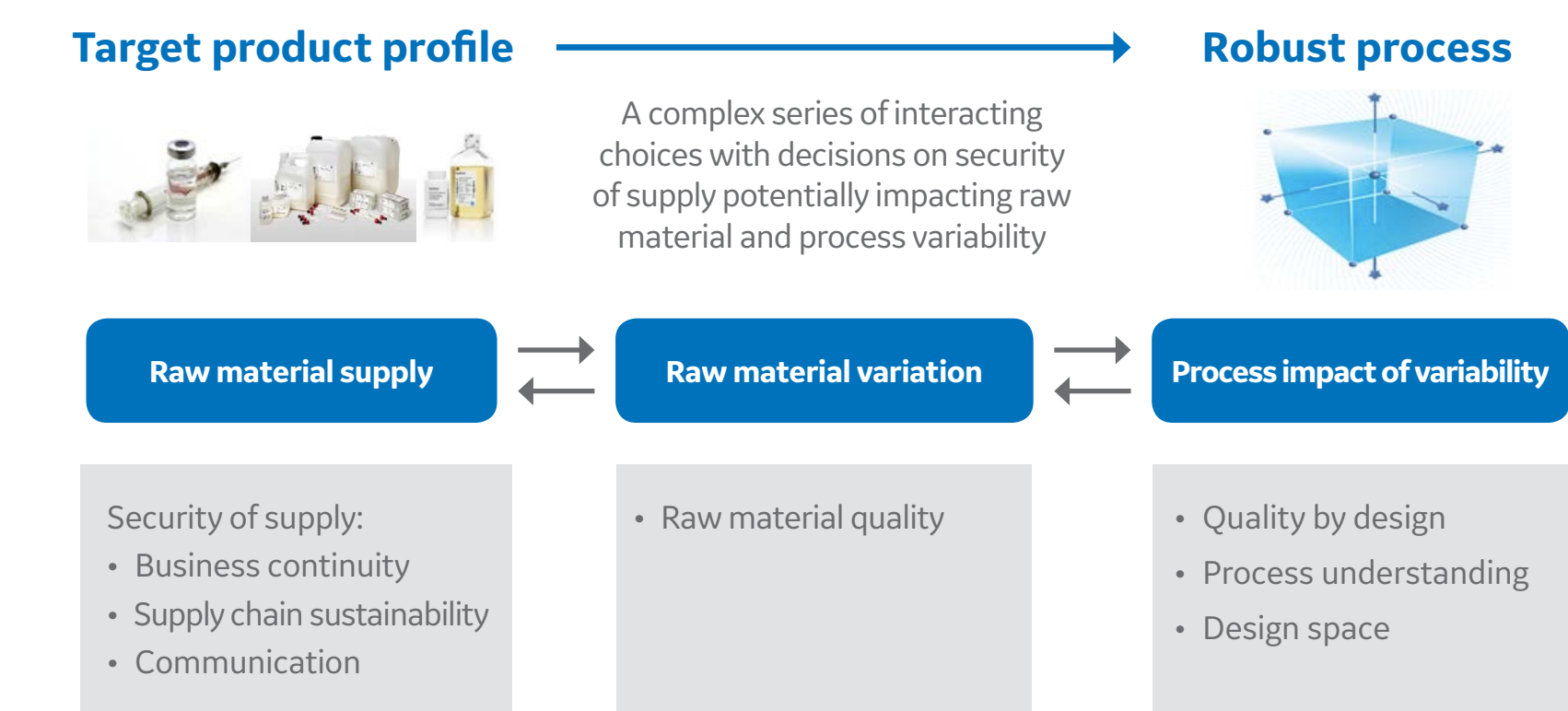
Second supplier agarose, Transfer dextran manufacturing, Modernize chromatography resin manufacturing. Includes chemical structures and product images.

Implementation of a second supplier of agarose

Leveraging ~ 50 years of experience using agarose

Flowchart showing the process from Adding second supplier to Emulsification, Crosslinking, and Ligand coupling. Includes a table of Key CQAs and Acceptance limits.

The raw material journey to robust processes



A continuum of challenges and successes

| Risk continuum | Raw material supply | Raw material variation | Process impact of variability |
|----------------|---|--|--|
| High | Sole source material with no or limited risk mitigation | Raw material is so variable it needs batch testing before use | Process on the edge of design space suffering periodic, poorly understood failure where raw materials are a major factor |
| Medium | Robust business continuity and safety stock programs | Variability is (partly) understood, though might not be completely controllable | Effects of variability better understood but might require custom product to ensure control |
| Low | Diversified supply chain, second sources, multiple production lines, second sites | Origins of variability well understood, and control over raw material sourcing and manufacturing eliminates risk | Process is designed to manage foreseeable variability in raw material with standard products. Adaptive process control |

Addressing supply risks at GE Healthcare

Security of supply is a holistic effort

At GE we carefully consider your needs for supply, business continuity, and transparency; driving near term improvements, but most importantly deliver you long term reliability, quality and performance.

- Holistic approach: Every day, hundreds of sourcing, quality, and manufacturing professionals work behind the scenes to provide security of supply to your manufacturing network.
- Supply risk management: Supply chain programs increase confidence by applying Quality by Design (QbD) principles and structured Risk Management.
- Personalized portfolio solutions: Each product portfolio has unique supply chain, quality and manufacturing needs. Tailored risk management enables more effective continuity programs.



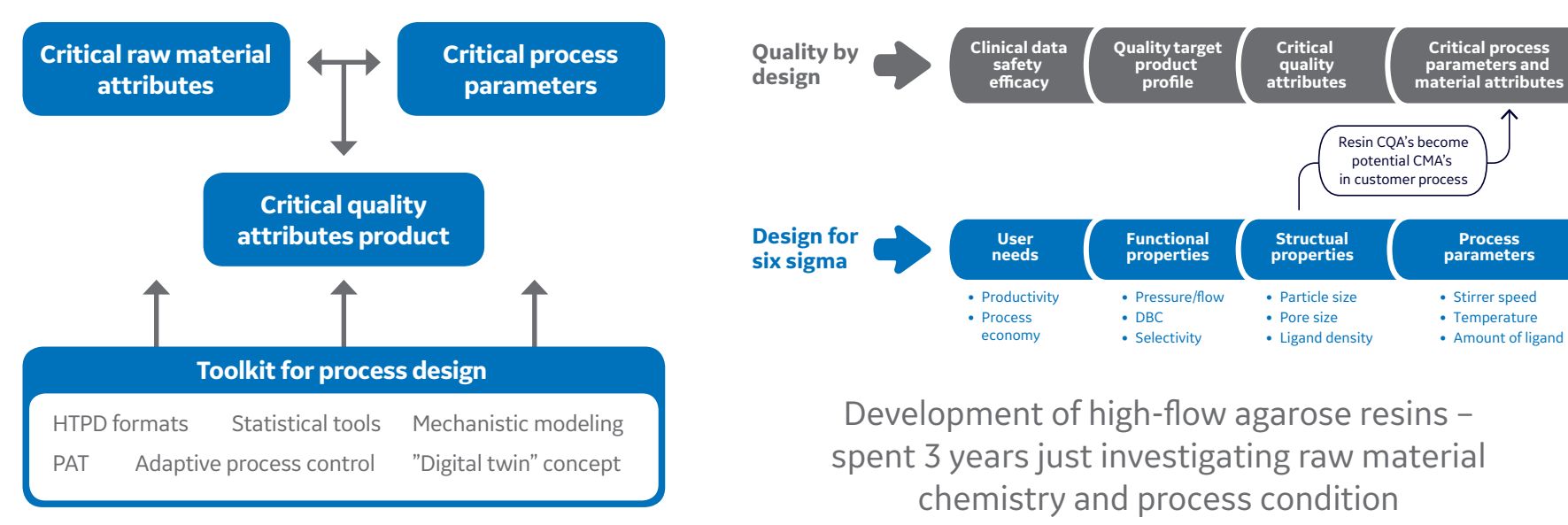
GE's security of supply program for chromatography resins

Resin program highlights: Global QMS, Capacity expansion, Second supplier program, Discontinuation policy, Delivery guidelines. Includes a diagram of the security of supply program and a table of program highlights.

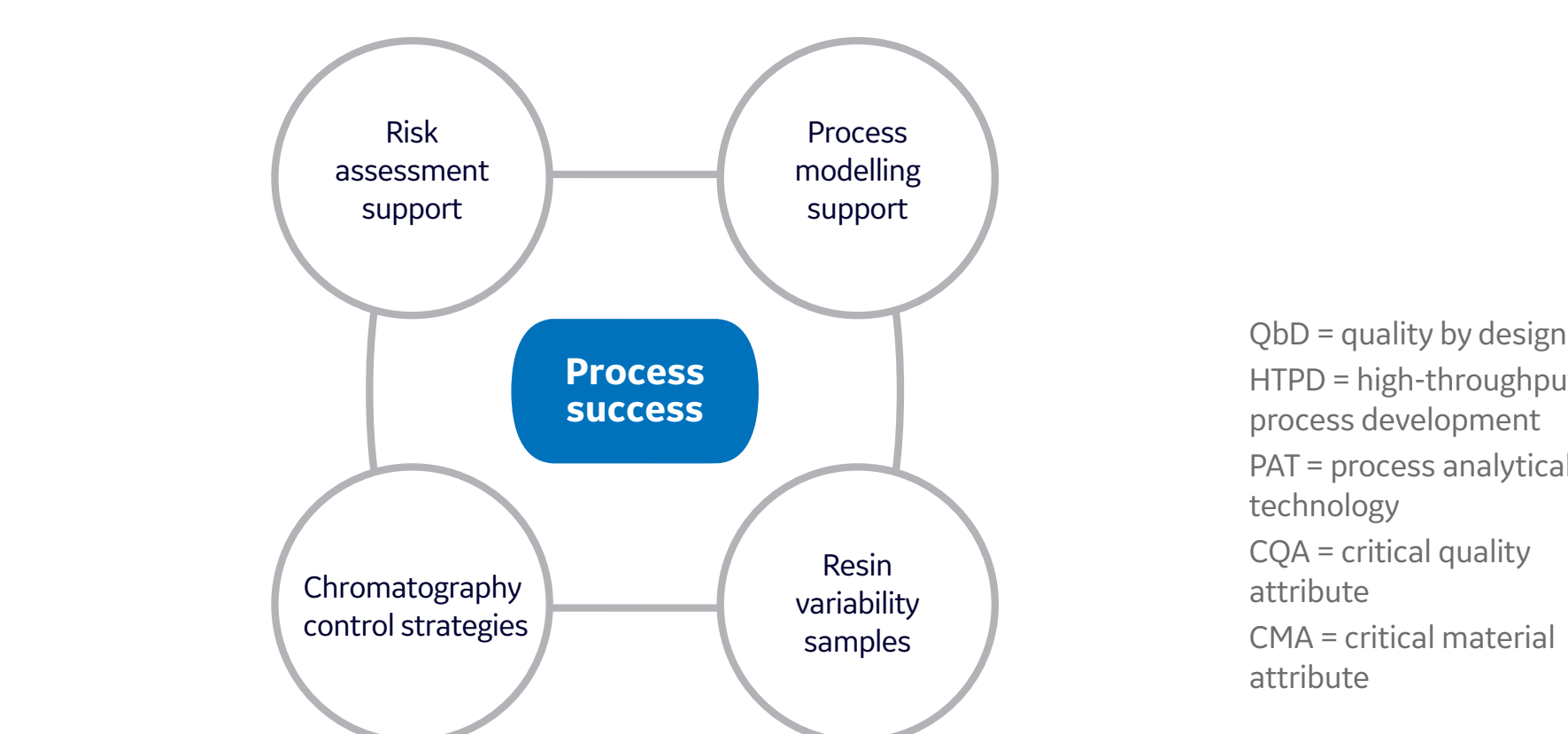
Manage variability

Minimizing the impact of variability: smart process design based on QbD principles

Development of chromatography resins mirrors and inputs into development of drug manufacturing processes



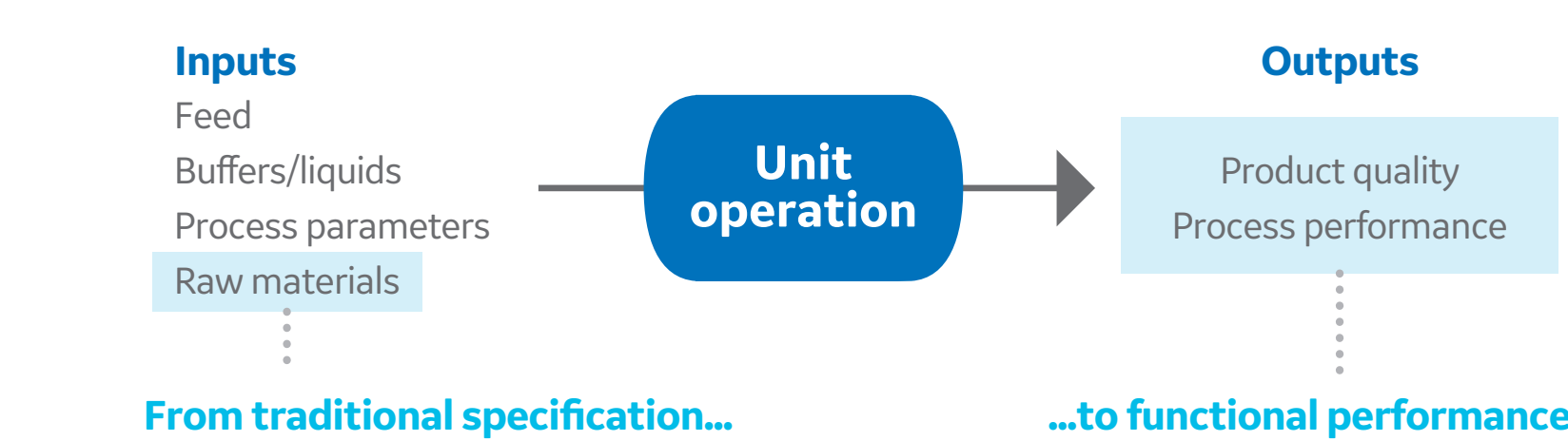
Suggested tools to assess the impact of resin attribute variability to generate process understanding



Conclusion

It is clear that transactional supplier-customer relationships need improvement and that long-term strategic partnerships around process life cycles are critical for success.

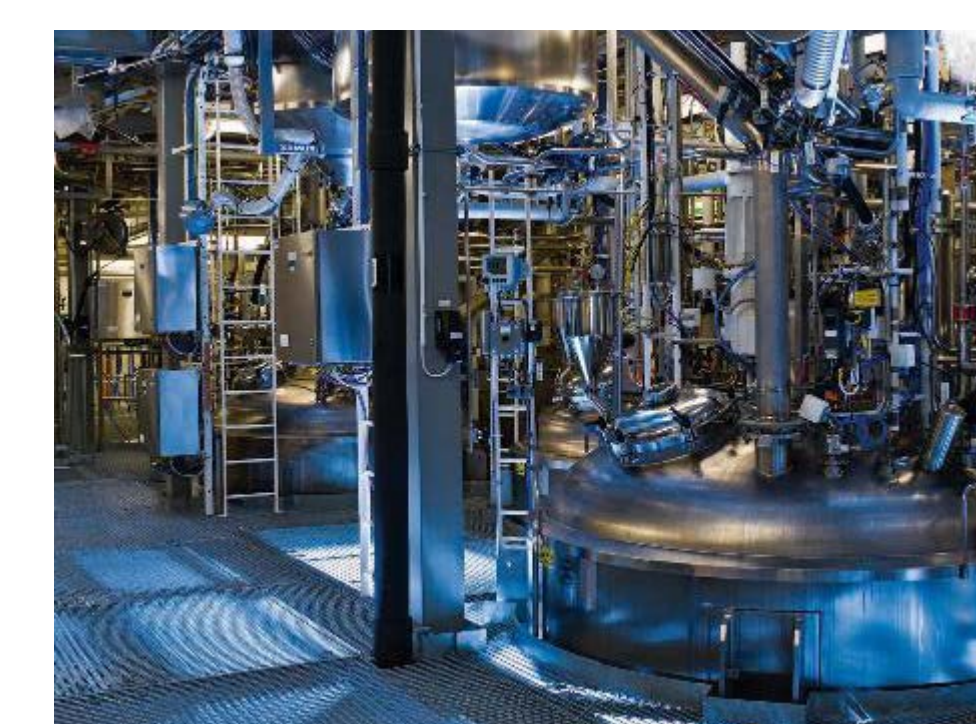
Collaboration can create a higher level of integration between manufacturing processes



"Collaboration occurs when companies work together to achieve common objectives. Such behavior requires a shift away from the traditional transactional relationship of customer/supplier." (1)

1. Patient-Centric Requirements for the Supply of Raw Materials into Biopharmaceutical Manufacturing, BPOG whitepaper

Control of raw materials continues to improve: complete understanding comes through collaboration



- Holistic control of raw materials from supply to understanding of raw material variability and impact on manufacturing processes and quality of biomolecules
- This creates a need for long-term strategic partnerships around process life cycles
- Transactional relationship is not good enough—supplier and user need to collaborate around a common goal with aligned incentives
- This is a big mindset change for both parties—requires courage and trust