A Guide to Biomanufacturing Facility & Site Design:

Optimize ROI via Purposeful Design

Introduction

The design and construction of Biomanufacturing MFG Facilities is a technical, complex and expensive endeavor that continues to evolve in response to innovations in equipment and manufacturing processes. At PTSI, we help clients navigate this process by expertly balancing technical needs, budgetary constraints, and timelines to ensure clients build facilities that meet the needs of today while planning for the growth of tomorrow.

Over the years, we've successfully worked with large, middle, and small biopharmaceutical clients in designing, constructing, operational readiness, and CQV of their biomanufacturing sites that meet their needs. This process starts with an understanding of the supply chain strategy, which balances internal manufacturing needs and outsourced contract development and manufacturing with trusted and reliable CDMO partners.

The key to successful execution of Biopharma MFG Facility Site design, construction, MFG operational readiness, and commissioning, qualification, and validation (CQV) projects is to understand our client's product process flow. This establishes the basis of design narrative, conceptual design drawings, project schedule, and budget which support our clients in gaining approval to proceed with the project. Our representatives shepherd our clients through the successful execution of their site projects per the plan, design, schedule, and budget.

This collaborative approach relies on a solid understanding of the dynamic regulatory landscape for the biopharma industry, combined with deep expertise in design, construction, CQV, process equipment, and raw materials partners. PTSI leverages over 20 years of engineering and biomanufacturing experience as client-side operations professional and another 15 years

The biopharma industry requires constant innovation to meet the growing demands of the world's health challenges. The push to be faster, more economical, have efficient quality systems, and produce safer therapeutics drives all aspects of our projects. With this, we have witnessed the expanded use of single-use technologies, modular cleanroom installations, outsourcing of raw materials (e.g., buffers, media, and purified (PUR)/water for injection (WFI) water), and contracted technical resources, all of which serve to optimize biomanufacturing efficiency.

Single-use technologies have changed the biopharma facility site design, decreased facility size and operational processes to deliver flexibility for facility planning and utilization strategies. Additionally, leveraging modular cleanroom components allows clients to expand capacity as needed with minimal downtime – rather than investing in space and equipment that may otherwise be under or over utilized. Finally, by leveraging outsourcing for non-critical bioprocessing steps such as manufacturing of raw materials (buffers, media, and PUR/ WFI water), clients have optimized their biopharma MFG facility site while realizing long-term strategic gains.

We believe that partnering with PTSI's experienced team allows our clients to be successful throughout the whole process not only for today but also for the future.

We've assembled this document as a collection of our learnings over the years – including several key discussion topics that are core to the successful execution of our client's projects.

Steven Sandoval: CEO/Operations Head
Pharmaceutical Technical Solutions Inc

Purpose & Scope

This report is intended to serve as a general guide for biopharma innovator and CDMO firms that are exploring new biopharma manufacturing facility site design, construction, CQV or retrofit projects. It is not intended to be comprehensive nor serve as a playbook of how to engage in manufacturing facility site design, construction, and CQV. For questions on topics that are not included in this guide, please contact us directly so that we may best serve you. PTSI can be contacted at ptsi@ptsi-ec.com or on our website: www.pharma-tech-solutions.com.

Key Concepts & Terms

Key concepts and terms used in this white paper include:

- **Biopharmaceutical:** A biologic-based therapeutic drug and includes biotechnology, gene therapy, viral vector, cell therapy, T Cell, CAR-T, mRNA, and vaccine industries
- **Bioprocessing/Biomanufacturing:** The methods and processes used to manufacture a biopharma drug
- **BOD:** Basis of Design
- **CapEx:** A one-time expenditure of funds, typically used to purchase capital equipment or construction facilities
- **CDMO:** Contract Development and Manufacturing Organization
- **CQV:** Commissioning, Qualification, and Validation
- **Continuous manufacturing:** Production of materials for 24/7
- **GMP:** Good Manufacturing Practices
- **MSAT:** Manufacturing Science and Technology
- **MFG:** Manufacturing
- **OpEx:** On-going/recurring operational expenditures typically associated with running operations.
- **ROM:** Rough Order of Magnitude

Trends in Bioprocessing Driving Facility Design

Several trends in bioprocessing have impacted the design, engineering, and construction of facilities used to manufacture biologics. Many of these trends have resulted in process improvements within biomanufacturing – resulting in changes in the way we think about biopharma manufacturing facility and site design, several of which include:

Increasing Titers

Improvements in bioprocessing technologies, processes, and raw materials have created substantial improvements in titers – resulting in improved batch performance. Due to the enhanced yields per batch, the demand for bigger facilities to house larger equipment or to accommodate larger processes has diminished over time. Consequently, the facilities that are being built today are incorporating more single-use process equipment with an integrated operations workflow reliant on strong partnerships with qualified suppliers that can provide pre-made and ready-to-use buffers, media, and PUR/WFI water.

Single-Use Technologies

It goes without saying that the pervasive adoption of single-use technologies has resulted in a net decrease in the demand for new stainless-steel biomanufacturing facilities. This has resulted in a reduction or elimination of traditional stainless-steel equipment typically required for each new facility.

Several key areas where single-use has replaced large stainless-steel systems:

- Bioreactors
- Downstream Processing
- Clean-in-place (CIP) Systems
- Large Buffer & Media Preparation Suites
- Clean Steam Generation/Distribution Systems
- PUR/WFI Water Production and Distribution Systems

The resulting switch to single-use has not only generated process efficiencies and faster speed to market, but clients also indicate that this switch has netted cost savings in the form of reduced workforce training and payroll costs, as well as CapEx and OpEx reductions.

Improved Partnerships with Critical Raw Material Suppliers

The biopharma industry (comprising both suppliers and manufacturers) has matured substantially in the past twenty years towards a greater understanding that critical raw material suppliers play an integral role in the manufacturing of therapeutics. For their part, suppliers have demonstrated a willingness to meet or exceed quality requirements established by biopharma companies in the manufacturing, processing, storage, and delivery of raw materials. While biomanufacturing remains a highly proprietary industry, biopharma manufacturers have seemingly increased their trust in and reliance on qualified supply chain partners to provide insights into manufacturing technologies and outsource non-core activities to help drive process efficiencies, time savings, and cost savings.

Consequently, biopharma manufacturers have increased their reliance on outsourcing of media, buffers, and/or PUR/WFI water to increase focus on core manufacturing and optimize facility efficiency.

It is important to note that while not all suppliers can provide these types of solutions (especially those who may be new to the market), there are many who understand the regulatory rigor that is required to meet the needs of biopharma companies and what that spotlight means for that company's suppliers. Those are the suppliers who are willing to adjust their business models to ensure that biopharma customers can be effective in their manufacturing and supply chain strategies.

Technological Innovation

Technological innovation is the leading driver in the development of efficient biomanufacturing facility and site design. Because each facility is designed around a process flow and production capacity unique to a particular biotherapeutic, the technology that is required for that specific biotherapeutic drives how facilities are designed and engineered. As a result, because the manufacturing of the technologies used in bioprocessing facilities continues to advance – so too does the design of the facility itself. Therefore, it is important to understand the technologies that will be deployed in each facility prior to the start of each project (referred to as the "Basis of Design").

Many of the technological innovations that have driven the evolution in facility design include:

- Improvements in the efficiency and reliability of single-use process equipment has resulted in smaller, more flexible facilities
- Introduction and adoption of modular cleanrooms has made it faster to construct facilities while allowing for faster product change over time
- Improved performance efficiencies of today's media and supplements have similarly resulted in smaller, more flexible facilities.

Inflationary Costs of Construction

One important reality (rather than a trend) that is driving biomanufacturing facility design and construction is that costs rise over time due to inflation. The International Monetary Fund (IMF) defines inflation as the "increase of prices for a basket of goods over time" [(1)]. The costs of construction is considered a specific basket of goods that is subject to inflationary pressure over time.

According to the US Federal Reserve Bank [(2)], the rate of inflation is provided as an index that measures the rise in the price of goods and services over time – this index is called the Consumer Price Index (CPI). Using the Fed's Inflation Calculator, we can measure how far a dollar spent in the past will stretch to equal today's dollar. By setting 2009 as the base year and 2025 as the current year, CPI increased from 100 to 146.57. What this means is that a $10 million facility construction project in 2009 will cost us $14.657 million to construct in 2025. However, inflation is measured across various industries. This measure from the US Federal Reserve Bank is used to demonstrate the general inflation conditions in the US Economy and may not serve as the best index for specialty biopharma facility manufacturing, nor are we sure if one truly exists. Consequently, the closest approximation of inflationary pressure within the construction industry may well be the Mortensen Construction Cost Index (MCCI).

The MCCI is an index that tracks the costs of non-residential construction projects across the US and in several key geographical markets. According to the MCCI, the national average for non-residential construction costs in 2024 is 186 – compared to 100 in its baseline year of 2009. According to this index, a $10 million facility built in 2009 would cost $18.6 million to construct in 2024.

What these two indices tell us is that purchasing power continues to erode over time – the question is to what degree does that affect the cost to construct biopharma manufacturing facilities? Given the specialty nature of the markets we serve, we believe that the costs to construct facilities today have outpaced inflation and are more closely approximated by the MCCI.

Knowing that costs will continue to rise (even as design is progressing), it is important to be programmatically mindful of facility needs today – meaning, what do you absolutely need vs. what can you outsource or do differently? The reality is that cost is a big driver of how facilities are being designed today.

References:

1 https://www.imf.org/en/Publications/fandd/issues/Series/Back-to-Basics/Inflation

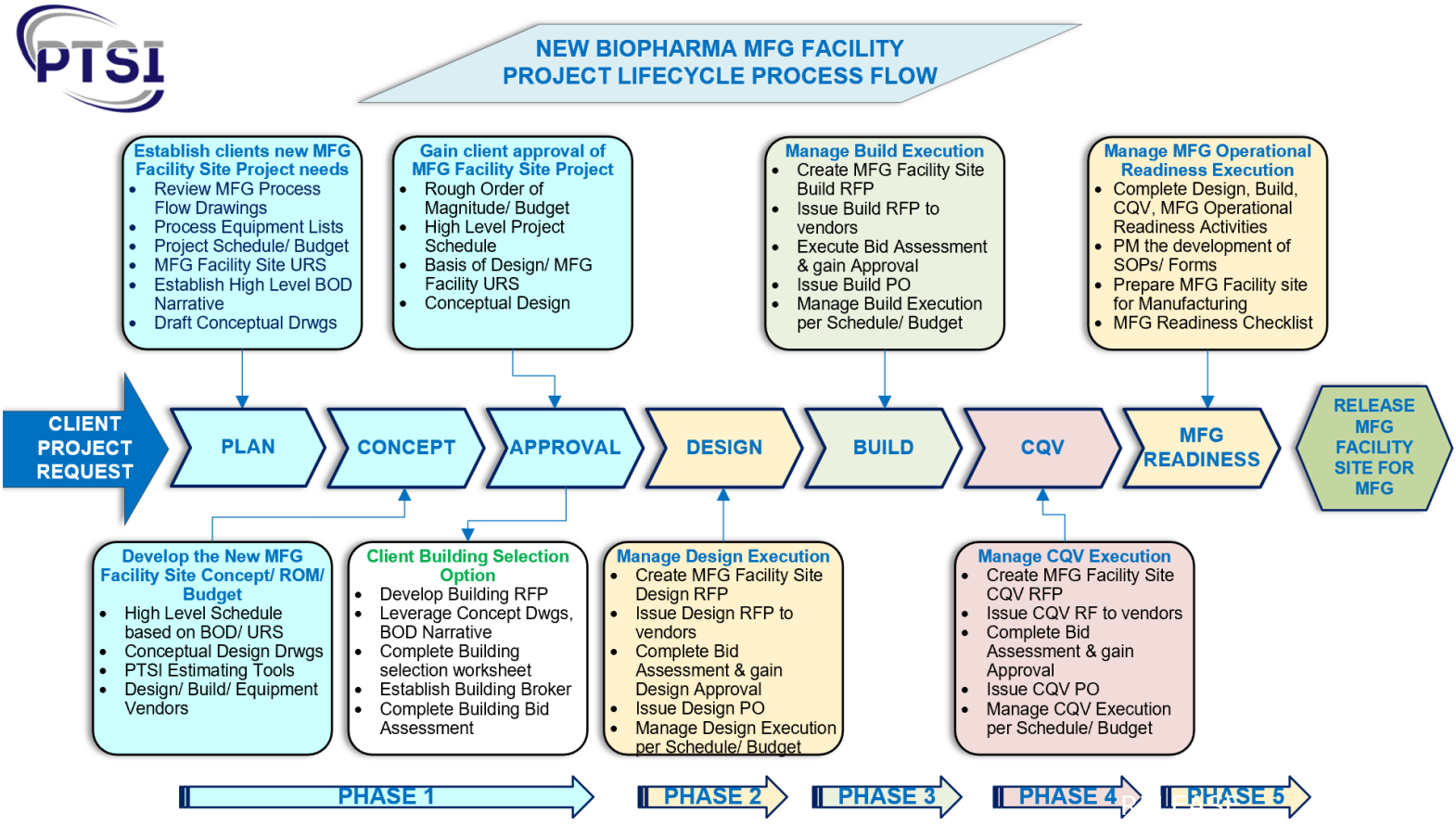
2 https://www.minneapolisfed.org/about-us/monetary-policy/inflation-calculator

Our Approach to Facility Design

PTSI works with biopharma drug innovators and CDMOs in defining requirements that support the design of new biomanufacturing facilities and sites. Facility planning requires a long-term view that balances programming needs, cost, timelines, materials, regulatory requirements, and labor – not only for today but well into the future. By taking a forward-looking approach to facility design, we advise clients on how to program the space they have to deliver operational efficiencies that optimize workflows. This approach includes a discussion of what to include as well as what not to include in the design of facilities.

Below is the approach we use to design and construct biomanufacturing facilities and sites.

New Biopharma MFG Facility Project Lifecycle Process Flow



* **Basis of Design (BOD) :** A document that outlines the project needs, assumptions and any inputs or considerations required to assist in the decision-making related to design.

Planning Phase

Planning is the first step in facility design and construction. It outlines the scope of work and other critical inputs and parameters that are necessary to guide the design process. Several key discussion topics covered in the planning phase include those highlighted below.

Project Scope

Scoping the project includes establishing a baseline of the project parameters, critical milestones, key inputs and drivers as well as any limitations that may affect the overall project. Several key questions to ask include:

- What is the purpose of the facility?
- What key functions will it house?
- What is the approximate square footage of the facility?
- How many people will it accommodate in each key functional area?
- What is the target date for design completion?
- What is the target date for start of construction?
- What is the target date for end of construction?
- What dates are immovable?
- What is the preliminary rough-order-magnitude (preliminary ROM) budget for the project (design, construction, facility readiness, equipment, fixtures & equipment, etc.)?

Programmatic Needs & Conceptual Design

Once the framework of the project has been established during the scoping exercise, a deeper discussion around the programmatic needs of the facility can begin. The programmatic discussion revolves around process flow, process equipment and early conceptual layouts. Several key questions to ask include:

- What is the process flow?
  - Product manufacturing
  - Finish/filling
  - Incoming raw materials
  - In-process goods
  - Finished goods inventory/warehousing
  - Outgoing shipments
- What is the equipment/system list?
- What should the conceptual layout look like?
- What is the preliminary BOD?

Site & Facility Selection Criteria

An important part of the planning process is understanding the criteria for site and facility selection. Several key actions and considerations include:

- Verify the clients' design requirements (Greenfield/Brownfield)
- Clarify if the site will be purchased or leased
- Clarify if the facility will be purchased or leased

- Leverage building owner and broker network in potential site selection options
- Negotiate with building owner on establishing a Tenant Improvement (TI) allowance that will impact CapEx strategy
- Discuss CDMO options that support Tech Transfer Process

Design Phase

The design phase of the project includes a detailed discussion of site layout, facility options, budgets, timelines and other execution specific considerations. Several key outputs of this phase include:

- A project ROM budget, based off the preliminary BOD
- A high-level schedule, based off the BOD
- Start engaging with vendors to validate the ROM by getting quotes for equipment, design, construction
- Establish a total ROM based off the conceptual design that includes manufacturing facility design, construction, CQV, and operational readiness

Construction Phase

This phase includes the construction of the facility in accordance to design, budget and schedules. Several key activities include:

- Write and finalize the construction RFP
- Issue to a minimum of three PTSI approved general contractors
- Assess the bids in response to the construction RFP and present it to client for approval
- Manage the construction contract negotiations
- Award the construction contract/PO to the vendor
- Manage the execution of the construction phase of the project
- Serve as primary point of contact with the general contractor and serve as project manager

Commissioning, Qualification & Validation (CQV) Phase

CQV is a critical step in the biopharma manufacturing facility construction process – focused on ensuring that the facilities, systems, and equipment will deliver high quality products. Key steps include:

- Develop the project's commissioning plan and obtain client approval
- Receive and verify the turnover packages from the general contractor
- Execute commissioning activities in accordance with the commissioning plan
- Develop validation RFP and issue to minimum of 3 PTSI approved vendors
- Assess the bids in response to the validation RFP and present bid assessment to the client for approval
- Manage the validation contract negotiations
- Award the validation contract/PO to the vendor
- Manage the execution of the validation phase of the project
- Serve as primary point of contact with the validation vendor and serve as project manager

Operational Readiness

After construction is complete, facilities must undergo a process known as "Operational Readiness." This step ensures that the first run for the facility is ready for the successful operational execution of the processes that it is intended to support.

At PTSI, we have established the following Operational Readiness Activities to support each project:

- **MSAT-Tech Transfer Readiness Activities**
  Including SOPs, process & support equipment systems list, batch records, sampling plans, bill of materials, process flow diagrams, critical process parameters
- **Supply Chain/GMP Warehouse Readiness Activities**
  Including establishing GMP warehouse SOPs/forms, raw materials, gowns and consumables, establishing supplier quality management SOPs
- **Quality Readiness Activities**
  Including quality manuals, Quality Management System (QMS) SOPs, site master file, risk-based business continuity plan, Electronic Document Management Database (EDMS)
- **Resource Plan**
  Including hiring, training and safety plans
- **Engineering Facility Readiness Activities**
  Including RCM program (PM, calibration, HEPA certification), CMMS equipment-system integration, EH & Safety plan, pest control, cleanroom final testing/ balancing and certification, IT systems (BMS, EMS, CMMS, ERP, ELN)
- **CQV Readiness Activities**
  Including commissioning plan (Equipment, Utilities, Facilities), substantial completion (floors, walls, ceilings, utilities), validation plan (cleanrooms, equipment and utilities), facility, labs, warehouse, and support areas
- **QC Lab Readiness Activities**
  Including lab equipment/system list, SOPs and ELN/LIMS, equipment/system method validation, sample management

Key Considerations in Biomanufacturing Facility & Site Design

Even before PTSI was established, our experts assisted in the design and qualification of large complex facilities for some of the world's largest biopharmaceutical companies all around the world. In the last 15 years, PTSI has assisted our clients on a variety of projects (large and small, new construction and retrofit). In this time, we've leveraged our expertise to help guide our clients to construct the best facility for their needs at a price they can afford.

In our role as advisors, several recurring themes emerged as we helped our clients navigate the technical and regulatory complexities associated with biomanufacturing facility and site design and construction.

This section highlights several of those key themes as lessons learned and includes the following:

- Design & manufacturing costs often exceed budgets
- Clients can reduce costs by eliminating media & buffer manufacturing suites
- A smooth process relies on the use of best practices

Key Consideration 1:

Controlling Costs

A central topic of discussion with each client is cost. Many clients are surprised to learn the all-in costs associated with building, furnishing, fitting, and validating facilities for operational readiness.

In our process, we seek to outline expectations early and quickly align on budgets, priorities, needs and wants. This includes an understanding of what it takes to get to "Operational Readiness." In our experience, the "Operational Readiness Costs" represent approximately 20-25% of the "Total Costs" of a project. Below is a table of projects completed in the past two years and the Construction Costs, Total Costs, and Operational Readiness Costs:

Table 1 | Construction Costs vs. Total Costs (Inc Operational Readiness)

Project	**Construction Costs** (M USD)	**Total Costs** (M USD)	**Operational Readiness Costs** (% of Total)
1	$ 4.65	$ 5.60	17%
2	$ 4.19	$ 5.20	19%
3	$ 5.37	$ 6.32	15%
4	$ 7.05	$ 8.54	49%
5	$ 14.98	$ 18.12	17%

"Construction Costs" defined as the cost to construct the facility

"Total Costs" defined as costs plus contingencies

"Operational Readiness Costs" defined as the costs to complete CQV, Supply Chain/Tech Transfer, CMMS, SOPs, MFG, Training and Staffing

For all projects, we recommend allocating 20-25% of the "Total Costs" towards Operational Readiness.

Key Consideration 2:

Eliminating PUR, WFI, Media & Buffer Prep Suites

While water systems such as PUR or WFI and buffer & media preparation suites are critical to the operations of biomanufacturing facilities, they are non-essential support activities that do not need to be physically located within the biomanufacturing facility or site footprint (essential activities include manufacturing Drug Substance (i.e., cell culture, separation, purification) and Drug Product (i.e., formulation, filling, inspection, packaging). Process liquid manufacturing activities (along with bulk water) can easily be outsourced to a qualified strategic supplier that has the capabilities to manufacture and deliver water, buffers, and media solutions ready-to-use.

PTSI advises clients to think critically about what aspects of their biomanufacturing facilities need to be designed within the footprint of their site. Outsourcing the manufacturing of buffers and media to a qualified supplier reduces a significant amount of one-time CapEx and ongoing OpEx – including accepting PUR or WFI water systems needed to support biomanufacturing.

Saving one-time CapEx

Our analysis indicates that clients can save on average 17% of their total Construction Costs if they eliminate onsite buffer and media preparation suites. The table below outlines the one-time cost savings that can be gained by eliminating the construction of media and buffer

Project	**Design/Construction Costs** (M USD)	**Cost of Media/Buffer Prep Suite** (M USD)	**Total Construction Costs** (M USD)
1	$ 3.88	$ 0.78	$ 4.66
2	$ 3.40	$ 0.79	$ 4.19
3	$ 4.47	$ 0.89	$ 5.37
4	$ 5.87	$ 1.18	$ 7.05
5	$ 12.48	$ 2.50	$ 14.98

Table 2 | Buffer & Media Preparation Suites CapEx

These cost savings are realized through the elimination or reduction of the following:

- Mixing equipment
- Water processing equipment such as WFI or Purified Water systems
- Large facility footprint
- Expensive air handling equipment and ductwork

By partnering with a reliable outsourcing partner, clients can avoid significant capital investments required to install and maintain additional WFI systems, skids, storage tanks, buffer filtration setups and other associated cleanroom infrastructure. These systems often become either bottlenecks or underutilized assets, depending on project flow, tying up capital and introducing unnecessary risk.

One-time cost savings also result in on-going operational savings.

Saving on-going OpEx

The on-going operational savings from reducing/eliminating buffer and media preparation suites as well as water systems results in a reduction in labor, utilities, training, testing, and compliance expenses that would have otherwise been required to support these suites.

Improved operational efficiency

The handling of buffer and media prep in-house consumes valuable team bandwidth and facility space for a non-revenue generating function. It increases maintenance, cleaning, and changeover requirements – all of which reduce operational efficiency. Outsourcing allows clients to redeploy staff and floor space toward higher value manufacturing activities, improving clients' dollar per square foot output and maximizing revenue potential.

Strategic benefits

Reducing or eliminating buffer and media preparation suites by outsourcing with a qualified supplier partner results in both tangible and intangible gains. While financial benefits are immediately apparent, the strategic benefits may outweigh the savings of today. By utilizing a mixed-operational strategy that balances outsourcing with in-house manufacturing, clients can remain flexible in response to changing business and economic concerns. This flexibility in growing, changing, and downsizing as needs change can sometimes prove to be invaluable.

One of the most common misconceptions around in-house solution prep is the true total cost of ownership. When factoring in labor, overhead, facility maintenance, procurement, supplier qualification and underutilized space – outsourcing often proves to be the more cost-effective and agile solution as it provides flexibility without long-term resource-intensive commitments.

Key Consideration 3:

Leveraging Best Practices

We encourage our clients to consider several of the following best practices aligned with industry best practices and regulatory standards that are worth noting:

Downgrade cleanroom classifications where appropriate

Clients will sometimes request Grade B cleanroom space when Grade C cleanroom space is sufficient to meet their quality needs and is aligned with industry standards (EU, FDA and ICH Guidelines). This reduction in classification saves money by reducing the requirements for HVAC and other cleanroom systems and equipment that may not be necessary to perform the tasks in that room.

Reduce size of classified space

Where feasible, evaluate whether it makes sense to reduce the footprint of the classified space and increase the size of support areas. This ensures that clients are building efficient facilities that are engineered to meet the operational demands of their workflows.

Get creative on HVAC design

At times a new replacement HVAC system may not be necessary. It is important to evaluate the best ways to provide air handling support with existing systems without sacrificing air quality and compliance specifications (i.e., air exchange, 100% fresh air to 80% recycled air).

Design efficient viral containment design

By designing facilities leveraging industry standards for viral containment pressure design, we design facilities that can accommodate multiproduct processes. This approach reduces cost, shrinks facility and site footprint requirements, and allows for enhanced operational flexibility.

Partner with general contractor & design firm to optimize design

PTSI client representatives control project costs through design, construction, CQV, and operational readiness activities. We challenge project costs throughout the lifecycle of the project and provide monthly project commitment and cashflow budget updates.

As an example, we were working on a client project where bids were coming in $8-12 million over the client's budget of $64 million. We worked with our general contractors to review materials, processes, and long-lead items that were affecting the project costs. We brought in some local general contractors and let the vendors know that they had a second opportunity to bid on the project. As a result we were able to bring the construction costs back within the project budget.

Conclusion

The most important advice that we share with our clients is to think strategically about utilizing classified space to get as much ROI as possible. This may mean that in order to maximize limited facility and site footprints, clients should remain open about evaluating strategic partnerships that fill operational needs, while minimizing incremental fixed CapEx and reducing recurring OpEx.

Selecting a Qualified Buffer, Media, and PUR/WFI Water Supplier

The on-site manufacturing and preparation of buffers and media (as well as other process solutions) is a time, resource, and space intensive activity that we recommend outsourcing due to the associated high OpEx and CapEx costs. These process steps not only require the staff and working knowledge that goes with human resources, but it requires expensive and space-consuming high-purity water systems such as purified water or water for injection that adds to the complexity of performing these tasks onsite. Outsourcing allows clients to better leverage current and future manufacturing capacity – without the burden of heavy fixed investment, while maintaining the responsiveness that is needed to support manufacturing demands. This section provides information on how to select a strategic partner to meet clients' operational needs.

How to Select a Strategic Partner

There are many large and small buffer and media providers that can successfully manufacture upstream and downstream solutions, while also providing ongoing logistics and warehousing support. These vendors are willing to work with biopharma manufacturers to ensure that the operational solution they design works for each client's needs. Below are the criteria that we've assembled for our clients to evaluate and find qualified vendors to meet their specific needs.

	Criteria	Description
1	Quality Management & Audit Performance	A qualified vendor must conform to ISO 13485 and have dedicated Class 7 cleanroom space. This ensures that vendors understand the quality rigor that will be required to perform according to the needs of biopharma customers.
2	Stability Studies	The ability to conduct stability studies on-site to ensure materials conform to the needs of the customers.
3	Segregated Animal-Origin Free and Animal Origin manufacturing	The ability to provide segregated manufacturing for solutions that are animal-origin free and manufacturing for potential solutions (e.g., media) that contain animal-origin components.
4	Tech Transfer	A repeatable and validated process for conducting tech transfer.
5	Collaborative	A willingness to work together to find cost-effective solutions that maintain the quality of the process and the product, such as BOM, lot sizes, manufacturing strategies and service level agreements.
6	Transparency	Willingness to conduct periodic (typically quarterly) business reviews to engage in forecasting discussions and/or to review issues to ensure supply chain continuity and stability.
7	Ability to Scale	The ability to scale small to mid-size projects to large-scale commercial production.
8	Project Management	A key measure of success for outsourcing partners is when they have a robust project management system to manage the needs of its various outsourced projects and any changes/modifications that those clients may request over time.
9	Escalation & Leadership	Outsourced vendors should provide their customers with an escalation plan when things go wrong and ensure that leadership is aware and on board with this plan.

Our Approach to Vendor Qualification

We utilize the following four pillars of supplier quality when qualifying new vendors:

- Regulatory Compliance
- Flexibility
- Reliability
- Customer Responsiveness

Regulatory Compliance is a non-negotiable standard for the vendors that we evaluate. We look not just at compliance but also at the creativeness with which this is achieved. With ever expanding growth in this sector, having an organization that not only understands regulations but also how to create a system to ensure that new processes can withstand regulatory scrutiny based on customer needs is crucial. Being able to understand customer needs and subsequently meeting those needs in a creative and compliant manner is necessary for the vendors that we work with.

Flexibility in meeting the needs of our clients is another requirement that we seek in our suppliers. As the biopharma industry continues to evolve and grow quickly, so must the supplier partners that seek to serve this industry. This flexibility should come in the form of customization and creativity that meets the needs of our clients.

Reliability is a crucial vendor qualification for a biopharma supplier. That supplier must consistently meet sourcing demands to avoid disruptions in the manufacturing and supply chain of life-saving therapeutics.

Customer Responsiveness is the final pillar that we use to evaluate our supplier partners. This responsiveness centers on the supplier's ability to provide comprehensive support when questions arise about materials used in the manufacturing processes.

Preferred Media & Buffer Supplier: GeminiBio®

Our preferred and qualified media and buffer supplier partner is **GeminiBio**. GeminiBio has successfully completed the vendor qualification process at PTSI and has proven to meet critical regulatory compliance standards, as well as meet key business and service requirements to give biologics manufacturers confidence when outsourcing their media and buffer prep.

Founded in 1985, GeminiBio has two manufacturing facilities in West Sacramento, California. The company has a 25,000 square foot facility that is dedicated to **Animal Origin Free (AOF)** upstream and downstream media and buffer manufacturing, as well as a 32,000 square foot facility that includes a cGMP warehouse and classified manufacturing suites for **Animal Origin (AO)** products. Both facilities are cGMP, and the company is ISO 13485:2016 certified and an FDA registered Class 1 Medical Device manufacturer.

We are particularly impressed with GeminiBio's manufacturing scalability and how the company's capabilities can help clients confidently increase their biologic manufacturing without exceeding GeminiBio's media and buffer prep capacity. In the context of AOF solutions, GeminiBio's facility includes a range of ISO 7 processing suites, including suites with 500-liter and 1,000-liter single use mixing vessels, and classified manufacturing space with 5,000-liter and 10,000-liter stainless-steel mixing vessels. With this wide diversity of AOF formulation capabilities, GeminiBio can provide customers with cGMP batch sizes spanning from 10-liters to 10,000-liters. Further, the company can fill aseptically into diverse containment types (rigid and flexible) and sizes (500 mL bottles to 1,000-liter pallet tanks). From the perspective of AO manufacturing, the company has segregated ISO 7 processing suites for Xeno Free (XF) and for AO products.

As noted above, GeminiBio's range of bioprocess liquid batch sizes allow the company to support the unique process liquid demands of a wide variety of biologic manufacturers, including:

- Large-scale monoclonal antibody (mAb) and plasmid DNA manufacturers;
- Small to mid-size batch requirements of AAV and LVV viral vector manufacturers; and
- Small batch size requirements, including both AOF and AO solutions, of Cell Therapy manufacturers.

Besides the AOF and AO process liquid manufacturing capabilities, the company has extensive cGMP warehousing capabilities, including temperature mapped and validated storage conditions at -20C, 2-8C, and controlled room temperature (CRT). Further, GeminiBio has validated processes related to both the movement and segregation of AOF and AO raw materials and finished goods.

Ultimately, we believe that GeminiBio has the capabilities, quality system, and customer service orientation to support biologic manufacturers. Outsourcing with a company like GeminiBio will allow biopharma companies to focus on their core manufacturing, while minimizing CapEx, OpEx, and oversight requirements associated with the ongoing management of on-site media and buffer preparation.

About PTSI

Pharmaceutical Technical Solutions Inc (PTSI) has been providing technical oversight and client representative support to biopharmaceutical and cell/gene therapy industries since 2010.

We leverage our extensive biopharma experience, the latest industry guidelines and established regulations to provide quality solutions to our clients' complex challenges.

PTSI professionals average over 15 years as 'the client.' This means that our professionals have worked in operational roles within biomanufacturing before joining PTSI. We use this insider knowledge to anticipate our clients' needs and provide innovative solutions. Our mission is to be the best in providing high quality, compliant, and proven biopharma solutions.

Our commitment to excellence, work ethic, and drive supports the achievement of our clients' objectives. Our high performance and results have consistently generated client confidence in the US and internationally for over 15 years.

The biopharma industry is highly competitive, costly, and ever-changing. Companies rely heavily on consultants for expertise and hands-on execution in all aspects of the business. Unfortunately, inexperienced consultants can negatively impact a client's business. PTSI has a vast array of in-depth knowledge and experience across all competencies:

- Conceptual Design & Engineering Expertise
- Construction Management & Oversight
- Quality Control Operational Readiness
- Quality Assurance Expertise
- Tech Transfer & Process Development
- Regulatory & Compliance Support
- Manufacturing Operational Readiness
- Reliability Centered Maintenance Program (CMMS)
- Supply Chain Strategy

PTSI works closely with biopharma companies to assist them in developing their biomanufacturing facility and site design, high level schedule, and budget. We specialize in providing experienced engineering, MFG, RCM, process development, quality control, project management, quality assurance, regulatory, and subject matter experts to support our clients. We seek to better understand not only the needs of our clients today but their needs for tomorrow.

Biomanufacturing facility and site planning should take a long-term view, balancing programming needs, cost, materials, labor, and regulatory requirements. We work with our clients in establishing their long-term supply chain strategy (e.g., clinical product development (IND/BLA), clinical/ commercial manufacturing facility and site design, construction, and CQV, utilization of CDMO partners). Taking a forward-looking approach to facility and site design, we advise clients on how best to program the space they have to deliver operational efficiencies that optimize workflows – but also on what to include (and often most importantly, what not to include) in the design of their biomanufacturing facilities.

Our strategic focus is on optimizing the biomanufacturing facility and site footprint within a set budget to meet all the programmatic needs of the client. Inevitably, all projects run into the challenge of not having the budget to support all the needs of the site. We work with clients to prioritize critical manufacturing needs within the biomanufacturing facility and site design and construction phases to ensure that core scientific IP and critical biomanufacturing functions are controlled and maintained by the client.

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