

PHARMACEUTICAL ENGINEERING®

Special Report
FACILITY OF THE FUTURE
May/June 2016

Are We There Yet?

Reprinted from
PHARMACEUTICAL ENGINEERING
THE OFFICIAL TECHNICAL MAGAZINE OF ISPE
MAY-JUNE 2016 VOL 36, NO 3
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Facility of the Future

Technological advancements such as wearable devices, continuous manufacturing, and 3D printing have significantly improved the products and services available to medical professionals and patients around the world. These and other innovations in numerous industries are the result of advances in materials science and concepts like the Internet of Things. As technology continues to develop, however, many in industry have begun to question if they have the right workforce, facilities, and technologies to produce equally innovative products, processes, and ideas.

Many organizations, including ISPE and the Global Pharmaceutical Manufacturing Leadership Forum (GPMLF), have been preparing for years, discussing and providing information to the pharmaceutical industry on how to handle these new technologies and how to prepare current and future workers to participate in this technological transformation.

The International Leadership Forum (ILF) is a group of 50 to 75 global leaders from more than 30 different companies engaged in the manufacture of key pharmaceutical products, as well as some vendors and service providers. The group meets biannually to address key topics in the pharmaceutical industry. In 2012 the ILF produced a document called the Global Positioning Strategy, which outlined six major elements that would provide platforms for alignment of key areas in the industry.

One of these elements was the Facility of the Future. To ensure that future manufacturing facilities were more agile and responsive to market changes, and focused more on customer's needs, the ILF recommended that the Facility of the Future be designed around the following concepts:

Use more portable and single-use technology, while utilizing flexible production lines, including the use of lean. The need to improve flexibility, increase productivity and efficiency, and reduce overall operating cost will require drastic changes to the pharmaceutical facility of the future if we are to compete successfully in this new and changing environment.

Use modular building strategies that allow for localization and rapid response or relocation to deploy manufacturing where and when needed.

Use quality by design concepts in new facility designs.

Utilize green and sustainable building concepts in the overall life cycle of all manufacturing facilities.

Ensure quick and efficient technology transfer processes so medicines can be delivered to the customer quickly and accurately.

Utilize process analytical technology while ensuring greater data connectivity and usage of analytics to drive improved performance.

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What Is the Facility of the Future?

In 2015, the ILF rebranded itself into an organization known as the Global Pharmaceutical Manufacturing Leader Forum (GPMLF). This group agreed to streamline and continue the focus on three key areas:

1. Supply chain robustness/supply need to rapidly evolve
2. New technology and plant-process design of the future
3. Update workforce of the future

The ISPE Strategic Plan 2016–2020 includes seven areas of prime focus for the organization over the next four years including:



ISPE Strategic Areas of Focus

The inclusion of the facilities of the future as one of ISPE’s seven key areas of focus over the next 4 years demonstrates the organization’s understanding that agile, efficient, sustainable, and compliant manufacturing facilities are absolutely required to support both patients and customers as we move into the future. ISPE is dedicated to preparing its membership (both individuals and companies) for a major transition as the industry begins to design and implement innovative technologies and concepts that will move the pharmaceutical industry toward the facility of the future.

To further emphasize and ensure the industry clearly recognizes the importance of these new types of facilities, which are focused on customer demand and speed of implementation, the ISPE annual Facility of the Year Award will, in 2017, introduce a new “Facility of the Future” award category. This new award category will highlight organizations and projects that implement new ways of thinking, feature innovative manufacturing of pharmaceutical products, and recognize teams and organizations that employ facility of the future concepts as well as other new technologies to advance the pharmaceutical industry.

As you will see in this series of articles, there are many definitions and assumptions about what a facility of the future includes and how it will better the manufacturer’s and customer’s daily and long-term goals. To remain at the forefront, an industry must continually examine how things are done and strive to create new ways to be innovative and transform the way of doing business.

Facility of the Future concepts attract the attention of many parties in the development and advancement of diverse industries, including governments, academic institutions, vendors, and service providers.

1. Governments are interested in new ways of manufacturing to ensure sustained employment for a particular industry or area of the state. Federal, state, and local governments succeed and fail based on employment for their constituents. It is well accepted that one manufacturing position usually creates three to four additional positions in a service or support industry. Government organizations in many countries are formulating strategies to help develop Facility of the Future environments for certain key industries they believe will create growth and economic advancement.
2. Academic institutions are continuously focused on Facility of the Future initiatives to ensure they produce graduates with the right technical and analytic skills to compete in the future labor market. Academic institutions also strive to know what future areas of research and development they should be exploring to be ahead of the technology road map.
3. Service providers and vendors want to supply new services, products, training, and expertise that give manufacturers new approaches, skill sets, and technology to improve agility, quality, and cycle time.

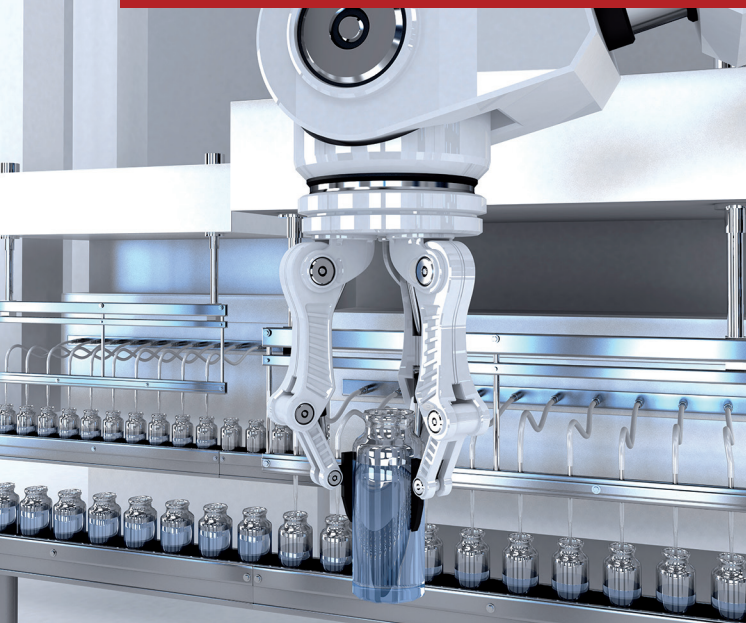
In 2017, FOYA will introduce a Facility of the Future category

Only with great collaboration between government, academic institutions, and the private sector can the maximum benefit of facility of the future be obtained. As noted previously, these new technologies will require additional employee training to develop new skills and to understand and implement the new practices brought about by technology advances. Collaboration with academic institutions in new areas of research and development, and working with governments to ensure the right environments are in place will allow these new technologies and methodologies to flourish.

What is clear in the pharmaceutical industry today is that leading industry organizations like ISPE and the GPMLF are putting great energy, effort, and resources into communicating facility of the future concepts and major developments within this field to their members and the pharmaceutical industry as a whole. This is an area of excitement and interest for ISPE leaders and membership.

ISPE has organized Facility of the Future forums in regional meetings around the world throughout 2016. Facility of the Future events or work streams were held in March in Frankfurt, Germany, and Raleigh, North Carolina, and in April in Shanghai, China, with strong participation and interest. ISPE will also conduct an important two-day session focused exclusively on Facility of the Future concepts in November 2016 in Bethesda, Maryland. ■

Jim Breen



Turning Opportunities into Reality

Pharmaceutical manufacturing has been conservative for many years. How conservative? From a manufacturing technology point of view very little has changed in the past half-century. In some selected areas, however, new technologies and regulations have begun to emerge.

A few pharma and biotech companies have shared their visionary strategies; some have even built pharmaceutical “Facility of the Future” concepts that have become operational. These include real-time-release manufacturing, functionally closed systems with low room classification, and continuous manufacturing of pharmaceutical drug products. While only few of these visionary experiences have been shared publicly, they still provide an opportunity to learn new best practices that differ significantly from previous state-of-the-art solutions.

Facilities of the Future initiative

To disseminate this knowledge as widely as possible, ISPE has launched a “Facilities of the Future” strategic initiative, hosting a number of events in Europe, China, and North America. At these gatherings, several companies have shared recent projects and current investments in next-generation solutions that point toward an agile and flexible manufacturing paradigm. With cooperation from regulators and technology suppliers, a number of new solutions and project experiences have been shared, followed by helpful discussions on the lessons learned.

In addition, the US Food and Drug Administration (FDA) has established the Emerging Technology Team—a specialized group within the Office of Pharmaceutical Quality that includes representation from the Office of Regulatory Affairs—to work directly with industry to help identify and resolve scientific

From a manufacturing technology point of view very little has changed in the past half-century

issues for new technologies. This provides opportunities for discussion and mutual development between regulators and industry. The ISPE Facilities of the Future initiative is a meeting ground for this cooperation.

Increasing demand

After several years with a low investment levels, project activities are once again high, with increased capacity demand for new or enhanced products, within biotech and chemical active pharmaceutical ingredients as well as injectables and traditional oral solid dosage products. Contract manufacturing organizations are also seeing increased capacity demand as more products are approved for local and global markets.

Some companies are concerned that these capacity demands are more than suppliers and engineering companies can handle, and that they run a risk for a capacity bottleneck. This is probably the new normal for pharma: After years of focus on patent expires and patent cliff concerns, a new wave of product approvals and a new generation of biosimilar products are approaching commercial manufacture.

This new reality also includes regulatory challenges from the world market as some countries establish new regulations or enforce practices that differ from mainstream international regulations. This can challenge the application of new technologies. But if Facilities of the Future are to supply the global marketplace, the challenge should be managed by cooperation with regulators on an international level.

As ISPE continues to stimulate innovation and best practice sharing worldwide, knowledge about current good manufacturing practices will increase. If new technologies are applied with careful consideration and management, they may be able to solve many traditional pharma manufacturing challenges. Pharmaceutical equipment and system suppliers also have many examples to share. And as suppliers often remind us, there’s no need to reinvent the wheel: Inspiration may also be drawn from industries outside the pharmaceutical world, as well.

So perhaps the time of the conservative pharmaceutical industry is coming to an end. Pharmaceutical manufacturing technology and solutions are starting to change, and practical experience with new and effective solutions provides a glimpse of the agility, flexibility, and quality envisioned in the FDA’s oft-quoted desired state for pharmaceutical manufacturing.

ISPE’s Facilities of the Future initiative may be a good way to get there. ■

Gert Moelgaard

The Workforce of the Future

Defining challenges and finding directions



One of the biggest decisions a manufacturer can make is whether its long-term strategic objectives are best served by upgrading existing facilities or by moving to new a location. Making this decision requires answers to a number of questions about the workforce:

- What technical knowledge and process skills will be required to meet future demands?
- How can we transfer them to different regions of the world?
- Do universities in the region teach the necessary scientific and engineering courses?
- How will trainers be trained and/or acquire proper qualification?
- What should we know about regional culture and lifestyle?
- What managerial style works best in each region? Is it contrary to our corporate style and values?
- What is the process for training all levels within organization?
- How will the company analyze workforce demand?
- What will strategy will we use to retain a skilled workforce, especially as the population ages and the industry loses the journeymen who know how to manufacture products?

Workforce development

The biopharmaceutical landscape is changing rapidly. Many multifunctional sites are being repurposed into as-yet-to-be-defined operational units or, in anticipation of product approval, are gearing up to handle new technology that will be deployed at a future date.

Yet while this is happening, 70% of biopharmaceutical industry workers remain stratified in scientific or manufacturing silos, and the industry, which has historically struggled with knowledge transfer, now faces an additional challenge: the emergent divide between technical and process workers. Overlap and cross-functional ability between the two are critical, and that criticality will increase significantly as the industry enters a new age of manufacturing.

Traditional job descriptions must and will change. Employee development programs must prepare workers to fill multiskilled roles that are often unique to each unit. Leaders from both manufacturing operations and the scientific community will be required to identify the skills and knowledge necessary, and ensure that the workforce has the tools they need to be successful. Enabling workforce success will result in success for the operational unit.

Education

Yesterday's workforce required a high school diploma. Today, many workers have college diplomas. Tomorrow's workforce will need postgraduate degrees. The conundrum is how to hire an "overly" qualified workforce, train them to the required skill level, and then retain that workforce to achieve product life cycle stability.

Whatever the employees' educational background, the work culture must offer job satisfaction, a sense of equality, and respect. It's also important to adhere to the region's cultural history. A one-size-fits-all monolithic corporate culture is doomed to fail. Finally, corporate policies addressing workforce culture must be established and strictly enforced; this reinforces the company's commitment to equality.

Millennials

Another factor in workforce development and satisfaction is generational: Millennials define success differently, and have different drivers for career decisions than their predecessors. Many from the United States and Europe have minimal loyalty to the corporation. Industry must learn what these drivers are and strive to create an environment that satisfies both corporate and individual objectives. Failure to do so will only erode employee loyalty and continuity as millennials seek employment elsewhere. Providing a place for employees to work that will improve their way of life and provide satisfaction that they are making a difference is a great place to start.

Leadership

Leadership will also be a challenge for global corporations that manufacture products and do business in different countries. We need to address and answer the following questions:

- How do we determine the ideal global leadership style and assess the gaps we likely have?
- If we examine the attributes of successful leaders in developed economies and compare them to those in emerging economies, can we identify the qualities required to lead a successful global operation?
- Access to huge markets and high profits are offset by the potential for failure. How do we train leaders to be proactive in their approach to leading the region?
- How do we build the succession plan? On what facts should it be based?
- How do we motivate staff so they are less likely to abandon ship?
- How do we create respect between management and workers?
- How can leaders make employees feel like winners?
- How do we convince process operators that producing products that meet specification the first time turns compliance into confirmation?

ISPE task team

The ISPE Global Pharmaceutical Manufacturer's Leadership Forum has been tasked with addressing these and other challenges that surround the Facility of the Future and the Workforce of the Future. These strategic objectives are crucial components of the biopharmaceutical industry's short- and long-term objectives to deliver lifesaving medicines around the world.

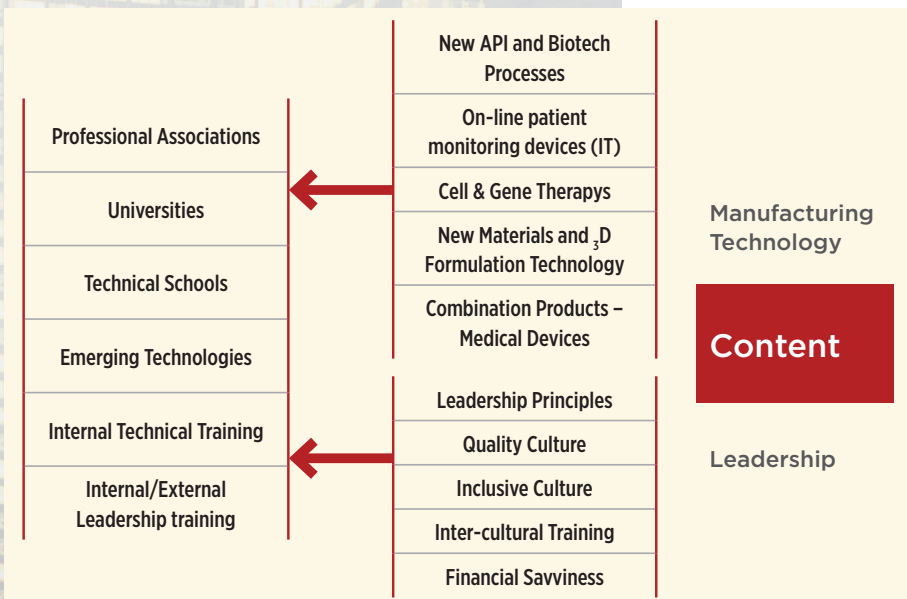
Employee development programs must prepare workers to fill multiskilled roles

Case study

My former company, Eisai Co., Ltd., restructured its R&D organization into 12 distinct units, split into therapeutic focus and riskier next-generation drugs. The company had a number of chemical entities that had been discovered years before but were deemed too toxic for human trials. They may now be able to utilize new delivery systems and scientific knowledge to take the drugs from the R&D shelves to next phase of development.

Eisai's reorganization provided the backing and stability of a large company, but by regrouping the workforce in smaller focused units created an entrepreneurial free-thinking environment provided a pathway for employees to expand their knowledge and skill. I don't know if Eisai deliberately established a work environment attractive to millennials, but it definitely provided opportunity and helped satisfy many millennials' desire to gain skill and knowledge.

This organizational setup will work in the process development and manufacturing sector as well, but it must be intentionally structured to best serve the workforce's needs and serve company objectives.



Millennials define success differently and have different drivers for career decisions than their predecessors

Figure 1: Knowledge sources for manufacturing technologies

The task force charter is to:

Create a process of ongoing understanding of the many cultural differences, geopolitical activities, national characteristics, and national norms to define diversity in our global “space” so that we can learn and adapt to lead, manage, motivate, and inspire our staff in all the regions of the world in which we do business.

Figure 1 illustrates knowledge sources (left) for manufacturing technologies (center). Establishing a workforce with the necessary knowledge and skills will require input from many—if not all—of these sources. Employees are also encouraged to never stop striving for knowledge.

The ISPE task team will focus on the knowledge and skills required for process operators, then work backward to process development and R&D. Process operators must know what a CPP is, how it is determined, and how it is related to quality issues. Employees in process development must have a clear understanding of the required specifications for the excipients used, and may even need to identify vendors that meet those specifications. R&D scientists must deliver basic science—and then it is interpreted by process development into the “voice of the product” or the applied science; process development staff uses this information to create technology transfer and training for process operators to insure manufacturing has minimal challenges.

Conclusion

The quest to produce high-quality, low-risk products at lower cost to meet market demand is often addressed through new technology, systems, infrastructure, and asset reliability. Yet a solid and reliable workforce should be established before any of these.

Every company and organizational unit should define the future workforce challenges they face in their region, and identify the strategies and objectives they should develop and execute for long-term success. Since organizational improvement is a journey with no final destination, these objectives will be continuous.

Taking the time to complete this thoughtful planning, however, will provide a road map for today and a GPS for tomorrow. If we neglect to plan for change and improvement, in 10–15 years we will not have achieved the goals for high-quality, safe, pure products and lower unit costs.

Planning for the facility and workforce of the future presents both challenges and opportunities—and that’s good news for the patients who depend on us to meet their needs today and tomorrow. ■

Larry Kranking



What Is the Facility of the Future?

“Facility (or plant) of the Future” is a great buzz phrase. Nobody can take issue with it. Why does it resonate with so many people; why are conference sessions on the subject always full? Why is everyone searching for the magic elixir of what it is and how to acquire it? Why is it so elusive? Are we already there? Does our mandate of quality and regulatory compliance help or hinder our ability to achieve efficient, world-class manufacturing operations?

But what are the characteristics of this mysterious facility of the future? What do we have to do to make it a reality, what are the challenges, what are the opportunities?

Pharmaceutical science may be close to entering its own “Moore’s Law” era

What are the external forces driving us to FoF?

Pharmaceutical science may be close to entering its own “Moore’s Law” era. Our understanding of biochemistry continues to increase—exponentially if you will. Computers are modeling physical chemistry, and our ability to efficiently identify or even to construct therapeutically potent molecules large and small is growing by leaps and bounds. In other words, the productivity of our laboratories—in terms of percent of molecules that prove therapeutic efficacy, will increase. This increase in “hit rate” for clinical trials, if it becomes reality, will drive down discovery costs. But this breakthrough science, if realized, will only put more pressure on engineering and manufacturing to deliver the processes and the facilities more quickly, with higher reliability, more throughput, and lower operating costs.

As costs to develop new drugs presumably declines, as our connected world makes product information more transparently available, as government and private payers demand lower prices for products, and as these new therapies treat previously untreatable and life-threatening or debilitating diseases, demand will only increase and the costs of goods sold will bear increased focus. We have experienced the significant decrease in the cost of computers while their capabilities have grown tremendously; should we not also expect a significant decrease in the cost of drugs in spite of significant increase in therapeutic value?

Diversity is the word when it comes to the global pharmaceutical market. Geography, politics, ethnicity, demographics, infrastructure, and regulatory domains all contribute to this diversity. Certain diseases thrive in certain environments, and in some cases, manufacturing proximity to disease source may drive manufacturing location. In some countries, some or

all manufacturing of drugs must be done in-country. Some diseases are prevalent in a given ethnic population but not others. Population age distributions are shifting, but at different rates in different countries. Different countries have different transportation infrastructure capabilities (road, rail, air, and storage along the way). Global regulators have yet to harmonize, and while progress is being made, regulatory diversity is still an issue for most companies. Lastly, tax rates vary considerably, which often trump all other factors when deciding where to manufacture.

Geographic diversity is reflected in supply chain complexity. Raw material sourcing, reliability of a given source, quality and variability of the source, and exposure of the source to natural or man-made disruptions are all important considerations. Raw material and finished goods protection, from storage conditions, transportation, to anti-counterfeiting, must be incorporated into the acquisition, manufacturing, and distribution processes.

It may not be easy to acquire the workforce that is needed to manufacture. In certain countries, aging populations mean expertise is retiring, and for too long companies have under-invested in transferring that expertise to the next generation, under-invested in developing and retaining talent, and under-invested in the health of their organizations, preferring to “rent” the expertise on an as-needed basis. Will that expertise be available, either in-house or on a contracted basis?

Companies will need to “up their game” when it comes to acquiring, training, and qualifying their manufacturing staff—both operations and maintenance. The good news is technology today offers a variety of methods to impart the necessary process understanding, equipment design, operating and maintenance principles, quality risks and control thereof, procedural requirements, and associated quality system controls—paper or computerized. In addition, some localities offer targeted university programs to help meet this challenge.

All these factors taken together are a wake-up call for factories that are “nimble”: they can accommodate manufacturing flexibility due to product

How do we bridge the “canyon” of technological differences between basic sciences that are light years ahead of applied sciences?

diversity, they can adapt to new technologies, they can be delivered quickly, and they are robust—they can tolerate variability small and large. Some will need to produce high volumes of a single product while others may be producing personalized doses.

What do we want from FoF?

How might we define this mystical facility of the future? Key attributes might include:

Achieve high tech metrics for process availability, process capability (Cpk): Most of us will admit that the pharmaceutical industry is not at the top of the performance list when it comes to common manufacturing quality and productivity metrics such as Cpk, availability, reliability, or batch rejection rates. Clearly, good manufacturing practice (GMP) regulatory compliance does not equate to world-class manufacturing measured against today’s tech industry standards.

Automation without tears: Fifteen years ago at the ISPE Annual Meeting plenary session, GlaxoSmithKline offered a video illustrating the potential integration of automation, information management, supply chain flexibility, and a global manufacturing network. One would think that fifteen years later, the vision portrayed in that movie would have become reality. For most companies, it is still a vision, if that. Companies spend a lot of time and money to implement distributed control systems and manufacturing





execution systems, yet most struggle mightily to achieve significant benefit from this investment.

Data analytics for process improvement: Our industry collects and reports process information and changes in an annual report to regulators. How many of us collect and analyze data to implement improvements on a continuous basis at the quality engineer and machine operator levels? Or do we only focus on that which regulatory filings demand? Do sister factories making the same products share information for common improvement? Are manufacturing observations, trends, problems readily shared as improvement opportunities, or covered up unless required for regulatory compliance?

Compliance at the push of a button: Compliance reporting cannot be avoided. Even today, however, companies are only beginning to take steps to automate the collection, analysis, and reporting from across their manufacturing network.

Flexible: Can easily accommodate multiple products requiring common manufacturing platforms and technologies. Most generic manufacturers find this challenge easy to overcome, and producers of personalized medicine will need to reinvent the quality system to control large-scale small-volume manufacturing. For those with a “campaign” mentality, can we reduce what is often an arduous changeover process?

Reliable: Can we schedule production runs with confidence that equipment will operate reliably? Can we predict machine failure? Do we know where we are exposed to single-point failure, and can we accept such failure based on business or quality critical factors? Are we overly reliant on detecting the occurrence of failure vs. preventing failure? Do we ignore anything that is not “GMP critical” at the risk of impacting our cost of goods sold?

Resilient to operator error: Operators are perhaps the least reliable part of a manufacturing operation. Can the manufacturing equipment and process withstand most operator errors, either through compensation by other means or at least identification when it happens before the impact reaches cost of goods sold? Do the equipment design, automation employment, and operating strategy work together to reduce the potential for operator errors?

Ease of implementing change: Considerations including flexibility, continuous improvement, etc., mean we want to implement change: frequently and easily. Do we have an IT-based change process, the supporting product and process knowledge, quality risk information, and competent internal resources that allow us to quickly assess and implement change as soon as the need is identified? Do we collect information that allows us to pinpoint root causes of problems and laser focus on the right change to improve the situation?

Low maintenance: How often do we have to shut down for routine or corrective maintenance? Some companies today have initiatives to shorten the duration of planned maintenance shutdowns, or increase the time interval between such shutdowns, or even eliminate them altogether. This requires a well-founded asset management strategy, synchronized with the specific manufacturing demands to minimize life cycle capital, operations and maintenance costs and reduce costs of goods sold. Unified communication devices and robust analysis algorithms can continually diagnose asset performance during use. This gives us new challenging issues for improving the efficiency of asset operations. One obvious result is condition-based maintenance that makes a diagnosis of the asset status from continuously monitored data and predicts an asset’s irregularities, and alerts operators to execute specific maintenance actions before serious problems happen.

Low energy usage: While energy costs may have plummeted globally over the past year or so, designing and operating an energy efficient plant will always be a driver. From passive solar heating and cooling, to production and operation of WFI systems, designing for energy conservation is an omnipresent consideration. Using a combination of geothermal and other techniques, modern factories can achieve minimal to zero net energy consumption.

Low environmental impact: Along with low energy usage comes low environmental impact: What does the process discharge to the environment, or what demands does the process place on a waste treatment system? This applies not only to liquid or gaseous discharge, but also the impact of component waste and gowning cleaning or disposal.

Easy to design, construct, commission, validate, operate: Simple designs, cookie-cutter factories, plug-and-play equipment modules, reusable automation, standardized design, procurement, fabrication, and commissioning processes, project information management systems, and use of paperless approaches all impact the cost and time required to deliver a facility. How can standardization help the human performance element? How can a sophisticated and highly automated facility help train the operators and maintenance staff using state-of-the-art knowledge management solutions?

Continuous processing and real-time release: The drivers for continuous processing include smaller equipment, higher utilization, lower costs, and more consistent quality. The amount of data collected, and the use of sophisticated process models and adaptive process control strategy will allow us to use real time release in most cases. Separately, industry is moving to product serialization, which should facilitate the acceptability of continuous processing. This “linkage” can be made by considering individual serialized packages time-stamped with time of manufacture, allowing traceability to the processing conditions and raw materials applicable to the product in that package.

We will need to move beyond product release decisions based on a few analytical pass/fail tests, to manufacturing based on detailed knowledge of in-process parameters and a sophisticated process control strategy. We will have continuous manufacturing data available upon which to make real time release decisions. Costs will come down and quality will go up.

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What specific strategies, tactics, and techniques might we use to achieve our facility of the future?

What do we need to do to achieve FoF?

First, which “facility of the future” is right for our situation? Are we a multinational company with a global supply chain? Are we a boutique niche player with a single plant and novel product technology? Are we acquiring new network capacity through mergers or acquisitions? Do we transfer product manufacturing technology across the globe, or across the campus?

From the C-suites and the offices of global management consultants come the top-down manufacturing supply chain strategies, based on some analysis of market demands, cost, and other factors that generally drive capital project budget realities and location decisions. From our understanding of the external forces at play and the desired attributes of our facility, available technologies, supplier capabilities, and many other considerations become the bottom up opportunities, challenges, and limitations on what we can achieve. We must integrate these top-down and bottom-up mandates and realities to forge our specific facility of the future.

What specific strategies, tactics, and techniques might we use to achieve our facility of the future? We must successfully integrate process knowledge, equipment and automation design, delivery and operation, personnel training and qualification within the constraints of a project schedule, budget, and quality/ regulatory requirements. Key elements to be integrated include:

- Understanding our processes and listen to the voice of the product: What does the product require from the equipment, systems, and process control strategy in order to be manufactured consistently and of high quality?
- Having a disciplined process to establish the requirements, design to those requirements, invest in design reviews, and then follow through with a well-planned and managed delivery, commissioning, and initial operations process.
- Designing for life cycle operating cost: This is required even before one commences design of FoF. Along with what the product requires, we need to move away from the “old way of engineering and designing manufacturing facilities.”
- Designing for reliability.
- Optimizing maintenance strategies.
- Improving use of automation and information management.
- Rethinking how operators are trained and qualified.
- Being passionate about risk management—not just quality risks, but business risks. Focusing on risk management and risk reduction, not just risk understanding and hazard detection.
- Be willing to challenge sacred cows of compliance practices: We must do nothing just for the sake of compliance.

Summary and conclusion

There can be many challenges and barriers to achieving our vision for a facility of the future. The obvious ones include compliance fears (doing something because we think regulators want to see it done that way), project delivery timelines, project budget limitations, and lack of sufficient talent/ skills/ experience in our workforce. How do we overcome these challenges?

How do we bridge the “canyon” of technological differences between basic sciences that are light years ahead of applied sciences? Applied science—how we manufacture product, has remained stagnate over the last 15–20 years with the exception of “spurts” of change such as some current continuous oral solid dosage manufacturing operations. For most of the changes, the only real change is the ability to collect real time data in a process analytical technology format. Little has changed in the actual operating principles of the equipment, systems, maintenance reliability, etc.

**How do we bridge the
“canyon” of technological
differences between
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applied sciences?**

Regulators have been pushing industry towards quality risk management as a more sophisticated, nuanced approach to GMP compliance. That being said, we are on a long journey to implement more significant change, and we must constantly adjust our compass as new paths emerge. Fundamentally, though, both regulators and industry need to seriously accelerate the adoption of new technologies, new methods of process and quality control, and other methods that promote flexibility, lower cost, and higher quality.

We must continue to explore new technologies, educate ourselves, our industry, and the regulators. We must achieve greater industry standardization in terms of project delivery methods, regulatory expectations, and human performance goals. We should look to other industries for benchmarks, novel technologies, and world-class manufacturing methodologies. We must accommodate and embrace change and improvement.

We are given a limited amount of time, money, and talent—never enough. We must understand the principles needed to minimize our cost of goods sold, we must identify the opportunities available to us in our project scenario, must work within an efficient project delivery system, and we must successfully integrate a program for the process, the staff, and the plant/equipment. If we do these things well—from concept design to full-scale operation, we can achieve that facility of the future, delivering better quality, significant therapeutic value, and greater quantities of product to our customer-patients, and providing our shareholders with a solid return on their investment. ■

Robert E. Chew

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