



FOYA | 2017

Facility of the Year Awards

RECOGNIZING INNOVATION. BY DESIGN.

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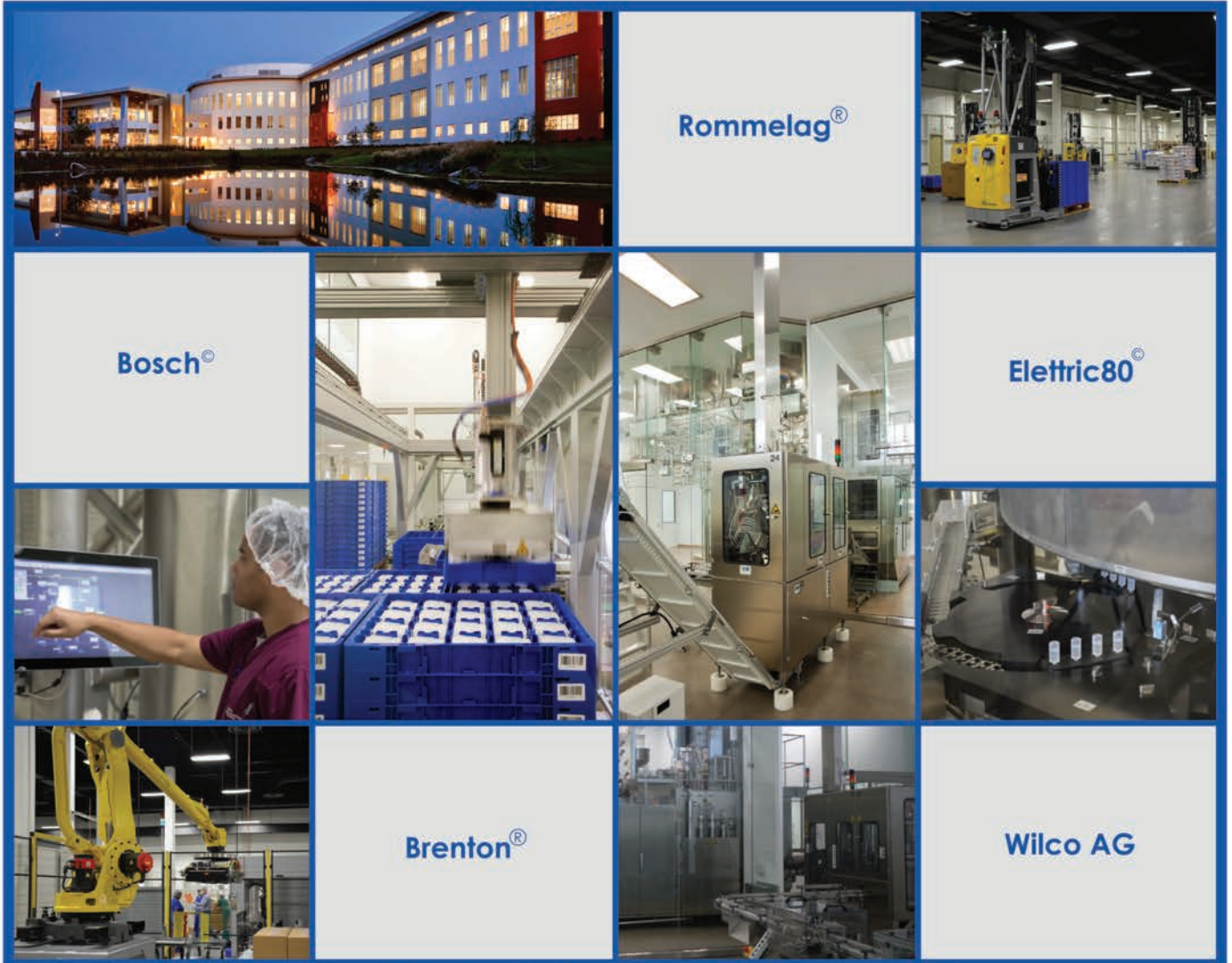




nephron

pharmaceuticals corporation

embracing technology to automate manufacturing and logistics



4500 12th Street Extension West Columbia, South Carolina 29172





2017 ACHIEVERS OF MANUFACTURING EXCELLENCE

CATEGORY WINNERS

Abbott Operational Excellence	7
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John E. Bournas

Excellence is more than an aspirational value. For members of the pharmaceutical manufacturing industry, excellence is a deeply embedded belief that drives a collective desire to improve the lives of patients. It manifests daily in the actions of more than 5 million pharmaceutical manufacturing employees around the world, and the relief it provides millions of patients in the form of medicines and medical devices.

As the representative of some 18,000 men and women working in this global industry, one of ISPE's roles is to shine a light on the beacons of excellence in pharmaceutical manufacturing. From buildings to systems to people, through our conference venues, publications, and award programs, we pay homage to the best and the brightest.

The FOYA program was created to celebrate six facets of manufacturing excellence: Project Execution, Facility Integration, Equipment Innovation, Sustainability, Process Innovation, and Operational Excellence. FOYA is also evolving to reflect paradigm shifts within the industry. And so in 2016 we added a new category to reflect the efforts of members who are developing solutions for the Facility of the Future. This strengthens the foundation of the FOYA program—the belief that patients benefit most when technology, innovation, and quality combine to produce manufacturing excellence.

This same ability to adapt, to not be defined or limited by what was, is present in the submissions of each FOYA category winner and honorable mention. We are proud to honor the eight winners who not only share our commitment to innovation—they also advance pharmaceutical manufacturing technology by demonstrating creativity and excellence in facility design, construction, and operations.

Reading through this year's submissions was inspiring. Our winners are exceptional in their ability to define problem statements and execute their solutions with distinction. Not only was culture the cornerstone of several of the winning projects, many demonstrated the relationship between corporate quality culture and operational excellence. Hailing from the United States, Puerto Rico, Ireland, and Indonesia, our 2017 winners also represent the diversity of thought that fuels intellectual discourse and debate, and fosters innovation.



Facility of the Year Awards 2017

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ISPE is an association rooted in the tradition of collaboration and knowledge sharing. It is our reason for being, and the reason our members join. We provide members with opportunities not only to learn from one another, we also make it possible for them to shape that learning to further pharmaceutical manufacturing innovation.

KNOWLEDGE TRANSFER

Since the first publication almost four decades ago, ISPE Guidance Documents have played a fundamental role in that learning process. The collective knowledge of the pharmaceutical manufacturing industry professionals who write them—on topics as diverse as biopharmaceutical process development and data integrity—encourages innovation, furthers technological advances, and facilitates regulatory compliance. Hundreds of members have collaborated, debated, and discussed to write Guidance Documents for their colleagues. They do it selflessly, and with the humility that makes the knowledge they share so well received by their peers.

Does this knowledge seep into the processes and mindsets that create award-winning FOYA submissions? Does it foster innovative thinking and imagination? I will leave that for you to judge as you read through this year's winning submissions. What is certain, from ISPE'S perspective, is that FOYA projects are a testament to the role innovation and excellence play in pharmaceutical manufacturing.

Cheers, then, to FOYA Category Winners Abbott (Operational Excellence), Bristol-Myers Squibb (Facility Integration), Cook Pharmica (Equipment Innovation), Eli Lilly and Company (Process Innovation and Facility of the Future), Jazz Pharmaceuticals (Project Execution), and Honorable Mentions Nephron Pharmaceuticals Corporation, Novartis-Penn Center for Advanced Cellular Therapies, and PT. Kalbio Global Medika.

John E. Bournas
ISPE CEO and President



FOYA | 2018

Facility of the Year Awards

It's an exciting time in our industry. Thanks to your innovative designs, we're changing the way we work and deliver quality medicines to the people who need them.

**SUBMIT YOUR
PROPOSAL TODAY.**

2018 Deadline: 20 November 2017

Innovation.
By Design.

www.FacilityOfTheYear.org



2017

Abbott
Operational Excellence
Operational Excellence—A
A New Quality Approach
Longford, Ireland

Bristol-Myers Squibb
Facility Integration
Biologics Development
Building and Clinical
Manufacturing Building
Devens, Massachusetts, US

Cook Pharmica
Equipment Innovation
Flexible Filling Line
Bloomington, Indiana, US

Eli Lilly and Company
*Process Innovation and
Facility of the Future*
Continuous Direct Compression
Manufacturing Kits 2 and 3
Indianapolis, Indiana, US (CM2)
and Carolina, Puerto Rico
(CM3)

Jazz Pharmaceuticals
Project Execution
Project Rock
Monksland, Athlone
Co. Roscommon, Ireland

PT. Kalbio Global Medika
Honorable Mention
Biotech Facility
Jakarta, Indonesia

**Nephron Pharmaceuticals
Corporation**
Honorable Mention
Nephron SC
West Columbia, South Carolina
US

**Novartis and University of
Pennsylvania**
Honorable Mention
Novartis-Penn Center for
Advanced Cellular Therapies
Philadelphia, Pennsylvania, US

2016

OVERALL WINNER
**Genentech, a Member of
the Roche Group**
Process Innovation
CCP2 Return to Service
Vacaville, California, US

Baxter BioPharma Solutions
Operational Excellence
Solutions Oncology
Manufacturing Expansion
Halle (Westfalen), Germany

Ethicon, LLC
Sustainability
San Lorenzo Conservation
Strategy
San Lorenzo, Puerto Rico

Janssen Vaccines AG
Project Execution
ZEBOV in B81J
Bern, Germany

Pfizer Inc.
Equipment Innovation
PCMM: Portable, Continuous,
Modular, and Miniature
Groton, Connecticut, US

Takara Bio Inc.
Facility Integration
Center for Gene and
Cell Processing
Construction Project
Kusatsu, Shiga, Japan

**Greater Pharma Manufacturing
Co. Ltd**
Honorable Mention
New Facility
Bangkok, Thailand

**University of Strathclyde,
CMAC**
Honorable Mention
Technology & Innovation Centre
Glasgow, Scotland

**West Pharmaceutical Services,
Inc.**
Honorable Mention
Ready-to-Sterilize (RS)
Expansion
Kinston, North Carolina, US

2015

OVERALL WINNER
AstraZeneca China
Project Execution
Market Supply Solid
Dose Facility
Taizhou, China

Astellas Pharma, Inc.
Equipment Innovation
Tube Packaging and
Labeling Equipment Project
Kerry, Ireland

IDT Biologika GmbH
Facility Integration
Biologics and Vaccines
Production Facility
Dessau, Germany

**Pharmalucence
Pharmaceuticals**
Honorable Mention
Construction of New
Aseptic Filling Facility
Billerica, Massachusetts, US

2014

OVERALL WINNER
Pfizer Ireland Pharmaceuticals
Operational Excellence
NSI Capacity Expansion
Grange Castle, Dublin, Ireland

**Boehringer Ingelheim
Pharma GmbH & Co. KG**
Equipment Innovation
Aseptic Area 5 and
Combi Line Facility
Biberach, Germany

F. Hoffmann–La Roche Ltd.
Sustainability
B250-Q2K Facility
Kaiseraugst, Switzerland

Grifols Therapeutics Inc.
Project Execution
Grifols North Fractionation
Facility
Clayton, North Carolina, US

**Patheon Pharma Services
(formerly DSM Biologics)**
Process Innovation
Biologics Plant of the Future
Brisbane, Australia

**Penn Pharmaceutical
Services Ltd.**
Facility Integration
Project PennDragon Contained
Manufacturing Facility
Tredegar, South Wales, UK

**WuXi Apttec
Pharmaceutical of China**
Honorable Mention
Fully Single Use mAB
Production Facility
Wuxi City, China

2013

OVERALL WINNER
**Novartis Vaccines
and Diagnostics**
Process Innovation
Flu Cell Culture Facility
Holly Springs, North Carolina,
US

Biogen Idec
Facility Integration
Flexible Volume Manufacturing
Project RTP
North Carolina, US

F. Hoffmann–La Roche Ltd.
Project Execution
TR&D Building
Basel, Switzerland

MedImmune
Equipment Innovation
UK Automation Upgrade
Project
Speke, Liverpool, England, UK

Merck & Co., Ltd.
Operational Excellence
Vaccine and Biologics Sterile
(VBSF) Project
County Carlow, Ireland

Morphotek, Inc.
Sustainability
Pilot Plant
Ambler, Pennsylvania, US



2012

OVERALL WINNER
Merck & Co., Inc.
Facility Integration
 Merck Vaccine Bulk Manufacturing Facility (VBF) Program of Projects
 Durham, North Carolina, US

Chiesi Farmaceutici S.p.A.
Sustainability
 Chiesi Farmaceutici Research and Development Centre Facility
 Parma, Italy

Eisai Pharmatechnology & Manufacturing Pvt. Ltd.
Project Execution
 Eisai Knowledge Centre Facility
 Andhra Pradesh, India

Rentschler Biotechnologie GmbH
Equipment Innovation
 REX III Manufacturing Facility
 Laupheim, Germany

Roche Diagnostics GmbH
Operational Excellence
 TP Expand Project
 Penzberg, Germany

National Institute for Bioprocessing Research and Training (NIBRT)
Honorable Mention
 Novel Collaboration for its New Greenfield Facility
 Dublin, Ireland

2011

OVERALL WINNER
MedImmune, LLC
Project Execution
 Frederick Manufacturing Center Expansion Facility
 Frederick, Maryland, US

F. Hoffmann-La Roche Ltd.
Process Innovation
 "MyDose" Clinical Supply Facility
 Kaiseraugst, Switzerland

Merck & Co., Inc.
Facility Integration
 Global Clinica Supplies Manufacturing, Packaging, and Warehouse Expansion Project
 Summit, New Jersey, US

Novartis Vaccines and Diagnostics GmbH
Equipment Innovation
 "MARS Project" (Marburg Site) Facility
 Marburg, Germany

Pfizer Health AB
Operational Excellence
 Project Pegasus – Bio 7 Manufacturing Facility
 Strängnäs, Sweden

Pfizer Manufacturing Deutschland GmbH
Sustainability
 Strategic Plant Restructuring and Energy Master Plan Project
 Freiburg, Germany

Shire HGT
Honorable Mention
 Project Atlas
 Building 400 Facility
 Lexington, Massachusetts, US

2010

OVERALL WINNER
Genentech
Project Execution
 Tuas, Singapore

Biogen Idec
Operational Excellence
 North Carolina, US

MannKind Corporation
Equipment Innovation and Process Innovation
 Connecticut, US

Pfizer Biotechnology Ireland
Sustainability
 County Cork, Ireland

Pfizer Ireland Pharmaceuticals
Facility Integration
 Dublin, Ireland

2009

OVERALL WINNER
Roche Pharma Biotech Production Basel
Project Execution
 Basel, Switzerland

Aseptic Technologies
Equipment Innovation
 Gembloux, Belgium

Centocor Biologics Ireland
Sustainability
 Ringaskiddy, Cork, Ireland

Centocor R&D Schaffhausen
Facility Integration
 Schaffhausen, Switzerland

hameln Pharmaceuticals Limited
Operational Excellence
 Hameln, Germany

Orchid Chemicals & Pharmaceuticals
Regional Excellence
 Aurangabad, India

2008

OVERALL WINNER
Pfizer Manufacturing Deutschland GmbH
Process Innovation
 Illertissen, Germany

Boehringer Ingelheim Pharma GmbH & Co. KG
Facility Integration
 Biberach, Germany

Bristol-Myers Squibb
Equipment Innovation
 New Brunswick, New Jersey, US

IDT Biologika GmbH
Operational Excellence
 Dessau-Rosslau, Germany

F. Hoffmann-La Roche AG
Project Execution
 Basel, Switzerland

2007

OVERALL WINNER
Genentech
Project Execution
 Oceanside, California, US

Cook Pharmica, LLC
Facility Integration
 Bloomington, Indiana, US

Shanghai Roche Pharmaceuticals, Limited
Project Execution
 Regional Excellence
 Shanghai, China

Taiyo Pharmaceutical Industry Co., Ltd.
Equipment Innovation
 Takayama City, Japan

Vetter Pharma-Fertigung GmbH & Co. KG
Process Innovation
 Ravensburg, Germany

2006

OVERALL WINNER
Baxter BioPharma Solutions
 Phase IV Vial and Syringe Filling Project
 Bloomington, Indiana, US

AstraZeneca
 Large Scale Laboratory Project
 Macclesfield, England, UK

Daiichi Asubio Pharma Co., Ltd.
 NBP (New Bio Plant) Project
 Tokyo, Japan

Janssen Pharmaceutica
 Small Volume Area Facility
 Geel, Belgium

Wyeth Pharmaceuticals
 The Wyeth BioPharma Campus at Grange Castle Project
 Dublin, Ireland

Biolex Therapeutics
Special Merit Recognition
 Pittsboro Phase II Facility Expansion Project
 Pittsboro, North Carolina, US

2005

OVERALL WINNER
Novo Nordisk A/S
 New Manufacturing Plant
 Hillerød, Denmark

Alkermes, Inc.
 Brickyard Square Manufacturing Site
 Cambridge, Massachusetts, US

Apotex, Inc.
 Expansion to its Etobicoke, Ontario, Manufacturing Facility
 Winnipeg, Manitoba, Canada

KOWA Company Ltd.
 New Addition to its Manufacturing Plant for Oral Solid Dosage Products
 Nagoya, Japan

Lundbeck Pharmaceuticals Ltd.
 New Manufacturing Facility at Seal Sands
 Middlesbrough, England, UK

RECOGNIZING AND REWARDING INNOVATION

James Breen, Chair, FOYA Judging Committee and Vice President/Lead, Biologics Expansion, Janssen Pharmaceuticals



James Breen, FOYA Judging Committee Chair

Photo: Yossi May, Washington Talent

Since 2004, a group of 10 to 15 leaders in the pharmaceutical industry, have met to judge the projects submitted for Facility of the Year Awards. These are leaders in owner organizations from all regions of the world, representing both small and large companies within the pharmaceutical and medical device industries. They all have extensive experience in their fields—engineering, manufacturing, and quality; most have international responsibilities. Several have lived or worked outside their native countries. They are experienced, knowledgeable, and understand the global landscape.

The judging season starts in January with a one-day meeting to review the FOYA submissions, which are submitted to ISPE in the fourth quarter of the preceding year. Submissions come from all corners of the world and represent projects in the pharmaceutical, medical, and biologic fields. Judges nominate one project for each of the FOYA awards. If they do not identify a project that demonstrates excellence in any one category, however, they will not award the category that year.

Judges arrive with their individual shortlists of projects that they have rated according to cost, schedule, safety, and capability. While they have a template to help them catalog their analyses, they have the freedom to use their expert judgment in reviewing each project.

At the initial committee meeting, the judges review each submission, discuss their individual merits within the submitted category, and consider whether they could qualify for other categories within the FOYA portfolio. This process allows for much dialogue, listening to each judge's assessment and determining whether the project is novel. This segment provides judges with a forum to discuss new industry trends, and how they are reflected in the submissions.

The judges' collective expertise and experience is brought to bear during the ensuing discussions and evaluations. Once they have screened each submission for compliance with the program requirements, the judges use their broad experience to understand the project: Do the proposed costs and schedule seem reasonable? Did the project team clearly articulate the accomplishment and the business value for the overall outcome outlined in the project paper? The judges also use their internal and external networks to benchmark the project information and ensure outcomes as stated were achieved.

One of the areas judges focus on is safety, and whether it was top of mind during project execution. They carefully review the safety portion of the submissions in terms of "days away, restricted or transferred," total recordable injury rate, and the general tone of the safety culture. This reflects the judges' experience that projects with a strong safety record will have better performance.

Judges then select the overall winner from among the category winners. The process involves several rounds of discussions, followed by a series of secret ballots. Once the winners have been selected the judges are sworn to secrecy until ISPE announces the category winners. The overall winner is revealed at the ISPE Annual Meeting in the fall.

While there are a limited number of category winners, judges reserve the right to recognize projects with Honorable Mentions. These are clearly successful projects that overcame significant challenges in planning, execution, and delivery.

One myth that I know all the judges would like to dispel is that only large complex projects win these awards. Nothing could be farther from the truth—the judges discuss this as they review the submissions. Most are small projects to im-

prove quality, reduce costs, transfer in new products, or implement new information technology solutions. The judges understand that these projects are critical to the success of the business at each facility, so we focus on and award smaller projects that demonstrate a good return.

This year we added a new category called Facility of the Future. The category was developed in response to the changing manufacturing environment to recognize the application and/or implementation of innovative design concepts, new technologies, and unique solutions that exemplify the next generation of agile, flexible, efficient, and effective new and existing life sciences facilities.

I have led the FOYA Judging Committee for the past five years and I have found it to be a wonderful experience, both personally and professionally. Having a group of leaders at these sessions allows us to share recent trends in the industry, discuss lessons learned from these projects, and explore how we can communicate these best practices across the entire ISPE membership to advance the industry. I have learned a great deal judging these projects from a technical and project management point of view, which allows me to perform my duties for my employer better and more efficiently while leveraging the latest trends in industry. I believe each ISPE FOYA judge would claim this same benefit.

I would like to thank the FOYA judges for volunteering their time as well as the companies that submitted projects. Selecting the final awards gets more difficult each year as the quality of project submissions increase.

Finally, we all enjoy working within an industry that improves the lives of our patients. To continue this mission as an industry, we must strive to improve our performance each day; FOYA allows us to recognize the effort of those that do. <>



ABBOTT

Abbott creates breakthrough products—in diagnostics, medical devices, nutrition, and branded generic pharmaceuticals—that help you, your family, and your community lead healthier lives, full of unlimited possibilities.

“The Abbott Longford site has increased productivity, improved changeover efficiencies, eliminated backorders, and enhanced product quality—while also reducing cost per unit, cycle times, equipment downtime, and inventory holdings.”



Project

Operational Excellence—A New Quality Approach

Location

Longford, Ireland

Project mission

Create a sustainable continuous improvement culture

Total campus area

Facility: 135,000 sq. ft.

Internal facility modifications: 5,300 sq. ft.



CULTURAL SHIFT BEGETS WIDESPREAD IMPROVEMENT

When the Abbott Diagnostics facility in Longford, Ireland, launched its project in 2012, its goal was to create a sustainable, continuous improvement culture that would deliver high-quality, safe, and effective diagnostic products. Five years later, the facility has generated millions of dollars in cost savings, product lead times have improved, inventories and energy consumption have been reduced, and employee morale has risen. The Longford facility may also have created a model project that it can deploy at Abbott's other facilities worldwide.

BEHAVIOR-FOCUSED MODEL

The 135,000-sq.-ft. Longford facility was established in 2004 and currently employs more than 350 people involved in the design, development, and manufacturing of in-vitro diagnostic products. The company's product portfolio includes diagnostic reagents for the detection of thyroid, fertility/pregnancy, cardiology, renal, and metabolic markers.

By 2012, the site had gone through its initial start-up phase and management at the facility

was looking to develop a sustainable growth strategy. It launched its operational excellence project with a view to building performance from the ground up. "This project is focused on creating a culture of long-term sustainable performance," says Everett Tucker, Division Vice President, Global Operations Strategy and Engineering, Diagnostic Division at Abbott. "It was about how we might create an environment where people are more empowered and more involved in how the business runs."

Management conducted benchmarking of other organizations, including a visit to another manufacturing company. "The company had a model that was based around behaviors in the factory, and it drove a lot of operational excellence behavior and activities at the company site," says Ciaran Corcoran, Site Director at the Longford facility. "That got us thinking that we didn't use this approach at our facility, and so we took action to build the 'Longford behaviors' and what are we doing around those."

Following further discussion and benchmarking, Abbott Diagnostics' management team reached the conclusion that the operational excellence model it wanted to follow was based on

one developed by the Shingo Institute, located at the Jon M. Huntsman School of Business at Utah State University. "That is when we really bolted the Shingo part onto our behaviors, because they both sat very well together," says Corcoran.

The Shingo Model is not an additional program or initiative that an organization integrates into its operations; according to the shingoprize.org website, it is a set of 10 guiding principles that are meant to anchor an organization's current initiatives and to fill the gaps in its efforts towards ideal results and enterprise excellence. Each principle plays a critical role in enabling an organization's culture, designing systems for continuous improvement, aligning principles, behaviors, and results across the enterprise, and achieving a sustainable culture of excellence.

PEOPLE LINKED TO STRATEGY

To avoid confusing employees by the introduction of new "Shingo behaviors," much effort was spent identifying and connecting existing Abbott behavioral expectations to the Shingo principles. In fact, the Longford behavioral standards

are well aligned with the Shingo dimensions of operational excellence as they specify that everyone in the organization needs to respectfully work together to deliver customer-focused results while finding ways to improve.

The site's functional departments develop their own local vision and strategy maps/balanced scorecards by aligning their goals to the site strategy. Departmental goals are formally agreed on an annual basis and cascaded through the organization. All departments contribute to site initiatives and develop their own department-level initiatives that support the attainment of their goals. The departmental strategy maps/balanced scorecards form the basis for visual management and give employees a clear line of sight into how their jobs are linked to both site and departmental strategy, enabling them to work in a coordinated and collaborative fashion.

"We are providing an ecosystem for employees to reach their full potential," says Corcoran. "People can very easily see a long-term career for themselves in the business and they know what's going on in the business because the whole thing is very visual, open, and transparent."

Corcoran feels that the openness and transparency enable him and his management team to anticipate risks. "We walk around the factory twice a week for about an hour and a half each time, and we go through various work centers all over the factory," he says. "The employees have visual boards, they talk about their metrics, about their achievements, and their challenges. By walking around and meeting people in this way, you are really showing everybody how engaged the management team is. And it enables us to make fast decisions: if there are any risks to the business then I have an ability to quickly identify and address them. The whole system is built around transparency and openness, and that enables us to see risks ahead of time and do something about them."

In illustrating his point, Corcoran describes how the company has placed demand and capacity visuals throughout the facility. Each department tracks the demand placed upon it over a period, and then plots it on a chart. "You can see the demand and capacity on a simple chart that we look at every week," he says. "Then, if we know that a project is coming in the next few months, we can ask the department if they can handle it. So, that drives anticipation and encourages different conversations about how we can

"BY WALKING AROUND AND MEETING PEOPLE IN THIS WAY, YOU ARE REALLY SHOWING EVERYBODY HOW ENGAGED THE MANAGEMENT TEAM IS. AND IT ENABLES US TO MAKE FAST DECISIONS."

level load or how we can move things around. And we start those conversations months ahead of time."

AWARD-WINNING RESULTS

Through its Operational Excellence project, the Longford facility has achieved cost savings totaling more than \$13 million across all spending areas. These savings were generated by the reduced use of raw materials, lower energy consumption, automation, batch-size optimization, and multiple process-improvement projects targeting the complete value chain. Furthermore, lead times have fallen by 38%, back orders have been eliminated and there has been a 15% reduction in distressed inventory.

As of November 2016, the facility had accumulated 3,755 lost time accident-free days. In

addition, the site has significantly reduced its carbon footprint by consuming less energy (energy usage fell by 23% between 2012 and 2015 despite test-volume growth), eliminating waste going to landfill, and creating an on-site biodiversity garden.

Employee morale at the site is high, and reflected in its excellent employee attendance record of at least 98%. Internal promotion rates are also high, attesting to the success of career mentoring and coaching programs. Furthermore, creating an awareness of the benefits of physical activity encourages all employees to become more active, and the site provides a supportive workplace environment for doing so.

Corporate social responsibility (CSR) is also a key focus of the Longford site. Employees volunteer a combined total of more than 2,000 hours





each year to the site's many CSR initiatives. The site has offered several workshops on operational excellence for staff of hospitals that use Abbott products and who are trying to introduce or reinforce lean principles.

For its efforts, Abbott's Longford facility has been recognized in Ireland and internationally, winning numerous awards, including the:

- 2013 and 2014 Plant of the Year Award, from Abbott Global Environment, Health Safety & Energy
- 2015 Medtech Company of the Year Award, from the Irish Medtech Association
- 2015 National Business Excellence Award, from the Irish Centre for Business Excellence
- 2015 Shingo Prize, from The Shingo Institute at the Jon M. Huntsman School of Business, Utah State University
- Special award for Behavioral Excellence for Safety, from the Shingo Institute, presented to Abbott Diagnostics Longford at the Shingo Awards ceremony in April 2016

Abbott Diagnostic Longford's operational excellence culture has become so well-entrenched that even the Shingo Institute's review committee was impressed. "They were impressed with the whole attitude in the facility, that the culture was so alive," says Corcoran.

According to Everett Tucker, the key to the success of the company's operational excellence program is that it "wasn't mandated or forced. It was an empowering, ground-up program that really stimulated and excited people. It isn't something that will simply die of its own weight once there is a change in leadership. And because of the progress that we made in Longford, we are looking to replicate this model at our other sites as well." ♦

KEY PROJECT PARTICIPANTS

MANUFACTURER /OWNER	Abbott Ireland Diagnostics Lisnamuck Co. Longford, Ireland
ENGINEER/ARCHITECT (A&E)	Agility/EM3 Business Centre Main Street Charleville Co. Cork, Ireland
ENGINEER/ARCHITECT (A&E); CONSTRUCTION MANAGER; MAIN/GENERAL CONTRACTOR; PIPING CONTRACTOR; HVAC SUBCONTRACTOR	Rockwell Engineering Millstreet Rd. Macroom Co. Cork, Ireland
AUTOMATION AND CONTROL SUPPLIER	Nicotra Gebhardt GmbH Gebhardtstrasse 19-25 74638 Waldenburg, Germany
ELECTRICAL CONTRACTOR	Frank McGowan & Sons Limited 15 Arcadia Court Athlone Co. Westmeath, Ireland
CIVIL CONTRACTOR	James Irwin Construction Ltd Unit 9 Dome Court Roscommon Co. Roscommon, Ireland
MAJOR EQUIPMENT SUPPLIERS	Bausch Germany GmbH Döllschützer Str. 1 D-07607 Hainspitz, Germany Pago Etikettiersysteme GmbH Gutenbergstrasse 9 DE-72631 Aichtal-Aich, Germany BBK Etikettier-und Sondermaschinenbau GmbH Dieselstrasse 18 D-64743 Beerfelden, Germany Portakabin Rosevill Business Park Turvey Ave. Donabate Co. Dublin, Ireland Lift Rite Ltd. Unit F1 Maynooth Business Campus Maynooth Co. Kildare, Ireland Telstar Technologies, SL Av/ Font i Sagué, 55 Parc Cientifici Tecnològic Orbital 40 08227 Terrassa Barcelona, Spain RTD Technology Ltd., T/A Asistec Unit 15A, Solus Tower Estate Corke Abbey Bray Co. Wicklow, Ireland Astra Clean Systems/Lighting Kingsway House 23A Marlborough Rd. Lancing, West Sussex, England BN15 8TR



BRISTOL-MYERS SQUIBB

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop, and deliver innovative medicines that help patients prevail over serious diseases.

“Modifications to the existing campus—additions to the utilities, parking garage, CUB, pipe rack, and storm water management—required a deliberate focus on planning and integration. The results were impressive, and the integration of this facility within BMS’s broader mission and network of assets made this submission stand out.”



Project

Biologics Development Building and Clinical Manufacturing Building

Location

Devens, Massachusetts, US

Project mission

Transition Bristol-Myers Squibb into a next-generation biopharmaceutical company

Total campus area

89 acres



FLEXIBILITY AND COLLABORATION ANCHOR EXPANSION

Adding a new facility to an existing campus is always a complex task, requiring advanced planning, adjustment to inevitable challenges, and exceptional collaboration among designers, scientists, construction crews, and teams from existing facilities. Global biopharmaceutical company Bristol-Myers Squibb (BMS) took things to another level when it combined two separate construction projects at its Devens, Massachusetts, campus: adding a biologics development building (BDB) and a clinical manufacturing building (CMB), all with minimal disruption to existing facilities.

Located 45 miles west of Boston, the Devens site is an 89-acre biologics campus that BMS is developing according to a multiphase master plan. The initial phase, budgeted at \$750 million, was completed between 2007 and 2009. It included the construction of a large-scale cell-culture building, a lab/office/cafeteria building, a central-utilities building (CUB), a wastewater treatment plant, a cryogenic storage building, a

warehouse, and a three-story parking garage.

The second phase, a \$280-million expansion aimed at accelerating the development and launch of innovative new medicines, was completed in January 2016. It added two physically connected buildings: the 230,000-square-foot four-story BDB and the 131,000-square-foot multistory CMB.

“Devens is one of our primary biologics production sites,” says Bryan Mann, Director, Capital Projects at BMS. “The driver was to build a development facility and a clinical manufacturing facility that would centrally integrate everything, from research all the way to production, and have all of those key items on the same site.”

KEEPING ALL INFORMED

BMS began planning for the expansion of the Devens campus in early 2013. Architect and Engineering (A&E) contracts were awarded for each building, with ARC/Architectural Resources Cambridge responsible for the BDB, and Clark, Richardson & Biskup (CRB) for the CMB. Lend-

lease Corporation was given the overall construction mandate.

As the designs for each building took shape over the following months, the BMS team decided that the two facilities should be built in parallel. This posed a challenge: how to construct two separate facilities, designed by two separate architects and built by a single construction manager, on a fully operational campus? It became apparent as well that the new construction would require several modifications to the existing campus, including additions to the utilities, parking garage, CUB, and pipe rack and storm water management facilities.

Needless to say, a high level of collaboration and coordination, along with innovative delivery methods, were required to execute the project.

“Between the A&E teams, BMS, and Lendlease, there was a lot of preplanning involved,” says Daniel Post, Associate Director-Technical Services, Engineering at BMS, who acted as project manager for the BDB. “We had to review which utilities had to be tied into the new buildings, and



would therefore be affected by construction, and we were able to segregate the new area from the rest of the site with fencing and good logistics.”

“During the preconstruction period we spent a lot of time planning to make sure that we could avoid impeding operations at the existing facility and separate the construction zone from the rest of the campus,” says Scott Tereshak, Project Executive for Lendlease. “With the help of the design teams, we also planned out where BMS intended to schedule shutdowns so we could coordinate the project schedule around them.”

Furthermore, the team developed a process to keep everyone on the site informed of upcoming activities. “We developed a ‘construction activities notice’ process,” explains CMB project manager Anthony Haskell, Associate Director, Project Manager at BMS. “Any activities related to the site followed this notification process; the completed form went out for review by all stakeholders. We held weekly meetings to review and coordinate this type of work with the site team. The goal was to minimize the impact to opera-

tions and site personnel. Planning was the key to success, and we have continued to use this process on other projects.”

OVERCOMING CHALLENGES

Groundbreaking at the site took place in February 2014. One year later, while the roof was in place, an unusually snowy winter saw close to 10 feet of snow fall over a six-week period. Construction crews spent many days shoveling snow instead of building the facilities.

The project team also faced several challenges unique to the simultaneous construction of two new facilities. A&E firms CRB and ARC collaborated to design a shared waste-processing system for both buildings, which saved time and money. The process created an additional challenge, however, because the underground portion of the system had to be installed before the slabs were poured for the BDB and CMB. Additionally, volume/capacity calculations for the CMB had to be done before the process line had been fully engineered.

The central utilities pipe rack had to be designed for two different buildings with two different needs, which required extensive coordination between the engineering teams. In addition, electrical conduit had to be looped through both buildings and reconnected back to an existing building so each facility could be served from two directions as well as allow for redundancy and future expansion. This required well-planned system shutdowns in addition to determining how to tie in to the electrical system without interrupting existing operations.

The project was completed on schedule and within budget, nonetheless. “The BDB was ready for occupation in November 2015,” says Post. “Staff moved in within a month, and two weeks from the initial move-in some groups were set up and doing science. The CMB staff moved in early 2016 as qualification was winding down and engineering runs were starting. Beneficial use was realized in April 2016.”

From all accounts employees working at the new facilities are exhilarated by the results.



“ONE OF THE THINGS WE DON’T WANT TO LOSE SIGHT OF IS THE INTEGRATION OF POTENTIAL NEW MEDICINES THROUGH COMMERCIAL MANUFACTURING TO GET THE MEDICATIONS TO THE PATIENT.”

“When we were all there for the ribbon-cutting and we walked around with the scientists, there was palpable excitement,” says Tereshak. “Employees knew how important it was for them to interact with the other people in the chain, going from process development all the way through commercial production.”

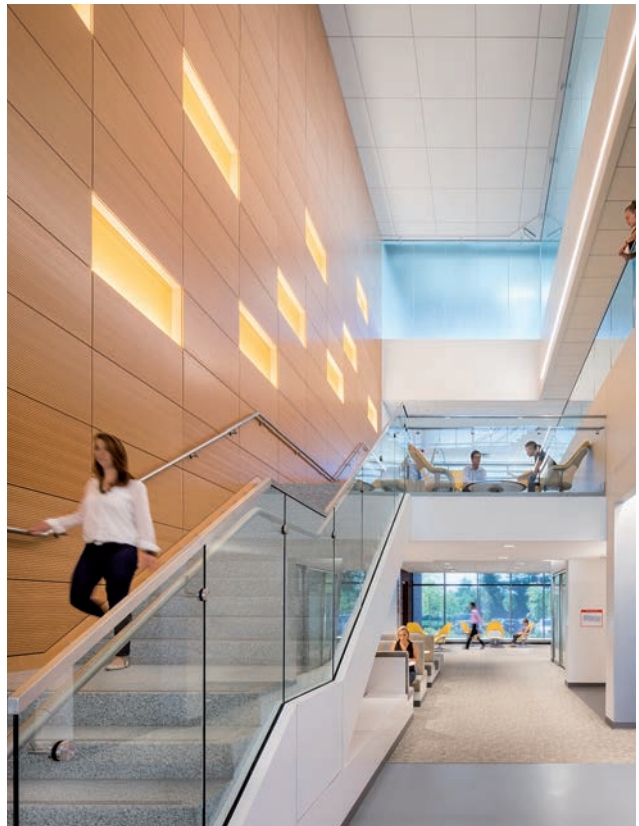
Reflecting on the successful project, Jeffreys Johnson, AIA, Principal in Charge at ARC, points to the collaboration between all the companies involved. “We saw a lot of challenges, but if we hadn’t worked together so closely and so well the challenges would have been much greater,” he says. “But it was a very collaborative process from the start, and that really did make it the successful project that it is.”

Ryan McDonough, Senior Associate, Biotechnology Core Team Leader at CRB, sums up the project this way: “The CMB is one of a small number of fully single-use manufacturing facilities in this industry. And one of the things that we don’t want to lose sight of is the integration of discovery of potential new medicines through commercial manufacturing to get the medications to the patient. Having that all on one campus is pretty important.”



KEY PROJECT PARTICIPANTS

MANUFACTURER/OWNER	Bristol-Myers Squibb 38 Jackson Rd. Devens, Massachusetts 01434 United States
ENGINEER/ARCHITECT (A&E)	ARC/Architectural Resources Cambridge 501 Boylston St., Suite 4101 Boston, Massachusetts 02116 United States Clark, Richardson & Biskup (CRB) 220 West Germantown Pike, Suite 170 Plymouth Meeting, Pennsylvania 19462 United States
CONSTRUCTION MANAGER	Lendlease (US) Construction LMB Inc. 20 City Square, 2nd Floor Boston, Massachusetts 02129 United States
STRUCTURAL ENGINEERS	Symmes Maini & McKee Associates (SMMA) 1000 Massachusetts Ave. Cambridge, Massachusetts 02138 United States SNC-Lavalin Project Services, Inc. 436 Creamery Way #100 Exton, Pennsylvania 19341 United States
MAJOR EQUIPMENT SUPPLIER	GE Healthcare 3350 North Ridge Ave. Arlington Heights, Illinois 60004 United States
SITE	VHB 99 High St., 10th Floor Boston, Massachusetts 02110 United States





COOK PHARMICA

Located in Bloomington, Indiana, Cook Pharmica is a privately held CDMO that provides biopharmaceutical companies with a unique one-source, one-location model for development, clinical, or commercial cell culture manufacturing, parenteral product manufacturing and secondary packaging.

“This unique collaboration between owner, suppliers, and engineering experts delivered a novel application of commercially available and custom-developed equipment innovation that drove superior commercial, market-changing technology, and supply chain flexibility on a “ready-to-use” vial platform.”



Project
Flexible Filling Line

Location
Bloomington, Indiana, US

Project mission
Leverage new technologies to add flexibility and capacity within an existing cGMP space

Total campus area
2,300 sq. ft.



INNOVATION AND INFLUENCE

Flexibility is a critical attribute for any successful contract development and manufacturing organization (CDMO). It can manifest itself in the ability to manufacture a wide variety of medicines or to rapidly accommodate new client requests. Cook Pharmica's recently completed Flexible Filling Line (FFL) project enables the company to achieve all this, along with the ability to manufacture vials, syringes, and cartridges from a single filling line.

Seeing strong market acceptance of its existing vial and syringe product lines, and conscious of a shift in the industry to extend the ready-to-use platform and utilize new capabilities for filling flexibility, Cook began planning to combine activities associated with what had traditionally been three filling lines into one line under barrier isolation, in one filling suite.

"With every filled unit representing a patient, we are excited about this capability and capacity to help our clients reach millions more patients," says Ryan Hawkins, Cook Pharmica's Vice Presi-

dent and Chief Operating Officer.

The concept for Cook Pharmica's flexible filling line began in 2010. "Over the next five years," says Hawkins, "things changed in the supply of ready-to-use vials and cartridges, as well as with robotic technology. The changes helped create more possibilities vs challenges associated with processing multiple formats on a single line."

Cook pursued the development of its concept with two trusted partners, OPTIMA Pharma, the worldwide leader in packaging technologies, including biopharmaceutical filling and packaging, and Nuova Ompi, a global producer of primary glass packaging for the pharmaceutical industry. By combining its product development and manufacturing knowledge with the expertise of a machine builder and a component supplier, Cook created a strong partnership to expand its current capability.

"This partnership was about working together, with a common goal of making a version of flexible filling that would benefit each company and possibly, the industry," says Hawkins.

SMOOTH DEPLOYMENT

Within 12 months of its official kickoff meeting in October 2014, Cook's FFL project staff began factory acceptance testing for the flexible filling line, including the lyophilizer, isolator, and fill line.

Cook had available cleanroom space adjacent to its existing filling operations, and to mitigate any disruptions to the site, Hawkins's team coordinated with suppliers to have the equipment installed during the plant's annual shutdown period in December 2015.

"We built this line to be a clinical workhorse, but we also intended it to be commercially capable. We are already doing engineering batches for clients, and we have a number of projects lined up, including the process performance qualification protocol, which is the last stage before commercialization."

ADVANCED TECHNOLOGY

OPTIMA Pharma's flexible filler is a first-of-its-kind solution, capable of filling syringes (up to 5 ml), vials (up to 30 ml) and cartridges (up to 3 ml). The FFL handles all components in a nested

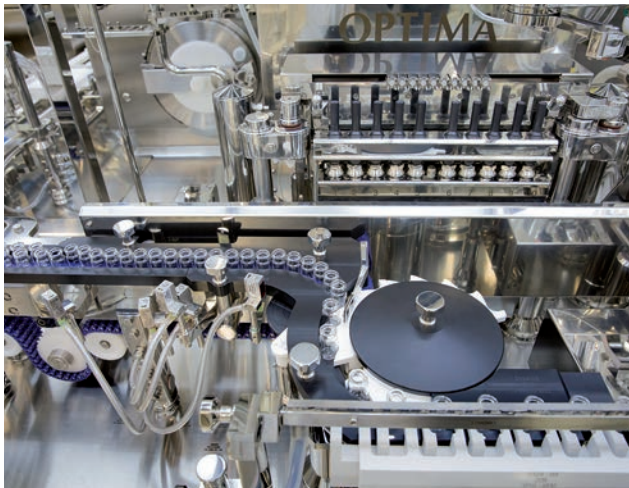
format, as well as vials in tray format, a newly available solution from Nuova Ompi. The line offers further flexibility by dosing via peristaltic pumps and a single-use disposable (SUD) product path or via time-pressure dosing steam-in-place capability.

Automated in-process check weighing and other advanced features ensure accurate dosing and minimal rejects. A 72-sq.-ft. freeze dryer coupled to the line enables manufacture of lyophilized products. The vial capper on the line serves both the new flexible filler and capping product from the adjacent commercial vial line.

The FFL uses barrier isolation technology to provide the highest level of aseptic processing. This includes new catalytic aeration technology that enables short bio-decontamination cycle times, which levels changeover times compared to lines that do not have automated decontamination. No-touch transfers and handling are facilitated through automation of component tub/tray de-bagging and de-lidding. In addition, robotic denesting/detraying, as well as automated lyophilizer loading and unloading, ensure simple and repeatable transitions and eliminate built-in operator involvement.

STRATEGIC AND INNOVATIVE

For Cook, the new FFL is a strategic enabler that allows the company to expand its manufacturing capabilities and support increased volumes of



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We are proud to have supplied

Cook Pharmica

with leading-edge modular
cleanroom technology for their
Flexible Filling Line (FFL) Facility.



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“AS A CDMO, WE MAY NOT HAVE OUR OWN PRODUCTS, YET THAT DOESN’T MEAN WE CAN’T INNOVATE OR INFLUENCE INDUSTRY.”

specialized products within its cGMP offering. The ability to process multiple configurations and formats results in a more cost-effective method of delivering value to customers and end users.

“With the addition of this line, we can now do capping on the FFL for anything that is liquid or lyophilized on our current vial line. It provides us flexibility in terms of format, capacity, and scheduling,” says Hawkins.

In reflecting on the project, Hawkins proudly notes its innovative nature. “It is not always easy to innovate in biopharma,” he says. “I would like to think our new platform could be a leading standard or part of a broader shift in industry. As a CDMO, we may not have our own products, yet that doesn’t mean we can’t innovate or influence industry.”



KEY PROJECT PARTICIPANTS

MANUFACTURER/OWNER	Cook Pharmica 1300 S. Patterson Dr. Bloomington, Indiana 47403 United States
ENGINEER/ARCHITECT (A&E)	IPS-Integrated Project Services, LLC 721 Arbor Way Suite 100 Blue Bell, Pennsylvania 19422 United States Plymouth Meeting, Pennsylvania 19462 United States
CONSTRUCTION MANAGER	Commissioning Agents, Inc. 652 N. Girls School Rd. Indianapolis, Indiana 46214 United States
HVAC SUBCONTRACTOR	Poynter Sheet Metal 775 Commerce Pkwy W. Dr. Greenwood, Indiana 46143 United States
MAJOR EQUIPMENT SUPPLIER	Optima pharma GmbH Otto-Hahn-Strasse 1 74523 Schwaebisch Hall, Germany
PROCESS ENGINEER	Core-Reliance 991 U.S. Highway 22 W. Ste. 200 Bridgewater, New Jersey 08807 United States
CIVIL/ARCHITECTURAL CONTRACTOR	Fox Construction 207 W. 10th St. Bloomington, Indiana 47404 United States
MECHANICAL CONTRACTOR	HFI 2010 Vernal Pike Bloomington, Indiana 47402 United States
HVAC AUTOMATION CONTRACTOR	Thermo Systems 84 Twin Rivers Dr. East Windsor, New Jersey 08520 United States
ELECTRICAL CONTRACTOR	Cassady Electrical Contractors 2200 W. Tapp Rd. Bloomington, Indiana 47403 United States
MODULAR/CLEAN ROOM CONTRACTOR	AES Clean Technologies, Inc. 422 Stump Rd. Montgomeryville, Pennsylvania 18936 United States
EQUIPMENT MOVE-IN CONTRACTOR	Cardinal Contracting 2300 South Tibbs Ave. Indianapolis, Indiana 46241 United States
ROOFING CONTRACTOR	Building Associates Inc. 3701 Jonathan Dr. Bloomington, Indiana 47404 United States
FLOORING CONTRACTOR	Cornerstone Flooring St. Patrick Drive Brownsburg, Indiana 46112 United States
FABRICATION/STEEL SETTING CONTRACTOR	Wilhelm Construction 3914 Prospect St. Indianapolis, Indiana 46203 United States
INSULATION CONTRACTOR	Gribbins Insulation 821 W. Johnson Dr. Terre Haute, Indiana 47802 United States
FIRE PROTECTION CONTRACTOR	Ryan Fire Protection 9740 E. 148th St. Noblesville, Indiana 46060 United States
TELECOMMUNICATIONS CONTRACTOR	Indiana Voice and Data 840 W. 17th St., #6. Bloomington, Indiana 47404 United States



CATEGORY WINNER
Process Innovation

CATEGORY WINNER
Facility of the Future

ELI LILLY AND COMPANY

Eli Lilly and Company is a global health care leader that unites caring with discovery to make life better for people around the world. It was founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today remains true to that mission in all its work.

“Eli Lilly and Company was named winner of the FOYA 2017 Process Innovation Award for their forward-thinking implementation of continuous direct compression (CDC) and other process innovations in oral solid dose (OSD) facilities across their manufacturing network.

“Lilly was also named winner of the FOYA Facility of the Future category for their process development, production platform commitment, and deployment of three replicate operational continuous OSD production facilities.”



Project

Continuous Direct Compression Manufacturing Kits 2 and 3

Location

Indianapolis, Indiana, US (CM2) and Carolina, Puerto Rico (CM3)

Project mission

Design and implement a network of state-of-the-art continuous manufacturing process facilities for commercialization and production of tablets

Total facility floor area (associated with project in existing facility)
CM2: 4,975 sq. ft. CM3: 4,720 sq. ft.



CONTINUOUS INNOVATIVE THINKING WINS TWICE

Continuous manufacturing (CM), one of the newest and most advanced production methods, is a hot topic in the pharmaceutical industry. For companies able to develop a reliable process, CM's benefits can include reduced costs, improved speed, and better quality control.

Global health care leader Eli Lilly and Company considers itself on the leading edge in its use of this technology. As part of its recently completed CM project, the company developed a CDC manufacturing process that it then deployed in two additional facilities.

About five years ago, Lilly began to consider the possibility of implementing CM for its oral solid dosage (OSD) products. The company's development group began to work with the technology, investing time and energy to ensure that it fully understood CM and its potential benefits and integrating PAT into the initiative. That ini-

tial project, known as CM1, was completed at the company's development facilities in Indianapolis, Indiana, US.

"The first thing you notice is that CM speeds up the development cycle on new products," says David Sternasty, Vice President, Corporate Engineering, Global Health, Safety, and Environmental at Lilly. "Under an older production model, a development scientist might make 16 or 32 discrete batches of product in a designed experiment that then have to be lab tested to determine how process parameters impact production. In a continuous processing unit, parameters are established by adjusting controls and, consequently, you can do multiple experiments very quickly. This is a huge advantage for development scientists, because it allows them to gain product understanding quickly. This was the reason, from a development standpoint, that we originally started moving to CM."

Integration was a central principle that influenced all aspects of the project. At the system level, feeding, mixing, and tablet compression unit operations are seamlessly integrated with online PAT and first-principles modeling to provide a comprehensive unified control strategy. The Lilly CM platform also relies on integration at the individual unit operational level.

The company designed a novel approach for its dispensing and feeding unit. Lilly's process is innovative because feeders are actively controlled as an integrated system rather than a series of independent set points using a cascade control loop, also known as ratio control. By designating a master feeder (typically the drug substance feeder) and modulating the other feeders in response to variation in the master feeder output, the concentration of formulation components is maintained more consistently. The powder feeder feedback control loops automatically adjust for raw material



ified in only 11 months and placed into service. “Because of the efficiencies, and the fact we were replicating an installation we had just completed,” says Pletcher, “we were able to reuse and leverage commissioning and qualification protocols as well as much of the design work. This approach has proved to be a very efficient and effective way to replicate units from one facility to another.”

Both CM2 and CM3 are functional replicates with identical equipment, layout, PAT instrumentation, and automation and control schemes. According to Sternasty, the design of both GMP equipment sets benefited from years of optimization and evolution work on the prototype CM1 installation.

“We have seen that a benefit with the CM

changes such as density and powder flow.

Additionally, the CM1 development unit taught the Lilly team learned to deal with other variables, such as environmental disturbances, vibration, and room-pressure changes. “These feeders are incredibly sensitive, and they are on very sensitive scales,” explains Timothy Pletcher, Lilly’s Associate Senior Consultant Engineer. “We learned that we needed to be mindful and design a system that could provide as much stability as possible. So we worked closely with our A&E [architecture and engineering] firm to design structurally independent platforms, such as on the midlevel feeders and upper-level feeders, which were mass-dampened to give us as much stability as we could achieve.”

EFFICIENT REPLICATION

In September 2014 Lilly determined that the CM1 platform was ready for use in a commercial manufacturing environment. The company launched the CM2 project, which it planned to integrate into the company’s existing OSD facility in Indianapolis. Building on lessons learned in the development phase, the CM2 line progressed quickly through construction, commissioning, and qualification; the unit was ready for production of three development molecules, in line with good manufacturing practice (GMP), in November 2015. A mere 15 months had elapsed between the company’s funding approval and its ability to produce commercial products destined for patients.

Installation of a second GMP unit (CM3) at an OSD manufacturing facility in Carolina, Puerto Rico, began in November 2015. The unit was qual-



“CONTINUOUS
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 INNOVATIVE WAY TO
 PROVIDE A RELIABLE, SAFE
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 MEDICINES, AND BRING
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 THE PIPELINE AS QUICKLY
 AS WE CAN.”

process is that there is no scale-up,” says Sternasty. “Because we are using continuously running equipment that is very small in scope, the equipment deployed in development is the same as that used in manufacturing. So there is no cost and time associated with scale-up and technology transfer. From a manufacturing standpoint, the capital investment is significantly lower, the equipment offers a more compact footprint, and the process uses less energy than what you would see in a traditional wet-granulation fluid-bed drying process. So we started on the course because of the gains we would see in development, and we have gained continued benefits all the way through to commercial manufacturing.”

For his part, Pletcher credits the teams’ close working relationship for the project’s success. “We had an unprecedented level of collaboration,” he says. “Finding ways to replicate that team effectiveness and cross-functional teamwork on other projects would be beneficial on any other endeavors that we undertake. The success of these projects was very much built on how effectively these groups worked together—from development to manufacturing.”

“Lilly is focused on innovation,” says Sternasty. “We believe that continuous manufacturing is an innovative way to provide a reliable, safe supply of high-quality medicines, and to be able to bring our product through the pipeline, from development to manufacturing, as quickly as we can. So, we are really very pleased with the results of what we have installed here.” ♦



KEY PROJECT PARTICIPANTS

MANUFACTURER/ OWNER	Eli Lilly and Company Lilly Corporate Center Indianapolis, Indiana 46285 United States	Lilly del Caribe PO Box 1198 Carolina, Puerto Rico 00986-1198
ENGINEER/ ARCHITECT (A&E)	Mussett Nicholas & Associates 502 S. West St. Indianapolis, Indiana 46225 United States	
ENGINEER/ ARCHITECT (A&E)	TLF Engineers 3901 W. 86th St., Ste. 200 Indianapolis, Indiana 46268 United States	Babilonia Engineering Group 1223 Cll Juan Ponce de Leon San Juan, Puerto Rico 00926
CONSTRUCTION MANAGER	Davis & Associates Inc. 2852 N. Webster Ave. Indianapolis, Indiana 46219 United States	Fluor Daniel Caribbean, Inc. Parkside Plaza Ste. 500 St. 2 No. 14 Metro Office Park Guaynabo, Puerto Rico 00969
MAIN/GENERAL CONTRACTOR/ PIPING SUBCONTRACTOR/ HVAC SUBCONTRACTOR	Davis & Associates, Inc. 2852 N. Webster Ave. Indianapolis, Indiana 46219 United States	Alproem Engineering Contractors 2135 Carr. 2 Ste. 15 Bayamon, Puerto Rico 00959-5259
AUTOMATION AND CONTROL SUPPLIER	Cornerstone Controls 8525 Northwest Boulevard Indianapolis, Indiana 46278 United States	Emerson Process Management Los Frailes Industrial Park 475 Calle C Ste. 501 Guaynabo, Puerto Rico 00969
	Prozess Technologies 6124 Delmar Blvd. St. Louis, Missouri 63112 United States	
MAJOR EQUIPMENT SUPPLIER	Korsch America 18 Bristol Dr. South Easton, Massachusetts 02375 United States	CDM 197 Stone Castle Road Rock Tavern, New York 12575 United States
	Bruker Optics, Inc. 5465 East Cheryl Parkway Madison, Wisconsin 53711 United States	
MAJOR EQUIPMENT SUPPLIER	Coperion K-Tron 590 Woodbury Glassboro Rd. Sewell, New Jersey 08080	
	Gericke USA, Inc. 14 World’s Fair Dr. Ste. C Somerset, New Jersey 08873-1364 United States	



JAZZ PHARMACEUTICALS

Jazz Pharmaceuticals focuses on improving patients' lives by identifying, developing, and commercializing meaningful products that address unmet medical needs.

“Without any prior experience in the building of manufacturing facilities, Jazz Pharmaceuticals put together a small team drawn on a variety of external sources, ensured that recruits were aligned with the company's culture and objectives, and delivered a greenfield-licensed facility against very aggressive targets.”



Project

Project Rock

Location

Monksland, Athlone
Co. Roscommon, Ireland

Project mission

Create a fully operational, FDA-approved manufacturing plant in Ireland by the end of 2016

Total campus area

55,627 sq. ft.



SCOPE, TIME, AND BUDGET: A ZERO-COMPROMISE APPROACH

Scope, time and budget: These are the key variable components of any project. If one of the three deviates from plan, the other two are always affected. But for Jazz Pharmaceuticals, compromise was not an option. The company's unwillingness to settle for something less than perfect led to the building of a state-of-the-art manufacturing facility in Athlone, Ireland.

In March 2013, Alan Mac Neice, Executive Director and Site Leader of the Athlone facility, was appointed to lead a project without defined parameters.

"In the early stages of the project, the scope of what we wanted to do wasn't clear," explains Mac Neice. "We wanted to improve the control of quality and the supply chain as these pertained to patients. Our aim was to pick several supply-chain operations or components and identify them as the most important areas for us to take control of. We looked at a huge range of options (e.g., manufacturing of raw materials, of the active ingredient, or of the drug product) and finally settled on manufacturing of the drug product, as well as packaging, labeling, and fin-

ishing, as the right things to do."

The drug in question, Xyrem, is used to treat narcolepsy. Jazz had seen significant growth in demand for Xyrem since 2005, and decided to build a new facility and manufacture the product on its own. This was a bold move for a company that had no prior manufacturing experience. Until then, Jazz had outsourced all its production; contract manufacturers had been producing Xyrem since 2005.

AHEAD OF SCHEDULE AND UNDER BUDGET

In October 2013, the Board of Directors approved the scope and budget for the company's plan to build a new facility on a 17.5-acre lot in Athlone, a town located in central Ireland between Galway and Dublin. The company had a budget of €46.2 million (\$50 million) and a target date of late June 2016 to obtain approval from the US Food and Drug Administration (FDA). The facility also had to be provisioned for future expansion and accommodate the manufacture of new products.

Following budget approval, Mac Neice and his team (of six at the time) completed the design

and submitted their planning application to the local authorities in Ireland. Groundbreaking took place on an extremely wet 10 February 2014. "We had had six months of rain practically every day that winter, which made us quite nervous," says Mac Neice. "Fortunately, it stopped raining the next day and we had dry weather for the next three months, which made our construction people very happy."

Mac Neice's team moved into a temporary office located a mere 200 meters from the project site in June 2014. "Our team spent their time working on parallel projects, such as manufacturing and quality management systems, writing the procedures, working out how the technology transfer would work, as well as reviewing and approving the design as it progressed," he says.

Between June and September 2014, Mac Neice grew his team to a full complement of 26. "They were working on all the things you need to do to have a fully operational pharmaceutical manufacturing site," says Mac Neice. "So when we moved into the building—which we did before it was finished in April 2015—we were able to hit the ground running by using the team to

THE PROJECT COMPLETED ITS PERFECT TRIO OF FULL-SCOPE IMPLEMENTATION, DELIVERED AHEAD OF SCHEDULE, AND UNDER BUDGET.

support the facility's commissioning and qualification. We were also able to start executing on our business systems, leading to the manufacture of validation batches at the end of October 2015, which led to regulatory submissions later that year and in early 2016."

On 8 April 2016, Ireland's Health Products Regulatory Authority granted authorizations for the manufacture of Xyrem and investigational medicinal products at the facility. Just over two months later, on June 27, the staff was informed that the US FDA had approved Jazz's Prior Approval Supplement (PAS) to manufacture Xyrem at its new facility.

The project came in 2.4% under budget, completing its perfect trio of full-scope implementation, delivered ahead of schedule, and under budget.

RECIPE FOR SUCCESS

According to Mac Neice, Jazz set out to achieve these goals right from the start. "Even with only 10% of the design done, we mapped it out and set the date on which we wanted FDA approval, which was to be 29 June 2016," he explains. "That was the fastest possible timeline. We always talked about the day; we didn't talk about the week or the month or the quarter. And the dynamic we set among all our business partners and our own team was that every day matters, which had a huge psychological impact on how people thought."

In terms of factors for success, Mac Neice says that what might have appeared to be weaknesses turned out to be great strengths. "We had no pre-existing infrastructure support or guidance on how to do this, which meant nobody was locked into a particular way of thinking. It meant we could really focus on what we wanted as an outcome.

"And the fact that the team was so small made decision-making very easy. Some of our business partners have remarked that these were key factors of success—that our team was small and how that allowed us to make decisions quickly."

Mac Neice also noted that it was his team's unwillingness to compromise on any aspect of

the project that led to its success. "All my life," he says, "I've been asked which is the most important component of the three—scope, time, or budget. On this project, all three components were equally important."


While his team knew that challenges and

short-term compromises were inevitable, they quickly adopted a mitigation plan. "At one point, we had a schedule challenge during the construction phase, which we addressed by deploying additional resources and working extra hours. So, we compromised on our budget. But once we had the plan in place to return to our schedule, we started exploring ways to recover that money from another part of the project. That's an example of our refusal to compromise on any of the three components in the long run. We might compromise on a short-term basis, but we always thought about how we could remediate or mitigate the compromise we had just made."





Additionally, the company made conscious efforts to build a strong working team and a culture where employees felt appreciated while also being challenged. “Our turnover rate has been very low. We have a culture where people were being challenged every day to be at their best, and to develop beyond it. That really ignites people. We targeted the type of people who would enjoy that kind of development and wanted to work in an environment that is constantly changing.”

Ultimately, Mac Neice says, the project’s success comes down to the team. “It was our staff who were successful in what they did, and this project has been a constant reminder to me that people create success. No matter what enablers you put in place, nothing will succeed unless your staff is successful. We’re a small team in a company that had never done anything like this before—in a town in the middle of Ireland—and we believed we could be world-class. Investing in people and in your business culture makes that happen.” 



KEY PROJECT PARTICIPANTS

MANUFACTURER/OWNER	Jazz Pharmaceuticals Monksland Athlone, Co. Roscommon, Ireland
ENGINEER/ARCHITECT (A&E)/ CONSTRUCTION MANAGER	PM Group Killakee House Belgard Square Tallaght, Dublin 24, Ireland
MAIN/GENERAL CONTRACTOR	John Sisk & Son Wilton Works Naas Road Clondalkin, Dublin 22, Ireland
ELECTRICAL CONTRACTOR	Suir Engineering Unit 9a Cleaboy Business Park Old Kilmeaden Road Waterford, Ireland
PIPING/HVAC SUBCONTRACTOR	Leo Lynch 16 Fonthill Industrial Park Fonthill Road North Clondalkin, Dublin 22, Ireland
AUTOMATION AND CONTROL SUPPLIER	Rockwell Automation IDA Business Park Carrigtwohill, Co. Cork, Ireland
MAJOR EQUIPMENT SUPPLIER	Marchesini Group S.P.A. Via Nazionale 100 40065 Pianoro Bologna, Italy Kells Stainless (ABEC) Cork Road Fermoy, Co. Cork, Ireland Extract Technology Bradley Junction Industrial Estate Leeds Road Huddersfield HD2 1UR, United Kingdom



PT. KALBIO GLOBAL MEDIKA

PT. Kalbio Global Medika is a biologics and biotechnology company, and wholly owned by Kalbe Farma, the largest healthcare provider in Indonesia and the largest publicly listed pharmaceutical company in Southeast Asia.

“A point of pride for Kalbio is their quality management system (QMS), designed in accordance with PIC/S standards. The QMS, which integrates all aspects of manufacturing, will support Kalbio’s ambitions to expand its products to regional and international markets.”



Project

Biotechnology Facility

Location

Jakarta, Indonesia

Project mission

Produce quality biotechnology products for local and international markets

Total facility floor area

Land: 118,402 sq. ft. Site: 180,015 sq. ft.



INCREASING EFFICIENCY WHILE REDUCING CARBON FOOTPRINT

Local firms make some 70% of all drugs consumed in Indonesia,* yet 90% of the raw materials required to make them are imported. Raw materials are susceptible to currency fluctuations, which can affect drug costs for patients. To control costs, the Indonesian government took steps to encourage in-country biologics and biotechnology manufacturing. PT Kalbe Farma, the country's largest pharmaceutical company, formed PT Kalbio Global Medika in response to the government's call to action.

Kalbio's Senior General Manager, Christopher Sweeney, jokes with a hint of pride that nothing would seem out of place if his facility were in San Diego or Boston, "except, perhaps, the palm trees." The \$35-million facility of almost 40,000 sq. ft. is built on a plot in the Cikarang Industrial Park on the east side of Jakarta.

Given its high quality-assurance standards, Kalbio faced challenges both during construction and when procuring equipment. Certain vendors didn't understand the fit and finish the company expected. In addition, the equipment requested was not necessarily the equipment vendors wanted to sell. "Some vendors think that because you are in the Far East and you are an Asian company, they can sell you any sort of system they find is more suitable for their own manufacturing purposes," says Sweeney. "We had a user requirement document stating what we wanted, and that wasn't the standard system that vendors had been selling across Southeast Asia."

The facility was completed in November 2016, 4% under budget. Kalbio expects to obtain its license to manufacture from Indonesia's National Drug and Food Control Agency (Badan Penga-

was Obat dan Makanan [BPOM]) in the second half of 2018.

AN EGALITARIAN STRUCTURE

As the project progressed through design and construction, Kalbio's management team adopted a staffing idea that Sweeney had seen when he worked in the United Kingdom. "We hired 30 postgraduates who were just getting out of college and we gave them a one-year training in biotech techniques," he says. "And we had great support from the international vendors because they saw the value of this. It was very pleasing to have the full support of Merck, GE, and Bioquell in helping us start up our facility."

* Source: Indonesian National Drug and Food Control Agency (Badan Pengawas Obat dan Makanan [BPOM])

Today, Kalbio employs approximately 90 people, with plans to expand to about 120 later in 2017. And as he does when talking about the facility, Sweeney speaks proudly of his staff, whose average age is 24. “They are all highly trained, educated, and motivated to get things done,” he says. “We also have a very egalitarian structure, an open-plan office, and an open-plan canteen; everybody is equal. We are all part of the same machine, we work as a team.”

INDUSTRY BEST PRACTICES

Seeing inefficiency in the process, Kalbio has used a progressive approach to validation. As part of their service delivery, vendors perform an installation qualification (IQ)/operational qualification (OQ) on all the company’s bespoke systems. To avoid duplication, the company has streamlined processes so that testing done, say, at the factory acceptance testing (FAT) or the site acceptance testing (SAT) stages is not repeated in the IQ or OQ stage. “We just reference the FAT and the SAT testing in the IQ or OQ documents,” says Sweeney, “thereby saving a lot of time and money.”

The company has also implemented a full quality management system that is compliant with PIC/S guidelines; Sweeney adds that Kalbio is one of the first biotech companies in Southeast Asia to adopt a risk-based approach to manufacturing.

Additionally, Kalbio set out to reduce its demand on resources. To this end, for example, the facility’s air handling units (AHU) condense 700 liters of water from the atmosphere per hour—for a total of 16 cubic meters of water per day—which is then reused. The AHUs are also turned down overnight to further reduce electricity demand. “Basically, we have tried to do as much as we can to reduce our carbon footprint,” says Sweeney. “And while it costs money to implement these measures, they save money in the long run.”

For Sweeney, receiving a 2017 FOYA Honorable Mention “is a great achievement for Kalbio, for my team, but also for the Indonesian biopharma industry. I hope it spurs other companies to do the same, and send in their FOYA applications when they have finished their facilities.” ♦



SWEENEY SPEAKS PROUDLY OF HIS STAFF, WHOSE AVERAGE AGE IS 24. “THEY’RE ALL HIGHLY TRAINED, EDUCATED, AND MOTIVATED TO GET THINGS DONE.”

KEY PROJECT PARTICIPANTS

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NEPHRON PHARMACEUTICALS CORPORATION

Nephron Pharmaceuticals specializes in blow-fill-seal (BFS) manufacturing, a technology in which a vial of medication is formed, filled, and sealed in a continuous process, without human intervention in a sterile, enclosed area.

“Nephron is being recognized for using and integrating a suite of industry-leading technologies such as laser-guided vehicles, automated warehousing, robotics, and track-and-trace technology. The company is also recognized for its significant infrastructure investment in West Columbia and its commitment to using local talent from nearby universities and trade schools. In addition, the facility’s viewing areas and access were designed to facilitate students’ and visitors’ exposure to the pharmaceutical industry, thereby helping to promote and advance pharmaceutical manufacturing careers.”



Project
Nephron SC

Project mission
Build a state-of-the-art automated manufacturing facility

Location
West Columbia, South Carolina, US

Total facility floor area
Land: 2,317,140 sq. ft. Site facility: 408,000 sq. ft.



AUTOMATED, STATE OF THE ART, AND COMMUNITY FOCUSED

When Nephron Pharmaceuticals Corporation was at full production capacity and no longer able to keep up with sales growth at its facility in Orlando, Florida, President and CEO Lou Kennedy knew something needed to be done: expand the existing facility or build a new one altogether. “We were selling everything that we could produce; we had no excess capacity,” says Kennedy. “So we purchased 60 acres in Orlando next to the original facility. However, several things occurred that made doing business in Orlando difficult, and Kennedy reached out to South Carolina, which welcomed Nephron with open arms.

Nephron now has a state-of-the-art facility featuring automated BFS manufacturing, robotics, laser-guided vehicles, and the most recent quality control and automation systems.

In February 2011, feasibility studies and design began on a new 408,000-sq.-ft. facility budgeted at \$245 million. Construction got underway a little more than a year later, in April 2012, in West Columbia, a city of approximately 15,000 located in the center of the state. The site was selected for

its many benefits, including proximity to universities and colleges, the state’s deep manufacturing labor pool, accessibility to three major interstate highways, and the ability to receive materials via rail car, which Kennedy says significantly lowers the costs of raw materials.

Although architects and engineers provided an initial construction estimate of three to five years, Kennedy and her team completed it all in a much shorter timeframe. “We completed the project—from implementation through validation, to obtaining FDA approval, to official opening in late 2015—in three years,” she says. “It was a really aggressive timeline, and we are very proud of that.”

STATE OF THE ART

Nephron designed its South Carolina facility to be a world leader in BFS manufacturing. The unique aspect of the new plant, which utilizes eight BFS machines to produce inhalation drugs, is its high level of automation. “We are making sterile drugs that require no human intervention, and that’s important because there is no chance for error,” says Kennedy. “Each piece of equip-

ment throughout our facility is custom-made, spec’d out by our own design engineers, and integral to making sterile aseptic medications and eliminating risk.”

The entire manufacturing process utilizes a variety of systems to operate with the utmost safety and efficiency. It includes:

- Automated filling via BFS technology: Rommelag BFS machines are used to form, fill, and seal vials in an aseptic environment with no human interaction, a technology that produces a highly repeatable and safe drug product.
- Automated warehousing: The Elettric80 warehouse and laser-guided vehicle system automatically retrieves and stores pallets of finished goods as well as works in progress.
- Automated packaging: Bosch packaging technology lines are used to package BFS products efficiently for sale to hospitals and home users. Packaging includes printing and verification operations to prevent counterfeiting and allow tracing of products through the supply chain.

“WE ARE MAKING STERILE DRUGS THAT REQUIRE NO HUMAN INTERVENTION, AND THAT’S IMPORTANT BECAUSE THERE IS NO CHANCE FOR ERROR”

- A laboratory information management system and MODA, a paperless quality-control microbiology solution, are used to automate and control Nephron’s laboratory systems.
- Plant-wide OSIsoft PI historian and manufacturing information systems are deployed as part of an overall automation strategy. These systems include a track-and-trace component that allows product in all phases of production to be accurately followed via barcodes and other verification methods.

“No BFS facility anywhere around the globe is as automated as ours,” says Kennedy. “While employees formulate the drugs at the start of the process using an automated formulation software, and then load trucks at the very end, every step in between is 100% automated. We are constantly tracking all the metrics, and through software we can adjust on every piece of equipment. This is a unique pharma plant.”

ABILITY TO EXPAND

The facility was also built with expansion in mind. “Our utilities are oversized so that as the company grows new lines can be added and the infrastructure can support the growth,” Kennedy says. Company growth can come from three sources: increased sales of currently manufactured inhalation solutions, sales of drug products that Nephron pursues based on market analysis, and sales of drug products on drug shortages lists that align with BFS technology.

Kennedy, and indeed all of Nephron’s 330 employees, take great pride in the new facility. Kennedy is especially pleased with the company’s contribution to the community. The building was designed so that all aspects of the production process are visible to visitors—which often include customers and schoolchildren. Nephron also has an intern program for college and high school students. “We’re trying to inspire young folks to pick careers in pharma and in high-tech manufacturing. I think that is a good testament of what the company hopes to encourage,” says Kennedy. 



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NOVARTIS AND UNIVERSITY OF PENNSYLVANIA

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Project
Novartis-Penn Center for Advanced Cellular Therapies

Location
Philadelphia, Pennsylvania, US

Project mission
Find more effective treatments for cancer via personalized medicine

Total facility floor area
23,610 sq. ft



ADVANCING INNOVATIVE CANCER THERAPIES

In August 2012 the Novartis Institutes for Bio-Medical Research, based in Cambridge, Massachusetts, and the University of Pennsylvania's Perelman School of Medicine (Penn Medicine) announced they had entered into an exclusive global research and licensing agreement. Under the alliance, Penn Medicine granted Novartis an exclusive worldwide license to the technologies used in an ongoing trial of patients with chronic lymphocytic leukemia (CLL) as well as future therapies based on chimeric antigen receptor (CAR) technology developed through the collaboration. As part of the agreement, Novartis invested \$20 million to establish the \$27-million Center for Advanced Cellular Therapies (CACT) and to support future research in CAR technology.

Construction on the CACT—formally known as the Novartis-Penn Center for Advanced Cellular Therapeutics—began in December 2014, and the facility opened in early 2016. It adjoins the existing cancer therapeutics floor in the Smilow Center for Translational Research, allowing it to be fully integrated into Penn Medicine's research and clinical operations. The CACT employs 100 highly specialized professionals working across 6,300 sq. ft. of cleanroom space specially de-

signed for cell engineering and 24,000 sq. ft. of laboratory and cell therapy manufacturing space with the capacity to manufacture cellular therapies for up to 400 patients per year.

"The CACT will allow us to leverage this progress to develop and test new approaches more quickly," says Carl H. June, MD, the Richard W. Vague Professor in Immunotherapy at Penn Medicine. "At the same time, we'll be able to expand our ability to manufacture personalized cell therapies for a greater number of trials."

A NEW SCIENTIFIC WORKPLACE CULTURE

Although the CACT is primarily a lab and research space, the project design team brought in experts from outside the fields of science and technology with a view to making the facility more efficient and effective. They also included specialists in corporate workplace design to create the best environment possible for employees.

Open-plan laboratories within the facility allow researchers from the center's four principal investigator (PI) teams to work together rather than in silos, as in many lab facilities. Each PI team works on different aspects of the research, which

requires specialized facilities: the clinical cell and vaccine production facility, a quality control lab, a transformational and correlative studies lab, and a product development lab. This approach promotes what the center calls a "new scientific workplace culture," which blurs the boundaries across disciplines and encourages collaboration.

The center was designed and built to meet current good manufacturing practice cleanroom standards, including ISO Class 10,000 cell processing rooms and ISO Class 100,000 support spaces. The flow of specimens, materials, and staff has also been carefully considered to ensure the highest standard of cleanliness throughout the facility.

These and other design decisions are intended to improve collaboration and communication among the teams, helping them increase speed to market and produce individual patient therapies more efficiently. The strategic layout and organization of lab equipment will also dramatically cut the time it takes to generate "hunter" cells: While it previously took a month to produce these therapeutic agents for each patient, the new facility will help reduce the time to two weeks.

The CACT advances this process through the

**NOVARTIS AND UNIVERSITY OF PENNSYLVANIA
HONORABLE MENTION**

different functional areas contained within the facility, such as vaccine development, assay development, and correlative studies of blood and other bio specimens, to examine how trial participants respond to the therapies they receive.

EXCITING NEW THERAPIES

In addition to continued trials in CLL, Penn has engineered T cell trials underway for other types of leukemia, as well as lymphoma, mesothelioma, myeloma, and neuroblastoma.

In 2014, the US Food and Drug Administration awarded breakthrough therapy designation to CTL019, an investigational CAR therapy for the treatment of relapsed and refractory adult and pediatric acute lymphoblastic leukemia. CTL019 is the first personalized cellular therapy for the treatment of cancer to receive this important classification.


Pioneered by Penn Medicine, this new application first removes a patient's T cells, then genetically reprograms them in the CACT's clinical cell and vaccine production facility. After being infused back into the patient, these hunter cells both multiply and attack, targeting tumor cells that express the DCD19 protein. Tests reveal that each single engineered cell can grow into an army of more than 10,000.

Ultimately, the CACT's objective is to develop new treatment options for life-threatening diseases. "This new joint center is testimony to the power that comes from merging academic discovery and the generation of new medicines," says Mark Fishman, President of Novartis Institutes for BioMedical Research. ◊


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