

A Strategic Assessment Tool for Modernizing Buffer Preparation in Biologics Facilities

THE CHALLENGE

The evolving biopharmaceutical ecosystem have significantly increased the complexity of the operations in biomanufacturing facilities. Organizations face challenges in improving production efficiency due to varying buffer volume requirements between different programs and production runs, making buffer management optimization difficult. Another complicating factor is selecting different buffer preparation technologies because their benefits often come with another trade-off. Some facilities initially default their strategy to the made-in-house (MIH) model due to the facility's design and preference, so all buffers and solutions are prepared internally. However, it is clear this is not scalable and new efficient technologies and strategies are required such as in-line dilution (ILD), in-line conditioning (ILC) system, and ready-to-use (RTU) solutions. A recent survey of bioproduction facilities suggests a gradual paradigm transition for buffer preparation technologies over the next decade.¹ Therefore, it has become more critical than ever for operations and facility teams to continuously review their buffer preparation roadmap.²⁻⁶

BUFFER PREPARATION STRATEGIES

A typical biomanufacturing facility can expect to utilize one or a combination of the following buffer preparation strategies:

- **MIH:** Preparing buffers through dissolving chemical powders and mixing liquids, usually in a dedicated buffer suite or logistics area. This maximizes internal control and leverages the economy of scale as buffer volume needs increase, but requiring significant infrastructure and manpower.

- **ILD:** Preparing buffers using concentrated stock solutions (e.g., 10X or 30X) thereby reducing storage space for dry powders and add operational flexibility.
- **ILC:** Mixing multiple stock solutions to generate the desired buffer composition and concentrations, offering adaptability to changing production needs.
- **RTU:** Outsourced pre-formulated 1X buffers that minimize in-house resources, enabling just in time production needs but possibly at a higher cost.

As biologics manufacturing becomes increasingly complex, buffer preparation strategies must align with operational efficiency, financial considerations and stringent regulatory requirements. For instance, large scale monoclonal antibodies (mAbs) production often generates medium (10,000-50,000 L/year) to high buffer volume demands (>50,000 L/year) that could overwhelm daily operations if addressed through traditional, preparation approaches. In continuous manufacturing programs, real-time buffer availability is essential due to the sequential dependency of process steps. Conversely, programs requiring relatively small buffer volumes per batch (<10,000 L/year) might not justify additional investments beyond the in-house buffer preparation infrastructure. Relying exclusively on MIH or any single preparation strategy can limit flexibility and amplify the risks associated with that method. To overcome these challenges, adopting a hybrid buffer preparation model that can integrate MIH, RTU, ILD and ILC strategies enables facilities to dynamically adjust their buffer preparation approach in response to fluctuating production demands.

		Cost				Supply Chain			Operational Strategy			
Buffer Demand	strategy	Direct Raw Material Cost	Capex Investments	Labor and QC Release Cost	Footprint & Storage Space	Availability & Risks	Speed & Delivery Timeline	Recipe Flexibility				
Low	Min	4	2	2	3	3	2	3				
	ILD	3	1	2	2	2	3	1				
	ILC	3	2	1	2	2	2	3				
	RTU	1	4	4	2	4	2	1				
Medium	Min	4	3	2	3	3	3	3				
	ILD	3	2	2	2	2	3	4				
	ILC	3	2	2	2	2	3	4				
	RTU	1	4	4	2	4	2	1				
High	Min	4	3	2	3	3	3	3				
	ILD	3	2	2	2	2	3	4				
	ILC	3	2	2	2	2	3	4				
	RTU	1	4	4	2	4	2	1				
Buffer Demand Level	A % of total cost	Process Step	Footprint & Storage	Strategy chosen	Assessment criteria	Direct raw material cost	Capex Investments	Labor & QC release cost	Footprint & Storage space	Availability & risks	Speed & delivery timeline	Recipe Flexibility
Low	30%	USP	10%	ILD	1. Importance weighting	1 (10% weight)	1 (20% weight)	3 (10% weight)	7 (20% weight)	2 (10% weight)	4 (10% weight)	3 (20% weight)
		DSP	60%	RTU	2. Importance weighting	1	4	4	4	4	4	3
		FFP	20%	RTU	3. Feasibility (initially)	1	4	4	4	4	4	3
		CSP	10%	RTU		1	4	4	4	4	4	3
Medium	30%	USP	10%	ILD	1. Importance weighting	2	2	3	4	2	3	1
		DSP	60%	ILD	2. Importance weighting	2	2	3	4	2	3	1
		FFP	20%	ILD	3. Feasibility (initially)	2	2	3	4	2	3	1
		CSP	10%	ILD		2	2	3	4	2	3	1
High	20%	USP	10%	ILD	1. Importance weighting	4	2	1	1	1	2	3
		DSP	60%	ILD	2. Importance weighting	4	2	1	1	1	1	2
		FFP	20%	ILD	3. Feasibility (initially)	4	2	1	1	1	1	2
		CSP	10%	ILD		4	2	1	1	1	1	2
		Total weighted score =										

Figure 1: Our Buffer Strategy Assessment Tool features a structured evaluation framework and a digital calculation sheet for analysis and decision-making.

THE ASSESSMENT TOOL FOR HYBRID BUFFER PREPARATION STRATEGY

The challenge for facility and operations leaders lies in selecting the right combination of strategies to meet fluctuating demand while balancing cost, footprint, labor and speed. To support the decision-making process, we have developed a Hybrid Buffer Strategy Assessment Tool designed to guide teams in evaluating which buffer preparation approaches may be most suitable for their operational goals (Figure 1). This tool introduces a structured, multi-criteria evaluation method that helps facilities assess potential hybrid strategies based on production volumes, process steps and site-specific priorities. Rather than focusing on a single variable such as cost or volume, this tool takes a broader view—enabling users to consider multiple decision factors simultaneously, including direct costs, footprint, speed and flexibility.

As an example, a hypothetical facility is evaluating three hybrid buffer preparation scenarios based on buffer demand scale and operational priorities, with Footprint & Storage ranked as the most important criterion and Flexibility as the least. The total buffer demand includes a mix of low volumes (10%), and

medium to high volumes (90%). Each scenario assumes a different buffer strategy approach across the different buffer demand segments.

The assessment tool calculated weighted scores for each scenario:

- **Scenario 1** (all MIH): Baseline, lowest score.
- **Scenario 2** (RTU for low volumes + MIH for medium and high volumes): +4.9% improvement by offloading small-volume preparation. This modest score improvement reflects the 10% of low volume buffer demand.
- **Scenario 3** (RTU for low volumes + ILI for medium volumes + ILC for high volumes): +53.4% improvement, showing the highest favorability by introducing efficient preparation technologies where impact is greatest (90% of buffer demand).

This analysis illustrates how hybrid strategies can significantly improve operational performance by aligning buffer preparation methods with demand levels and facility constraints. This represents a step toward more data-driven and strategic buffer management planning in biopharmaceutical operations.

As biomanufacturing becomes more dynamic and diverse, buffer preparation strategies must evolve accordingly. The Hybrid Buffer Strategy Tool described here and other quantitative, structured assessment tools such as Total Cost of Ownership (TCO) models can be used to support critical investment decisions. In addition, periodic assessments to evaluate performance and efficiency can be extremely valuable particularly as facilities and priorities evolve.

We encourage manufacturers to use tools like Avantor's Hybrid Buffer Strategy Tool to support data-driven decision-making and drive operational efficiency. There's no better time to evaluate your buffer preparation approach and ensure it meets the evolving demands of today's biomanufacturing landscape.

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