



Leaford Blevins and Tom Gerbo

Facility design can affect the bottom line in biopharmaceutical manufacturing. The authors offer insights about what to look for and what to consider in facility design — whether you're retrofitting an existing facility or building from the ground up.

Reducing Costs by Facility Design

Adaptable design and selection of a suitable property contribute significantly to cost effectiveness in biotech manufacturing operations.

Pharmaceutical concerns, for example, require a unique set of cleanliness specifications, building code regulations for safety compliance, and energy efficiency issues that will determine bottom line profitability in the long run.

Choosing the Right Building

Choosing the proper site location is the first key. Pharmaceutical producers often choose existing buildings in light industrial parks that require extensive conversion. When looking for such a building, it is important to check several key factors.

Yard space. Often existing structures consume most of the property, with minimum space for parking. For pharmaceutical manufacturing needs, however, seek a property with available yard area to accommodate tanks, chillers, emergency generators, haz-mat storage trailers, and the like. Failure to take yard space into consideration may result in inadequate parking areas, or in awkward, inefficient yard design.

Ceiling height. It is extremely important to select a building with high ceilings to incorporate interstitial space for ductwork, plumbing, light fixtures, and so forth. In fact, less than 23 feet in interior clear height becomes problematic.

Roof strength. The roof must be of sufficiently solid construction to support the heavy load of large air handling units. If possible, avoid site-cast concrete panels or masonry buildings; steel or other light construction materials are a better choice. The reason: duct penetration in concrete is limited and installing intake louvers will pose engineering issues that could be averted.

Flexibility. In pharmaceutical design, low weight-bearing interior walls made of brick or concrete masonry units (CMU) should be rejected, if possible. These do not allow for the wall movements that are often required when subdividing space for fire or hazardous chemical control areas. Optimally, control areas should be unrestricted, but multitenant subleasing may restrict available subdivisions required by code. When seeking to lease, owners should seek single tenant buildings or a site with as few tenants as possible, or develop a legal understanding regarding the ability to subdivide areas of their tenant space into additional control areas.

Safety. The dual safety needs of personnel and product are paramount in a drug manufacturing plant. Chemically derived drug products are cause for concern in spread of fire, for example. The amount of chemical in use bears on fire codes and the building's occupancy classification, which ranges from B to H1. To best meet safety criteria, examine the perimeter area of the building compared to the interior floor area. A general rule for a well-planned, adaptable lab is a structure in which a minimum of 25% of its perimeter wall is exterior wall.

Cleanliness Is Key

A drug manufacturing lab obviously requires a high level of cleanliness. Depending on the type of operation within a facility, the operation can demand Class 100 cleanroom standards for filling operations to Class 10,000 or 100,000 for less stringent operations (synthesis or precipitation operations). Although often much smaller than a semiconductor lab, the space should be devised similarly. The clean space should encompass cleanable surfaces, no-dust ledges, and seamless flooring that is impervious to chemical spills.

Stringent air requirements hold. Although air recirculation in a typical cleanroom can include 10–20% new air, a chemical or drug

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manufacturing area does not have the luxury of recirculating air. Because of the presence of flammable and toxic substances, there must be a high rate of air change and no return is permitted. Thus, 100% outside air is required, and it must undergo prefiltration and ultrafiltration processes to ensure 99% purity.

In the programming stage, multiple pathways must be designed for movement of personnel, raw materials, and finished product so that each is defined and carefully controlled with minimal crossovers. Defining equipment location and how materials move through the manufacturing process in light of staff movement will maintain critical clean areas.

Maintainability of relative air pressure in the people pathway also aids in preserving cleanliness. A system of cascading air flow (from highest to lowest pressure) from manufacturing area, to airlock, to a gowning area, to a second airlock, and to corridor ensures air will be most clean in critical clean areas.

Placement of equipment and controls outside the clean room to limit maintenance personnel traffic also has a positive effect. In addition, the clean room size is reduced, thus reducing the volume of air needed to be changed, while simultaneously increasing energy efficiency.

Designing for Nimbleness

Existing structures have their limits. But when a company designs a new facility, it's possible to take flexibility and adaptability to a whole new level.

In the late 1990s, for example, Ventana Medical Systems, Inc., a Tucson, AZ, manufacturer of histology lab equipment and chemical reagents, had been experiencing rapid growth and was projecting exponential growth from 1998–2003. At the time, the company's employees were scattered across eight buildings and 70,000 ft² on the west side of Tucson, mostly in commercial property not designed for precise scientific work. It needed to select a site that could unify its workforce and build a lab flexible enough to reflect market fluctuations.

Ventana's goals were ambitious: It wished to be the primary driver in automating histology labs worldwide. Yet, besides manufacturing slide readers and microtome equipment, it is a large supplier of the chemical reagents used for slide stains. To keep pace in an ever-changing

market, architects were tasked with creating a facility that could nimbly expand or contract particular programs for either wet (reagent consumables) or dry (slide-staining instrumentation) lab manufacturing.

When our firm's Tucson office was selected for the job, planners first conducted an analysis of the three overall components of the operation — R&D, Quality Assurance–Quality Control, and manufacturing. To determine the size and scope of a facility that would ultimately become a three-building complex, architects examined the company's existing product line, its predictions for future sales, and the anticipated growth of its research and development labs.

Following extensive evaluation, planners programmed an 85,600-ft² manufacturing facility including 59,200-ft² R&D laboratories and engineering building and 37,600-ft² corporate headquarters. The 19-acre site provided expansion area for an additional 40,000-ft² building.

From these findings, they determined interior work areas modularly based on the lowest common denominator, or smallest lab building block, that could accommodate all three classifications.

Modularity was assimilated into the overall master plan. Predetermined, repeatable patterns incorporated valves, dampers, wiring, and outlets in mechanical, electrical, and plumbing systems. The main infrastructure was laid out so that walls could be moved in increments, utilities could be interchanged, and even air could be borrowed from one space to the next.

Flexibility was carried through between the wet and dry manufacturing labs and between manufacturing and R&D labs. If the reagent side grew more rapidly the plant could accommodate a shift toward it, and if manufacturing space reached critical mass, R&D could be displaced and easily moved into new construction on the site.

Changes continue to be a constant at Ventana. As the company grew from start-up to the \$300 million company it is today, management philosophies dictated modification of manufacturing areas such as bulk formulation. At the same time, manufacturing processes also shifted from a nonclean to a semiclean environment. With adaptability built in, these changes are relatively easy to accomplish. Minor modifications made to air handling

equipment such as exchanging diffusers for HEPA filters can elevate a space from nonclean to a semiclean level. Because of the open design, manufacturing lines that were inconceivable during initial planning stages can now be accommodated. Because it included change in its original plans, the company was not designed into a corner. It continues to have room to maneuver.

Movers and Shakers

Moving operations from eight disparate locations into one facility, particularly when equipment is not to be entirely replaced, typically shuts down production, or at minimum causes production delays at a plant. This was not the case with Ventana.

With the help of two move managers and a project coordinator, one of whom had successfully completed a relocation of a research lab at Johns Hopkins University, equipment was methodically cataloged over the course of the construction process. Working about six months out from the targeted occupancy date, the move managers formed a detailed move plan in cooperation with Ventana, the building contractor, and the moving company. Through a combination of selected equipment replacement, stock warehousing, scheduling downtime, and staggering relocation, operations were scarcely disrupted. The actual move took barely a month.

Site selection was another key to Ventana's success. It selected a site on a desert plateau, at the foot of the Santa Catalina Mountains in picturesque Oro Valley on the northern outskirts of Tucson. This location provides a reverse commute for most of its employees. The design reflects the logical, efficient image the company wished to project to researchers, clients, and investment bankers, while the façade incorporates colors reminiscent of the Arizona sunsets. The biotech firm also used early renderings of the sleek, streamlined building as a recruitment tool to attract top-notch employees.

Today Ventana has grown twice as fast as projected, but because the design concept was pure enough it is able to withstand the test of time and supports future growth. **BPI**