

# How to Stay One Step Ahead of Biopharma Supply Chain Constraints

## INTRODUCTION

Supply chain disruptions are not a new concern for the world of biotech and biopharma. As the industry pushes to develop therapeutics faster and more efficiently, the need for bioprocess raw materials is mounting – and there are simply not enough. While much focus has been placed on active pharmaceutical ingredients (APIs) used for small molecule drugs, another real problem is the implications for those companies producing biologic therapies and ensuring they have the right bioprocess materials.<sup>1</sup> The consumables needed to develop drug therapeutics, which include filter media and cell cultures, single-use components, and vials and syringes, are becoming more difficult to source in adequate amounts.<sup>1</sup> This paper examines single-use supply constraints that interfere with bioprocess operations and have been exacerbated by the COVID-19 pandemic and highlights Entegris solutions that can help minimize production delays.

## COVID-19: A THORN IN SUPPLY CONSTRAINTS

The COVID-19 pandemic has only exacerbated supply chain constraints. With more than 300 different COVID-19 vaccines, antivirals, and other therapies<sup>2</sup> currently in development and more being explored each day, the demand for bioprocessing materials and consumables has continued to outweigh supply. Consequently, the amount of supply challenges has grown immensely, which includes:<sup>3</sup>

- Reluctance to receive raw materials from impacted area
- Sourcing
- Site closures
- Transportation
- Introduction of counterfeit material
- Lack of coordination and supply chain traceability

### The Need for a Reliable Supply Partner

To resolve many of these setbacks, companies must cultivate a deeper relationship with suppliers. Understanding how suppliers plan to minimize disruptions can be crucial. Clear, consistent communication can help pharmaceutical companies better react to upstream disruptions and tackle demand management.

It is also becoming abundantly clear that supply chain mapping (SCM) is not optional – it must be considered by biopharma companies. Knowing the source of materials as well as having them verified for integrity, quality, and availability is critical and a requirement to pass regulatory agency approvals. However, to accomplish this, there must be a collaborative relationship and approach taken between suppliers and drug manufacturers. By doing so, drug manufacturers can ensure that their products meet regulatory guidelines and are also safe for patients. Making this collaborative style approach more standard will benefit both end users and the biopharma industry as a whole.<sup>4</sup>

### Supply Chain Constraints Impact on Mixing Operations

One area that may be especially vulnerable to supply chain constraints is mixing operations within the single-use bioprocess. Each process train can require up to 15 – 25 mixer bags for various reagents, buffers, media, and intermediates. If a company cannot purchase enough of their single-use mixer bags and impellers, the entire process is impacted.

Currently, most single-use mixers use hardware that requires vendor specific bags to drive the impellers. Therefore, these bags are not just a consumable supply challenge, but due to a lack of bag supply, could become an asset utilization challenge. A company may decide to change the technology they are currently using, but this also entails hardware lead time and of course, capital cost challenges.



Figure 1. Entegris single-use mixing system.

What's more, single-use processing systems are a required material to operate plant capacity. For example, single-use bioprocess trains are most often designed on a concept of integrated unit operations, which may contain a bill of materials in the hundreds. If one assembly is unavailable, the entire process is brought to a halt, resulting in drug development and commercial operations delays.

## THE ENTEGRIS SOLUTION

As a dedicated supply partner, Entegris has made significant investments in raw materials and components. They have not only increased their capacity but have also maintained critical operations by relying on business continuity plans and leveraging trusted supply partnerships. This has allowed them to maintain industry-leading time to delivery compared to other suppliers that have virtually shut down customers with their inability to supply and meet production timelines.

More specifically, they can deliver mixing solutions quickly, often in as little as six weeks for standard designs. Their single-use mixers can effectively mix a wide range of reagents, buffers, media, and intermediates. They deploy their mixer rapidly with simple, effective hardware and often can adapt the mixer bag to operate within existing mixer hardware because the mixing action is based on recirculation. With multiple inlet and outlet connection options for closed sterile process integration this mixing system maximizes simplicity, ease-of-use, and affordability when storing, recirculating, and mixing biopharmaceuticals in a single-use bag, Figure 2.

The mixing bag is fitted into a reusable conical drum and runs with a simple peristaltic pump, minimizing capital costs. This unique system rapidly recirculates to homogeneity in minutes, saving time and money without sacrificing quality or consistency.

In addition, the simple and intuitive design of the single-use consumables requires less operator training and minimizes the risk of mishandling.

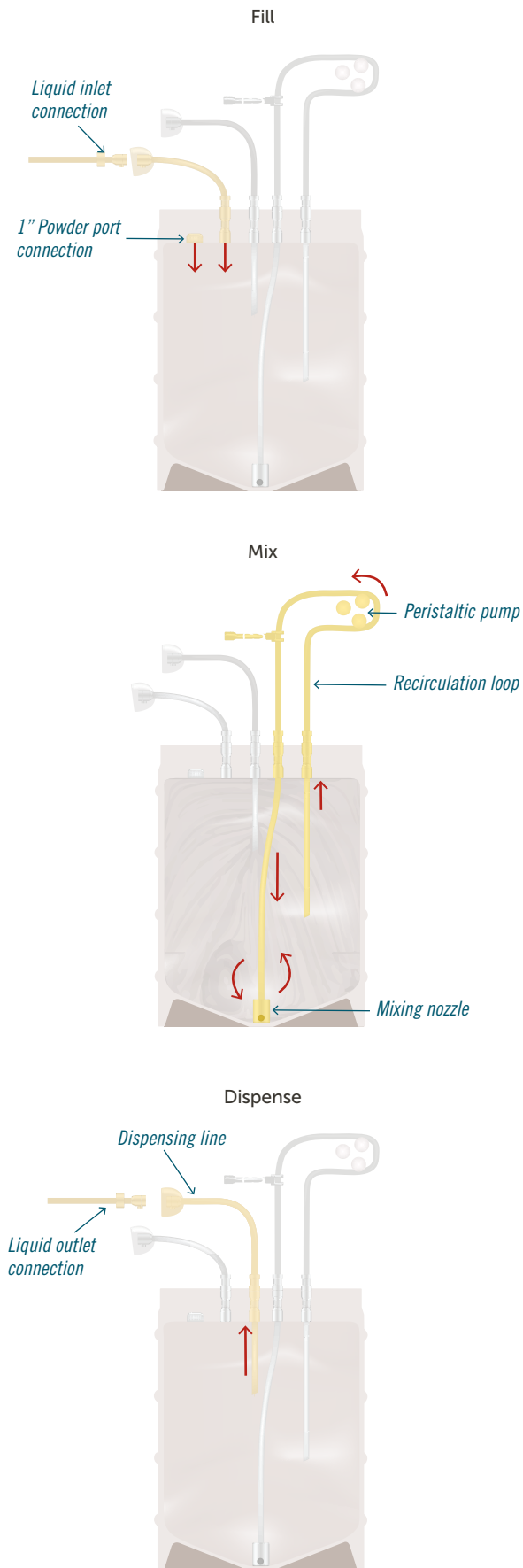


Figure 2. The Entegris mixing system maximizes simplicity, ease of use, and affordability.

But perhaps most importantly, fast development and delivery times minimize the risk of production delays in the processing suite. Entegris collaborates to design and deliver a solution that meets specific, unique customer needs. Currently, custom configured product lead times from confirmed order to delivery are 10 to 12 weeks, Figure 3.

### Custom Design Decisions

- Process application
- Bag size
- Tubing size/length
- Port size/quantity
- Connectors
- 3D bag outer container dimensions
- Gamma sterilization 25 – 40 kGy

### SUMMARY

Today's biotechnology and biopharmaceutical industry is facing ever increasing threats to their supply chain. The COVID-19 pandemic has further intensified the issue, making access to critical raw materials an even more difficult route to navigate.

Entegris has had the foresight to plan accordingly and ensure its supply is robust, minimizing the risk of production delays. And with the Entegris mixing system, designed to offer ease of use, customization, and flexibility, manufacturers no longer have to worry about their mixing processes. They can have peace of mind knowing that their buffer and media will be mixed correctly and efficiently, a requirement for high quality, reliable, life sciences manufacturing.

### Industry's Shortest Product Lead Times from Concept to Delivery



Figure 3. With the industry's shortest lead times, which include customization, Entegris can help minimize production delays.

### ABOUT ENTEGRIS

Entegris is a world-class supplier of advanced materials and process solutions for the semiconductor and other high-tech industries. Entegris is ISO 9001 certified and has manufacturing, customer service, and/or research facilities in the United States, Canada, China, France, Germany, Israel, Japan, Malaysia, Singapore, South Korea, and Taiwan. Additional information can be found at [entegris.com](http://entegris.com).

## References

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<sup>2</sup>Milken Institute's *COVID-19 Treatment and Vaccine Tracker*. <https://covid-19tracker.milkeninstitute.org>

<sup>3</sup>Kulkarni, N. *Managing supply chain disruptions in the pharmaceutical industry*. CRB Group. <https://www.crbgroup.com/insights/managing-supply-chain-disruptions/>

<sup>4</sup>*Supply Chain Mapping: A Best Practice for the Biopharma Industry?* BioPhorum Operations Group Ltd. [https://www.biophorum.com/wp-content/uploads/bp\\_downloads/Supply-chain-mapping-best-practice-April-2018.pdf/](https://www.biophorum.com/wp-content/uploads/bp_downloads/Supply-chain-mapping-best-practice-April-2018.pdf/)

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