



Plan for success with your process liquid and buffer preparation

White paper

Introduction

Preparation for manufacturing is a complex and challenging undertaking. Process liquids and buffers are important components within the bioprocessing workflow, and preparation of these solutions can be very resource intensive. The fiscal impact of process liquid and buffer preparation in the total cost of ownership (TCO) goes beyond capital and operational expenditures. There are numerous hidden costs associated with inefficiencies, contamination, batch failures, and personnel devoted to manufacturing process liquids and buffers.

Setting the groundwork for successful scale-up is essential for getting a therapeutic to market quickly and efficiently, but navigating the unknowns associated with this process can be challenging. A greater awareness of common operational inefficiencies, risks, and financial burdens can improve the overall spend visibility to obtain a more accurate assessment of the TCO. In addition to “known” costs such as personnel, equipment, and physical space, TCO includes “hidden” costs such as process inefficiencies and quality errors. Greater visibility and awareness of hidden costs can inform how you approach the next stages as your business expands and your production demands increase.

Plan for operational efficiency

Sourcing from a reliable chemical supplier is an essential component in scaling up your process liquids and buffers. Often, several suppliers will be needed to obtain all the raw materials required for various buffers and process liquids. In times of chemical shortages and delays, or unexpected increases in demand, managing the logistics of alternate sources requires additional time and labor. Managing multiple supplier relationships individually and coordinating inbound material receipt can be a very resource-intensive process. Without consolidated orders, freight and shipping expenses will be higher, for multiple individual shipments.

Beyond procurement challenges, raw materials need to undergo quality control (QC) testing prior to preparation for process liquids and buffers. The documentation, validation, and training associated with these processes also present challenges to facilities that must allocate personnel and equipment. Inefficiencies in any step of this process can increase the risk of production delays.

Outsourcing process liquid and buffer preparation can increase workflow efficiencies and support scale-up. The right partner can help reduce total costs by managing your supply chain and identifying compliant suppliers to ensure quality standards are maintained when sourcing raw materials for buffer production. With the right support, you can mitigate supply disruptions, increase order accuracy, and improve productivity. Depending on your scale-up needs, the right partner can provide ready-to-hydrate dry powders in standard or custom packaging or ready-to-use process liquids in bioprocess containers. They can further support by handling multiple buffer solution calculations to help reduce risk of pH errors, performing audits, and testing multiple lots. With extensive knowledge in liquid stability, the right partner can confidently deliver large volumes of liquids and buffer concentrates suited for your needs. With larger batch sizes, QC testing can be consolidated, further increasing workflow efficiencies.

Mitigate your risks

When handling chemicals, you must comply with and adhere to Environmental, Health and Safety (EHS) regulations. Buffer formulations that include corrosive or hazardous chemicals require additional processes, protocols, and special equipment that pose potential safety risks for personnel. Furthermore, the tendency for some powders to clump or be prone to static charge increases the labor associated with preparation and cleanup. To reduce the possibility of cross-contamination and particulate risk exposure, most material handling takes place under a laminar flow hood or in a ventilated space, which has the potential to conflict with other core activities. Manual material handling of large drums, along with repetitive motions, are safety risks with in-house preparation.

Misformulations and batch failures are common and can be costly due to the waste that is generated. Identifying the primary causes of these issues will give you visibility into how to improve processes and reduce waste. To reduce production delays when there is batch failure or unplanned demand, a safety stock is often stored on-site. However, safety stock requires sufficient warehouse space for storage and careful management to ensure the right amount is maintained. Additional costs can arise if too much material is kept and expires before it is used.

Contamination and operator error are primary causes of batch failure. Finding qualified personnel for buffer preparation activities may require additional time and effort due to talent shortages affecting many industries. An experienced outsourcing partner can help ensure accurate preparation of process liquids and buffers and reduce risks, allowing you to allocate resources to core activities. The right partner understands the careful calculations required to make quality process liquids and buffers, has the expertise to evaluate stability profiles, and can determine appropriate packaging for chemical class.

Maximize your facility and processes

The capital investment for a facility suitable for manufacturing vaccines and therapeutic products can range from \$500 million to \$1 billion [1]. Setting up a new facility can take 5 to 10 years. If scale-up is needed, capacity is often expanded by setting up suites in parallel or investing in equipment. Financial loss is a risk if these facilities are underutilized. Buffer preparation is a highly resource-intensive activity that

requires significant floor space. Buffers make up the largest volume of downstream processing components, and thus can be challenging to store [2]. Outsourcing process liquids and buffers and utilizing in-line dilution (ILD) technologies can help reduce your resource and space constraints while reducing capital costs. Although tank volumes are reduced with concentrated buffers and ILD, the overall number of tanks remains the same and the floor space required to house those tanks will always be a capacity limitation. Outsourcing buffer preparation can help biomanufacturers save time and reduce or avoid capital expenditures. Biomanufacturers can then consider investments in resources and activities to help scale growth.

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

There are opportunities to assess workflows for areas for potential improvement by conducting a Gemba walk. The right outsourcing partner will have lean specialists that can work directly with front-line personnel to identify areas of waste, risk, and value to develop a plan of action to eliminate key pain points and increase efficiencies. Depending on needs, they can provide the facility space and skilled staff to create quality buffers offsite for just-in-time (JIT) delivery. When buffer preparation is outsourced, facilities can devote personnel and equipment to high-value core activities.

Conclusions

Preparation of process liquids and buffers shifts resources away from core activities. The weigh-dispense-hydration process is filled with inefficiencies, risks, and failures that can increase time and costs across your workflows and result in production delays. Setting a strong foundation to establish a scalable process for buffer preparation while navigating the myriad resource challenges from time, personnel, investments, and space can be a daunting task.

Outsourcing buffer preparation to an experienced partner like Thermo Fisher Scientific helps ensure accuracy in formulation and consistency to minimize risks in your weigh-dispense-hydration workflow. The lean specialists at Thermo Fisher can provide key insights across your process workflow, reducing your need for large capital and operational expenditures. The process liquid and buffer preparation chemical specialists will help you improve efficiencies and ensure accuracy of your buffer formulations so you can focus on producing life-changing therapies.

References

1. Sarkis M, Bernardi A, Shah N et al. (2021) Emerging challenges and opportunities in pharmaceutical manufacturing and distribution. *Processes*. 9(3):457.
2. Fabbrini D, Simonini C, Lundkvist J et al. (December 13, 2017) Addressing the challenge of complex buffer management: an in-line conditioning collaboration. *BioProcess International*. <https://bioprocessintl.com/downstream-processing/separation-purification/addressing-the-challenge-of-complex-buffer-management-an-in-line-conditioning-collaboration/>

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

Risks
<ul style="list-style-type: none">• Batch failures and unplanned demand• Variable production schedules as a result of unplanned orders• Delayed timelines to accommodate desired growth and production increases• Change notifications and MOC from suppliers and regulators
Operational inefficiencies
<ul style="list-style-type: none">• Resources, time, and space required to support supply chain and product pre-production activities• Managing multiple suppliers and shifting lead times• Long durations from product receipt to material release• Excessive safety stock volumes that reduce inventory turnover• Difficulties with product supply planning, poor on-time-in-full (OTIF) performance, and JIT delivery needs
Financial burdens
<ul style="list-style-type: none">• Significant capital expenditures on raw material and safety stock inventory• High overhead costs for personnel not directly involved in quality and manufacturing activities• Inefficient capital expenditure in warehouse space• High operating expenses for preparing chemicals to be used in manufacturing• High supply chain management operational expenses

Case study spotlight

Situation

A clinical-stage biotherapeutics company faced challenges in scaling its manufacturing operations with existing resources to expedite development of its SARS-CoV-2 immunotherapy. To support the desired rapid pace of development, the company had decided to outsource manufacturing of 10 different buffers. However, the company received delayed communications regarding lead time issues and any 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 while preparing buffers, causing delays
- Inefficient supply chain and lack of communications regarding poor lead times, affecting planned development timelines
- Warehouse was over capacity and unable to support storage of buffers; a 10,000 ft² expansion would be needed to support the scale-up

There was a strong possibility of delay in first-in-human (FIH) trials; thus, management sought alternative partners who could reliably supply the outsourced buffers to advance the development of their product without incurring additional capital (CapEx) and operational (OpEx) expenditures.

Solution

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

Results

The company was able to focus its valuable resources on the SARS-CoV-2 immunotherapy development for FIH trials without expanding warehouse capacity, investing in new equipment, or increasing head count. As a result, it avoided \$2.2M in CapEx and saved \$368K annually in OpEx. Additionally, the process liquids were delivered on a predetermined schedule aligned with capacity availability, thereby avoiding significant capital expenditures while also providing some improvements to lead times.

\$2.2M CapEx avoidance

\$1.7M for facility expansion, including warehouse space to store buffers and raw materials

\$0.5M for equipment, space, and facility upgrades

\$368K OpEx annual savings

to support current manufacturing resources without increasing head count by 3 technicians and 1 manager

Find out more at thermofisher.com/simplifybufferprep

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