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Bioprocess optimization

Plan for success in process liquid and buffer preparation

Introduction

Preparing to manufacture a biotherapeutic is a complex and challenging endeavor. Process liquids and buffers are critical components in the bioprocessing workflow, and their preparation can be extremely resource-intensive. The fiscal impact of process liquid and buffer preparation on the total cost of ownership (TCO) goes beyond capital and operational expenditures. There are many hidden costs associated with inefficiency, contamination, batch failure, and dedicating personnel to manufacturing process liquids and buffers.

Laying the groundwork for successful scale-up is essential to getting a therapeutic to market quickly and efficiently, but navigating the unknowns can be challenging. A greater awareness of common operational inefficiencies, risks, and related financial burdens can improve overall spend visibility and enable more accurate assessment of TCO. In addition to the known costs of personnel, equipment, and physical space, TCO includes hidden costs that arise from process inefficiencies and quality errors (Table 1). Greater visibility and awareness of these hidden costs can inform how you approach the next stage as your business expands and production demands increase.

Table 1. Hidden costs that can adversely impact speed to clinical trials and market.

Risks	Operational inefficiencies	Financial burdens
• Batch failure • Unanticipated demand • Variable production schedules due to unexpected orders • Timeline delays to accommodate desired growth and increases in production • Manufacturing overhead cost (MOC) • Change notifications from suppliers and regulators	• Devoting resources, time, and space to support supply chain and pre-production activities • Managing multiple suppliers and shifting lead times • Long duration from product receipt to material release • Maintaining excessive safety stock volumes to reduce inventory turnover	• Difficulties with product supply planning, poor on-time-in-full (OTIF) delivery performance, and just-in-time (JIT) delivery costs • Significant capital expenditure (CapEx) to maintain raw material and safety stock inventory • High overhead costs for personnel not directly involved with quality and manufacturing activities • Inefficient CapEx for warehouse space • High operational expenditure (OpEx) to prepare chemicals for use in manufacturing • High OpEx for supply chain management

Plan for operational efficiency

Sourcing from a reliable chemical supplier is essential to efficiently scale up process liquid and buffer preparation. It is often necessary to obtain the raw materials required for different buffers and process liquids from multiple suppliers. In times of chemical shortages, delays, or unexpected increases in demand, managing the logistics of alternate sourcing requires additional time and labor. Managing multiple supplier relationships and coordinating inbound material receipt can be a highly resource-intensive process. Freight and shipping expenses for multiple individual orders are also higher than they are for consolidated orders.

Beyond these procurement challenges, raw materials must undergo quality control (QC) testing before they can be used to prepare process liquids and buffers. The documentation, validation, and training associated with QC testing present additional challenges to facilities that must allocate personnel and equipment for these activities. Inefficiency at any stage of this process can increase the risk of production delays.

Outsourcing process liquid and buffer preparation can both increase workflow efficiency and support scale-up. The right supplier can help you reduce your TCO by managing your supply chain and identifying compliant suppliers to help ensure quality standards are maintained when sourcing raw materials for buffer production. With the right support, you can mitigate supply disruptions, improve the accuracy of orders, and increase productivity. Depending on your scale-up needs, the right supplier can provide ready-to-hydrate powders in standard or custom packaging, or ready-to-use process liquids in bioprocess containers. They can provide additional support by handling buffer solution calculations to help reduce risks associated with pH errors, performing audits, and testing multiple lots.

With extensive knowledge about liquid stability, the right partner can confidently deliver large volumes of liquids and buffer concentrates suited for your needs. QC testing can also be consolidated for larger batch sizes, further increasing workflow efficiency.

Mitigate risk

Handling chemicals safely requires strict adherence to environmental, health, and safety (EHS) regulations. Buffers that contain corrosive or hazardous chemicals pose potential safety risks for personnel, so preparing and handling them requires additional processes, protocols, and special equipment. The tendency of some powders to clump or accumulate static charge increases the amount of labor associated with preparation and cleanup. Most material handling is done in laminar flow hoods or well-ventilated spaces to reduce the risk of cross-contamination and particulate exposure, which has the potential to conflict with other core activities. Manual handling of large drums and repetitive motion are also safety risks associated with in-house preparation.

Misformulation and batch failure are common, and they can be costly due to the waste that is generated. Identifying the root causes of these problems will provide insight that can help you improve your processes and reduce waste. To avoid production delays in the event of a batch failure or unexpected uptick in demand, safety stocks are often stored on-site. However, safety stocks require careful management and sufficient warehouse space for storage to ensure the right quantities are maintained. Additional costs can arise if too much material is held that expires before it can be used.

Contamination and operator error are primary causes of batch failure. However, finding qualified personnel for buffer preparation activities may require additional time and effort due to talent shortages that are affecting many industries. An experienced outsourcing supplier can accurately prepare your process liquids and buffers and reduce risk, allowing you to allocate more resources to core activities. The right supplier will understand the careful calculations required to make quality process liquids and buffers, and will also be able to evaluate stability profiles and identify appropriate packaging materials based on chemical class.

Maximize your capabilities

The capital outlay for a facility that is suitable for manufacturing vaccines and therapeutic products ranges from $500 million to $1 billion [1], and setting up a new facility can take anywhere from five to ten years. When scale-up is needed, capacity is often expanded by setting up suites in parallel or investing in new equipment. However, financial loss is a risk when new facilities or equipment are underutilized.

Buffer preparation is a highly resource-intensive activity that requires a significant amount of floorspace. Buffers collectively make up the largest volume of downstream processing components, so they can also be challenging to store [2]. Although tank volumes will be smaller if concentrated buffers and in-line dilution (ILD) technology are used, the overall number of tanks will remain the same, and the floorspace required to house the tanks will always be a capacity constraint. Outsourcing process liquid and buffer preparation and utilizing ILD technology can mitigate resource and space constraints, save time, and reduce capital costs. Biomanufacturers can then consider investing in resources and activities that help scale growth.

Preparing process liquids and buffers requires personnel with experience in handling large liquid volumes and pre-blended powders. When talent shortages are an issue, hiring a qualified team can be challenging. Some facilities are unable to divert personnel to buffer preparation activities, so they find support through outsourcing. An experienced outsourcing supplier can provide qualified personnel who will work as an extension of the team.

A process (Gemba) walk is an opportunity to assess workflows and identify potential areas for improvement. The right outsourcing partner will have lean specialists who can work directly with front-line personnel to identify areas of waste, risk, and value and develop a plan of action to eliminate key pain points and increase efficiency. Depending on needs, they can also provide the facility space and skilled staff to create quality buffers off-site for JIT delivery. When buffer preparation is outsourced, facilities can devote personnel and equipment to high-value core activities.

Conclusion

Preparation of process liquids and buffers shifts resources away from core activities. The weigh-dispense-hydration process is also full of inefficiencies, risks, and potential for failures that can increase costs across workflows and cause production delays. However, creating a strong foundation to establish a scalable process for buffer preparation while navigating myriad resource challenges can be a daunting task.

Outsourcing buffer preparation to an experienced supplier like Thermo Fisher Scientific can help you improve consistency and minimize risk in your weigh-dispense-hydration workflow. The lean specialists at Thermo Fisher can provide key insights across your process workflow and reduce the need for large capital and operational expenditures. Our team of chemical specialists can help you increase efficiency and the accuracy of your buffer formulations, allowing you to focus on producing life-changing therapies.

Case study spotlight

Situation

A clinical-stage biotherapeutics company faced challenges in scaling manufacturing operations, with its existing resources, to expedite development of its immunotherapies. To support the rapid pace of development desired, the company decided to outsource manufacturing of 10 different buffers. However, the company received delayed communications about issues with lead times and small-volume (<200 L) requests from the supplier. As a result, the company faced the following challenges:

- Operational inefficiencies in the weigh-dispense-hydration suites during buffer preparation, which led to delays
- Inefficient supply chain and lack of communication regarding long lead times, affecting planned development timelines
- Warehouse that was over capacity and unable to support buffer storage
- Scale-up that would require a 10,000 ft^2 expansion

There was a strong possibility that their first-in-human (FIH) trials would be delayed. Management thus sought alternative partners who could reliably supply outsourced buffers to advance the development of their product without incurring additional CapEx and OpEx.

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Solution

Thermo Fisher Scientific collaborated with the company's Chief Scientific Officer and Purification Manager to better understand their unique needs for their highest-priority buffers. Premade process liquids ready to use for manufacturing offered the best solution for the company's situation. By collaborating with Thermo Fisher, the customer received premade buffers through Thermo Scientific™ Process Liquid Preparation Services.

Result

The company was able to focus its valuable resources on immunotherapy development for FIH trials without expanding its warehouse capacity, investing in new equipment, or increasing its head count. As a result, the company enjoyed $2.2 million in CapEx avoidance and saved $368,000 annually in OpEx. Process liquids were also delivered on a predetermined schedule that aligned with available capacity, enabling the company to experience improvements in lead times while avoiding significant capital expenditures.

$2.2M CapEx avoidance

$1.7M for facility expansion, including warehouse space to store buffers and raw materials; **$500K** for equipment, space, and facility upgrades.

$368K OpEx annual savings

Savings could be used to support current manufacturing resources without increasing head count by 3 technicians and 1 manager.

References

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