A publication of
The Williamsburg BioProcessing Foundation

November/December 2004

BioProcessing™ JOURNAL

Advances & Trends In Biological Product Development

Vol. 3 No. 6

www.bioprocessingjournal.com

A Project Approach for the Design, Construction, and Validation of Multi-Functional, Multi-Product, Pilot-Scale Biopharmaceutical Facilities

By ROSHNI DUTTON and GEOFF SHEFFRIN

It has been reported that the biotechnology-derived medicines area of the pharmaceutical industry led to 133 marketed entities with sales of $22 billion by the year 2001.[1] By 2002, the therapeutic protein market had reached $32 billion, with biologics representing more than 50 percent of all drugs approved by FDA — up from a modest 16 percent in 1995.[2] The biopharmaceutical market is predicted to grow to $50 billion by 2008.[1] Currently, approximately 40 percent of biopharmaceutical products are in Phase I and Phase II clinical trials.[2] It is anticipated that from 2003 to 2008 there will be a more than 45-fold increase in demand for access to product development facilities capable of supplying clinical material.[3]

While still modest by comparison to the total pharmaceutical market of $430 billion in 2002, the biopharmaceutical sector is growing more than twice as fast as that of traditional pharmaceuticals and the accelerating growth of the biopharmaceutical market is straining the capacity of the industry to respond.[2] Globally, large-scale capacity is actively being added, both internally and by contract manufacturing organizations (CMOs). With approximately 300 percent additional large-scale capacity scheduled to come on line, it is anticipated that commercial needs will be met through 2008.[2] However, whether in-house or outsourced, clearly there is an impending need for additional multi-functional, multi-product, pilot-scale development facilities.

A biopharmaceutical facility of any reasonable size can take three to five years, or even longer, to deliver from concept to the point of fully validated functionality. The complexity and risk of a timely delivery is compounded when the facility must be designed to accommodate multiple products, multiple processes (that are normally yet to be defined), parallel product processing, and campaigning. Such is often the case for a development facility.

With more than a decade of established growth, biotechnology still brings with it the excitement of new, leading-edge discovery and execution. However, just because the field has so much that is new does not mean that that the process of creating and delivering a large-scale validated development facility needs totally new and innovative techniques. Our experience has shown that the right combination of tried and tested approaches with some new twists on how things are done can give very effective results. Speed to market with a safe and efficacious drug is always the critical success factor with any new pharmaceutical entity. When considering new and innovative properties, it is the "yet to be defined" factors that can cause considerable and sometimes unnecessary delay, particularly at the development phase. These unknown factors have a direct impact on the facility project plan, the scope, and the execution.

All projects of any scale start with a very basic project management concept — Do you want it good, fast, or cheap? Pick two out of three. In pharmaceuticals one requirement is a given: This is a highly structured and regulated industry, so good is the only option and a must in any pharmaceutical project. So, do you want it fast or cheap? You cannot have both.

Currently, we are involved in the design, construction, and validation of an Aventis Pasteur 42,000-square-foot, multi-functional, multi-product, pilot-scale viral vaccine development facility, which features both parallel product processing and product campaigning capabilities.[4] First conceptualized in 1999, concept design for this facility began in July 2000 and we are currently in the middle of validation with anticipated completion by December 2004. During this project, we have learned a number of valuable lessons (Table 1), and have taken the opportunity to refine our process methodology.

What follows, based on our experience on several projects, including the Aventis Pasteur project, is the descrip-

Roshni Dutton, Ph.D. *(roshni.dutton@simpatico.ca) is president, BioProcess Assist, Ontario, Canada; Geoff Sheffrin, P.Eng., C.Eng. is principal, OBK Technology, Ontario, Canada.*

tion of a process methodology that walks the fine line between the quickest (functionally compliant) delivery date and the most cost-effective achievement of the validated end result for a multi-functional, multi-product, pilot-scale biopharmaceutical development facility.

The Project Team

Before the project can begin, a project team must be assembled. A good project team is of the utmost importance to the success of the project. While it is not necessary to assemble an entire team immediately, it is critical that the core members are assigned and dedicate 100 percent of their time throughout the life of the project. For larger projects, we have found that a core team of only three individuals works well:

Owner's Project Team Core Members:

- Project leader/design-Process owner
- Project manager
- Project engineering manager

This trio is complemented by a diverse group of skills and experience, namely:

External Team Members:

- Architectural
- Contract general manager (GM)
- Facilities engineering (mechanical, electrical, structural, process)

Additional internal team members on an "as needed" basis:

- Users/owners
- Quality assurance (QA)
- Regulatory assurance (RA)
- Finance and accounting
- Operations and maintenance

The first essential of a successful project is to have a "process owner." This person knows all the technical needs and requirements of the entity from start to finish. They are senior enough and have the authority to be able to make decisions, yet junior enough to be the hands-on knowledgeable expert. This person is the hub of the project from start to finish. This individual is the keeper of the concept and a focal point for all issues, discussions, alternatives, and decisions from above and below, both internal and external. It is their responsibility to keep the project on track with respect to scope, user requirements, and functionality. This individual should be the designated authority on all decisions.

The project manager controls the administrative functions of budgeting and scheduling for the overall project. This individual is the troubleshooter and prod to keep the project on time and on budget. The project manager is responsible for allocating resources and coordinating interactions of the extended project team.

The project engineering manager is responsible for coordinating the design, procurement, construction, and installation and commissioning activities. This individual interfaces with all internal and external parties, including construction trades and vendors. The project engineering manager acts as a partner with the architect and construction general manager. We do not advocate the project engineering manager acting as the project's construction general manager for any project of significant scale.

The external team members should also be dedicated to the project, but are not required for 100 percent of the project life or 100 percent of their time. These people must be identified and put in place early enough to blend in smoothly with the project schedule. In choosing these individuals, from sole sourcing or through open requests for proposals (RFPs), the most important criterion is quality-based selection. Only a team of knowledgeable and experienced individuals can bring about a timely, cost-effective, and high quality project outcome.

As with the external team members, specific individuals should be assigned as members of the internal team, available on an as-needed basis. These individuals are also not required for 100 percent of the project life or 100 percent of their time.

None of the above is new, but is a vital reconfirmation of what must be (and often is not) in place for success.

Table 1. Project Chronology Summary (lessons learned)
Successfully delivering a biopharmaceutical facility, from concept through construction to validation, depends on good planning for the project process, the budget, and the design. A strong knowledgeable dedicated internal core team and extended design and construction team are critical.

- Good, fast or cheap? Good is a given, so, pick two out of three.
- Select the process owner and project core team.
- Use the three-step approach for the project plan (concept, preliminary, and full scope engineering) and the budget.
- Start with concept engineering — get input from everyone and then get input from everyone again.
- Create a concept budget and time (limit).
- Create a user requirement specification.
- Use concurrent activity planning to define the validated end-point.
- Select the engineering and architectural partners — use quality-based selection.
- Start preliminary engineering.
- Create a preliminary budget.
- Full-scope project engineering.
- Create a project implementation plan and define a process control program.
- Design qualification — seek input from regulatory bodies.
- Lock in the design.
- Select the construction and commissioning contractor partner (and any other major contracted service providers) — use quality based selection.
- Final budget.
- Create the detail design specification.
- Break ground — start the construction process.
- Create the various functional requirement specifications.
- Fully plan the validation requirements.
- Lock in the compliance standard.
- Assemble documentation as construction proceeds.
- Start IQ execution as soon as commissioning starts.
- Start OQ execution as soon as commissioning ends.
- Deliver PQ execution effectively and early.
- Celebrate the success.

The Project Stages

The traditional approach to project delivery is through a sequence of distinct steps. These are: project approval, preliminary design, budget, detail design, bid and tender, build, commission, and validation. The project approval step usually implies an approved budget. This in the absence of the conceptual design or the preliminary engineering, usually presents the first major hurdle — an inadequately defined budget created when the scope was not well known will haunt the project to its conclusion. The critical aspect of a successful, efficient process is to shrink this traditional sequential project delivery approach while managing the risk. The key to efficient project delivery is to divide the project into a set of distinct deliverables that are set to an overlapping, concurrent schedule (Fig. 1):

- Conceptual design
- Preliminary or functional design
- Detailed design
- Design qualification
- Project implementation plan
- Construction
- Installation and commissioning
- Validation

The first five deliverables can be lumped together as the planning portion of the project, while the last three deliverables are the project execution. The old saying "measure twice, cut once" applies: Take the time up front to get it right and thus ensure a smooth and efficient project execution. Dollars spent during the planning stages can be the most cost effective monies spent on a project if they clearly define project expectations and the project scope and returning costs.

As depicted in Figure 2, an adaptation of the validation V Model can be applied to the planning portion of the project.[5] An iterative, back-and-forth approach can be taken throughout the planning portion of the project. As the project progresses through this stage, the number of control and information documents increases, as do the deterrents to change.

To deliver the project cost-effectively and in a timely manner, the detail invested at the start of the process is critical in making the best use of financial and team resources. The key to success is "concurrent activity." Concurrent activ-

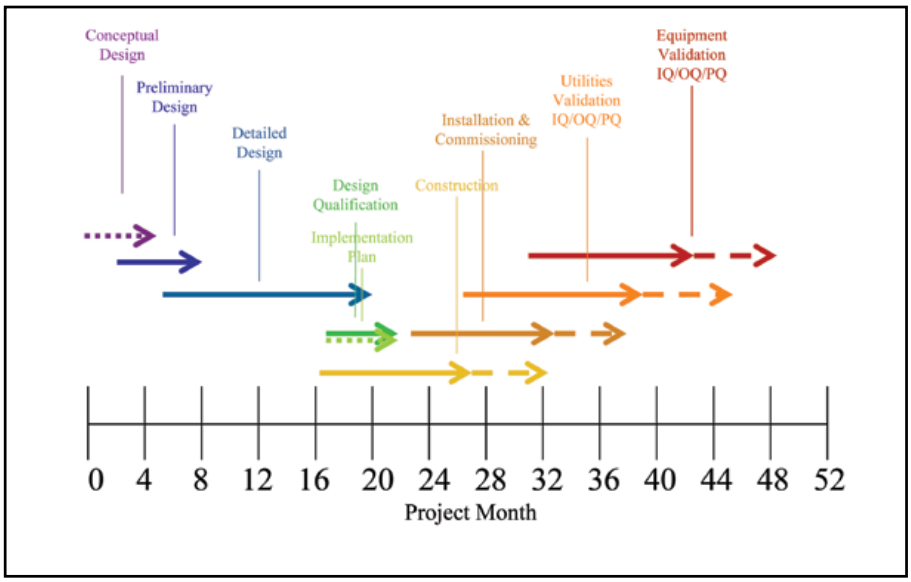

Figure 1. Overlapping and Concurrent Schedule for Facility Design, Construction, and Validation Project. With a knowledgeable dedicated project team, this schedule walks the fine line between cheap and fast with low risk to quality.

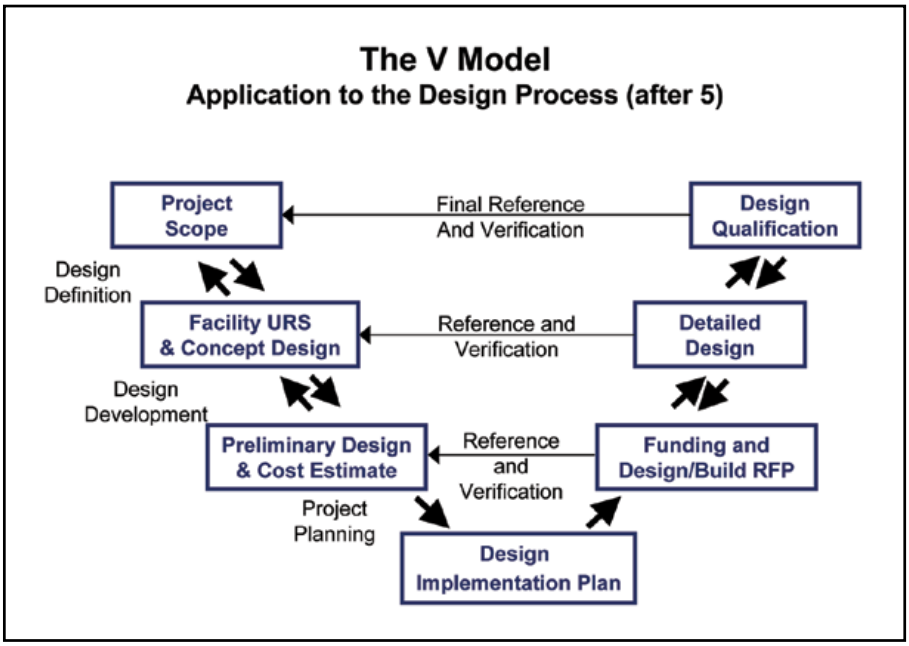

Figure 2. Application of the V Model (after 5) to the planning phase of a (biopharmaceutical) facility construction project. The project scope serves as the basis for the facility user requirement specification (URS) and conceptual design, which in turn serves as the basis for the preliminary design and cost estimate. The design implementation plan is developed out of the preliminary design, which together are used to secure the project funding, and to form the basis for the detailed design, construction, and validation. The detailed design can be referenced back to the facility URS, while the design qualification ultimately checks the detailed design against the project scope.

ity requires that the validated endpoints of both the facility and the process be identified at the concept engineering stage. This ensures that the full scope of the requirements is identified early and as completely as possible (however, with new processes and new technology, the term "completely" is relative).

The Conceptual Design

It is the core team's task to resist the temptation to charge ahead. Instead, the team should invest a small part of the overall time up-front in a "conceptual design" activity, which normally will last from two to four months at the front end of the project and cost between 0.1 and 0.2% of the overall intended budget (Table 2). For a $100 million facility this amounts to approximately $100,000 to $200,000, small change for the amount of time saved and the definition that it provides later in the process. This is a paper exercise that is not governed by controlled documents (and hence not subject to change control). Exploring alternatives and making changes are quick and cheap. The elements of the conceptual design include:

- Process scope
- Draft facility user requirements specification (URS)
- Physical space needs
- Major equipment and utility needs
- Required adjacencies
- Cleanroom classifications and containment requirements
- Alternative concept design sketches and GMP flows
- Outline: project implementation plan (PIP)
- Gross budget estimate: ±35% (square footage estimate), or ±30% (factors estimate)
- Draft process flow diagrams (PFDs)

While conversion of the development and clinical manufacturing facility into the full manufacturing facility is often the case, a company should consider the development pipeline and ensure that there are adequate facilities for the early clinical manufacturing and late stage clinical manufacturing as well as for launch and full manufacturing. Allowing a development manufacturing facility to launch can be problematic if it prevents other drug candidates in development from getting into the clinics in a timely fashion. Hence, conversion to full manufacturing should only be considered if alternate development and clinical manufacturing facilities are available.

For our multi-functional, multi-product development facility, one of the earliest decision-making challenges was, "Will this be a development facility, a manufacturing facility, or a combination of both?" Many facilities of this kind are a combination of both. The reason is that while in the development phase any drug candidate will need to progress through Phase I, II, and III clinical trials and, if successful at each step, will then need to be manufactured in launch quantities. Frequently, such facilities are later adapted to dedicated manufacture of a licensed product. Such future modifications and expansions should be considered in the design.

With the project scope set, the core team can sketch out the elements of the conceptual design. Traditionally, dedicated facility design is centered around the process. A defined process sets the scope and scale of all components of the facility, from warehousing through utilities to cleanroom requirements. A multi-product development facility has no specified process to hang the design on. Instead, the design must be based on a combination of substitute criteria:

- Model processes
- Industry-standard unit operations
- Flexible unit operation sequence/ configuration
- Reasonable unit operation scale; preferably skid-mounted, portable, or semi-portable
- Multiple segregated rooms or suites; preferably capable of connection or interaction

The balance between good laboratory practice (GLP) and good manufacturing practice (GMP) space in a development facility is often difficult to assess at the beginning. Even more of a challenge is to determine how much GMP space is needed and how this is broken down into functional operating areas (Fig. 3). With too few suites, the processes compete for development

Table 2. The three-step approach to project planning, including budgeting. Time and a relatively small cost invested up front in quality planning will ensure a smooth and efficient project delivery, without major design or budget surprises.

Process Steps	Approximate Cost*	Advantage
Concept Engineering	0.1%–0.2% of the final validated cost of the project	For a modest expense this allows many detail elements to be considered which refine the scope, technical detail, and budget needs.
Preliminary Engineering	1%–2% of the final validated cost of the project	Clarifies the scope to a high degree of confidence and substantially improves the planned time to deliver and the budget accuracy.
Final Engineering and Project Management	10%–13% of the final validated cost of the project (incrementally 9%–11%)	The previous steps provide a solid framework that minimizes the risk of surprises.

* Cost includes the cost of validation and the cost of the previous steps.

time. With too many suites, the cost is unnecessarily high. If the suites are too small the development needs are compromised, yet if they are too large then maintenance and operating cost is too high, particularly for Class A/B environments (Table 3). In addition to considerations of cleanroom classification, the requirement for biosafety level (BSL) containment must be decided (BSL1, 2, 3, or 4).

It is important throughout the process to seek out input from as many users and owners as possible. Be sure to include representatives from QA, RA, and maintenance and operations.

Once the concept engineering is in place, it is important to summarize the concept information into a draft of the URS. This is a comprehensive document that outlines all facets of the deliverables from the project. It covers the total building as well as all services and utilities, support equipment, and process equipment. The draft URS is the primary deliverable of the conceptual design, and will become the first controlled document of the project. However, it is important to allow the URS to remain in draft form throughout the conceptual design stage and well into the preliminary design stage of the project.

To the degree known, the process for delivering the final entity should also be documented at this time as a draft of the PIP.

With the early steps of the overall program outlined and an initial version of a budget available, the challenge is always, "How do we get there as quickly as possible within budget?" The potential success of a project is often made more difficult by two events that happen at the beginning of the process:

- Capital needs to be approved before any serious work can commence
- Once approved, the senior decision makers want to see physical progress quickly

The conceptual design and costing estimate can often be financed without a formal budget. Even so, for most organizations it is unusual to have a three-step approach to a budget (preliminary design, detailed design, and construction and validation). One solution to this dilemma is to merge the conceptual and preliminary designs, creating a single-step budget process based on the preliminary costing estimate and including a generous (± 20%) contingency.

The Preliminary Design

The deliverable of the preliminary, or functional, design is a reasonably complete "working" draft floor plan that will serve as the model for the detailed design. The preliminary design is the translation of the draft URS into a picture of what it will look like and how it will work. The elements of the preliminary design include:

- Approved URS (this is the first key information document and the first control document)

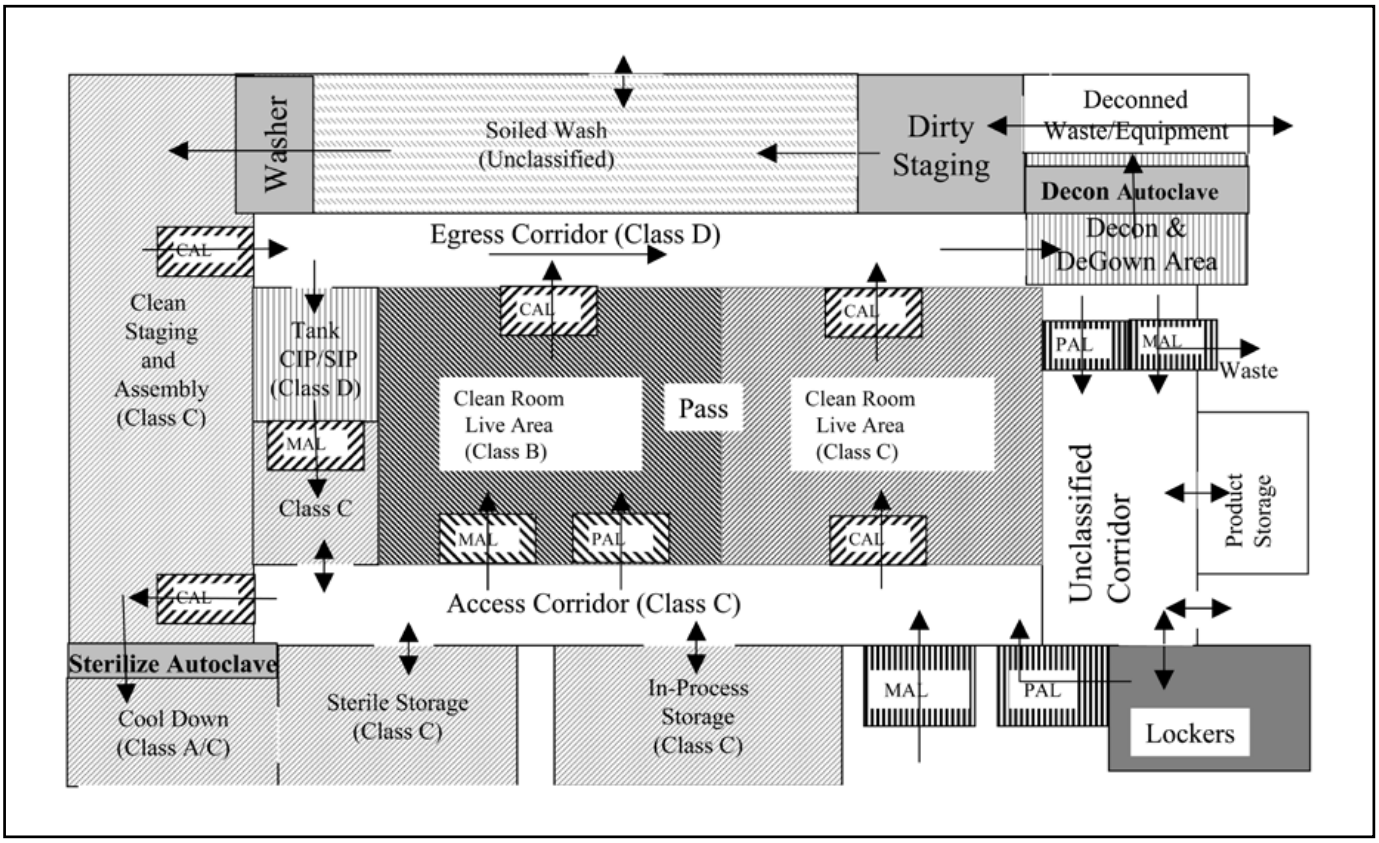

Figure 3. GMP Biomanufacturing Facility Generalized Concept. The GMP area of the facility is self-contained, with unidirectional flows ingressing from dirty to clean and egressing from clean to dirty. Internal suites can be segregated for parallel processing, yet integrated/connected for larger scale processing of one product. MAL = material air lock; PAL = personnel air lock; CAL = combined air lock.

- Site location and alternatives
  - Addition, renovation, brown field, or greenfield
- Process flow diagrams (PFDs)
- Preliminary equipment list
- Initial space needs estimate
- Preliminary floor plan, flow patterns, classifications, and containment
- Preliminary (*draft*) piping and instrumentation diagrams (P&IDs)
- *Draft* functional requirements specification (FRS)
- *Draft* project implementation plan (PIP)
- *Draft* quality management program (QMP)
  - Design qualification (DQ)
  - Validation master plan (VMP)
- *Draft* detailed design specification (DDS)
- Initial timelines for site preparation, construction, commissioning, and validation
- Internal and external resource needs
- Costing budget, probably to +/- 20% (quantity survey)
- Capital acquisition request (for internal projects), or funding procurement documents for detail design capital (this is the second key information document)
- Request(s) for proposal for detailed design and construction (this is the third key information document)

As shown in Figure 1, the preliminary design can overlap and merge with the conceptual design. Unless internal resources are extensive and broad based, it is likely that key engineering and architectural contract partners will need to be engaged. This should be done as the draft URS is completed (at the end of the conceptual design stage). This group will be required to expand upon the user requirements and commence with the detail design specification, which in turn leads to the various functional requirement specifications being developed. For these to be effective documents, they must be developed in the context of "designing from the validated end-result back." For this reason, the QA validation representative should also be brought on board at this time.

There were a number of considerations peculiar to the multi-product development facility that include:

- Parallel multi-product utilization and segregation of suites
  - Aerosolized potassium iodide (KI) study
- Campaigning of suites
  - Disinfection studies
- Multiple suite utilization patterns
  - Adjacencies
    - Pass-throughs
    - Material transfer stations and closed system tank-to-tank piping transfer
    - Cleanroom dumbwaiter
- Roughed-in utility drops
- Future retrofitting and expansion capabilities

In the absence of a specified process or processes, the PFDs for the multi-product development facility are based on model processes that are typical for the types of products being developed. Basic unit operations for upstream, downstream, and (if applicable) fill and finish operations are listed, with alternative technology options for each unit operation. This can be thought of as a "LEGO block" approach that can be configured and re-configured into a variety of PFDs. Sizing is based on a combination of off-the-shelf equipment, maximum flexibility, and maximum portability. Wherever feasible, disposables, stand-alone equipment, and semi-portable skid mounted unit operations should be specified.

Numbers and sizes of rooms and suites, together with their classifications and adjacencies, were then specified for both GMP and GLP areas of the facility. The alternatives explored in the conceptual stage should be reduced to one or two options, and the floor plans and equipment layouts sketched. Future changes and expansions should be incorporated into the layout. For example, hallways, corridors, elevators, and doorways should be sized to facilitate relocation of equipment and skid-mounted unit operations; adjacencies and room allocations should be arranged to accommodate changing processing patterns; main flow patterns and knockout panels should be located to facilitate future expansion; and structural and mechanical space, as well as utility sizing should be specified to allow for near- and mid-term expansion.

The engineering team members can now develop the draft P&IDs and FRS. Utilities should be provided for all of the technology options and sized to accommodate the configuration of the technologies into a PFD that maximizes utility types and consumption. Utility requirements can be multiplied by a factor for near-term expansion, and drops/outlets roughed in and capped off. Mechanical space can be provided for mid-term expansion, with planned tie-ins for duplicated or enlarged utility equipment, storage systems, and circulation loops.

With the initial timelines and resources estimated and the preliminary engineering in place, the information can now be summarized into a final draft of the URS and submitted for approval. The outline PIP should now be fleshed out into draft form, and the QMP can be drafted, with particular emphasis at this point in the project on the design qualification.

By the end of the funding process, the design alternatives should be reduced to a single set plan. The preliminary design package is used to secure funding and for contract design and construction services.

Detailed Design

The detailed design is a direct translation of the preliminary design into detailed plans and specifications for construction. The elements of the detailed design include:

- FRS and P&ID (first and second control documents)
- Process engineering, architectural, mechanical, electrical, and control drawings
- Initial construction and validation schedule (Gantt chart)
- Flow diagrams and descriptions for personnel, materials, and air (third control document)
- Detailed equipment list: specifications, requirements documentation, and space and service needs (fourth control document)
- DDS (fifth control document)
- QMP (sixth control document); This does not need to be project-specific
  - DQ
  - VMP (seventh control document)
- Costing to +/- 10% (detailed costing estimate)
- Funding procurement documents for construction, equipment, and validation capital (fourth key information)

To continue to deliver best time and best cost, two more things now became critical. One was to select construction and commissioning contractor (and any other major contracted service providers) and engage them as early as possible as partners in the process. This is important for two principal reasons. Reason one is that instead of spending time on the "tender/bid/award/mobilize" process, the preferred contractor is selected and pre-qualified as a partner before the project breaks ground. Reason two is that the right contractor can bring a wealth of experience to the process, the project, and the execution plan, and can plan mobilization more quickly and effectively by knowing weeks (sometimes months) ahead of the upcoming needs.

Table 3. Environmental Particulates Cleanroom Classifications
As the classification of cleanliness increases from undefined to Class A, the cost of operating and maintaining the cleanroom increases exponentially.

ISO Class	European Class*	Traditional US Classifications** Static (Particles Per Cubic Foot)	Traditional US Classifications** Dynamic (Particles Per Cubic Foot)
5	A	100	100
6	B	1000	10000
7	C	10000	100000
8	D	100000	undefined

*classifications according to European GMP guidelines.
**classifications according to FDA GMP guidelines

The second is planning the validation requirements, which ensures that the documentation required for validation starts to flow almost as soon as the project breaks ground. Installation qualification (IQ) would commence with the pre-commissioning, operational qualification (OQ) would be well under way by the time commissioning ends, and performance qualification (PQ) should be a simple step for the facility and its utilities (Fig. 1). Process-related validation, if taken into consideration from the beginning of the project, should also flow quickly and smoothly with its own IQ being active by the end of commissioning.

We strongly advocate the three-step approach to the project plan and evolution as well as the budget (Table 2). To start with concept engineering and a commensurate minor budget, then progress to preliminary engineering with its own budget, before getting to the full implementation phase adds immeasurably to the success of both the budget and the stakeholders' financial expectations. This can be achieved even in conjunction with overlapping and concurrent execution of the project stages.

Design Qualification

Verifying the detailed design as compliant with regulations, reflective of user requirements, and as an accurate and complete translation of the project scope is critical. A DQ, which is a requirement under European Commission (EC) regulations, is not yet an FDA requirement. Nevertheless, a formal and complete check of the project plans prior to major expenditure of time and money on the project execution is obviously beneficial. The DQ can be performed as the detailed design is closing, and concurrently with the final drafting of the PIP, site preparation, and the initiation of construction (Fig. 1).

With the validated end result planned to the best degree possible, and once the design has evolved to a stage where the detail is being translated into the building and construction process, it is important to lock in the compliance standard. This is because compliance standards constantly move forward. If they are allowed to frequently add to the scope of the project then execution gets extended, costs increase, and a ripple effect continues to impact the execution process. (Caveat: There are always exceptions, but they need to be absolutely critical and a major threat to the viability of the facility or process if not acted upon.) It is advisable to review the design with the regulatory bodies in conjunction with executing the DQ. When the DQ is finalized, the design should be locked in.

Any changes that are made after this point require not only costly construction change orders, but also complex and extensive change control, with a partial re-execution of DQ.

Project Implementation Plan

The PIP is created as the design progresses from preliminary through detailed stages. The PIP should include the process control program (PCP), which details how to keep the construction process on track and on budget. The PIP should be locked in as the detailed design is nearing completion, and in conjunction with execution of the DQ. At the same time, project execution can get underway with site preparation and initiation of construction, controlled through the draft PIP.

Construction, Installation and Commissioning, and Validation

With the planning stage complete, verified, and locked in, project execution should flow smoothly. There will always be surprises along the way, but these will be minimized by the effort put into quality planning. With an effective PCP, the most critical aspect of construction execution becomes communication and coordination.

Documentation that accompanies the execution portion of the project includes:

- VMP (seventh control document)
- Commissioning schedule (included in PIP)
- Validation schedule (included in PIP)
- Complete-as-built drawings, specifications, contracts, purchase orders, schedules, documentation, and signed off commissioning reports (control documentation)
- IQs, OQs, PQs, and related documentation (control documentation)

Validation can be an intricate, complex process at the best of times, and particularly so for a multi-functional, multi-product biopharmaceutical facility with intentions of parallel processing and campaigning. By having thought through all the prospective validation requirements from the outset, delays in protocol preparation, review and approval for every step of the validation process can be almost entirely eliminated, particularly if protocol templates have been developed with care and forethought.

The validation execution sub-team should include QA, operators, maintenance and operations, and engineering. The engineering project manager, who remains with the project throughout the validation stage, acts as the knowledge expert and interface between the validation personnel and vendors and construction personnel.

As described above, validation planning and execution can be performed on a concurrent and overlapping schedule with project planning, construction, installation, and commissioning (Fig. 1). With the VMP in place by the end of the detailed design stage, the individual validation documents can begin to be generated during the DQ. Facility acceptance tests (FATs) and site acceptance tests (SATs) can be tailored to comply with many of the IQ and OQ requirements, greatly reducing the formal validation activities. This approach also allows for the most effective use of vendors' expertise for validation execution and for transfer of technology to the owners and operators.

REFERENCES

1. David S. Biopharmaceutical contract manufacturing; an overview. *BioProcessing J.* 2003;3:33–35.
2. Norland R. The Ottawa Life Science Council [OSLC]. *The Canadian Bioprocessing Initiative, A Bold Initiative to Make Canada and Ontario a Global Leader in the Bioprocessing of Therapeutic Proteins.* OLSC; 2003 April <http://199.243.172.12/attributes/documents/pdf/Canadian Bioprocessing Initiative Executive Summary.pdf>
3. Fox S. HighTech Business Decisions. *Biopharmaceutical Contract Manufacturing 2003 — Serving the Growing Need for Biopharmaceutical Production*; 2003 August.
4. Dutton R. A multi-functional viral vaccine development facility. *Paper presented at 6th Annual Williamsburg Bioprocessing Foundation Facilities for Mammalian Cell Products Conference*; 2003 October 13–15; Coronado, CA.
5. The International Society for Pharmaceutical Engineering [ISPE]. *ISPE Baseline Pharmaceutical Engineering Guides. Volume 5: Commissioning and Qualification for Pharmaceutical Facilities and Equipment Baseline Guide.* Tampa, FL: ISPE; 2001 March.

Acronyms

BSL — biosafety level

DDS — detailed design specification

DQ — design qualification

FAT — facility acceptance test

FRS — functional requirements specification

GLP — good laboratory practice

GM — general manager

GMP — good manufacturing practice

IQ — installation qualification

KI — potassium iodide

OQ — operational qualification

P&ID — piping and instrumentation diagram

PCP — process control program

PIP — project implementation plan

PFD — process flow diagram

PQ — performance qualification

QA — quality assurance

QMP — quality management program

RA — regulatory assurance

RFP — request for proposal

SAT — site acceptance test

URS — user requirements specification

VMP — validation master plan