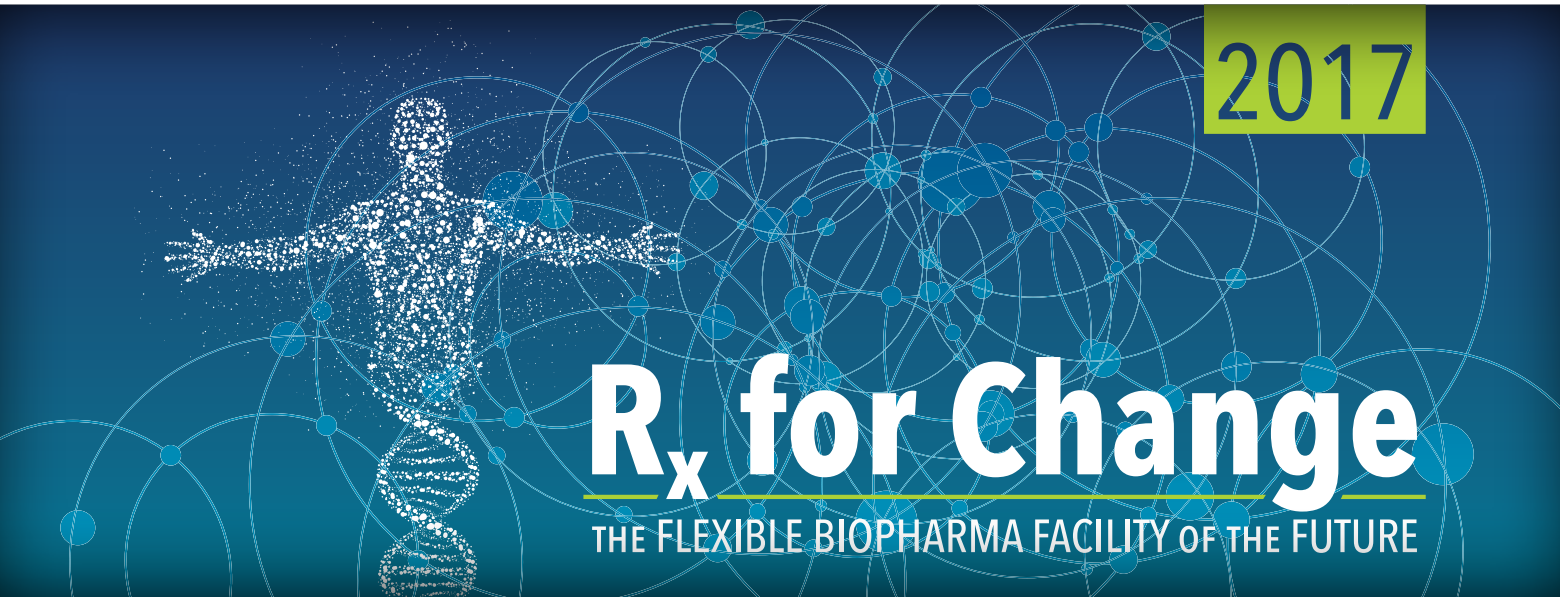
DESIGN FLEX 2030



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Industrial Asset Management Council

SIOR FOUNDATION

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This paper is part of the DesignFlex2030 initiative, commissioned by IAMC and SIOR to explore new design approaches that could lead to more flexible, adaptable, and sustainable industrial facilities in the future. Other papers in this series include "Recipe for Change: the Flexible Food Processing Plant of the Future," published in September, 2015.

FOREWORD

In the not-so-distant future, the biopharmaceutical industry is likely to completely eclipse the current-day pharmaceutical industry in terms of numbers of products and dollar value.

This speaks to the need for a more flexible facility, one that can adapt as market conditions change, as technology continues to alter manufacturing processes, and as the ever-flowing pipeline of scientific discovery yields new medicines.

Take note, commercial real estate industry! Today's approach—building a single-purpose, inflexible plant with permanently installed equipment, taking maximum depreciation early, and moving on when the book value zeros out—just isn't going to work tomorrow.

Actually, it's already not working well. The biggest cost of facility inflexibility is local jobs. It means shuttered facilities, heavy carrying costs, and hard-to-fill-space. It creates environmental hazards and causes blight. It results in wasted human, financial, natural, and cultural resources.

But there is a better way. We know it. It's the reason that the Industrial Asset Management Council (IAMC) and the Society of Industrial and Office Realtors (SIOR) initiated the DesignFlex2030 project—to explore new design approaches that could lead to more flexible, adaptable, and sustainable industrial facilities in the future.

This paper, *Rx for Change: the Biopharmaceutical Facility of the Future*, is part of a series of white papers under the DesignFlex2030 umbrella. It offers a way forward, with striking architecture, modular design, and an open interior. It will enable rapid change-out for quick, efficient, and cost-effective re-purposing and re-use as needs and users change.

We want to acknowledge IAMC and its Executive Director Tate Godfrey, and SIOR, led by Richard Hollander in this project's early stages and now Robert Hammond, along with their staffs for their commitment to this multi-year effort. We thank Cresa and IAMC Education & Research Committee co-chairs Ken Hagaman and Wayne Young for their support.

Our sincerest gratitude goes to Burns & McDonnell and Fluor, leading industrial and architectural firms that lent some of their most talented staff to this work. Our extraordinarily talented design team dedicated hours on end to this project, indicating a passion and a desire to truly make a difference. We thank our technical advisors from leading life sciences companies who helped ensure that the future vision was rooted in the practical realities of the biopharmaceutical lifecycle from molecular discovery to drug delivery.

We thank Joel Parker, Director, IAMC Professional Education & Research and DesignFlex2030 Project Lead, who is always there, making sure things get done. Our thanks also go to Ann Moline, the paper's author and researcher, and to the designers, Sean Scantland and Richard Nenoff.

Ron Grossmann, *Novartis Pharmaceuticals Corporation*

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TABLE OF CONTENTS

INTRODUCTION

THE DESIGNFLEX 2030 BIOPHARMA BASE CASE CHALLENGE

The team will design a flexible biologics manufacturing facility that includes cell culture/fermentation, purification and initial filling. The core flexibility concepts will support rapid plant reconfiguration for batch and continuous processing, cell line variation, multiple production scales, multiple purification technologies, and multiple primary container configurations.

The exterior envelope will feature an eye-catching and architecturally significant design and landscape that also incorporates sustainable functionalities such as daylighting along with futuristic assumptions on employee commuting and building use patterns/facility siting.

What will the biopharmaceutical facility of the future look like? What if we upended the traditional thinking about how such life sciences facilities are designed, built, and used?

How can innovative industrial facilities design, breakthrough technology, and changes in culture, process, and approach lead to more efficiency, greater throughput, and increased flexibility?

The DFlex2030 Biopharma Design Team—comprised of visionary life sciences architects, engineers, and manufacturing process experts from Burns & McDonnell and Fluor—set out to answer to these questions.

Building on their own track record of industry design experience and research, they gathered additional input from top biopharma facilities users, including their own clients. Technical advisors from leading life sciences companies joined in the effort, helping to validate the direction and approach.

Armed with information, this powerhouse team identified key issues with the way life sciences facilities are built and used today. They also uncovered emerging trends that are likely to impact the way biopharma facilities are designed and used in the future. These discussions yielded a list of priorities to address and a decision on the base case design challenge.

The result of the team's work is a conceptual design framework that starts as a monoclonal antibody production facility. It addresses current facilities problems, accounts for new and emerging technologies, and accommodates fundamental changes in the life sciences value chain. Woven into the design is the latest thinking on how to optimize industrial workplaces. New technologies, materials, and processes—some of which are not yet on the market—are part of the design as well.

This white paper showcases renderings of a next generation, fully flexible, highly efficient biopharma facility. Benefits include:

- Adaptability to rapid change
- Rapid transition from pilot to full production
- Multiple processes and functions under a single roof
- Higher throughput
- Increased efficiency
- Energy savings
- Lower real estate portfolio costs over time
- Ease of resale

The team's creative vision blends beautiful form with world-class functionality. This is a conceptual design for a workplace that appeals to a multi-generational professional workforce. It is a new approach to the industrial workplace—the facility itself is part of the draw. It's a place where people will want to work, giving the company an edge in the increasingly high-stakes competition to attract and retain top talent.

Soaring glass panels with a thin film solar membrane make for a light-filled, energy-efficient workplace. The graceful curve of the roof creates a distinctive architectural vision that allows for expansion without re-architecting the visual lines.

The green roof and wind turbines add environmental benefits including controlled stormwater runoff and reduced reliance on non-renewable power. Water features and "grasscrete" add to the distinctive style, reduce heat island effect, and limit dependency on increasingly scarce external water resources. With an emphasis on modularity, the external layout accommodates additional expansion. The changing nature of transportation is addressed with public transit connections adaptable to future innovations and upgrades and parking for personal transportation vehicles. A perimeter road allows for the fire access required for this type of facility, along with a smooth flow of traffic for shipping and receiving.

Flexible internal spaces are also modular in design, creating a hackable interior that allows for swift scale up or scale down. It can accommodate multiple processes, multiple products, and multiple functionalities. Airy and open corridors bisect the facility for easy access, allowing for better collaboration and adequate space for modular movement.

Unlike traditional industrial monoliths, the DesignFlex biopharma facility is a signature structure that adds value for communities. Rapid and cost-effective conversion to completely different uses exponentially ups the facility's re-sale potential.

WHAT WILL INFLUENCE FUTURE BIOPHARMA FACILITIES?

In an informal, anecdotal survey conducted by the DesignFlex2030 Design Team, biopharma facilities users confirmed what the team had suspected: that the evolution in the biopharma value chain will impact future facilities decisions. This evolution is creating conflicting needs—for a facility at once capable of highly efficient, large-scale production capacity and rapid throughput of small-scale, genetically tailored therapies.

To date, the industry has often responded by building separate, stand-alone facilities with permanently installed equipment to produce a single product. When demand wanes or the outdated facility has run its course, it is shuttered. The reason? It is often more expensive to retool an aging life sciences facility than to build new, facilities users said. So, companies are left with legacy facilities that they wind up selling for pennies on the dollar.

7 DISRUPTIVE INDUSTRY TRENDS & PRESSURES

Here are the top seven disruptive industry trends and pressures that will affect the future design of life sciences facilities, as identified by facilities users themselves.

1. Process, equipment, and technology innovations

Increased reliance on single use/disposable production, shift to continuous processing, and smaller footprint: "What we used to do in a 600,000 square foot plant we're now doing in a 200,000 square foot plant," says one life sciences company real estate advisor. "Our landscape is littered with closed and rusting plants that aren't usable anymore because of disruptive technological innovations." For instance, more widespread use of 3D/4D printing for identical cell lines likely will replace the need for breeding colonies of live animals for research and for mammalian cell culture manufacturing—thus reducing vivarium space needs. Facilities implications of the innovation trend include:

- Open and flexible space
- Portable, easy-to-install, self-contained processing units
- Flooring that can support heavy loads
- Plug-and-play utilities connections
- Decentralized, segregated HVAC and controls for production of multiple products and a variety of processes

2. New therapy discoveries, changes in drug development, fast-tracked regulatory approvals & personalized medicine

New discoveries, such as inhalation therapies, are changing the way drugs are delivered to patients. The future in new drug development is in using the body's own immune system to fight diseases. Personalized medicine, with the emphasis on developing specific therapies that are genetically tailored to meet individual needs, means a shift from large manufacturing process to small-scale lab processes. Regulatory authorities will have local outlets to fast-track new molecules, meaning a shorter time to market. Facilities implications include:

- Co-location of central lab, pilot, and production for increased collaboration
- Smaller footprints
- Smaller batch processing
- Agile facility capable of rapid change-outs, integration of next-generation equipment, and production of multiple products using multiple processes

3. Cloud-based R&D

Early research and discovery experimentation will always require a certain amount of hands-on bench work, according to one of the Design Team's technical advisors, an R&D workplace effectiveness specialist. "So, the bench is never going away," she says. However, as the research matures, cloud-based experimental platforms allow for high throughput parallel processing across a range of variables such as samples, acidity, and temperature. "It becomes a robust 'what if' platform with perfect traceability. Run the experiment repeatedly with the exact same parameters and you get exactly the same results," according to the advisor. Facilities implications include:

- Central lab linked to CROs around the world
- Fewer benches
- Co-location of central lab with pilot and production for increased collaboration

4. Drive for higher throughput, lower cost & optimized utilization

The average cost from new molecule discovery to regulatory approval today tops $2.6 billion,[1] climbing from more than $1 billion in the early 2000s and up from about $179 million in the 1970s. Based on this trend, drug development costs are not expected to decline. Many experts also suggest that the era of the blockbuster drug is over, given the rise of personalized medicine and custom treatments. No longer will companies be able to recoup as much of their drug development costs or fund as much new research from profits earned on sales of blockbusters.

BY THE NUMBERS: TODAY'S BIOPHARMA INDUSTRY

APPROVALS
- Novel medicines approved, 2015: 56
- Medicines approved since 2000: more than 550
- Only 2 of 10 marketed drugs return revenues that match or exceed R&D costs

RESEARCH AND DEVELOPMENT
- R&D 2015: $91.92 billion, est.
- Domestic R&D as a percentage of sales, 2015: 94.95%
- Total R&D as apercentage of total sales, 2015: 97.98%
- Average time to develop a drug: more than 10 years
- Drugs entering clinical trials resulting in an approved medicine: less than 12%

MEDICINES IN DEVELOPMENT
- Medicines in development around the world: 7,000
- Potential first-in-class medicines in clinical development globally: 70%
- Medicines in development for rare disease: more than 450

ECONOMIC IMPACT OF THE BIOPHARMACEUTICAL SECTOR
- Direct jobs: more than 850,000
- Total jobs: nearly 4.5 million

Source: PhRMA

1 There are multiple sources for these figures, including drugmaker Eli Lilly and the Pharmaceutical Manufacturers' Association (PhRMA) (http://phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf). See also: J.A. DiMasi and H.G. Grabowski. "The Cost of Biopharmaceutical R&D: Is Biotech Different?" Managerial and Decision Economics 2007; 28(4–5): 469–479; J. Mestre Ferrandiz, J. Sussex, and A. Towse. "The R&D Cost of a New Medicine." London, UK: Office of Health Economics, 2012; S.M. Paul, et al. "How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge." Nature Reviews Drug Discovery 2010; 9: 203–214.

A recent paper from the Bio-Process Systems Alliance spells this out. "Blockbuster drugs are a rarity now, and no one can afford the inefficiencies in discovery with high capital costs,"[2] the authors write.

According to Mario Phillips, president of Single-Use Technologies at Pall Life Sciences, this means even more pressure to squeeze costs out of processes, to increase yields in shorter times, and to optimize processes. Interviewed in BioPharm International, Phillips noted that "with the current cost pressures facing the industry, the number one challenge for biopharmaceutical companies can often be determining the economic viability of a facility design—the goal is to find a design that best minimizes capital investment and long-term operational costs in the facility, while still meeting the production needs the company has."[3]

This push for better-faster-cheaper also will require more collaboration early on, says Fluor's biopharma manufacturing process expert and DesignFlex team member Hector Davila. "Rather than scientists and researchers driving the train on how they are going to process, produce, and deliver the product, it is going to require a collaborative effort from the very beginning." This collaboration includes scientists, technologists, facilities staff, process engineers, and designers to identify optimal process and delivery platforms for maximum quality, speed, savings and efficiency. Facilities implications include:

- Flexibility to expand and contract quickly to meet business needs
- Rapid upgrades and modernization
- Speed to embrace technological innovation such as continuous processing and process analytical technology (PAT)
- Shift from fixed to disposable equipment
- Ability to change out processes quickly, easily and with limited disruption
- Collaborative space
- Co-located functional areas

5. Competition from biosimilars

"In biotech, there is a brewing dog-fight between biologics and biosimilars," says Fluor's Director of Technology, Manufacturing, and Life Sciences and DesignFlex team member Timothy McNeill. "This means even greater pressure on cost and time to market. It also speaks to having a simple and flexible facility design because this will make it quicker and easier to change out and qualify for the next use—plus shorter time to delivery for the facility." Facilities implications include:

- Limited use of permanently installed equipment
- Scalable, adaptable design
- Nimble global real estate strategy to accommodate swift ramp up from pilot to full production, fill-and-finish, and global distribution to maximize patent-protected timeframe

6. Workforce issues

With the increasing capacity of self-contained disposable processes and a growing reliance on robotics, it's likely that biopharma facilities of the future will require fewer people—as in other industrial workplaces. However, the highly sophisticated nature of the work—and the brain trust that represents the core of the company's ability to continually innovate—means that companies will continue to vie for the best and brightest scientific talent.

US Bureau of Labor Statistics estimates indicate that even with the increased emphasis on educating young people for careers in science, technology, engineering, and mathematics (STEM), labor shortages in private science-and-technology-based industry will continue. Over the next decade, businesses will need about 1 million more STEM professionals than the US is currently producing, according to the BLS' economic projections.[4]

Researchers at Georgetown University in Washington DC recently chronicled the gap for American companies. In their "Recovery 2020" study, authors Anthony P. Carnevale, Nicole Smith, and Jeff Strohl suggest that the US will require 8.5 million new STEM workers even before the year 2020, but that the country will fall far short of this number. One reason for the shortfall is a massive wave of retirement as the post-World War II baby boomer generation ages out of the workforce. A second reason for the expected shortage is an increase in the number of new jobs created that will require technical skill sets: the report predicts a 26 percent increase in new demand for such workers from 2010 to 2020 and beyond.[5]

As the nature of the work itself evolves, different work styles will need to be accommodated, especially in an industry that prizes both individual discovery and collaborative innovation. Facilities implications include:

- Location considerations:
  - research and higher education institutions
  - existing industry cluster
  - strong quality of life metrics
  - access to public transit and commuter options
- Flexible office and research space
- Collaborative areas
- Attractive work environment
- Green and sustainable design features
- Transparency and accountability

At a time when the pharmaceutical industry faces negative publicity over issues ranging from corporate relocations and tax inversion schemes to the high cost of drugs and seemingly opaque pricing policies, there is a stronger push for greater transparency and accountability. In June 2016, Vermont became the first state in the country to require justification for drug price increases. Other states are considering similar legislation.[6] These corporate governance pressures could have a trickle-down effect on facilities design. Facilities implications include:

- Welcoming, public-friendly spaces
- Site flow that accommodates public tours but protects proprietary processes
- Security

> "Take a look into the future…push the boundaries of the possible!"
>
> – **Wayne Young,** *speaking to the DesignFlex2030 biopharma design team*

2 Kapp et al, "Roadmap to Implementation of Single-use Systems," Bio-Process Systems Alliance, April 2010. http://www.bpsalliance.org/wp-content/uploads/2014/06/BPSA-Economics-White-Paper-2010.pdf

3 Haigney, Susan. "Challenges, and Trends in Biopharma Facility Design," BioPharm International, Volume 27, Issue 9, September 1, 2014. http://www.biopharminternational.com/challenges-and-trends-biopharma-facility-design

4 Yi Xue and Richard C. Larson, "Stem Crisis or Stem Surplus? Yes and Yes," Monthly Labor Review, US Department of Labor, Bureau of Labor Statistics, May, 2015. http://www.bls.gov/opub/mlr/2015/article/stem-crisis-or-stem-surplus-yes-and-yes.htm

5 Carnevale, Anthony P; Smith, Nicole; Strohl, Jeff. "Recovery 2020. Job Growth and Education Requirements through 2020" Center for Education and the Workforce, Georgetown University, June 2013. http://cew.georgetown.edu/recovery2020

6 "Vermont becomes first state to require drug makers to justify price hikes," Stat, June , 2016. https://www.statnews.com/pharmalot/2016/06/06/vermont-drug-prices-transparency/

FINDING A FUTURE-PROOF APPROACH

Based on this input from facilities users and their own industry expertise, the team set out to find a way to meet changing biopharma facilities needs within the same footprint—for a lifespan that would extend to the year 2030 and beyond.

Meeting weekly over the course of several months, the team discussed the implications of trends and shared knowledge on leading edge process innovations and design approaches.

Burns & McDonnell's Wayne Young, who moderated many of the discussions, encouraged the team to use their collective imaginations and focus on a futuristic vision. "This is your opportunity to take a look into the future," he told the group at the outset. "It's fine to use concepts that may be emerging now, but don't limit yourselves to what's available now. Push the boundaries of the possible!"

During their discussions, team members also noted the not-insignificant hurdle to be overcome in changing industry culture and mindset to embrace a new way of thinking.

"In this industry, it's about evolution, rather than revolution," explains team member and Fluor life sciences architect Todd Mion. "We needed a way to upend current thinking without scaring away the industry. We wanted to design a facility that could accommodate variable scale, variable purification, continuous and batch processing, and PAT. We needed utilities that can be routed anywhere. And we needed to accommodate future innovation." Ultimately, this led to the modular, plug-and-play approach.

ABOUT THE DESIGNFLEX2030 MONOCLONAL ANTI-BODY FACILITY OF THE FUTURE

The following pages detail key aspects of the Design Team's flexible biopharma facility of the future.

FACILITY HIGHLIGHTS

Designed to address the articulated challenges and needs of facilities users themselves, the renderings incorporate technologies, materials, processes, innovations, and approaches that are emerging now and that are on the future horizon.

Modular site design and layout

- Expandable and adaptable facility
- Add, remove, and exchange self-contained functional modules as needed

360-degree architecture

- Attractive exterior from all sides
- Light-filled facility adds to positive work environment
- Adapts for other users, such as university or semiconductor fabrication
- Enhances resale value
- Increases economic development value

Integrated facility

- Universal manufacturing space for multiple products or single product
- Accommodates latest process technology including single use disposable reactors and large scale purification
- Co-located research and development, pilot, administrative, and fill-and-finish enables stronger collaboration, innovation, and breakthrough

Modular and wall panel clean rooms/manufacturing spaces

- Plug and play
- Slide in and slide out
- Higher facility throughput due to reduced disruption for cleaning and qualifying
- Allows Single Use, Large Dose Upstream and Large Dose Downstream to be modified or reconfigured as needed
- Individual units can work independently or combined for modular process
- Ability to alter internal spaces with minimal construction disruption
- Unlimited plant flexibility that allows the most costly part of drug production to be adaptable and reusable

Modular Research & Development labs

- Designed for full flexibility
- Use individually or combined to create small pilot operation without disrupting existing production

Modular fill-and-finish units

- On-site capacity for speed-to-market
- Templatized design for reproduction anywhere in the world
- Ship modules to other locations based on global demand

Raised access flooring

- Ultimate load capacity
- Concrete-filled steel floors
- Underground utilities corridor
- Ease of conversion for semiconductor and data center environments

Solar and wind technologies

- Solar pavement panels
- Inductive charged, "plugless" parking spaces and ground pad systems
- High efficiency peel and stick thin film solar collectors on administration building
- Dynamic tint adjustment: photovoltaic glass on sides of the building exposed to light can generate power, allow for natural daylight, and filter the amount of sun exposure
- Large and small wind turbines: generate electrical power for large energy use equipment; ability to upgrade as technology evolves

Green roof

- Manages storm water
- Helps microclimate
- Binds dust particles
- Reduces noise
- Protects roof from UV breakdown

Leading-edge building materials

- Color-changing interior paint
  - identifies spaces by function to reduce risk of cross-contamination
  - reduces painting and renovation costs
  - flexibility for branding and rebranding
  - selling point for a developer that needs to accommodate a new tenant
- Color-changing exterior rain cladding accent tiles
  - improves insulation
  - more efficient heating and cooling
  - enables renovations without structural interference to minimize disruption and reduce cost
  - more flexibility for space identification
  - adds to re-sale value through ease of re-branding
- Smog-eating exterior rain screen tiles
  - concrete rain screen with bonded titanium dioxide
  - removes nitrogen oxide from atmosphere
- Cellular grass pavers ("grasscrete") on large public paved areas
  - reduces Heat Island effect
  - decreases rain water run-off
  - improves air quality

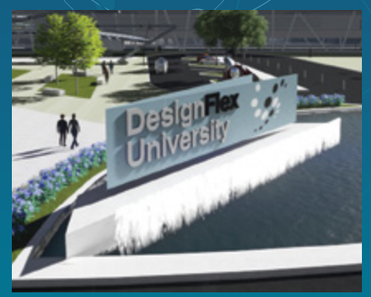
Next-gen utilities

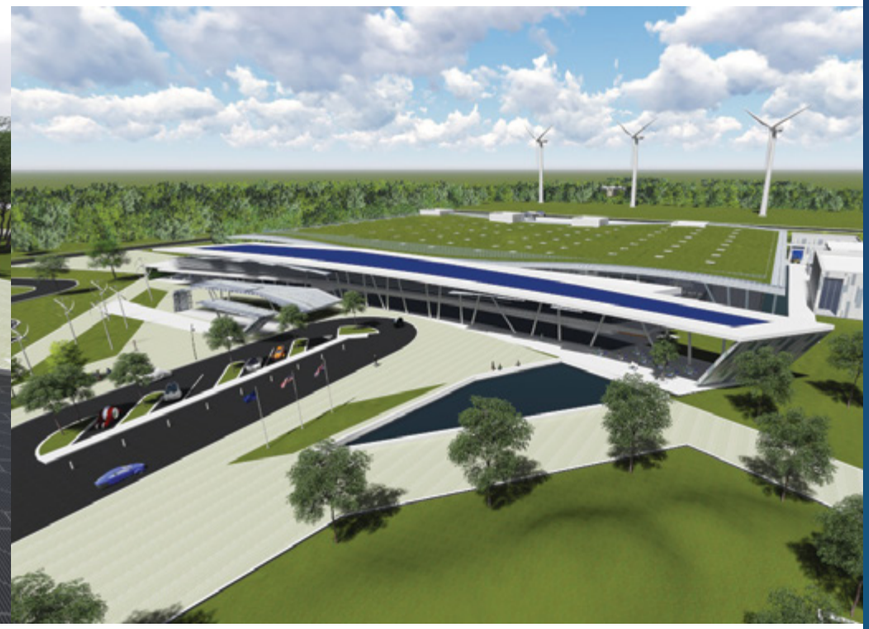
- Insulated corrugated cardboard ductwork
  - replaces semi-permanent metal ductwork
  - lightweight flatpacks for reduced shipping costs
  - easily removable
  - recyclable
  - water-resistant
  - fire-retardant
- Predictive HVAC maintenance software
- Solar-powered HVAC supplemented by natural gas
- Ice-powered air conditioning to cool large spaces

Advanced technologies

- Biometric security and access control
- Autonomous cars and personalized transportation
- Unmanned aerial vehicles (UAVs) for shipping and receiving
- Anti-gravity pallet lift
- Humanoid robots with charging stations for sack loading
  - reduces contamination risks in clean rooms
  - reduces workplace injury claims
  - lowers head count costs

SITE DESIGN





THE BIG IDEA

Design an external shell on an expandable site that can be used for virtually any purpose: from monoclonal antibody production to semicondctor fabrication to university lecture hall.

The undulating rooftop design allows for continuous expansion while retaining the facility's achitectural integrity. Using a completely modular design approach, any part of the site, including the parking lot, could be adapted to a diffierent use—the ultimate flexible facility.

THE PROBLEM IT SOLVES

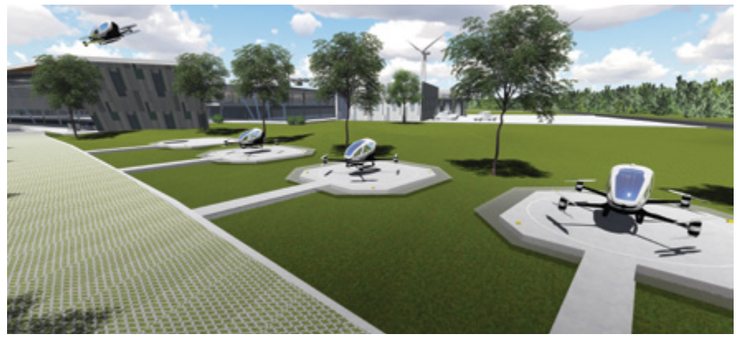
Today's biopharma facilities are built for today's use, with no thought about tomorrow. There is often little focus on the external site layout, other than practical issues, such as how many cars the parking lot can accommodate. Site and facility design limitations make it difficult to add on to or reconfigure the footprint.

"Down the road, this locks them into a corner," says Mion. "There's no viable future approach other than dismantling the building and starting over somewhere else."

HOW IT WORKS

Populate the space with prefabricated modules, housed in an exterior envelope that can take any form desired. Administration and R&D buildings are connected through transition corridors with the universal manufacturing space and support buildings—all of which are based on modular design for ease of repurposing.

A perimeter road carries traffic around the grounds in a smooth flow. The road can be pushed back as the facility expands to ensure compliance with the locality's construction standards and to accommodate changing traffic patterns. A striking design creates a sense of place, making for a positive and welcoming work environment that can attract top talent.



"The greatest advantage in this design is flexibility. It is like the lungs: it expands and contracts as needed. You can do big, heavy production yields. You can manipulate the insides to adapt for new technologies without shutting down. And you can rebrand it for a totally different use."

–**Edwin Paoli Perez,** *Design Team member and Fluor biopharma process expert*

UNIVERSAL MANUFACTURING SPACE

THE BIG IDEA

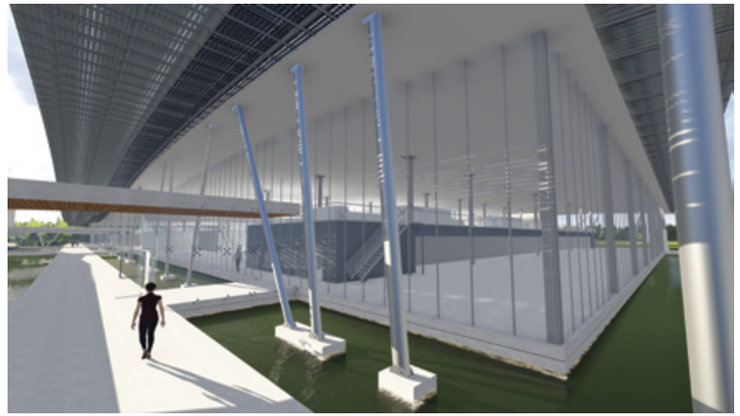
Minimize use of structural columns and maximize open space for total flexibility. The configuration allows for massive ramp up for a single blockbuster drug. It can produce anything from monoclonal anti-bodies to small molecule, oral solid dosing—in massive quanities or on a small scale. Manufacturing of multiple products can take place at the same time, using both continuous and batch production approaches, depending on what works best. Separate modules can house pilot production of new drugs in the clinical trial stage. The entire facility can be quickly retooled to meet a massive sudden demand for a vaccine or medicine in the event of an international public health emergency.

THE PROBLEM IT SOLVES

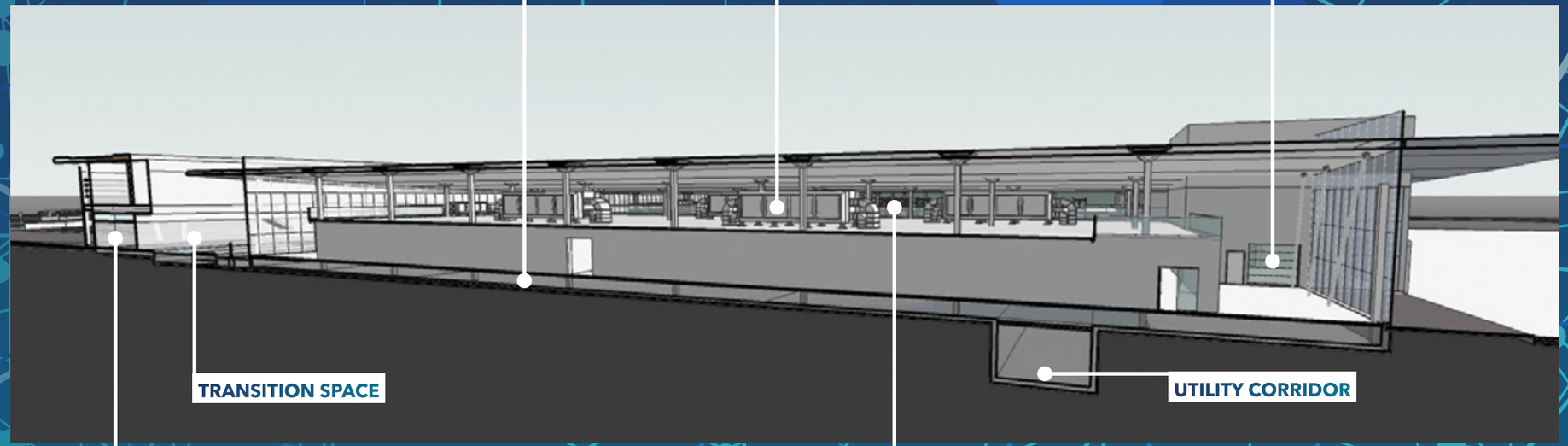
Today, biopharma facilities are often built around a single product. Permanently installed equipment and structural supports create obstacles for expansion or rapid change out. The spacing of concrete columns 40-50 feet apart, along with the multiple reconfigurations for process piping and utilities through years of remodeling all pose limits to flexibility. This makes it difficult to add capacity, switch to a different product, or run multiple processes at the same time. "Single use biopharma facilities are unviable, uneconomical, and uncompetitive," says McNeill.

Companies that try to introduce a new product or process into a plant rigidly configured for a different use face several risks, according to Dr. Tim Sandle, the head of the microbiology department at London-based Bio Products Laboratory Limited. Writing in the peer-reviewed Journal of Validation Technology, he says that such facilities simply may not be able to adopt the new process and its associated technology, posing time-to-market problems. Or, the company may try to force fit the new process or product into the existing layout, which might not allow for the optimal work or process flow. "This can mean introducing time delays or even increasing the risk of cross-contamination. An example might be the path of clean (or sterilized) equipment needing to cross the path of dirty (yet to be cleaned) equipment," he notes.[7] It also severely limits reuse potential.

The difficulty in reselling unwanted pharma real estate is a challenge not just for the owners of the real estate, but for economic developers who are concerned about the broader negative impact of vacant and deteriorating buildings in their communities.



7 Tim Sandle, Ph.D "Risk Considerations for Aging Pharmaceutical Facilities," Journal of Validation Technology, Institute of Validation Technology, April 26, 2016.



KEY FEATURES & FUNCTIONALITIES OF UNIVERSAL MANUFACTURING SPACE

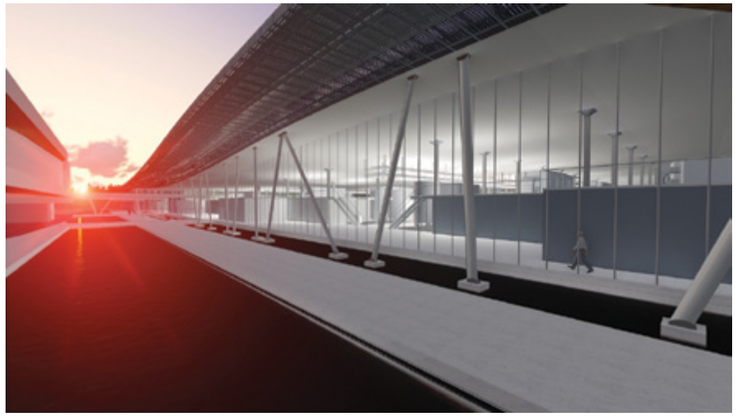
- Wide open area to accommodate single module functionality or connected modules for high capacity production
- Self-contained & accessible individual rooftop HVAC units for ease of control, monitoring & repair
- Retractable glass walls for daylighting and ease of module installation/removal
- Underground utility corridor and raised flooring system for ease of transition to other uses, like semiconductor fabrication
- Separation of gowning from administration/lab areas, centralized at transition locations before entering manufacturing support modules for better control of clean environment, security,and isolation of HVAC units

HOW IT WORKS

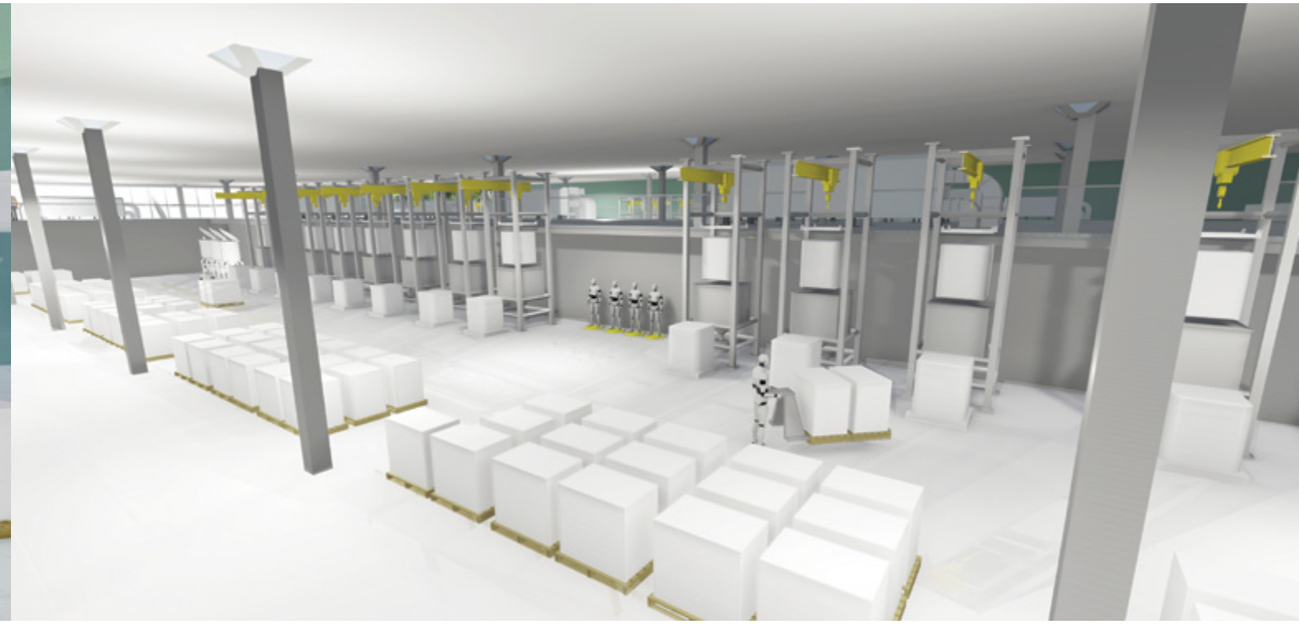
Biologics production requires several processes, including fermentation, purification, and fill-and-finish. Rather than building clean rooms as permanent structural elements, embed process equipment into self-contained modular/podular clean room units on skids that can be moved in and out with ease.

Modules can be stacked on top of each other or side-by-side to add capacity or for another process. Modules are self-supported with their own mechanical capabilities. The wide open, warehouse-like space, uninterrupted by difficult-to-move structural columns, essentially becomes a "future-proof" manufacturing area that can easily accommodate the latest generation process innovations without costly facility renovations. It also allows for easy conversion to other uses, upping the resale value.

"Basically, it works like the inside of a large open space in an airport terminal. But just imagine if you could relocate the airline check in areas, security and even baggage claim as needed through the years, without harming the core structure or envelope. AND, on top of that, you have full flexibility for utilities—that's the BIG IDEA!" says Mion.



SINGLE-USE BAG DELIVERY SYSTEM



THE BIG IDEA

Use disposable systems for up- and downstream production, eliminating cleaning and cleaning validation. Initially limited to smaller capacity processes, recent advances have meant that within the next few years, continuous reactors will be able to accommodate 3,000-4,000 liter capacity. By 2030, these reactors will handle even larger scale capacity requirements. The DesignFlex facility allows for open and flexible space to accommodate future capacity increases.

THE PROBLEM IT SOLVES

Contamination is one of the biggest concerns of biopharma manufacturers. At each step, from biosynthesis to formulation, materials must be validated to eliminate contamination risks. They invest heavily in processes to keep manufacturing areas and the massive stainless steel tanks in which processes take place ultraclean.

Use of disposables in upstream bioprocessing eliminates the cleaning and cleaning validation, because the containers are discarded after a single use. This reduces risks, saves time, minimizes consumption of highly purified water, and lowers costs. Single-use technologies "provide a means for smaller, cheaper, greener, safer and faster development and production," according to a recent study by a leading German biotechnical association, Dechema Biotechnologie.[8]

HOW IT WORKS

Use large disposable plastic bags for storage and transport of buffers and media in an airtight, dust-free process. The media bags—large enough to handle 5,000 liters of material—are connected via large volume plastic tubing that feeds into the reactors, where continuous perfusion takes place.

The mobile media bags are located near the reactors to minimize the length of the tubing runs—avoiding clutter and reducing risk of damage. The tubing itself is disposable as well, so there is no permanent equipment to be cleaned or validated.

8 Eibel et al, "Single-use Technology in Biopharmaceutical Production," Dechema, March 2012. http://www.bpsalliance.org/wp-content/uploads/2014/06/BPSA-Economics-White-Paper-2010.pdf

ABOVE & FACING PAGE: Single-use bag delivery system.

LEFT: Universal manufacturing space - Single dose

TANK FARMS FOR UPSTREAM & DOWNSTREAM PURIFICATION

THE BIG IDEA

Create fully portable tank farm by mounting stainless steel tanks on movable skids within modules built on plug-and-play power amplifier units(PAUs). Place individual HVAC units on an upper level for easy access, reachable via an overhead walkway.

THE PROBLEM IT SOLVES

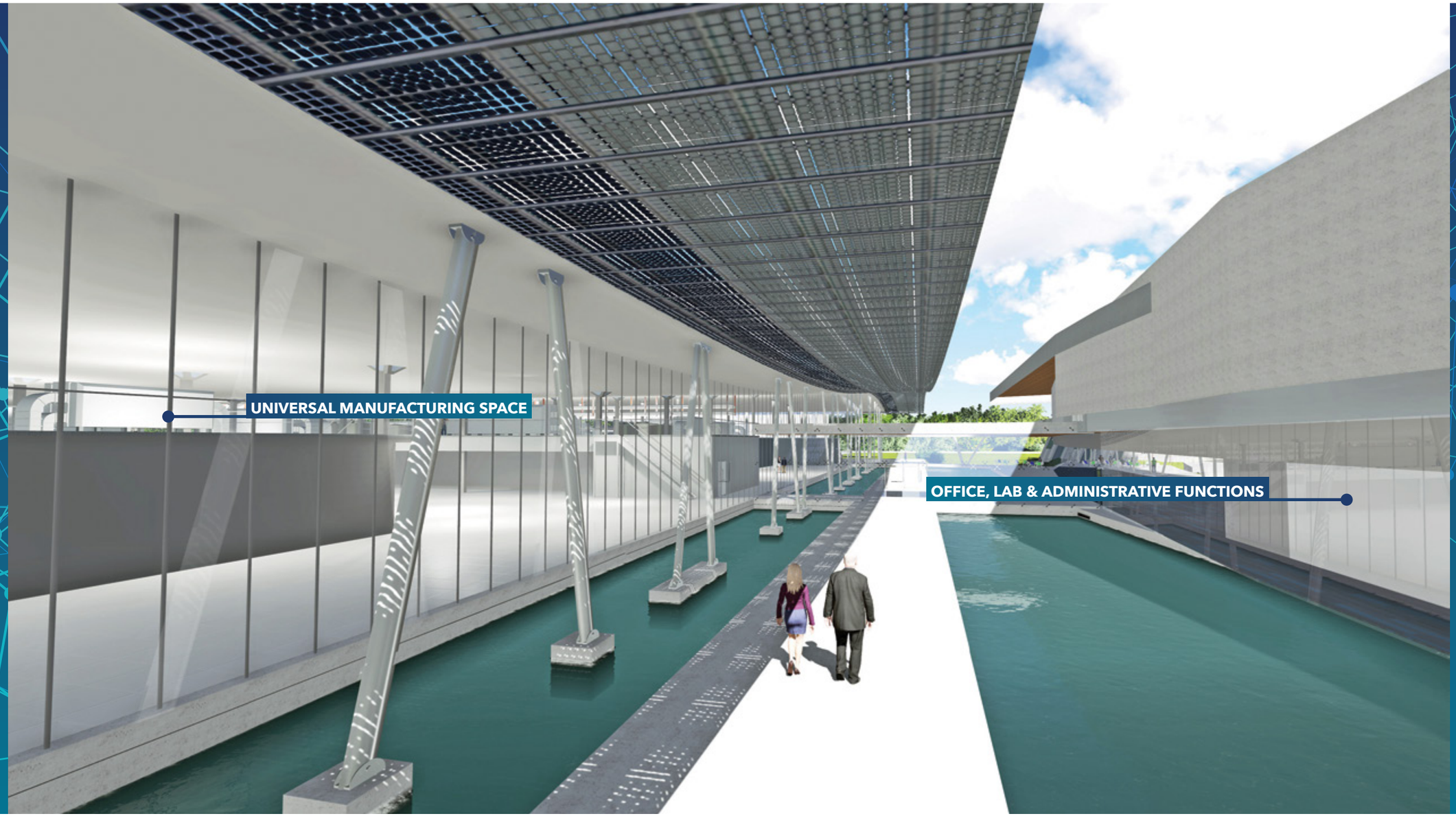
Permanently installed, highly complex purification equipment comes with a hefty price tag. It is a major reason for the high cost to construct new biopharma facilities. And…it is permanent. So, the potential to reuse the facility for other purposes—or even to change out aging equipment—is limited.

Modular systems are of higher quality, cost less, have shorter delivery cycles, and arrive ready to operate.[9] As demand increases, tank modules can be added easily with no need for new construction. In fact, the entire facility could be given over to produce more material for a blockbuster drug. As demand wanes, manufacturing can be scaled back again and tanks can be cleaned and reused for another process.

HOW IT WORKS

The tanks are mounted on industrial pedestals affixed to skids that can slide in and out through retractable walls without disrupting other processes. The overhead pipe rack system adds flexibility since certain processes require top-down connections. The raised floor system creates space for an underground utility corridor that is hooked up from below, with all chemicals flowing from the tank farm modules to the outside. Water flows through the underflooring as well. Without overhead piping that must be disconnected, tanks can be replaced more easily and with less disruption to other activities. The entire unit is contained within a module that can be moved in or out, with plug-and-play readiness.

9 "Why Build a Modular System?" IFS Solutions. http://ifsolutions.com/index.php/why-modular, accessed July 20, 2016.


UNIVERSAL MANUFACTURING SPACE
OFFICE, LAB & ADMINISTRATIVE FUNCTIONS

SHIPPING & RECEIVING

THE BIG IDEA

Give each function inside the facility its own shipping and receiving area, including single use, large-scale upstream, large-scale downstream, pilot, and research and development.

As transport evolves, the modularization of these functional areas allows for additions and upgrades without disruption. Drones with large-scale capacity can pick up or deliver everything from biologic waste to finished product to full modular units. Truck transport may still be part of a company's logistics equation in 2030 and beyond, and this design accommodates conventional truck traffic as well.

THE PROBLEM IT SOLVES

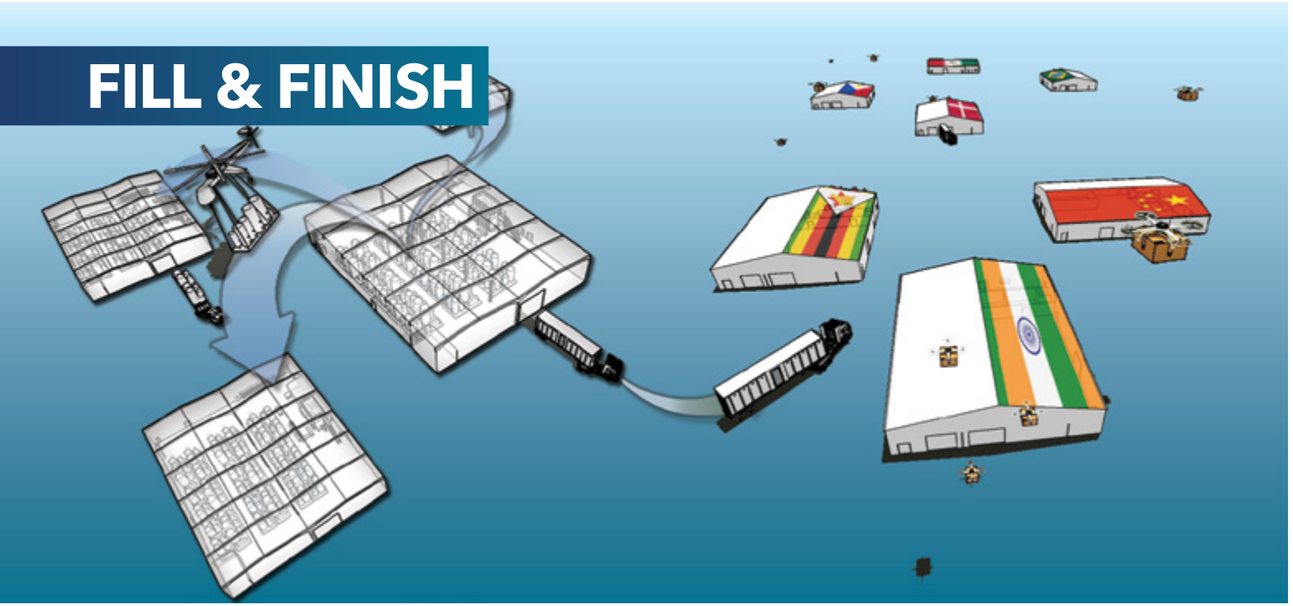
Decentralizing shipping and receiving areas by process keeps activities separate. This significantly reduces the risk of cross-contamination. Traffic also can flow more freely through the grounds.

HOW IT WORKS

Color-coding throughout the entire building serves as a visual reminder to direct traffic to the right point in the building. Already an accepted industry best practice, color coding reduces the risk of cross contamination, which poses an even greater concern in a facility where multiple processes are taking place. When a change to a new product occurs, paint colors can change as well, with the touch of a button.

A perimeter road lets trucks access individual shipping and receiving areas without causing traffic backups. The road can be pushed back as the building expands to meet new needs. Ample open space can accommodate new forms of transportation, such as drones or autonomous vehicles—or even an underground pneumatic tube tunnel system.

FILL & FINISH



Standardized, prefabricated fill-and-finish modules can be located anywhere in the world, sliding with equal ease into a low-cost, warehouse shell or architecturally significant, place-making building.

THE BIG IDEA

Commission pre-fabricated fill-and-finish modules that can snap into other modules on site for co-location advantages or work as stand-alone units anywhere in the world, depending on market demand. A raised floor system allows for complete process access below. Modularized individual HVAC systems attach from above. Internal design offers flexibility for continuous operations and lights-out, 24-7 packaging to maximize production capacity.

THE PROBLEM IT SOLVES

From the moment a drug wins federal approval, the clock starts ticking toward patent expiration. With the advent of biosimilars, there will be increased pressure to maximize the drug's revenue potential. Being ready to go with full production from the moment of federal approval is critical to achieving revenue goals.

The fill-and-finish unit's internal flexibility also addresses the shift toward personalized medicine. "Inside the fill-and-finish module of the future, small scale, single-use formulation can co-exist with large-scale, continuous operations," notes Burns & McDonnell's David Krumm, an architect and Design Team member. 3D/4D printing capabilities enable even more options.

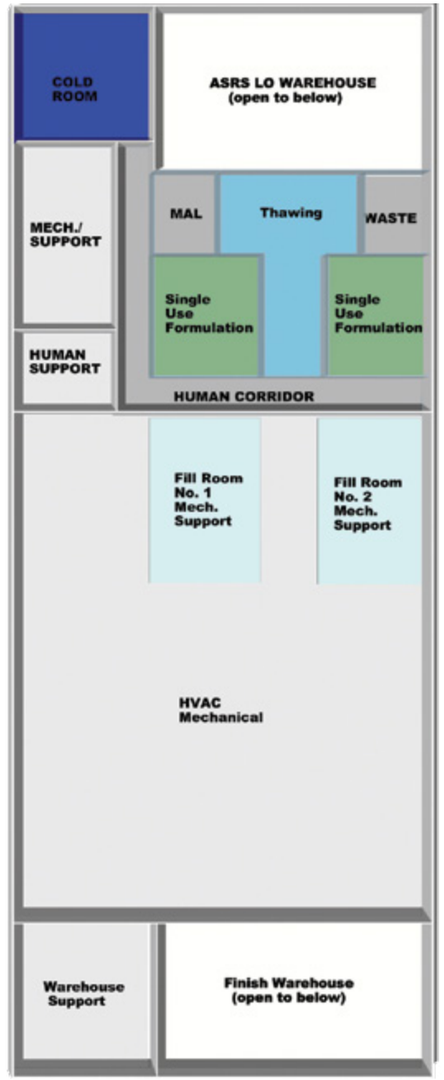
HOW IT WORKS

Add modules to existing facility to meet initial demand. Clone the design for additional modules, and ship globally to where demand is highest to lower transportation costs. By replicating a tried-and-true design, risks are reduced, increasing efficiency with each cloned facility platform.[10]

Follow the incentives and market demand for specific locations. Modules can be housed in easy-to-assemble, low-cost warehouse-like structures. Or, they could slip into a more elaborately designed exterior to integrate into a cityscape.

10 Salinas, Mike. "Modular Facility Design: A Cost-effective Option in the Post-Blockbuster Drug Era," M&W Group, 2015. http://www.mwgroup.net/wp-content/uploads/2014/11/Modular-Facility-Design_MWGroup.pdf, accessed July 20, 2016.

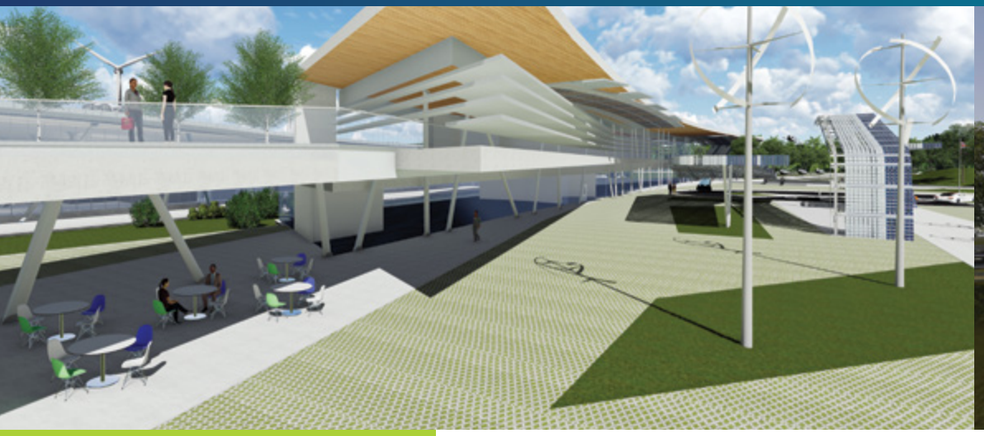
INSIDE THE FILL & FINISH MODULE

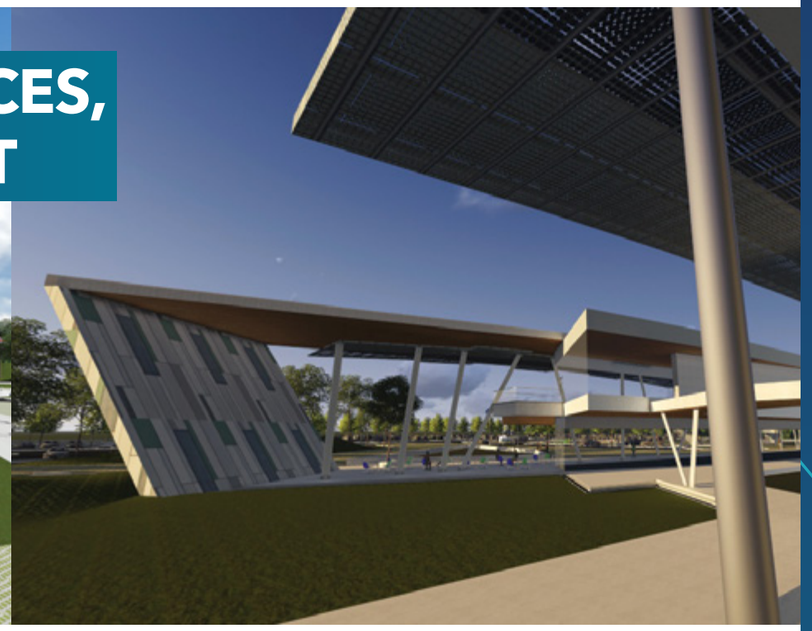


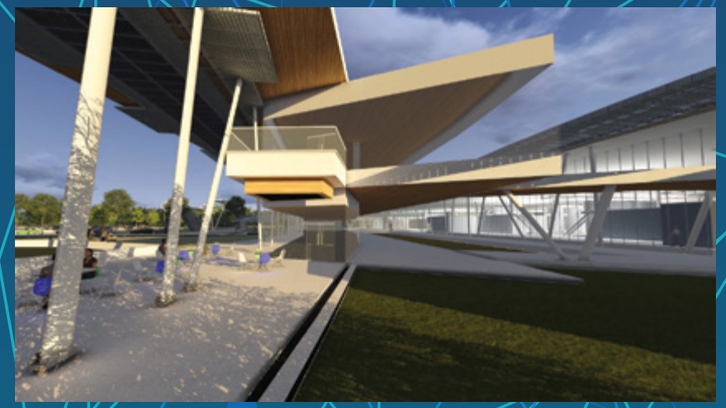
LEGEND

- ISO 5
- ISO 7
- ISO 8
- GRADE D
- NON-CLASSIFIED
- COLD ROOM

TRANSITIONAL SPACES, OFFICES, CO-LOCATED R&D, AND PILOT







THE BIG IDEA

Maximize open areas with walkways that transect the facility, using minimal permanent structural support for ease of change, co-location, and collaboration.

The transition space between the administration wing and the manufacturing space can be adapted for additional manufacturing capacity if needed. Separate gowning areas are adjacent to each process unit, connected by walkways to office areas. This makes life easier for quality staff, who will no longer have to remain gowned all day long. A more collaborative environment is created through co-location of offices, central R&D, pilot and manufacturing.

THE PROBLEM IT SOLVES

A key co-location benefit is in process development for the pilot manufacturing unit. At every clinical trial stage, different product amounts are required. It can be a challenge to optimize this process each time, figuring out how to produce the required quantity when it is needed.

By co-locating R&D, pilot, and large-scale manufacturing processes, an important knowledge flow is enabled. As the pilot unit produces what's needed for the next clinical trial stage, the product and process can be tweaked. "So, if you have to make a change, you can easily go back and talk to the early R&D team, and do some re-jiggering," explains one of the Design Team's technical advisors. The advisor, who manages the capital portfolio of a life sciences company and leads its workplace effectiveness group, notes that physical proximity makes it easier to partner the development team with the production group, enabling collaboration on new technologies that could enhance the production process. "Working together, once you create the process, you can engineer the process so it becomes standardized, which paves the way for increased efficiency and flexibility," she says.

Creating a physical space that invites collaboration also encourages interaction and dialogue between scientists and process experts. Such dialogue could yield lower-cost, more effective approaches to drug delivery, says team member Davila. "Today, the scientists are the ones who decide how the drug is to be delivered—say as an injectable—but this might not necessarily be the optimal way from a process, fill-and-finish, or patient delivery standpoint." Davila adds that this more collaborative approach could unearth cost savings that ultimately could translate to lower drug prices for consumers.

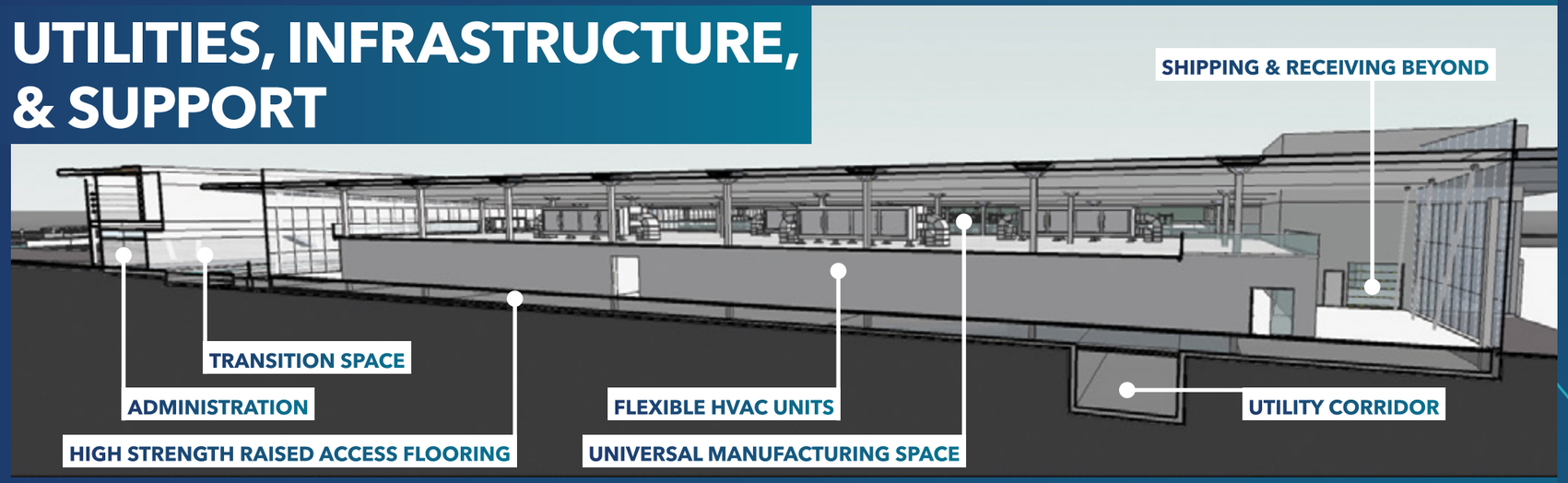
In addition, even in an age of digital connectivity, there's an inherent value in physical proximity. "We could do a much better job if labs and offices weren't as separated," says another team advisor, who also works in the area of workplace effectiveness. "Working in more collaborative spaces provides a better working environment for everybody."

HOW IT WORKS

A less traditional plan creates comfortable places in which to work collaboratively or individually. Co-located lab areas—also modulized—are designed for maximum flexibility as well. This allows for shared core instrumentation. It also facilitates the processes required to develop new molecular entities.

In addition, the flexibility allows for the addition of new job roles and different kinds of collaboration. For example, increasingly, bioinformaticists will design and analyze experiments in partnership with bench scientists, who will run the experiments.

UTILITIES, INFRASTRUCTURE, & SUPPORT



THE BIG IDEA

Build the entire structure on a heavy-duty raised floor and run a utility corridor underneath. This approach accommodates extremely heavy weight and allows access for repair and alteration. It also minimizes the need for permanent structural components, enabling re-use.

Vertical chases connect modular racks above with the utility core below. Water features flowing along transitional corridors and at the entry are collection points for rainwater and cache basins for purified, reclaimed wastewater from manufacturing processes. The water is recycled for use in heating and cooling and landscaping, to reduce reliance on external water sources.

Conventional metal duct work is replaced with super strong insulated corrugated cardboard that is 100 percent recyclable, water resistant, and fire retardant.

Use leading edge HVAC systems with emerging technologies including:

- Predictive maintenance software to warn of potential problems before a major failure occurs
- Thermally driven air conditioning: solar-powered HVAC supplemented by natural gas
- Ice-powered air conditioning: units can freeze up to 85 gallons of water each night for 6 hours of daily cooling capabilities for large spaces

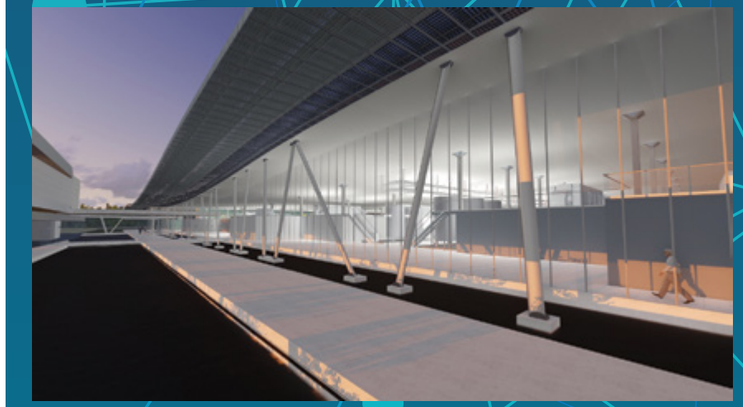
THE PROBLEM IT SOLVES

Permanently embedded utilities in the ceiling are among the single biggest obstacles to facility adaptation and re-use. They are hard to access, making repairs difficult and disruptive. This can slow down throughput, creating a domino effect of delays that could have revenue implications.

This configuration significantly increases the flexibility of the facility. Utilities can be added or removed as needed. Personnel can access utilities through the underground service level. Individual HVAC units take the place of centralized HVAC for increased control, reduced variability, and less disruptive repair in process areas.

HOW IT WORKS

Utilites can be structured with ceiling mounted modular rack installations above equipment. Or, they can be placed under the raised flooring to allow for readily accessible, free-range flexible installs. Large utilities are housed in an underground utility core. This allows them to pull from the mechanical support area outside, fed either from below the equipment or through the vertical chases connecting the racks above.



THE LONG VIEW

Adopting the approach as proposed here requires an evolution in mindset, from thinking only about today to looking ahead through many tomorrows. This may mean reconsidering the financial and location calculus as new facilities are planned down the road.

COST ADVANTAGES

It's no secret that life sciences facilities cost a lot of money and take a long time to build. The typical cost to build a new life sciences production facility hovers in the $500 million range, but can soar upwards of $1 billion.[11] It's a reason there's a rush to recover costs through tax incentives. It's also a reason that users try to stay in an obsolete building even though it cannot accommodate newer processes—which reduces operational efficiency even more.

What happens to these facilities after their owners deem them unusable, at the end of a 15-20 year span?

Managers of pharma companies' corporate real estate portfolios say that it's a struggle to figure out what to do with these legacy buildings, often weighed down with permanently installed, outdated equipment.

Because the facilities devalue quickly given this lack of flexibility—and the cost to repurpose them can outweigh the cost of building new—the typical financial approach is to maximize depreciation early, for a tax benefit. When and if the facility does sell, the price will likely be a tiny fraction of the original cost to build.

These legacy facilities are not particularly valuable assets from an economic development perspective either. The same inflexibility that poses re-use challenges within the same company or same industry is amplified when considering reuse for an entirely different purpose.

One recent sale highlights the issues in off-loading outdated life sciences facilities in stark detail. After deciding that its 1960s-era poultry vaccination research and manufacturing facility in the Maryland Eastern shore town of Salisbury could no longer be used "due to functional obsolescence,"[12] its owner, Merial, a division of French pharmaceutical conglomerate Sanofi, determined that the only thing to do was to sell. The 68,000 sf building, sat vacant for more than two years. Finally, in July 2016, the facility was sold to a local church for $1.5 million.

This shift toward more flexibility is already underway because things are changing so fast that there's a real risk of early obsolescence otherwise. Virginia's regional Inova Health System has taken this into consideration. The health care system is repurposing ExxonMobil's vacated 118-acre, five-building campus in the suburbs of Washington, DC into a center for cancer research and genome sequencing. The existing buildings are being gutted and interiors redesigned for maximum flexibility. Additional pad sites will become new facilities—also with adaptability as a key focus.

The reason for this approach? "What they need today is not necessarily what they are going to need tomorrow," says Dr. Gerald Gordon, president of the Fairfax County VA Economic Development Authority.

Inova's future plans for the site include the ability to accommodate college-style lecture halls as well as high school classrooms, in addition to wet lab space and pilot production facilities, plus residential units, health care facilities and retail, as part of a complete life sciences community. "This speaks to flexibility and being able to have the facilities morph into anything they need them to be," Gordon says.

The cost advantage in the flexible design approach as proposed in this paper lies in the ability to extend a facility's life span well beyond the typical 15-20 year average today. Because the building can be continually repurposed as needs change and technology evolves, when new products come on line, this same facility can accommodate them—eliminating the need to shell out carrying costs for vacant real estate AND the need to build something new.

Over time, this could significantly reduce:

- carrying costs for legacy facilities
- the time, resources, and expenses associated with siting, designing and constructing a new facility
- the size of the real estate portfolio and the costs associated with managing it

COMPANY	LOCATION	TOTAL INVESTMENT	PURPOSE
Athenex	Dunkirk, NY	$1.5 billion	Biologic cancer treatments
Baxalta *(formerly Baxter Life Sciences)*	Covington, GA	$1.3 billion	Plasma fractionation, purification, fill-finish, testing lab
Biogen IDEC	Solothurn, Switzerland	$1 billion	Large molecule, protein-based medicines
Bristol-Meyers Squibb	Dublin, Ireland	$900 million	Biologic-based medicines in multiple therapy areas
Boehringer Ingelheim	Wien, Austria	$545 million	Large-scale biopharma production facility for active ingredients using cell cultures
Hospira, Inc.	Andhra Pradesh, India	$390 million	Fill-and-finish for sterile injectable
Novo-Nordisk NA	Clayton, NC	$1.2 billion	Diabetes finished products and diabetes active pharmaceutical ingredients manufacturing
Roche	Suzhou, China	$470 million *(450 million Swiss francs)*	Diagnostics manufacturing
Samsung Biologics	Incheon, South Korea	$720 million *(850 million won)*	Large-scale biologics contract manufacturing organization
Sanofi	Flanders, Belgium	$339 million	Expansion; monoclonal antibody therapy for B-cell chronic lymphocytic leukemia
Vertex Pharmaceuticals	Boston, MA	$800 million	Headquarters

Source: Site Selection New Plants Database, corporate press releases

11 See a sampling of recent projects here: http://www.pharmaceutical-technology.com/projects/biogen/; In 2012, Baxter Life Sciences announced a $1 billion investment to construct a new facility in Covington Georgia (http://www.baxter.com/news-media/newsroom/press-releases/2012/04_19_12_expansion.page)

12 See press release: http://svnmiller.com/wesley-cox-sells-high-profile-pharmaceutical-facility/

SITE SELECTION & LOCATION

While some of the variables may change, the site selection calculus for biopharma facilities in the future will likely remain the same. According to location consultant Andrew Shapiro, the two key factors for today's life sciences site selectors are not going to change: proximity to markets and access to talent.

Shapiro, a principal with Biggins Lacy Shapiro & Company, advises corporations on the range of location-related issues, including site selection, incentives, energy and local land use regulations.

"Location trends in this industry are largely driven by market demand and market proximity today," he says. "If anything, I see this trend picking up more momentum in the future."

The ability to hire a qualified STEM workforce is another major influencer. Looking out 20-30 years, some tasks that require people today could be handled by robots and automated processes, particularly in fill-and-finish facilities. But for research-oriented functions, companies will continue to prioritize locations where scientific skillsets are readily available. "If you aren't looking at a recognized scientific innovation cluster, it could become even harder to find the talent you need," Shapiro says.

Biologics clusters typically emerge in regions with strong research institutions, a highly skilled and mobile workforce, access to a constantly renewing supply of talent, availability of capital, and an attractive quality of life, he notes.

Already, there's somewhat of an arms race going on to attract the best and the brightest. As Shapiro notes in a January 2016 article for Trade and Industry Development magazine, "Life scientists are the new 'rock stars,' recruited with the same zeal that would drive a major league baseball team to sign a Cy Young Award winner."

Given the competition for talent and the anticipated needs that aren't going way—even in an automated future—companies will begin to look deeper into the local education systems. Looking ahead, a robust K-12 school system won't just be a quality-of-life amenity to attract highly educated workers who want good schools for their kids.

In fact, it will be critical to ensuring that the company will be able to meet its long-term skilled workforce needs, according to Shapiro. "The farsighted site selector will… also investigate the state of the local K-12 educational system because it's a known fact that the U.S. is graduating an insufficient number of high school students with grounding in the technical disciplines and thus little or no interest in STEM careers," he writes in the magazine piece.[13]

Incentives, regulatory climate, and tax regime will also continue to play an important role in companies' location decisions. However, Shapiro notes that these issues will come into play only after companies have narrowed down their search to a specific region identified for market proximity reasons.

13 Shapiro, Andrew, "How the Bio-Pharma Industry Chooses the Best US Locations," Trade and Industry Development, January, 2016. http://www.tradeandindustrydev.com/industry/bio-pharmaceuticals/how-bio-pharma-industry-chooses-best-us-locations-11165

AREAS FOR FUTURE EXPLORATION & RESEARCH

Several important aspects of the biopharmaceutical value chain fell outside the flexibility-focused scope of this paper. They, too, are likely to influence future biopharma real estate portfolios.

GETTING DRUGS "THE FINAL MILE"

As the transportation industry undergoes massive transformation, so will the biopharmaceuticals distribution model. In their discussions, the team considered the logistics issues in getting medicines that last mile in the most challenging situations: reaching remote or cut-off locations during humanitarian crises, such as those caused by natural disaster, epidemic outbreak, or war.

The team met with Dr. Stephanie Kayden, a Harvard Medical School professor, emergency room physician, and humanitarian logistics expert to understand more about the obstacles faced by medical professionals on the ground inside a disaster or crisis zone.

Dr. Kayden acknowledged that reliable delivery and storage of medicines in field hospital situations is a significant challenge today—and will continue to be in the future. Among the issues: high theft risk, packaging that can break or open easily, medical waste disposal, complicated technology, and unreliable electricity.

What the team thought was the obvious and practical solution—design a modular, ready-to-go, "pharmacy-in-a-box" and deliver it direct to the field hospital by drone or blimp—in fact, might not be the answer, according to Dr. Kayden.

"Drones are already an issue," she said. "In many developing countries, people are suspicious of them because they can't necessarily rely on the government as a force for good. So, when they see giant boxes descending from the sky, they may think, 'that thing is either going to bomb me or spy on me!' Either way isn't good."

In the future, drones will become a more familiar presence. However, this familiarity may give rise to new challenges, she said. "The suspicion might go away. But then, people are going to know that the drones carrying supplies have value. So, they may start shooting them down for their own use or for sale on the black market."

When asked by the design team about future innovations in the cold chain—from drug creation to consumption—that would make a real difference, Dr. Kayden responded quickly. "Heat stability for medicines, like a heat-stable measles vaccine, number one. And number two, a simple, power-free self-cooling medical storage facility where the architecture of the structure itself keeps things cool and maintains optimal storage temperatures. These are the best things you as biopharma design innovators could do for us!"

Ultimately, the group determined that finding a solution to these highly complex problems deserved its own focus—an effort outside their specific flexibility challenge. However, several of Fluor's Design Team members are involved in a separate project that partners the company with the World Health Organization to address some of these issues.

THE FUTURE OF BIOPHARMA R&D

The biopharma R&D environment is changing rapidly. Advanced equipment and smart technologies are enabling high content screening for drug discovery and efficient live cell imaging and image data acquisition from

huge volumes of samples. After the initial discovery of a molecule of interest, these same technologies and advanced equipment allow for testing to take place anywhere in the world, linked through the cloud. "This kind of testing in the cloud is on a molecular level—gas and liquid chromatography, cell sorting, and robotic handling for experimental replication—to ensure repeatability and robustness," notes one Design Team technical advisor.

The Design Team's facility accommodates lab space. However, the team decided that the topic of what will go on inside those labs deserves its own design challenge—one which also falls outside the original charge to the team.

Indeed, the process of reimaging future labs in a more flexible way has already begun. "Universal Flex Labs allow them (tenants) to move walls in a flexible way and lab equipment in a flexible way so that they can change their workspaces to adapt them as they take on new projects without completely gutting or reconstructing their spaces,"[14] notes a recent article in Globe Street.

At one large biopharma company, the Workplace Effectiveness team—which pulls together staff from Real Estate, Space and Scenario Planning, and Neighborhood Work Environments in a comprehensive effort to optimize the workplace ecosystem—is looking at this issue closely. The team includes R&D staff, pilot process experts, manufacturing staff, as well as the company's associate real estate director. The goal is to identify a network of places that inspire innovation to improve patients' lives. Simple changes are already underway at this company: transparent glass windows for viewing into the labs to monitor experiments and equipment, open areas for collaboration, and breakaway office areas for heads-down, serious concentration time. The questions being asked now range from how to embed predictive technologies that could forecast epidemics to how to solve medical problems for just one person—and, importantly, how this will impact the physical R&D environments going forward.

PROCESS ANALYTICAL TECHNOLOGY & QUALITY BY DESIGN

Process Analytical Technology and Quality by Design are systems that make use of technology and data analytics to help control variation in manufacturing processes to ensure final product quality.[15]

The growing recognition of the value in embedding these approaches will further impact the way biologics are developed and manufactured in the future—as well as the spaces in which these activities take place.

It is clear that the trend toward adapting such systems will influence processes and affect all aspects of biopharma operations, ranging from the regulatory environment to corporate financial strategy.

Here again, the team did not address specific future implications, to stay true to the original flexibility challenge. However, the nature of the team's proposed facility would allow for easier adoption of these approaches, given the open nature of the space and the lack of permanently fixed, high-cost equipment.

14 Jordan, John, "In life sciences, it's all about the amenities," Globe Street, March 29, 2016. http://www.globest.com/sites/johnjordan/2016/03/29/in-life-sciences-its-all-about-amenities/

15 PriceWaterhouseCoopers, "Process Analytical Technologies and Quality by Design," 2015. https://www.pwc.com/gx/en/pharma-life-sciences/pdf/pwc-pharma-pat-qbd.pdf

CONCLUSION: A FUTURE-PROOF FACILITY

What's happening in the New York City market today captures the conundrum for today's owners of a life sciences facility real estate portfolio.

In 2015, 40 percent of the city's existing pharma space was vacant. At the same time, millions of dollars were being invested in a growing cluster of start-up biopharma companies, many of which are linked to the city's burgeoning academic research centers. In 2014 alone, the National Institutes of Health provided $1.5 billion in funding for New York City's public and private life sciences initiatives.

A surge in demand for new space has led to a life sciences construction boom in pockets of the metro area, including Midtown and South Midtown Manhattan, Brooklyn, and Harlem. Jones Lang LaSalle reports 2.45 million square feet under construction as of 2015.[16]

With lots of existing space available, why the construction boom? It's a classic supply-demand disconnect: The available supply doesn't meet what's being demanded by this new generation of biopharma companies.

In a nutshell, this is the economic argument for building with maximum flexibility. By incorporating the design elements proposed in this paper, life sciences facility users can:

- Minimize the risk of obsolescence
- Optimize facility usability even as needs change
- Improve valuation and reduce time on the market at point of resale
- Boost manufacturing efficiency
- Lower the risk of cross-contamination
- Reduce energy costs
- Adapt to changing workplace cultures

The approach yields a future-proof facility—one that can easily adapt to and integrate multiple iterations of technological change, scientific breakthrough, and process innovation. This hackable design ethos removes permanent physical barriers so that the building can morph into whatever shape or form is needed at the time, in a lifespan that exceeds the imagination.

16 The data and market statistics in this section are attributed to Jones Lang LaSalle, Life Sciences Outlook New York City, 2015. http://www.us.jll.com/united-states/en-us/Research/US-New-York-Life-Science-Outlook-2015-JLL.pdf

GLOSSARY OF TERMS

BIOINFORMATICS: The science of modeling biopharma's essential building blocks, including biomolecules and biologic systems, through the use of databases and computers.

BIOLOGICS: A biological medicine is a drug with an active ingredient made from a biological source. There are three steps in the biologics manufacturing process: 1) cell culture, which features process line development, cell expansion, and cell culture; 2) recovery and purification, including harvest, a multi-step purification process, and virus inactivation and removal; and 3) formulation to distribution, which begins with filling and finishing, followed by packing and storage, quality assurance and characterization, and stability testing.

BIOPHARMACEUTICALS: Drugs that are produced through the use of biotechnology (technology involving live organisms) and with complex, large biological molecules.

BIOSIMILARS: A biopharmaceutical that is developed to be similar to a preexisting biological medicine, known as the reference medicine. Biosimilars can only be sold once the patent of the reference medicine expires.

BUFFERS AND MEDIA: External additives that are critical to the production of biologics. Buffers purify the biologic by adjusting its acidity while media promote cell growth.

CLEAN ROOM: A production area with a highly controlled atmosphere to minimize any possible contamination from outside sources, such as human skin or hair and airborne contaminants. Each clean room has its own gowning process to sterilize visitors before entry, which may include lab coats, hair- and beard nets, booties, and safety glasses.

CONTRACT RESEARCH ORGANIZATION (CRO): A pharma or biopharma contractor that provides a wide range of outsourced research and development services.

CROSS-CONTAMINATION: Cross-contamination occurs when one biopharma product's airborne (or otherwise transported) byproducts interfere with the development or performance of another. This is a key risk for biopharma manufacturers because contaminated products must be discarded and processes must be halted for thorough cleaning and purification, resulting in higher costs and production delays.

FILL-AND-FINISH: The physical assembly of the drug, done via sterile procedure. Filling involves incorporating the active ingredients into the drug. Finishing involves sealing the product and preparing it for the end user. These are the final steps in the drug manufacturing process before packaging and distribution.

MONOCLONAL ANTIBODIES: Biologic agents designed to fight one specific disease or infection. They are made by combining a single antibody-producing cell (extracted from an animal such as a mouse) with a cell of an antigen (such as cancer), allowing the cell to grow and divide indefinitely.

NOVEL MEDICINE: A new drug that has received approval for manufacture and sale from the United States Food and Drug Administration. This approval typically comes after a long process involving several intermediate steps, beginning with the submission and approval of an Investigational New Drug (IND) application, featuring data on the potential success of the drug in concept. Following acceptance of the IND, the company begins the multi-phased clinical trial stage. At every step, the company is required to submit additional data and information.

PHARMACEUTICALS: Drugs produced using chemical means and small, simple molecules.

PILOT PRODUCTION: This key step in the drug manufacturing process involves testing every aspect of the drug being manufactured, including the facilities, batch sizes, and ingredients, before the facilities and procedures are finalized. Some contract manufacturing organizations (CMOs) offer outsourced pilot production as part of the range of services they provide to pharma companies.

QUALITY CONTROL: The testing, analysis, sampling, and establishment of specifications to ensure all aspects of the drug manufacturing process—ingredients, machinery, packing materials, and processes—are up to the necessary standards for consistency, purity, and strength.

WET LAB: A laboratory equipped with appropriate plumbing, ventilation, and equipment to allow for hands-on scientific research and experimentation.

Sources for glossary terms: 2016 Pharmaceutical Health Information System Glossary; Amgen; bio.org; biopharma.com; Biopharminternational; Bioreality.com; Merriam-Webster; National Institutes of Health; pharmaceuticaldrugmanufacturers.com; Pharmaceutical Online; Pharmacist.com; Pharmtech.com; US Food and Drug Administration.

REFERENCES

ARTICLES, REPORTS, & PUBLICATIONS

Baxter Life Sciences. "Baxter Announces Biologics Capacity Expansion," press release April 19, 2012. http://www.baxter.com/news-media/newsroom/press-releases/2012/04_19_12_expansion.page

Carnevale, Anthony P; Smith, Nicole; Strohl, Jeff. "Recovery 2020. Job Growth and Education Requirements through 2020" Center for Education and the Workforce, Georgetown University, June 2013. http://cew.georgetown.edu/recovery2020

Davila, Hector T. "How to Optimize Continuous OSD Manufacturing," Pharmaceutical Manufacturing, April 18, 2013. http://www.pharmamanufacturing.com/articles/2013/1304-optimizeosdmanufacturing/

DiMasi, J. A. and Grabowski, H.G. "The Cost of Biopharmaceutical R&D: Is Biotech Different?" Managerial and Decision Economics 2007; 28(4–5): 469–479.

Eibel et al, "Single-use Technology in Biopharmaceutical Production," Dechema, March 2012. http://www.bpsalliance.org/wp-content/uploads/2014/06/BPSA-Economics-White-Paper-2010.pdf

Haigney, Susan. "Challenges, and Trends in Biopharma Facility Design," BioPharm International, Volume 27, Issue 9, September 1, 2014. http://www.biopharminternational.com/challenges-and-trends-biopharma-facility-design

IFS Solutions. "Why Build a Modular System?" http://ifsolutions.com/index.php/why-modular Accessed July 20, 2016.

Jones Lang LaSalle. "Life Sciences Outlook New York City, 2015." http://www.us.jll.com/united-states/en-us/Research/US-New-York-Life-Science-Outlook-2015-JLL.pdf

Jordan, John. "In life sciences, it's all about the amenities," Globe Street, March 29, 2016. http://www.globest.com/sites/johnjordan/2016/03/29/in-life-sciences-its-all-about-amenities/

Kapp et al, "Roadmap to Implementation of Single-use Systems," Bio-Process Systems Alliance, April 2010. http://www.bpsalliance.org/wp-content/uploads/2014/06/BPSA-Economics-White-Paper-2010.pdf

Larson, Richard C. and Yi, Xue. "Stem Crisis or Stem Surplus? Yes and Yes," Monthly Labor Review, US Department of Labor, Bureau of Labor Statistics, May, 2015. http://www.bls.gov/opub/mlr/2015/article/stem-crisis-or-stem-surplus-yes-and-yes.htm

MestreFerrandiz, J., Sussex, J, and Towse, A. "The R&D Cost of a New Medicine." London, UK: Office of Health Economics, 2012. https://www.ohe.org/publications/rd-cost-new-medicine

Paul, S.M. et al. "How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge." Nature Reviews Drug Discovery 2010; 9: 203–214. http://www.nature.com/nrd/journal/v9/n3/full/nrd3078.html

Pharmaceutical Research and Manufacturers of America. "2016 biopharmaceutical research industry profile," Washington, DC; April 2016. http://phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf

Pharmaceutical Technology. "Biogen Idec Pharmaceutical Production Facility, Denmark," http://www.pharmaceutical-technology.com/projects/biogen/ Accessed July 21, 2016.

PriceWaterhouseCoopers. "Process Analytical Technologies and Quality by Design," 2015. https://www.pwc.com/gx/en/pharma-life-sciences/pdf/pwc-pharma-pat-qbd.pdf

Sandle, Tim, Ph.D. "Risk Considerations for Aging Pharmaceutical Facilities," Journal of Validation Technology, Institute of Validation Technology, April 26, 2016. www.ivtnetwork.com

Shanley, Agnes. "Aging Facilities: Aseptic Manufacturing Faces the Future," Pharmaceutical Technology, Volume 2015 eBook, Issue 2, May 15, 2015. http://www.pharmtech.com/aging-facilities-aseptic-manufacturing-faces-future

Shapiro, Andrew, "How the Bio-Pharma Industry Chooses the Best US Locations," Trade and Industry Development, January, 2016. http://www.tradeandindustrydev.com/industry/bio-pharmaceuticals/how-bio-pharma-industry-chooses-best-us-locations-11165

StatNews. "Vermont becomes first state to require drug makers to justify price hikes," June , 2016. https://www.statnews.com/pharmalot/2016/06/06/vermont-drug-prices-transparency/

Salinas, Mike. "Modular Facility Design: A Cost-effective Option in the Post-Blockbuster Drug Era," M&W Group, November 2014. http://www.mwgroup.net/wp-content/uploads/2014/11/Modular-Facility-Design_MWGroup.pdf

AUDIO

Bebinger, Martha, "Inventing A Machine That Spits Out Drugs In A Whole New Way," All Things Considered, National Public Radio, May 23, 2016. http://www.npr.org/sections/health-shots/2016/05/23/478576727/inventing-a-machine-that-spits-out-pills-a-whole-new-way

WEBSITES

Chromasun, solar powered air conditioning
http://chromasun.com/CHW.html

Comx
http://www.comxusa.com/concrete-filled-steel-access-floor-systems

Daxner International
http://www.daxner-international.com/en/Products/Big-bag-handling/Big-bag-loading-systems/23-Big-bag-loading-system-ECO-LIFT-1500

GatorDuct, disposable corrugated cardboard ductwork
http://www.gatorduct.com/

GE Renewable Energy
https://www.gerenewableenergy.com/wind-energy.html

IceEnergy, ice-powered air conditioning
https://www.ice-energy.com/

Innovative Glass
http://www.innovativeglasscorp.com/

Onyx Solar
http://www.onyxsolar.com/

Plascore
http://www.plascore.com/honeycomb/cleanrooms/

Starrco
https://www.starrco.com/modular-clean-rooms/

Sustainable Paving Systems
http://www.sustainablepavingsystems.com/products/grasscrete/

Wind-Works
http://www.wind-works.org/cms/index.php?id=17

ZinCo Green Roof Systems
http://www.zinco-usa.com/

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