

# How can outsourcing buffer preparation help meet the world's urgent need for a SARS-CoV-2 vaccine?

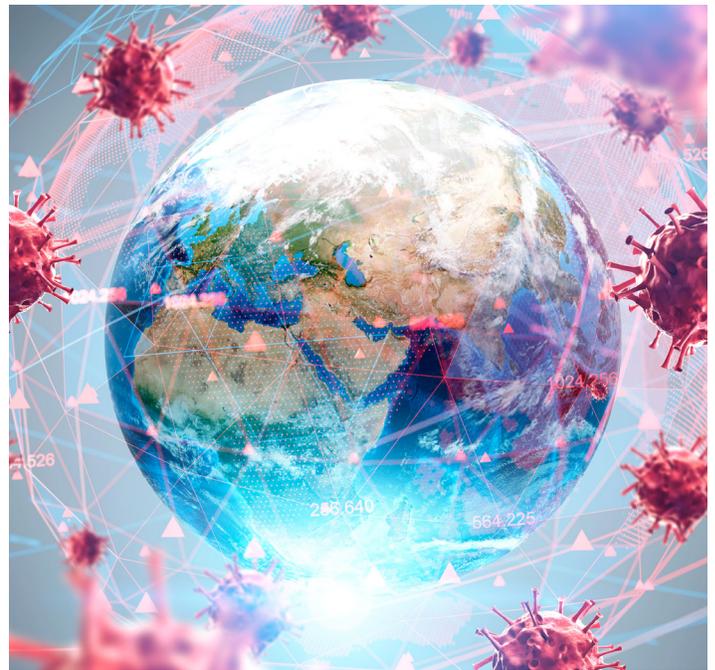
As the SARS-CoV-2 crisis maintains its grip on the world, the pressure to develop and distribute effective treatments and vaccines continues to mount. To spare as many people as possible from this deadly disease, treatments and vaccines that are developed for human use will need to be produced and distributed in massive quantities. So far, there is no approved treatments or vaccines available worldwide. To meet the worldwide demand, drug companies will have to scale up their manufacturing capabilities dramatically.

As numerous therapeutic drug and vaccine candidates make their way through human clinical trials, companies are already planning for how to manufacture any successful molecule on a global scale.

In this planning, the preparation of process liquids and buffers should be considered. These solutions are indispensable for drug development and manufacturing as buffer production remains an important part of the facility footprint, labor requirements, and equipment costs, but can be a logistical challenge. During a crisis, like the current SARS-CoV-2 crisis, buffer outsourcing can be essential to increase manufacturing capacity and speed. Sufficient buffer supplies of appropriate quality will be key to meeting the future large-scale manufacturing needs of any SARS-CoV-2 therapeutic or vaccine.

## Navigating the decision-making process

Buffers are essential in all stages of the production of biological drugs; therefore, they are important for every manufacturer. Managing the logistics and the large number of components involved with buffer manufacturing and storage requires extensive amounts of time and labor, as well as facility space.



This has led to an increase in the number of manufacturers seeking alternative options to in-house buffer preparation, a consideration even more paramount during a global crisis.

Outsourcing is a continuum of options based on specific manufacturing needs—a fit-for-purpose solution, not one-size-fits-all. Outsourcing can help:

- Scale manufacturing processes efficiently
- Streamline production workflows
- Improve quality and compliance
- Free up valuable skilled staff, as well as space

Outsourcing has been gaining momentum in the industry over the last six years<sup>1</sup>, thereby allowing buffer preparation simplification to become a strategic imperative for many organizations. This is particularly true for downstream processes, where the volume and number of buffers required for multiple purification steps is significant and complex. Such a shift is encouraging manufacturers to consider outsourcing and explore how it could positively impact their operations.

There are significant benefits to be gained from using an outsource partner for process liquid and buffer preparation and supply. It can enable organizations to stay Lean and maximize their limited resources most effectively. It also lays the groundwork for easy scale-up and provides an assurance of supply to minimize production delays.

The clear opportunities offered by outsourcing are accompanied by concerns such as a sense of loss of control, a risk that quality may deviate from what is expected or required, or a potential lack of integration with your own processes. However, these issues can be reduced or eliminated with thoughtful planning and collaboration.

There are also a considerable number of advantages that are afforded by supplier programs (such as safety stock and excess inventory), which should be factored into the decision-making process. In addition, utilizing outsourcing partners enables manufacturers to benefit from enhanced quality control and efficiencies of scale that may be otherwise difficult to achieve.

### **Maximize manufacturing facility footprint**

Buffers are the largest component of downstream processing by volume<sup>2</sup>, and as such, storage can be a challenge for many manufacturers. The need to store 25,000L of ready-made buffer, for example, creates a large amount of facility dead space. Even with appropriate temperature warehousing, every buffer has a shelf life after which it becomes unviable. Working with an end-to-end partner that can source these chemicals for process liquids/buffers, manufacture in dry or liquid formats under cGMP manufacturing, and provide storage and assurance of supply capabilities is critical for vaccine and therapeutic manufacturers to meet the aggressive timelines and goals.

Buffer preparation and storage for a standard monoclonal antibody treatment can require up to 30% of a facility's valuable floor space, which could be otherwise used to expand manufacturing capacity. A simple solution to reclaim some or all this footprint is to outsource buffer preparation entirely, eliminating the need for mixing tanks and their maintenance, with the added benefit that capital and operating costs are reduced as a result.

Manufacturing capacity is a critical issue. Even before the crisis, vaccine and therapeutic production was near capacity. Building a facility typically takes around three years, and planning begins only after proof of concept because the risk of failure is high. During a crisis, however, companies made a major shift in their risk mindset. They are arranging manufacturing before they have all the scientific data. Utilizing an outsource partner's cGMP warehousing and taking advantage of just-in-time delivery, so that only the right amount of buffer is delivered exactly when it is needed, significantly reduces on-site storage needs.

### **Reduce testing, ensure quality**

When deciding to outsource, it should be kept in mind that there is an extensive amount of work that can be done by the supplier. Responsibility for procurement and QC testing of salts, liquid preparation, filtration, quarantine, and finished good testing, as well as the documentation, procedures, validation, and training that accompany these, are all removed when outsourcing.

Simply managing all aspects of the buffer production process and scheduling these to fit "just-in-time" product manufacturing processes are tangible benefits that can also be gained.

Buffer performance does not need to be compromised. Selecting an outsource partner with a robust quality management system and employing high-functioning processes and continuous improvement approaches will ensure the production of the highest-quality buffers. Product consistency can be enhanced by preparing buffers in the larger batch sizes that are achievable when outsourcing, compared with the multiple, smaller batches that are often produced when buffer is prepared in-house. This, coupled with in-depth knowledge of liquid stability, can potentially enhance buffer performance.

## **Additional support and insight**

Working with a partner that has a depth of experience and understanding in buffer preparation can be invaluable. For example, a chemical capability team can employ

its experience to review your formulation specifications, highlighting any concerns about solubility limits or other formulation challenges. An outsourcing partner can also provide critical insights on appropriate packaging and can help avoid mechanical failures or exposure to any unwanted extractables or leachables.

Additionally, some buffer formulations are more complex than others. This can cause challenges when it comes to preparation and storage. The need to handle caustic or toxic chemicals, or special production conditions such as cold processing to maintain stability, can very quickly drive an escalation in production costs.

Offering a technical sounding board, an outsourcing partner's expert team will be able to make recommendations that could improve the formulation of your buffer, preempt issues, and help ensure ready integration with your processes.

## **Drive operational excellence and continuous improvement**

Outsourcing buffer preparation can also provide the opportunity to implement new technologies and approaches to stay at the forefront of the industry.

In-line dilution (ILD) has become a more popular option for buffer preparation as it uses concentrated buffer constituents, helping minimize the need for storing large volumes. Reducing facility usage in this manner can significantly reduce the capital costs involved with buffer preparation. The considerably smaller volumes utilized in ILD also mean that it is possible to use single-use bags, reducing capital costs further. The chemistry involved in preparing concentrated buffers is both complex and a relatively new field; therefore, it can be extremely useful to have access to an outsource partner's expertise in areas such as solubility limits and organic stability profiles.

The benefits that come with outsourcing buffer preparation can play an important part in driving efficiency and continuous improvement efforts for an organization.

## **Do the economics make sense?**

When prioritizing assignment of finite capital investment funds, outsourcing noncore functions is an option. For outsourcing process liquids, and specifically buffers, basing this important decision on data is vital, since there is often more than one option that can deliver measurable benefits.

Understanding your current costs is a key first step, and an economic modeling tool<sup>3</sup> is a good way to define these by quantifying the trade-offs and helping identify the potential benefits that can be achieved. By inputting data unique to your facility (i.e., detailed utility spend, labor costs, equipment, building cost, and buffer ingredients), it is possible to calculate a breakdown of annual expenses related to buffer production, and to determine a cost per liter. The analysis will facilitate informed decision-making when it comes to outsourcing.

As well as directly comparing overall costs, the cost-efficiency of individual steps should also be considered. For example, buying pre-weighed components can remove the time and effort needed to dispense and weigh the required raw materials, as well as reduce any requirements for special handling capabilities.

Using the common buffer formulation of 0.1 M sodium hydroxide (NaOH) as an example, Figure 1 shows how attractive the economics of outsourcing can be, simply based on the larger batch sizes achievable through an outsource partner. The five-fold increase in lot size compared to the typical lot size in-house translates into significant annual savings, as well as reductions in prep time, lot testing, and per-liter cost.

Producing buffers at scale is often a core element of delivering production and cost efficiencies, and some large organizations can produce their buffers as effectively as an outsource partner. However, even for these types of organizations, facility redesign and new facility future-proofing can often tip the balance in favor of an outsource option.

	In-house	Outsourced <sup>4</sup>
Batch size	2,000 L	10,000 L
Batches per year	20	4
QC releases	20	4
Prep time (2,000 L)	4 hours	1 hour
Annual prep time	10 days	2.5 days
Total batch cost	\$11,500	\$35,000
Cost per liter	\$5.75	\$3.50
Labor costs per year	\$230,000	\$140,000

<b>\$90,000</b> annual savings	<b>75% reduction</b> in prep time	<b>80% reduction</b> in lot testing
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**Figure 1.** Cost analysis of outsourcing manufacture of 0.1 M NaOH buffer, compared to typical in-house manufacture, to illustrate the potential time and cost savings that can be achieved.

Production economics are not always the sole driver behind the decision to outsource; organizations still make the decision to outsource because of the broader benefits, and these are not always as easy to quantify. When building a new facility, and perhaps transitioning from stainless steel into single-use, it can be an excellent opportunity to design a facility with increased productivity per square meter by outsourcing non-core elements of the manufacturing process, like buffer production.

## So, can you afford not to outsource?

Getting it right from the start is vital; invest time up front to ensure that priorities are clear and the production needs can be met. An outsourcing partner should enhance your manufacturing and relieve time pressures.

Drug manufacturing demands will rapidly increase with the eventual approval of one or several SARS-CoV-2 treatments and vaccines. Buffer outsourcing can help drug manufacturers focus on core manufacturing and reallocate capital and operating expenditures to advance drug development and production. A more efficient manufacturing process in turn will help speed the distribution of critical treatments or vaccines, helping save lives around the world.

Working closely together will result in the identification of a tailored solution that's fit-for-purpose *and* cost-effective.

With over 30 years of experience, Thermo Scientific™ Production Chemicals and Services helps biologic developers and manufacturers mitigate risks, improve operational efficiencies, and reduce total cost of ownership by simplifying the process liquid/buffer preparation workflow and streamlining the supply chain activities for cGMP chemicals. As a result, companies around the world who partner with Production Chemicals and Services can accelerate their speed-to-market, speed-to-clinic, and innovation: manufacturing millions of doses of lifesaving vaccines and biotherapeutics.

## References

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3. "The Total Cost of Buffer Preparation and Handling." BioProcess International, December 5, 2016. <https://bioprocessintl.com/ask-the-experts/total-cost-of-buffer-preparation-handling/>.
4. Data supplied by Thermo Fisher Scientific.

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