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2014

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2014 Facility of the Year Awards Program: A Decade of Excellence

For the past decade, the Facility of the Year Awards (FOYA) has provided a paramount platform to celebrate innovations in pharmaceutical manufacturing. FOYA's industry spotlights focus on quality projects which apply technological advancements, state-of-the-art manufacturing strategies, and cost-effective operations to produce pharmaceuticals that raise the standard of living on a global scale.

From preventative vaccines to advancements in cancer treatments, FOYA, driven by their goal of quality through manufacturing advancement, has collected and shared cutting-edge methods successfully carried-out by our industry peers. Sharing industry accomplishments in facility design and operations drives a competitive quality into pharmaceutical products, as well as exposing more effective ways to deliver services. FOYA and the participating facilities, contribute to an unparalleled source of inspiration benefitting the health of patients and the strength of



F. Hoffmann-La Roche Ltd.

pharmaceutical commerce. By continuing to showcase, share, and celebrate efficacious facilities, the pharmaceutical industry can continue to strive toward their highest potential in quality and corporate achievement.

The FOYA program recognizes innovative projects and the visionaries behind the designs, processes, and construction that enhance the delivery of a quality project, as well as reduce the cost of producing high-quality medicines. The awards program effectively spotlights the accomplishments, shared commitment, and dedication of individuals in companies that advance our industry and inspire continuous progress in pharmaceutical products serving the health of patients worldwide.

The facilities chosen are outstanding examples of innovation and advancement for each piece of the manufacturing puzzle. The facilities are models of practical application of manufacturing theories and consistent follow-through on a specific level which ultimately enhances the quality of a final product. Be-

ing honored in a category acknowledges those firms who constructed, validated, and equipped the facility demonstrating their ingenuity of design and vision. Award categories and their respective winning companies include:

- **Boehringer Ingelheim Pharma GmbH & Co. KG** winner of the Facility of the Year Award in the category of *Equipment Innovation* for its Aseptic Area 5 and Combi Line facility in Biberach, Germany.
- **F. Hoffmann-La Roche** winner of the Facility of the Year Award in the category of *Sustainability* for its B250-Q2K facility in Kaiseraugst, Switzerland.
- **Grifols Therapeutics Inc.** winner of the Facility of the Year Award in the category of *Project Execution* for its Grifols North Fractionation Facility in Clayton, North Carolina, US.
- **Patheon Pharma Services** (formerly DSM Biologics) winner of



Boehringer Ingelheim Pharma GmbH & Co. KG



Grifols Therapeutics Inc.

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Patheon Pharma Services

the Facility of the Year Award in the category of *Process Innovation* for its Biologics Plant of the Future in Brisbane, Australia.

- **Penn Pharmaceutical Services Ltd.** winner of the Facility of the Year Award in the category of *Facility Integration* for its Project PennDragon-Contained Manufacturing Facility in Tredegar, South Wales, UK.
- **Pfizer Ireland Pharmaceuticals** winner of the Facility of the Year Award in the category of *Operational Excellence* for its NSI Capacity Expansion in Grange Castle, Dublin, Ireland.

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- **WuXi Apptec Pharmaceutical of China**, *Honorable Mention* in the category of *Process Innovation* for its Fully Single Use mAB Production Facility in Wuxi City, China.

Over the past 10 years, submissions for the Facility of the Year Awards program have been received from 30 different countries and territories making FOYA a true representation of global excellence in pharmaceutical manufacturing. Each submission was reviewed by an independent, blue-ribbon judging panel consisting of global senior-level executives from all aspects of the industry. These industry professionals included:



Penn Pharmaceutical Services Limited

- **Jim Breen, Chair** – Vice President, Worldwide Engineering and Technical Operations, Johnson & Johnson
- **Chaz Calitri** – Vice President, Global Engineering, Pfizer, Inc.
- **Chris Chen** – Sr. Vice President and Chief Technology Officer Biologics Services WuXi AppTec Co., Ltd.
- **Sanjit S. Lamba** – Managing Director and Head of Global Procurement Strategy, Eisai Pharmatechnology and Manufacturing
- **Brian H. Lange, P.E.** – Operations Director, NA Operations and Merck Consumer Care, Merck & Co. Inc.
- **Andy Skibo** – Regional Vice President, Biologics-Supply, MedImmune/AstraZeneca



Pfizer Ireland Pharmaceuticals

- **Ron Trudeau** – Vice President, Facilities Engineering Services, Baxter Healthcare

The 2014 FOYA overall winner will be announced during the plenary session at the **2014 ISPE Annual Meeting** which will be held from 12 to 15 October 2014 at Caesar's Palace, in Las Vegas, Nevada. During the Annual Meeting, the FOYA program will be highlighted and the 2014 category winners and the 2014 overall winner will be honored; there will be an education track that offers insight from 2014 category winners on their winning projects.

FOYA award winners also will be formally recognized as part of the ISPE exhibit at the **2014 Pharma EXPO** which will be held 2 to 5 November 2014 at McCormick Place in Chicago, Illinois. This world class exhibition, sponsored by ISPE and PMMI, will include a conference which will be covering topics on the latest technological and regulatory trends, best practices and practical applications of science and technology throughout the entire pharmaceutical lifecycle. 



WuXi AppTec Biopharmaceuticals Co., Ltd.



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Boehringer Ingelheim

Transparency and Flexibility Supports Aseptic Success

Introduction

After a two year period of concept development, **Boehringer Ingelheim (BI)** endorsed the **Aseptic Area 5 and Combi Line** project in Biberach/Riß, Germany to implement a new facility for aseptic manufacturing of biopharmaceutical drug products. This campus is not only one of the major BI research and development centers, but it is also the home of one of the largest facilities dedicated to biopharmaceuticals. This facility provides the entire value chain from cell line and process development to commercial cell culture manufacturing to the aseptic production of various finished drug product dosage forms. More than 1,600 employees contribute to the various activities in Process Development, Biopharma Operations, Biopharma Quality Unit as well as all engineering, supply chain, and logistic



Aerial view.

functions. These services are provided for BI's internal products and for global partners in its strategic contract manufacturing business for biopharmaceuticals.

Boehringer Ingelheim's original production building, F113, was built in the early 1970s. The 57,528 square meters floor area includes two production levels, five office levels at the east and west side, and mezzanines above the production floors allowing a very flexible asset. Central utilities and the building's framework are located in the center of the facility. In addition, the basement hosts a central gowning area for personnel and storage areas for pull/push concepts in biopharma cold chain logistics. With this clear building structure and a height between production levels of 7.5 m (approx. 24.6 ft), building F113 was ideal for new aseptic production areas.

The Aseptic Area 5 Project Team faced multiple challenges in restructuring for aseptic production such as:

Boehringer Ingelheim

Category Winner – Equipment Innovation

Project: F113 Aseptic Area 5 and Combi Line

Location: Germany

Project Mission: a modular concept for capacity expansion.

Site Size: 483,390 m² (5,203,167 sq. ft.) / **Project**

Size: 1,635 m² (17,599 sq. ft.)

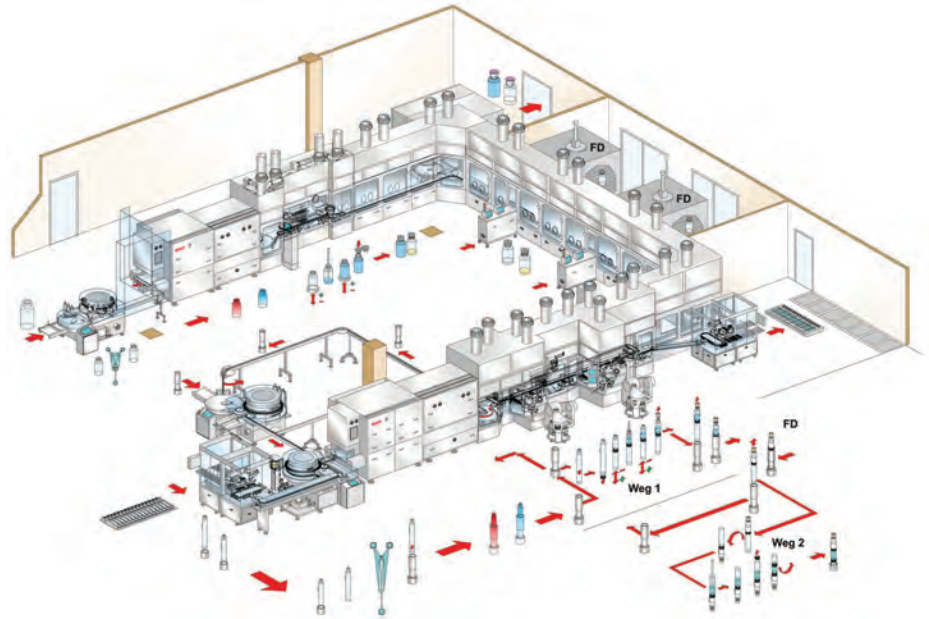
Duration of Construction: 36 months

- Constructing a multiple product facility
- Leveraging synergies with existing operations
- Installing the latest technologies with respect to regulatory requirements for aseptic processing of biopharmaceuticals.
- Variable options for large product campaigns and economic smaller scale products

Boehringer Ingelheim, recipient of the ISPE 2014 Facility of the Year Award for Equipment Innovation, developed and executed Aseptic Area 5 and Combi Line with its own interdisciplinary project team. The project was further supported by industry machine experts and global pharmaceutical service partners excelling in operating infrastructure.

Areas were implemented in two phases:

- Construction Phase 1 (Aseptic Area 5)*
- Utilities and HVAC systems



3-D simulation of the complete machinery installation.

- Airlocks
- Peripheric equipment

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Construction Phase 2 (Combi Line)

- Filling unit for liquid and lyo-cartridges and vials
- Detraying and retraying units
- Corresponding washing and siliconizing equipment
- Capping unit

Optimal Transparency

The facilities of the Aseptic Area 5 Project are all constructed with glass cleanroom walls to achieve optimal transparency for visitors, operators, and authorities. Transparency was not only a target for physical construction, but also for the batch documentation and all process data recording systems. In order to achieve optimal transparency, air returns were also made of glass panels. This allows insight to all processes from the surrounding "E-corridor" around the Aseptic Area 5 for supervisors, clients, and regulators. In addition to the perk of natural light, Aseptic Area 5's glass panels provides a unique opportunity for interaction between those inside of the cleanroom and those on the outside without gowning or breaking the clean barrier. Boehringer Ingelheim's innovative conceptual designs provide practical functionality to industry standard manufacturing.

Transparency also played a role in batch documentation and additional process data recording systems. In 2008, the project core team initiated a plan, including workshops, to integrate Aseptic Area 5 into Boehringer Ingelheim's Biopharma's automation concept. Based on the existing support Boehringer Ingelheim's Enterprise Resource Planning (ERP) system and the Manufacturing Execution System (MES), the new facility

“Transparency and flexibility were central themes throughout Boehringer Ingelheim's Aseptic Area 5 and Combi Line project. The selection of this project as winner of the equipment innovation category was not for a single innovation, but for the combination of multiple innovations.

– FOYA Judges

had to integrate all manufacturing processes into the Electronic Batch Recording (EBR) system. This enabled Aseptic Area 5 to become an almost paperless facility.

Twenty-seven different package units with a variety of differing software solutions are integrated. The EBR system in use at Aseptic Area 5 provides operators with step by step guidance for all manual or automated working steps. Batch reports are generated by each package unit and automatically integrated into the EBR. This increases GMP compliance and allows efficient batch record review, archiving, and centralized data evaluation. Boehringer Ingelheim's system integration provides remote access for maintenance and access to all production data from the office network.

Flexibility Leads to Innovation

Boehringer Ingelheim persevered through this project with their openness to flexibility. Overcoming large campaign manufacturing and small scale products led to the innovative use of line layout and customized equipment solutions. The U-shape line design allowed flexible usage of individual processing units, while maximizing operational time of the area during decontamination of separate isolators on the line. The development of a custom carrier system for the transport of cartridges throughout the line enabled proper handling to prevent tipping during their movement. The team also planned for flexibility of moving products from existing suites into this new area by ensuring filling equipment could handle many different size components. Boehringer Ingelheim's most effective innovation for equipment is the flexible isolators concept. The team developed five individual isolators for each individual piece of major equipment. This allows parallel activities such as transfer



Surrounding corridor with view in the Aseptic Area 5.



Vial filling with automatic loading and unloading units.

operations, setup or decontamination to occur within each isolator at the same time. Connections through “mousehole” ports

enable transfers of components between the different isolators during operation.

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Why Our Project Should Win

The following is an excerpt from Boehringer Ingelheim's submission, stating in their own words, the top reasons why their project should win the ISPE 2014 Facility of the Year Award:

- Flexible concept for facility utilization and modular integration
- Innovative solutions for aseptic processing of biopharmaceuticals (liquid and lyophilized) into vials and cartridges
- Small ecological footprint by integration into an existing building
- Transparency in construction and batch records (EBR)
- Short project timelines and early start of payback applying the modular concept

Modern Isolator Construction

The installation of new facilities in a production building, which is in cGMP-operation, requires stringent and consequent separation of operative production areas and areas under construction. The "preliminary" wall in the ISO 7 area built to separate operative Phase I from the Phase II construction was fabricated of solid metal. Cleanroom conditions for the operatives were validated upon initiation, but cleanroom parameters like pressure differences, temperature, relative humidity, and non-viable particle counts were continuously monitored and inspected daily. After finalization of Phase II, the equipment underwent a summer shutdown during which the metal separating wall was deconstructed. After a successful cleanroom validation, the Combi Line was then integrated into the Aseptic Area 5 manufacturing concept. This made joint use of supportive equipment, personnel-, and material-airlocks.

Looking ahead, Boehringer will demonstrate another advantage of modern cleanroom design in isolator construction for rapid facility integration. This anticipated approach will be ap-

Key Project Participants

Designer/Architect: Boehringer Ingelheim Pharma GmbH & Co. KG
(See ad on page 13)

Engineer: Klett-Ingenieur-GmbH

Construction Manager: Goerg Lemcke

Piping Subcontractor: Kinetics Germany GmbH

HVAC Subcontractor: Daldrop + Dr.Ing.Huber GmbH + Co. KG

Automation and Control Supplier: Actemium Controlmatic GmbH

Equipment Suppliers: Robert Bosch GmbH (filling lines/isolators) and HOF Sonderanlagenbau GmbH (lyos) (See ad on page 9)



Inside isolator IR safety.

plied with the integration of an additional module consisting of a vial filling line in isolator technology, two additional smaller lyophilizers, and the required supportive equipment. This next module is called "Aseptic Area 6" and is scheduled "ready for production" in Quarter 3 2016.

Conclusion

The culmination of many innovations led to the selection of Boehringer Ingelheim's Aseptic Area 5 and Combi Line for the winner of the equipment innovation award. Optimal transparency as a central theme was evident by the innovative use of glass cleanroom walls, air returns, and technical space which allowed easy observation, convenient communication between operators, and efficient use of exterior daylight. This is an example of a project team challenging the standard and making imaginative and effective use of innovation as a way to improve the way facilities are operated. 



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F. Hoffmann-La Roche Ltd.

Positive Energy Balance in Sustainability

Introduction

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalized healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the World Health Organization (WHO) Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials, and chemotherapy.

Roche's new **B250-Q2K** laboratory facility in Kaiseraugst, Switzerland was forethought to further develop the Basel site and consolidate the analytical work on pharmaceutical production. Building 250 (B250), the new analytical laboratory, houses Quality Control (QC) and Quality Assurance (QA) staff



Aerial view.

who are responsible for carrying out all QA activities related to drugs manufactured or packed in Basel/Kaiseraugst as well as CMOs.

From its inception B250, the Roche Analytical Laboratory, was conceived with a focus on sustainability. The overall facility design followed the Roche Corporate Architectural guidelines ensuring a focus on facility lifecycle and "timeless elegance." The adopted building concepts guaranteed maximum flexibility allowing for fast and simple adaptations to meet future requirements. The result of the team's efforts is an exceptional 130,000 square foot facility that exceeds Switzerland's strict legal energy efficiency requirements by 40%. Applying novel designs and innovative process methods earned F. Hoffmann-La Roche Ltd.'s Kaiseraugst project the **ISPE 2014 Facility of the Year Award for Sustainability**.

Project Overview

Building 250 is a modern and inspired solution to Basel's QC and QA operations from several older laboratory buildings. By

F. Hoffmann-La Roche Ltd.

Category Winner – Sustainability


Project: B250 – Q2K (Quality to Kaiseraugst)

Location: Kaiseraugst, Switzerland

Project Mission: build a new laboratory building for quality assurance and quality control.

Size: 13,000 sq. m. (139,931 sq. ft.)

Duration of Construction: 20 months

A man with dark hair and glasses, wearing a white button-down shirt, stands in a pharmaceutical factory. He is leaning against a piece of machinery. The background shows a clean, industrial environment with stainless steel equipment and bright lighting.

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Open ceiling infrastructure in standard lab.

developing lean work processes into the layout, Roche modified influenceable workflows to reduce cycle time by up to 50%. The newly designed open plan laboratories in combination with the “flow line” maximized flexibility, facilitated efficiency, and promoted communication during the entire product quality analysis process.

Laboratories for QC and office spaces for QA are located in the new Q2K building and concentrate on the following functions:

- Analysis for incoming materials such as packaging materials
- Support, monitoring, and troubleshooting for manufacturing

- and packaging processes such as cleaning validation analytics, environmental monitoring, and special analytics
- Release and stability testing of drug products from the Kaiseraugst and Basel site, and manufactured by CMOs.
- Release and stability testing of drug substances from Basel Biotech production

For Roche, creating an identity for QC and QA in their new location was a top priority. Essential user support and enthusiastic acceptance enabled users to adapt quickly to new lean workflows. This display of employee esteem also contributes awareness to building care and equipment up-keep. Outstanding color concepts and ergonomically designed furniture were additional high standards for office and laboratory areas. Airy staircases enhanced by art and attractive social zones invited comfortable functionality.

Project Spirit

Roche Project Management invested in the facility’s success by fostering open, vertical relationships with internal and external staff, as well as financial stakeholders. Leadership teams modernized the traditional hierarchy system by generating equality and recognizing the expertise of all team members. Ideas, perspectives, and the general pool of knowledge proactively mitigated manpower risks and potential delays. The high value of trust and clarity allowed an exceptionally transparent resource management strategy and highly organized processes and facilitation patterns.

Why Our Project Should Win

The following is an excerpt from Roche’s submission, stating in their own words, the top reasons why their project should win the ISPE 2014 Facility of the Year Award:

Stellar Project Execution

- Total inclusion and interaction across nationalities, gender and hierarchies resulted in a huge knowledge pool, the project team was highly engaged and felt a deep emotional attachment to the project.
- Exemplary pursuance and expansion of the established project execution processes, achieved outstanding results regarding quality, time and cost.
- Advanced employment of controlling tools and intricately detailed mock-ups ensured high standard execution.
- Consequent 3D-modelling for all trades generated an understanding of modular technical equipment between the contractors.

Pioneering Facility Integration

- Exploitation of the synergy potential was surpassed.
- Active creation of identity.

- Integrative involvement of users and fulfilment of their needs and requirements in a futuristic way.
- Added values via aesthetic design features create an emotional connection between employees and their building.

Passionate Sustainability

- Sustainable practices keenly executed in all areas, even if small and seemingly insignificant.
- Overall energy concept fervently embraced and adhered to.
- Intelligent combination of work within given parameters produced a total greater than the sum of its parts.
- Energy efficiency of stipulated legal and corporate standards increased by 100%.

World Class Operational Excellence

- Transcended the initial workflow analysis model.
- Spearheaded implementation of the custom made lean management process.
- Consequent and futuristic translation from process into space through the modular building concept.
- Repetitive questioning and reviews achieved the optimal user group allocation throughout the building.

Efficiency beyond Legislation

The overall building design follows the Roche Corporate Architecture guidelines, which guarantees timeless elegance. Sustainability awareness was prioritized throughout development. High quality materials were conscientiously chosen for aesthetic value and energy balance enhancing maintenance and cost savings throughout the facility's lifecycle.

Innovative Infrastructure

The building concept of B250 supports maximal flexibility and modularity allowing for practical and unobtrusive adaptations. The static framework system and parapets maximize floor space and clear the zone of interfering ceiling supports. Thinking outside the availability of open market offerings, Roche B250-Q2K team adapted existing options to design open ceilings in lab areas. This innovative modification allowed more accessible and operable infrastructure zones. Roche's open ceiling infrastructure provided innovative and integrated support for:

- Electrical conduits and rails
- Air supply
- Gas distribution and connection points
- Suspended open racks and media columns
- Light fittings
- Cooling panels

Maximizing Light and Reducing Energy

A novel combination of glass elements and blinds was developed to project maximum daylight inside the room. These

ridged, but delicate lamellas can only be used when protected from weather conditions. Their structure also provides an anti-glare solution while allowing natural light deep inside the room and views of the exterior even when closed. Roche's Q2K project team implemented Close Cavity Façade (CCF) to protect the lamellas which is composed of a triple glass thermal isolation layer on the inside and a simple glass pane on the outside of the element. The cavity is constantly supplied by compressed air to prevent diffusion and condensation.

“B250 – Q2K is an example of what can be achieved when one combines a commitment to sustainability with an innovative project team.

– FOYA Judges

From the project's onset, Roche's B250-Q2K team aspired to go beyond current environmental legislation with an energy concept based on legal stipulations and user requirements. Parameter calculations were defined by simulations using state-of-the-art technology and enhanced synergy design. Combining multiple energy-saving measures, energy consumption was reduced by an additional 40% when compared to other buildings in accordance with legal requirements. B250-Q2K's energy saving measures included:



Close Cavity Façade (CCF) is composed of a triple glass thermal isolation layer on the inside and a simple glass pane on the outside.

- Heat recovery from neighboring existing data center
- Rooftop solar panels for warm water production
- A water conservation green roof which hosts an environmentally friendly habitat for insects

Energy Efficient Air Exchange

Air exchange in the B250 facility underwent a radical design innovation reducing operating air change rate to 50% of the design rate for normal operation to approximately four times per hour. Zones requiring a lower air rate exchange were separated from lab areas. The air volume was then regulated to an 'on demand' program rather than scheduled, automatic provisions. This employs a two-step reaction including cooling panels which further reduces energy needs.

Roche's method to adapt air exchange to real need for efficient rate reduction:

Approaches:

- Extensive analysis of both external and internal heat load
- Detection of overall energy consumption, "point of use" tracking

Solutions:

- Reduce rate of air change by 50% during the day and 75% at night
- Increase air change rate locally only during high heat generation or when fume hoods are in operation
- Adapt duct pressure and air temperature supply

To ensure the designed energy consumption target was met, monitoring technology for energy consumption was implemented from the onset. After completion Roche had monitored the building consumption over a 12 month period and compared measured values with model based values. This helped to ensure no energy was wasted by wrongly set controllers.

Conclusion

In a world of "good enough," Roche's Q2K facility found uniqueness and exceptional success through vertical planning and the inspiration of a project team committed to going over and beyond current legislative requirements. By generating a cooperative culture where all perspectives held value, Roche empowered the development of a facility full of innovative designs and energy efficient processes. Compelled to create an emotional connection for their employees, Q2K's project team


Key Project Participants

Designer/Architect: Nissen Wentzlaff Architekten BSA SIA AG
Construction Manager/General Contractor: Itten+Brechbühl AG
Piping Subcontractors: Alltech AG, Baier AG, Cofely AG
HVAC Subcontractor: Cofely AG
Automation and Control Supplier: Siemens Schweiz AG
Laboratory furnituresuppliers: Waldner GmbH



Solar panels on the green roof.

added aesthetic, yet efficient features to create user identification at the new location. The overlap in planning and execution phases reduced Roche's construction to a 20 month duration. Residential challenges were overcome by constant and proactive communication with area stakeholders and authorities leading to a reduction of regular permit periods.

Roche's dedication to environmental protection is reflected in the group's policies. These standards were consistently applied to the B250-Q2K project. The development of B250 as an energy efficient facility was a priority from concept development. Regular energy reviews were carried out ensuring in-house standards were met or exceeded. By skillful combinations of energy-saving measures, energy consumption was heavily reduced. Requiring only a quarter of the energy of other buildings of similar size, Q2K is a primary example of low-energy construction. B250-Q2K's project team invested an immense effort to ensure the positive hidden energy balance of materials throughout construction of the facility. Consistent quality, innovation, and proactive streamlining are evident throughout Q2K. Roche's project team was fervent to go beyond current environmental requirements and developed a concept that established optimal and state-of-the-art sustainable synergies. 



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Taking Bioscience Into the 21st Century

Introduction

Grifols, the third largest producer of plasma derived medicines, found inspiration by developing innovative healthcare services and products while maintaining the highest quality and safety ethical standards for patients around the world.

Grifols employs a workforce of 13,200, each committed to serving patients affected by life-threatening conditions, such as chronic obstructive pulmonary disease, hemophilia, and genetic emphysema.

In 2009, the Clayton site was owned and operated by Talecris Biotherapeutics. Their senior management developed a plan for Grifols to construct a next generation fractionation facility. Even though Grifols acquired Talecris Biotherapeutics toward the end of construction, the project team never slowed the momentum.

Grifols' North Fractionation Facility (NFF) is located in Clayton, North Carolina, US and leads the industry with the most advanced technology for plasma fractionation. The NFF facility operates with closed, fully automated manufacturing, delivering products in a safe, quality conscious, and efficient manner. For this project, Grifols also developed a completely new disk stack centrifuge and an innovative automated bottle opener. With the team's in-depth knowledge the facility was



Exterior view of south and east side of NFF.

built on schedule and with a quality level that facilitated a smooth commissioning and start-up phase resulting in the selection of NFF for the **ISPE 2014 Facility of the Year Award for Project Execution**.

Innovation in Plasma Fractionation

Fractionation is the starting process developed more than 75 years ago for separating proteins from human plasma. Fractionation begins with thousands of tested individual 800 ml human blood plasma donations combined into a common pool. This pool is divided into various components via successive precipitation and separation steps. The solid phases are referred to as "pastes" and are enriched with key proteins (Factor VIII, IgG, Albumin, etc.). These pastes are further purified in typical downstreams, which are used in classic bioscience processes using chromatography, ultra filtration, and nano filtration steps. Plasma fractionation has most commonly been conducted in a Grade C/D cold room environment, without natural light, creating a challenging environment for any maintenance of equipment or manufacturing operations. From the project's beginning, Grifols set out to modernize and overcome this challenge by maximizing the application of closed process systems,

Grifols Therapeutics Inc.

Category Winner – Project Execution

Project: Grifols North Fractionation Facility (NFF)

Location: Clayton, North Carolina, US

Project Mission: to provide Grifols' patients with a safe and reliable supply of life saving therapies.

Size: 13,935 sq. m. (150,000 sq. ft.)

Duration of Construction: 24 months



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This facility represents the leading edge of improved quality assurance and has raised the bar for the fractionation industry. Starting with the design and flow through validation, an integrated information management plan was used to guarantee data quality. Below are some of the significant contributions used by the Grifols team in achieving this new industry standard.

Process Technology Advances

NFF applied modern design techniques to set a ground-breaking 21st century standard in achieving a reproducible, automated, and efficient fractionation.

- Minimized residence time for thawed plasma to increase cryoprecipitate yield
- Used highly automated process controls to minimize errors and to allow sub-freezing processes to be operated within an ambient environment
- Maximized equipment utilization to decrease the overall capital investment
- Minimized open product handling to reduce cleanroom requirements and associated costs
- Increased throughput and efficiencies by developing adequate process conditions for the world's largest batch size (up to 9,000 L of plasma)
- Provided enhanced bioburden control through application of SIP throughout the production train

Equipment Technology Advances

Grifols invented, developed, and applied state of the art bioscience equipment design to established industry standards enhancing process repeatability, control, and throughput.

- Implemented closed processing systems throughout the entire facility to minimize human interactions
- Invented and constructed a novel plasma bottle opening, pooling, and thawing train replacing manual batch-thawing
- Developed a semi-continuous thawing system decreasing residence time and improving heat transfer capability
- Developed a disc-stack centrifuge fulfilling the unique requirements of plasma fractionation



Completely closed processing allows the 12,000 L processing reactors to be placed in the unclassified technical core.

- Designed the centrifuge (split-machine) to minimize cleanroom space and provide easy maintenance access from the technical area
- Customized use of linear actuators to open and close the paste collection units to enhancing process ergonomics and operator safety

Advances in Facility Technology Design

Grifols' NFF project team delivered an efficacious layout for process, personnel, material, and waste flows creating an optimal environment for operators.



Automated bottle opener - robotics prevent human interaction and potential contamination.

- Minimized cleanroom requirements through the use of closed processing and by employing a rigid empty cleanroom policy
- Eliminated traditional cold room environments through process technology and control
- Contained all primary manufacturing functions on a single operating level while vertically integrating the logistics flow for raw materials and products
- Designed second floor process areas allowing for easy installation of super skids
- Optimized use of glass to enhance operational communication and provide viewing corridors for patients and visitors

Project Culture

Grifols' project began by staffing its project team with full time, cross-functional professionals to support an integrated design organization with productive communication. Driven by the goal to build an environment of respect, trust, and consistency, a rigorous contractor evaluation process selected the highest prerequisite experience in design and construction. The members of the NFF project steering team continued for the life of the project. The "one" team included expert representatives from Engineering, Procurement, Construction Management, and Validation or EPCM(V), who participated in steering meetings each month with Clayton site management. User

“The project culture we sought to achieve was greatly facilitated by the use of the selected partner where the parties could build a level of common understanding of the articulated project goals and develop a solid relationship of trust.

– Grifols

requirements and design solutions were consistently reviewed by a steering committee providing necessary and time-relevant ratifications. Having a single team from concept to completion promoted a single point of accountability, continuity of intent, and elimination of redundant functions. The key attribute to this successful collaboration was the acceptance of "one" team where each team member's value was recognized and respected. In order to assure all steering committee interests were incorporated from conceptual design, the team including Grifols engineering and architect partners (Fluor) spent the

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first several months at the Clayton site. This approach allowed all functional groups to actively participate in the various areas of conceptual development.

Grifols' project quickly moved into detailed engineering/procurement as the design was sequenced between construction schedule and IFC documentation. Firm decisions made in basic design and close collaboration with procurement and engineering enabled the project to purchase major equipment early enough to support detailed design. Engineers worked closely with key expert vendors to customize equipment elements and make purchases that assured quality and qualification data collection.

A successful, achievable budget was established during the preliminary engineering phase. Early infusion of constructabil-

ity in the design allowed enhancements including a permanent load-in platform, installation of a bridge crane, and early planning for large modules. As a result of the aggressive project timeline and plasma fractionation's multiple repetitive unit operations conceptual designers chose modular construction techniques. A key to NFF's achievable budget was constructing major equipment modules on-site allowing assembly to run concurrent to building construction. As architectural finishes were completed, modules were immediately inspected and directly installed by available equipment. Post-project construction, the fabrication facility now acts as a general site warehouse. Careful planning in concept design and implementation of the modular approach resulted in strengthened qual-

Why Our Project Should Win

The following is an excerpt from Grifols' submission, stating in their own words, the top reasons why their project should win the ISPE 2014 Facility of the Year Award:

1. Reduced Risk to Product Quality

- Validated a closed process to eliminate contamination risk and reduce the cleanroom space
- Collaborated with Grifols Engineering to develop a robotic bottle opening system to eliminate potential plasma contact with operators
- Employed automation systems reducing human error and increase process repeatability

2. Manufacturing Efficiency

- Effected a 100% increase in site output to 6MML
- Lowered labor per liter fractionated by 40%
- Increased process yield between 8 and 15% across fractions produced by leveraging Grifols advanced understanding of processing human plasma
- Achieved a 31% reduction in energy per liter with closed process in ambient space
- Reduced chemical costs by \$1 million annually by employing bulk chemical storage and distribution

3. Implementation of Innovative Equipment and Technology

- Built a fully automated processing train reducing cycle times, improve yield, and minimize human intervention
- Developed in-house process utilizing horizontal thaw vessels, ABO, and precipitation reactors
- Collaborated with GEA Westfalia to develop the industry's first disc-stack centrifuge for fractionation, featuring closed processing, CIP systems operating in ambient conditions
- Designed automation of paste collection vessels to enhance ergonomics and operator safety, reducing cycle time and located drives in technical space
- Achieved a 90% reduction in medical waste generation per liter fractionated

4. Facility Integration

- Produced a modern, sustainable facility that eliminate harsh cold work environments, while achieving excellent functional arrangements resulting in a minimization of material movement
- Contained manufacturing operations on a single level
- Minimized cleanroom footprint to 12% of gross space
- Directing vertical transfer between levels produced simplified horizontal flow paths
- Applied broad use of windows and natural light while eliminating cold rooms

5. Project Execution Approach to Accommodate Innovation and Meet Project Goals

- Overcame change of ownership mid construction due to Grifols commitment to excellence
- Fully integrated, co-located project team consisting of both owner and EPCM(V) contractor staff allowed for the concurrent design and construction schedule to work
- Used onsite fabrication shop and super skid approach saving four months and 15% of cost
- Assembled pilot centrifuge installation to develop and debug software
- Employed international design office (Poland) to lower design costs
- Designed facility and coordinated construction sequences with comprehensive 3-D model
- Leveraged RV/IV commissioning data for use in final qualification package
- Leveraged supply of unusable plasma to complete 10 pre-qualification ETP runs to completely debug the facility prior to validation
- Created MIV partnership for a vertically integrated controls solution
- Developed operations and maintenance staffing and procedures in parallel with design



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ity assurance, enhanced safety, and a reduction of the overall project schedule and cost.

Conclusion


The commitment of the Grifols 'project team contributed to the success of NFF. Seamless preplanning and post project execution resulted in achieving expectations in all initial goals, including standards in quality, operability, and maintainability. The project met cost targets and schedule timeframes estab-

Key Project Participants

Owner Representative: Grifols Therapeutics Engineering
Designer/Architect/Engineer: EFDEE (Fluor Corporation)
Construction Manager/General Contractor: Fluor Corporation, Inc.
Piping Subcontractors: Intermech, Inc. and JJ Kirlin
HVAC Subcontractor: Gamewell Mechanical, Inc.
I & E Subcontractors: Omni Instrumentation Services, Inc. and Cooper Electrical
Automation and Control Suppliers: Emerson Process Management (*See ad on page 21*) and R.E. Mason Company
Major Equipment Suppliers/Contractors: Grifols Engineering, S.A. and GEA Westfalia
Super Skid Fabricator: UltraPure Systems, Inc.



Centrifuge suite with two paste collection vessels containing the centrifuge bowls.

lished at preliminary engineering in November 2009. Team collaborations guided by a cross functional steering committee was a key factor to NFF's success. Grifols' choice to execute with a systematic approach of option development, evaluation, review, and selection provided the necessary framework to satisfy all project objectives and build a highly innovative, new plasma fractionation facility. 

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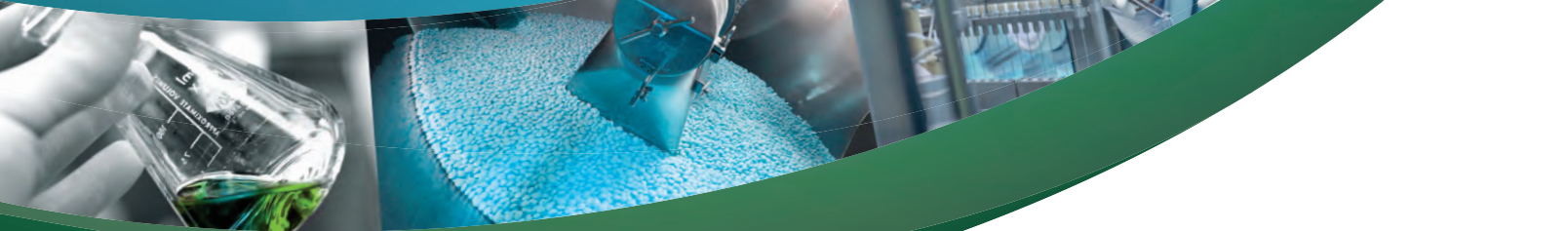
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Patheon Pharma Services Mammalian Cell Culture's Plant of the Future

Introduction

Patheon Pharma Services, formerly DSM Biologics (DSMB) is an outsourcing manufacturing partner with nine sites in Europe, the US, and Australia. Patheon's **Biologics Plant of the Future (BPOF)**, the new Brisbane, Australian facility was cooperatively built through a partnership with Biopharmaceuticals Australia, the government of Queensland, and the Commonwealth of Australia. DSMB, now Patheon Pharma, was selected as the international contract manufacturing organization partner to design and operate the Brisbane facility to emphasize the incorporation and integration of a new generation of flexible and single-use bioprocessing technologies in a facility optimized for multi-product manufacturing operations.

The BPOF is a single purpose-designed building: it has six functional levels in total with two, eight meter high processing floors. One processing floor is as yet unfitted and provides expansion space to double facility capacity. The facility is an integral part Queensland's Translational Research Institute (TRI) which co-locates the site with four leading research institutes. TRI, including the BPOF, is located on campus at Princess Alexandra Hospital (PAH), Queensland's second largest hospital, in

Patheon Pharma Services

Category Winner – Process Innovation

Project: DSM Biologics Plant of the Future (BPOF)

Location: Brisbane, Queensland, Australia

Project Mission: design and construct a world-class, cGMP scale-up biopharmaceuticals manufacturing facility.

Size: 5,000 sq. m (54,000 sq. ft.)

Duration of Construction: 36 months



Front view of Patheon's BPOF.

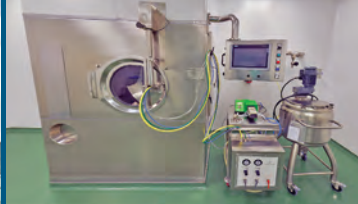
Woolloongabba, Brisbane. Through the presence of BPOF, TRI is one of only a few places in the world where new biopharmaceuticals and treatments can be discovered, produced, clinically tested, and manufactured in one location.

Patheon's Biologics Plant of the Future will increase mam-

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Viewing corridor looking down into the multi-product cell culture suite.

malian cell culture capabilities in all stages from preclinical through to Phase III and commercial manufacturing. This state-of-the-art and purpose-built cGMP manufacturing plant

will produce mammalian-based biologics (such as APIs) for preclinical and clinical trials, as well as for market. The facility is unparalleled for size and scope in Australia and was officially opened in October 2013. The facility was inspected by Australia's regulatory body, the Therapeutic Goods Administration (TGA), and awarded a manufacturing license in January 2014.

The Brisbane facility is Patheon's biopharmaceuticals production's blueprint for a "biologics plant of the future." Using industry-standard and their own innovative proprietary technologies for the optimization of therapeutic biopharmaceutical manufacturing earned Brisbane's BPOF facility the **ISPE 2014 Facility of the Year award for Process Innovation.**

Construction Methodology

The BPOF building is a concrete framed, six story, metal clad

Why Our Project Should Win

The following is an excerpt from Patheon's submission, stating in their own words, the top reasons why their project should win the ISPE 2014 Facility of the Year Award:

Process Innovation

In Patheon's Biologics Plant of the Future (BPOF), highly innovative bioprocesses are provided at commercial scale for the first time. By increasing titer and reducing the number of unit operations, these innovations can significantly increase the manufacturing efficiency and reduce the cost of goods by as much as 70% for important new therapeutics such as monoclonal antibodies. Our BPOF project has benefitted from the advantages in process intensification provided by these innovations to reduce the manufacturing footprint and provide a highly cost-effective manufacturing environment.

Equipment Innovation

To be an effective CMO, the equipment design for the BPOF has had to satisfy a wide range of manufacturing process variants and scales and not be customized only to Patheon proprietary operations. A set of highly flexible manufacturing equipment has been developed to support manufacturing scales that vary by more than 10 fold and accommodate all conventional processing routes. The BPOF equipment has been designed in accordance with Quality by Design (QbD) principles to allow a direct transfer from Patheon's smaller-scale facility in Europe. The offerings of multiple vendors have been integrated to provide fit-for-purpose unit operations.

Design Innovation

Our facility design has successfully reduced the size of process cleanrooms and avoided the congestion that can arise when process equipment is surrounded by a multitude of mobile vessels. The layout has managed the extensive use of single-use technology by focusing on equipment mobility and minimizing the distances that equipment must travel during operations.

Operational Excellence

The Brisbane BPOF project has integrated the technological developments of recent years to provide an optimized biopharmaceutical contract manufacturing facility. Intensified and simplified processes lower the costs of manufacturing. Equipment and facility design increase facility effectiveness.

Project Execution

Our project faced a number of unusual challenges, particularly:

- The large number of stakeholders, including a combination of governments and private interests
- Our facility is part of a research precinct within a public hospital
- The absence within Australia of experience in the design or construction of mammalian cell biopharmaceutical facilities
- A project team working in three entirely separate time zones

We used a flexible and adaptive execution approach to overcome these challenges, but with rigorous application of project management disciplines, such as project roadmaps, delivery to due dates, pass-gate reviews and endless communication.

structure with six functional levels. The facility sits atop a ground level, parking garage which is shared with the adjacent TRI building. It has two, eight meter high processing floors allowing for substantial interstitial service space. The facility shares goods loading facilities and certain base-building utility infrastructure with TRI, but is otherwise a standalone facility.

A fully functional design provided the following specific features:

- Fully trafficable ceilings
- Heat recovery
- WFI generation via multi-effect distillation columns
- State of the art building and environmental management systems
- Minimized waste treatment through chemical treatment prior to discharge

The facility construction methodology opted for a stick build approach, largely due to the complexity of services required for each room and an inclusion of an external elevated viewing area. This window into the production suites provides the ability to showcase the facility without gowning and entering the manufacturing area.

“The implication of this technology [XD[®] and RHOBUST[®]] combination is far-reaching. It not only enables higher output from a smaller manufacturing facility footprint with reduced processing times, it also significantly reduces the cost of goods, and decreases the investment costs for a dedicated production facility.

– Patheon

Today's Technologies

Patheon's Biologics Plant of the Future (BPOF) was designed by an expert international team of biological scientists and bioengineers, and leveraging over 25 years of in-house mammalian cell culture processing experience. The facility incorporates technology, first in use at commercial scale, in both the upstream and downstream areas which is novel both in individual process areas and end-to-end biopharmaceutical production. These innovative uses in technology intensify and simplify mammalian



Chromatography system with inline dilution and buffer conditioning capacity.

cell processing and create an opportunity to provide customers outsourcing manufacturing at up to 70% lower cost of goods.

XD[®] Technology

Patheon's patented XD[®] technology works in a continuous media feeding mode with a filtration unit to retain both the cells and the recombinant protein in the bioreactor to generate industry-leading product titers. The constant nutrient supply and the removal of potentially toxic metabolites result in a more optimal environment for the cells to grow and to reach higher cell densities. In comparison to a standard fed-batch process, the XD[®] process regime allows straightforward implementation without extensive feed development. The XD[®] process is robust and scalable, while still maintaining consistent product quality. The XD[®] process



XD[®] bioreactor generating high cell density cell culture and product titer.

produces very high cell densities while still retaining high cell viability at the end of the batch, resulting in a very high volumetric productivity. At the end of the cell culture (approx. 14 days), the harvest (a single bioreactor volume) is processed as one batch. The technology has been used successfully with all the relevant mammalian production cell lines (CHO, hybridoma, myeloma and PER.C6[®] cell line) with 5 to 15 fold increases in recombinant protein titers being achieved. Within the BPOF facility, XD[®] technology has been scaled-up to 500 liter bioreactors; each 500 liter XD[®] unit being equivalent to 5,000 liters of capacity (average) when using conventional cell culture technology.

“*The combination of XD[®] technology upstream, RHOBUST[®] technology downstream, and the extensive implementation of single-use technology throughout the plant truly makes DSM Biologics facility an outstanding example of process innovation on a broad scale.*

– FOYA Judges

RHOBUST[®] Technology

The RHOBUST[®] technology is a second generation Expanded Bed Adsorption (EBA) technology that provides a sophisticated solution to multiple process steps by combining clarification and product capture into one single step in the first downstream process unit operation. The RHOBUST[®] technology utilizes a new generation of agarose beads that are prepared from a homogeneous mixture of agarose and tungsten carbide (10 vol%) and consequently have a high density (3 g/mL). This allows processing to occur at higher flow rates in the expanded bed mode when compared to the flow rates used for packed bed chromatography.

Due to the operation in the expanded bed mode, crude harvest can be directly loaded onto the column. Cells flow through the expanded bed, while product is captured directly from the

culture medium. Labor intensive procedures such as column packing and qualification under high pressure conditions are not required, resulting in less process time and clean room occupancy. The process is scalable from 1-2 cm diameter laboratory columns up to 10 cm diameter intermediate scale columns and finally to full-scale production columns. Standard ligand chemistries such as Protein A, ion exchange and mixed mode are available for the capture of monoclonal antibodies or other recombinant proteins. New functionalities can be developed for the capture of specific biopharmaceutical products.



Rhobust[®] Expanded bed absorption chromatography column displaying level control of the bed height.

Conclusion

Patheon's Biologics Plant of the Future found success through their extensive implementation of single use technology throughout all production areas on a highly flexible platform. Their patented XD[®] technology incorporates technology similar to perfusion, but operates at increased cell densities and high titers while retaining the product inside the bioreactor during perfusion. In addition, downstream RHOBUST[®] technology incorporates next generation expanded bed chromatography in a fresh configuration allowing full commercialization of this technology.

Although this technology has been theoretically familiar for more than 20 years, Patheon's proprietary use cross linked agarose beads on a tungsten carbide substrate allowing for high particle density evolving this technology from theory to commercial application. Their RHOBUST[®] technology greatly simplifies harvest and recovery steps by eliminating equipment and process steps in addition to both the product loss and QC/QA exposure involved in multiple step operations. BPOF sets an industry standard as this newly implemented technology may offer breakthrough improvements to biopharmaceutical production in multiple applications. In conclusion, the combination of XD[®] technology upstream, RHOBUST[®] technology downstream, and extensive implementation of single-use technology throughout the plant truly makes the BPOF facility an outstanding example of process innovation on a broad scale. **(E)**

Key Project Participants

Designer/Architect: Wilson Architects / Donovan Hill Associates

Engineers: M+W Process Industries GmbH (concept design) and Amec (schematic and detailed design/procurement, commissioning engineering)

Construction Manager/General Contractor: Watpac Construction Pty Ltd.

Piping Subcontractor: Triple-Nine Stainless

HVAC Subcontractor: AE Smith

Automation and Control Supplier: ZI-ARGUS / Siemens – Industrial Automation

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—Henry Yuan, Pharmaceutical Engineering Postgraduate, Tianjin University, China



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Penn Pharmaceutical Services Limited The Pillars of Lean Manufacturing

Introduction

Penn Pharmaceutical Services Ltd. is a long established pharmaceutical company providing integrated drug development, clinical trial supply, manufacturing, and packaging services to the international healthcare industry. Clients can choose Penn Pharma as a full development partner or choose core services as a stand-alone offering. The company operates from two sites in South Wales, UK employing nearly 300 highly skilled staff. The co-location of operational and project management teams provides clients with clear communication and rapid project decisions.

Penn Pharma launched **Project PennDragon** in 2012 in response to an increased demand for oral solid dose oncology outsourcing, building on Penn's history and heritage in processing potent molecules. The aim of the project was to create a new solid dose facility to house small and large scale equipment capable of manufacturing 1 kg to 120 kg batch sizes using full containment in-line with ISPE guidelines. The facility was to be integrated into the existing Penn site with a key aspect of the design being the ability to process multiple products at the same time. The facility design required the flexibility to support



Exterior of the new Contained Manufacturing Facility (CMF).

customers throughout development, clinical, and commercial supply of their products. The 15,100 sq ft (1,400 sq m) new facility expansion site consisted of part of an existing building and a staff car park. This required significant “enabling works” to ensure business continuity as the new facility was integrated into an existing operational area within its 12 month construction timeline.

The result is that Penn has successfully created a facility capable of clinical and commercial production of oral solid dose coated tablets and capsules delivering batch sizes from development scale of 1 kg to commercial scale of 120 kg. In the outsourcing space, there is no other solid dose facility with this level of engineered containment combined with automated in process cleaning systems. Penn Pharma's facility is a contained manufacturing operation utilizing leading edge engineering which enables “speed to market” delivery for clients, while continuing to ensure the highest level of cleaning, operator safety, and environmental controls. Leading the industry trend to target more niche medicines, the PennDragon Project is a role model for small and flexible facilities and is the recipient of the **ISPE 2014 Facility of the Year Award for Facility Integration.**

Scope and Design

Considerable effort was put into developing a comprehensive project scope to ensure that objectives were clear to all and

Penn Pharmaceutical Services Limited

Category Winner – Facility Integration

Project: Project Penndragon – Contained Manufacturing Facility

Location: Tredegar, Gwent, United Kingdom

Project Mission: to create a multiple use API solid dose facility capable of handling batch sizes up to 120 kg for molecules with OELs down to 0.01 microgram/m³.

Size: 1,400 sq. m. (15,100 sq. ft.)

Duration of Construction: 19 months



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Contained manufacturing with a difference



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achievable. A project management approach was implemented for scope, design, and implementation requiring a focused and strict project governance from the Project Steering Group (PSG). A detailed project plan was developed with assigned resources establishing a clear understanding of priorities and task accountability.

The scope of the project was to create a unique offering in the contract development and manufacturing space. Penn Pharma designed the facility to eliminate the need for Personal Protective Equipment (PPE) in routine operations. The forefront of the project was the entire small and large batch scale processes. These were fully contained, integrated trans-

fer processes and wash in place systems. By minimizing scope creep and keeping attention on the pre-established timing plan, progress was maintained throughout the course of the project. Direct access to the PSG allowed for rapid decision making to manage any change, risk or issue that arose thus preventing any serious impact on progress.

Design Objectives

Objectives for the new oral solid dose facility were based on the pillars of lean manufacturing: safety, quality, delivery, cost, and a strong focus on the company's workforce.

Why Our Project Should Win

The following is an excerpt from Penn Pharma's submission, stating in their own words, the top reasons why their project should win the ISPE 2014 Facility of the Year Award:

Application of Lean Six Sigma to equipment and facility innovation.

The overall conceptual design, using value stream mapping, design for manufacture and lean six sigma techniques ensured a smooth and efficient start-up of the plant's operation. Central to the whole philosophy was an innovative, engineered powder handling solution, where every aspect of the solid dose process is fully contained and held at a relative negative pressure, so there is no open processing at any stage of the operation. The creative deployment of automated and validated wash in place, wet in place and wash off line technologies was linked to a modern effluent treatment system. This ensures robust cleaning validation with repeatable processes which mitigate the risks associated with cross contamination in a multi-API facility. Finally, the design allows geometric scale up from 1 kg to 120 kg, with flexibility to switch between small and large scale process streams. Added to this is the option for customers to select disposable technologies to improve speed to market and reduce development and clinical costs.

Great teamwork.

The most outstanding aspect of this project that deserves recognition is the capability of the core project team from Penn. Their technical ability on facility design, chemical engineering, formulation development, validation, regulatory oversight and overall operational project management is exemplary. This small number of subject matter experts, with empowerment and teamwork, has demonstrated "best in class" delivery of a complex and demanding facility design and build.

Speed to market and project execution.

To take a car park and turn it into a facility capable of producing potent, coated tablets in less than 12 months is a phenomenal achievement in this industry sector. This required clarity of purpose, clear project goals and robust performance

management against key performance indicators. Every week the project team presented progress against a 6 point project report out tracker. This ensured that there was no "scope creep" and thus the overall project was delivered on time, to budget and to the required high specification.

Leadership in health, safety and environmental responsibility.

In a business that has an exceptional safety record, the whole facility design focused on engineering solutions, to eradicate the use of personal protective equipment in routine operations. Operator safety was central to the philosophy and design. In addition, the building was designed with BREEAM in mind. BREEAM is the world's foremost environmental assessment method and rating system for buildings and is used in more than 50 countries. This sets the standard for best practice in sustainable building design, construction and operation, and has become one of the most comprehensive and widely recognized measures of a building's environmental performance. It encourages designers, clients and others to think about low carbon and low impact design, minimizing the energy demands created by a building before considering energy efficiency and low carbon technologies. Finally, a new effluent management system was installed to ensure that any waste discharged was below the limits set by the local water authority, reinforcing Penn Pharma's ethical approach to protecting the local environment.

Stakeholder satisfaction-external client and internal staff.

As a contract manufacturing organization, Penn Pharma has to ensure that customers have trust in our ability to deliver. This is particularly pronounced in the case of potent drugs where lack of attention to detail can have serious consequences. The measure of how successful Penn Pharma has been in building a facility and organization that customers trust, has been the number and breadth of projects already won and the positive comments on design and safety received from customers, auditors and regulatory bodies alike. This demonstrates the level of confidence that Penn Pharma has created in the marketplace with this new investment. Customers have readily stated that they "love it" during project visits and audits.



Tablet film coater room.

Safety

The facility was designed to handle active compounds with Occupational Exposure Limits (OELs) down to $0.01 \mu\text{g}/\text{m}^3$ based on an 8 hour Time Weighted Average (TWA). The fundamental approach involved a negative pressure equipment design philosophy that would eliminate the need for Personal Protective Equipment (PPE) in routine operations.

Quality

The new contained manufacturing operation had to meet the regulatory needs of the global markets supported by the existing site including the USA, Japan, South America, and Europe. The facility equipment train designs incorporated the principles of Quality by Design (QbD) and an Failure-Modes-Effects-Analysis (FMEA) approach working closely with the Medicines and Healthcare Products Regulatory Agency (MHRA) from day one.

Delivery

The facility design needed to be flexible enough to support customers through development, clinical and commercial supply. The accelerated timescale had an expectation to deliver an operational facility in only 12 months from the start of construction.

Cost

PennDragon CMF was very much a “build it and they will come” approach, based on Penn’s analysis of the potent outsourcing market. A budget limit was set of £14m (approx. \$23 million) to include the cost of a new purpose built facility with dedicated utilities and the purchase of all solid dose equipment and inclusive of the design, construction, and project management fees. The Welsh Government assisted with financial support and linked capital funding to create new jobs in the pharmaceutical and life sciences industry sector in South Wales.

Nothing could be compromised on quality or safety, so with aggressive time lines, equipment sourcing was central to the success of the PennDragon project. A robust FMEA selection process and commercial bid analysis was undertaken to secure leading edge equipment, at a competitive market price.

People

With an initial core team of just six project members, supported by an external project design and construction contractor, the focus was on speed to market. The team had the full complement of formulation, quality, validation, engineering, regulatory and operational skills required to make the rapid decisions required to deliver success.

Equipment Best Practices

Project PennDragon combined the use of leading industry best practices. Equipment selection was based on geometric scale-up allowing clients to partner with Penn at an early stage and take their product from initial formulation development to commercial production, limiting scale-up risk and associated costs. The small, dedicated project team implemented a rigorous equipment selection process. This involved the use of a structured evaluation matrix shortlisting and selecting various individual equipment items required to construct a “world class” processing facility. The exercise was repeated for every key item of equipment, before taking the shortlisted suppliers into a final commercial bid process.

Design Best Practices

The design features of the facility and its utilities were chosen to comply with global industry standards and guidelines, including: WHO, ISPE, PIC/S, EMA, FDA, USP, and JP. The quality management system of the facility incorporates ICH



The through the wall PharmaConnect System.



Fully contained product transfer in large scale granulation.



Integrated utilities for tablet coaters.

Q8, Q9, and Q10 in its product design, technology transfer and quality processes ensuring a quality and continuous improvement mindset throughout the organization.

The facility cross-contamination risks are managed by:

- Ensuring each machine is operated at a relative negative pressure
- Using single pass air in the supplied HVAC systems with terminal, safe change, HEPA filters in place
- Ensuring that room pressures are negative, relative to the adjacent room or corridor
- Deploying airlocks in rooms identified as higher risk from the FMEA analysis
- Providing separate, dedicated utilities to the new unit
- Deploying wash in place, wet in place or wash of line systems for equipment, valves, IBCs integrated with disposable technology wherever possible
- Testing all equipment, prior to every production run, using pressure decay testing. All processes and transfers were

Key Project Participants

Designer/Architects: Mark Dean-Netscher, PPSL and Scitech Ltd.
(See ad on page 41)

Engineers: Rory Jones and David O'Connell, PPSL and Scitech Ltd.
(See ad on page 41)

Construction Managers: Chris Saunders, Cupperscales Engineering Services Ltd. on behalf of PPSL and Richard Godden, Scitech Ltd. (See ad on page 41)

Piping Subcontractor: Norstead

HVAC Subcontractor: Parker Environmental Services

Automation and Control Supplier: Schneider Electric Ltd.


Equipment Suppliers: GEA Pharma Systems and Robert Bosch GmbH

“Significant effort was put into the front end of the project to ensure that the facility design allowed a modular approach. This enabled multiple work packages to be implemented at the same time, thereby reducing the overall timescale to 10 months.

– FOYA Judges

validated following the ISPE guidance on SMEPAC testing, by an independent body (VEGA)

Conclusion

In September 2013, the Penn Contained Manufacturing Facility (CMF) was officially opened for business and instantly attracted clients from Europe, USA, and Japan. Penn Pharma is realizing its vision of becoming a preferred partner of choice for the supply of solid oral dose formulations containing potent molecules for both investigational and commercial use. The contained manufacturing facility was built with leading edge equipment using engineered containment enabling Penn to deliver “speed to market” for clients, but more importantly ensuring the highest levels of cleaning, environmental controls and above all else, operator safety. As the pharmaceutical industry is targeting more specialist niche medicines, smaller and more flexible facilities able to manage highly potent molecules are of critical importance. Penn offers a state-of-the-art facility, adhering to the latest industry guidelines delivering contained manufacturing with a difference. 

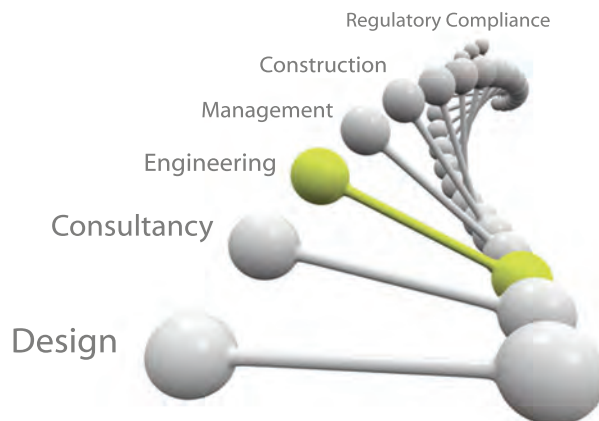


Scitech is proud to have partnered Penn Pharmaceuticals as it wins ISPE Facility of the Year 2014 for Facility Integration

Penn's new facility for the manufacture of oral solid dosage medicines with OELs down to $0.01\mu\text{g}/\text{m}^3$ designed and built by Scitech



Scitech is an employee owned, highly specialised and skilled business offering a full range of engineering, construction and professional services, specifically designed and packaged to suit the needs of the life science sectors. Whatever the requirement Scitech has the experience and the skill sets to be able to deliver. It's in our DNA



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Pfizer Ireland Pharmaceuticals Expanding a Vision of Empowerment and Operational Excellence

Introduction

Pfizer Ireland Pharmaceuticals' manufacturing plant is located on a 90-acre site at the Grange Castle Business Park in Clondalkin, South County Dublin. Grange Castle officially opened in 2005 with approximately 1,000 professionals focusing on biopharmaceuticals and vaccines. The Grange Castle collective site is one of Pfizer's many Biotech Operating Units implementing state-of-the-art technology, cutting edge thinking, and production expertise resulting in quality-driven products which improve the health of a global population.

Pfizer's **Network Strategy Implementation (NSI) Capacity Expansion** began with key challenges. Significant demolition of an existing vial filling and inspection facility, new construction, start-up, and integration activities were to take place without disruption of supply. To



Aerial view of Grange Castle.

Pfizer Ireland Pharmaceuticals Category Winner – Operational Excellence

Project: NSI Capacity Expansion

Location: Pfizer Ireland Pharmaceuticals, Dublin

Project Mission: increase manufacturing capacity for Prevenar® and Somavert®.

Size: Two suites with a total of 8,200 sq. m. (88,264 sq. ft.)

Duration of Construction: 21 months

succeed under such circumstances, Pfizer chose implementation under the direction of an integrated team, including members with operations, technical, and engineering backgrounds. Key to NSI Capacity Expansion's success was the early involvement of facility users in the project team which ensured all requirements were identified, as well as achieved.

An established team was designated early in design and remained in-situ for the full project lifecycle, including PV batch production. The commissioning and verification phases of the project were self-executed by Pfizer using their pre-existing team plus supplemental project resources. This phase used best practice approaches from previous Pfizer projects and fully integrated operations functions during execution.

NSI Capacity Expansion was delivered on target under an aggressive timeline from preliminary design to verification in 21 months with GMP batch production occurring at 26 months.

A proud partner



Novartis US Flu Cell Culture Facility | Holly Springs, NC

2014 FoYA Operational Excellence Category Winner

2014 PFIZER IRELAND PHARMACEUTICALS



2013 **NOVARTIS U.S. FLU CELL CULTURE FACILITY**
Holly Springs, NC

**NATIONAL INSTITUTE FOR BIOPROCESSING
RESEARCH AND TRAINING (NIBRT)**
Dublin, Ireland

2012 **CHIESI FARMACEUTICI RESEARCH AND
DEVELOPMENT CENTRE**
Parma, Italy

**CONFIDENTIAL CLIENT, VACCINE BULK
MANUFACTURING FACILITY**
Durham, NC

2011 *FoYA Honorable Mention for:*
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Lexington, MA

GENENTECH ECP1, E.COLI PRODUCTION FACILITY
Tuas, Singapore

**PFIZER BIOTECHNOLOGY IRELAND, MONOCLONAL
ANTIBODIES (mAbs) SMALL-SCALE FACILITY**
Cork, Ireland

2010 **MANKIND CORPORATION, TECHNOSPHERE
MANUFACTURING FACILITY**
Danbury, CT

**PFIZER IRELAND PHARMACEUTICALS, ASEPTIC
MANUFACTURING FACILITY**
Dun Laoghaire, Ireland

2006 **WYETH PHARMACEUTICALS, THE WYETH
BIOPHARMA CAMPUS AT GRANGE CASTLE**
Clondalkin, Ireland

We congratulate all of our clients on their award recognition over the years.

Compared to benchmark data from other global biotechnology projects, Pfizer's completion schedule exceeds the industry benchmark average by 30%. The upfront planning and early team engagement ensured reciprocal functionality in delivering support to all project milestones earning Pfizer's NSI Capacity Expansion the ISPE **2014 Facility of the Year Award for Operational Excellence**.

Project Overview

Project NSI Capacity Expansion encompassed an addition of two facility suites (Suite 2 and Suite 4) and involved 8,200 sq m of newly constructed manufacturing space. Suite 2 is located on the first floor of the manufacturing suite and designated for increased manufacturing of Prevenar 13v[®], a global vaccine for Pneumococcal disease. To support the additional capacity

requirement for Prevenar 13v[®], the Suite 2 design incorporated additional fallow space for future expansion. The process rooms were designed around "plug and play" operations with mobile vessels and movable processing skids. Each generic station within the suite is supported by transfer panels, utility panels and ceiling hubs enabling multiple process steps including: buffer preparation, lyophilization, activation, diafiltration, conjugation, chromatography, and bulk filling. The facility can support both aqueous and solvent based processing and includes equipment preparation, wash, and sanitization areas. Grange Castle's Suite 2 was designed to accommodate a 2x process scale-up as part of the transfer from existing facilities. Together with the existing vaccine conjugation capacity at Grange Castle, the completion of Suite 2 will enable Pfizer to supply 100 million dose equivalents of Prevenar 13v[®] each year.

Why Our Project Should Win

The following is an excerpt from Pfizer's submission, stating in their own words, the top reasons why their project should win the 2014 Facility of the Year Award:

Facility Integration

- The project successfully executed \$160 million of capital investment across the existing site. Capacity expansion of DS suites along with Warehouse and QC upgrades were required. The complex nature of this integrations lead to many unique challenges.
- Constructed two new manufacturing facilities by demolishing an existing vial filling which was "sandwiched" between two live commercial manufacturing areas (producing DS and DP material for Pfizer's top selling vaccine Prevenar13v. (Sales in 2013 were in the order of approx.. \$4 billion). All existing utilities and services had to be traced, disconnected, isolated and made safe without interruption the adjacent live commercial manufacturing suites.

Excellence in Project Execution

- This complex integration project was designed, built and qualified to a point where batch production could proceed in just over two years. This represents a 30% improvement against the average time for this scope, based on the industry benchmarks established for similar sized retrofit projects.
- The overall cost came in 3% under budget (excluding contingency).
- New and innovative approaches to project challenges such as delivering the operational readiness program. Our approach to set up the integrate project team allowed for rapid decision making which was key to keeping this fast-track project on schedule.

People /Team

- Knowledge and experience. Having a project team which is

experienced in all facets of project execution and operations is necessary so that the team has the abilities to recognize areas which are suitable for self-execution, versus areas where external expertise is required.

- Empowerment. The individuals and team are empowered to make decisions in support of project execution. The demands of modern project schedules make this a prerequisite to success.
- Integrated project team. A cross functional team with complementary skills that were committed to the fast track nature of this project. The team held themselves mutually accountable for delivering the project on time.

Operation Excellence

- Supported the development of a capable innovate, empowered and engaged operations technician team who were key decision makers during the design phase of the project and felt ownership for those key decision
- Standardized a highly complex and multifaceted biotech process through the implementation of standard work. Implementing 5S for design, ensuring flow and flexibility of people, process and product to enforcing Pfizer vision of "building for the future."

Safety and Quality

- NSI Project had an excellent safety performance with >1 million man-hours executed without an incident, with a recordable incident rate (TRIR) of 0.3. The safety program is best in class in Pfizer.
- The facility build quality is of a very high standard with <3% project re-work levels for mechanical and electrical with little to no end user modifications required at handover.
- NSI project team executed 33 Process Validation (PV) batches with a 100% success rate across 6 separate products, with a right first time metric of 85%.



Process flexibility – “plug and play”.

Suite 4, located on the ground floor of the MS building, was constructed to facilitate small to medium scale biotech manufacturing processes, including the acromegaly therapy Somavert®.

“The vision was clear to design, create, and implement a world class manufacturing environment through engaged, innovative, and proud colleagues which touch the product daily.

– Pfizer Ireland

To support the Somavert® process, the facility includes space and equipment for: buffer preparation, pegylation, chromatography, ultrafiltration and diafiltration, and bulk drug substance filling. Similar to the Suite 2 expansion for Prevenar 13v®, the facility also includes equipment preparation, wash, and sanitization facilities. At capacity, the facility will support global Somavert® demand while maintaining capacity for two other products of similar scale. An additional feature of the Suite 4 facility is its physical flows and HVAC design allowing operations as a stand-alone process or grouping with an adjacent clinical facility.

Empowering Operational Excellence

Implementing the Operational Excellence (OE) Program was integral to the development of NSI Capacity Expansion Project's strategy. Pfizer's initial vision included novel approaches

and the empowerment of colleagues to increase efficiency, drive innovation, and reduce costs.

Lean Management Systems

Pfizer's NSI project team created a Lean Management System (LMS) strategy to consolidate the tools and concepts required for a successful expansion. NSI Capacity Expansion was based on the following foundational elements in order to mitigate plausible risks and optimize productivity:

- **5S** was the preliminary method to initiate a design with efficient flow of people and product through the operational facilities. A 3D NSI Capacity Expansion model established the course and positioning of equipment, doors, windows, and storage areas. An innovative approach created by design technicians

called the “the cardboard phase” used cardboard cut-outs for all pieces of equipment, storage systems, vessels, buffer tanks, and other critical machinery. These stand-in pieces tested the accuracy of the conceptual flow and early 5S room plans. The final phase was creating the visual workplace which included creating specific places for the full operational kit in order to reduce motion waste.

- The most complex element of Pfizer's LMS was NSI Capacity Expansion's **standard work design** and implementation. Product complexity required 200 full maps directing processes and supporting activities.
- Pfizer's encouraged all NSI Capacity Expansion project team members to train on the 6-Sigma Toolkit. Many transactional Method 1 projects provided optimal solutions for plant systems using Voice of the Customer (VOC), Value Add/Non



Use of glazing to maximize natural light.

Value Add (VA/NVA) analysis, and Failure Modes and Effects Analysis (FMEA). Reactive M1s for investigation issues led to root cause identifications and early resolutions.

Innovative Operational Process Models

NSI's success was a result of an effectively developed operational model complete with prolific agility and flexibility. Instead of applying a traditional leadership hierarchy, Pfizer approached plant organization by establishing self-directed, high performance teams. Allowing team members authoritative independence empowered and motivated the workforce resulting in vested and high quality performance. Multi-disciplinary groups were also formed as **cell teams** which consisted of operations, QA, technical services, and engineering. These expert teams supported distinct and specialized elements of the production process through applicable proficiency and problem solving discussions. The NSI project team also undertook their own continuous progress by implementing a 360-degree feedback mechanism which worked toward improving individual performance and team dynamics.

NSI Capacity Expansion also exhibited project distinctiveness and manufacturing innovation with the following key decisions during concept design and project maturation:

- Disposable technologies were used throughout the facility to ensure optimization of clean utilities, minimize start-up time, lower capital cost, and enhance adaptation flexibility.
- Buffers, which could be completed in advance, were prepared in fixed SS vessels then hard-piped into process rooms or by disposable bags.
- Team members deployed Electronic Batch Records (EBRs) to support batch execution
- Process analytical technologies including: pirani gauges for lyophilization, hand-held NIR spectroscopy, and the Charles River Endosafe® endotoxin test system.
- Piloted project named Automatic Data Aggregation, Visualization, and Evaluation (ADAVE) was launched to create a



Technician interaction with Electronic Batch Records (EBRs) using Human Machine Interface (HMI).

future state informatics solution for all uni-variate process data. A fully automated data aggregation, monitoring and reporting solution was delivered.

“Besides planning and implementing this project, the project team had a high interest in making sure that these new manufacturing suites included not only the latest technologies (EBR, PAT and disposable bag), but also lean thinking.

– FOYA Judges

Conclusion

Pfizer's upfront early planning and early engagement of the core team members developed ownership and inspiration to complete a successful project. Not only did NSI Capacity Expansion prosper with operational excellence, project teams emphasized a “green approach” and held an excellent safety record with over one million hours worked. Both expansion suites are fully adaptable and cater a varied and expanding portfolio of Pfizer products and processes. The NSI Capacity Expansion project team built in modernized flexibility to facilitate further advances in technology and innovation, as well as continuous improvement in full facility manufacturing. Using these principles as drivers, Pfizer's expansion suites fulfilled their vision of building a biologics “plant of the future.”

Key Project Participants

Designer/Architect/Engineer: Jacobs Engineering Ireland (See ad on page 43)

Construction Manager/General Contractor: John Sisk & Son Ltd.

Piping/HVAC Subcontractor: HA O'Neill Ltd.

Automation and Control Supplier: Zenith Technologies Ltd.



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in what they do...



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WuXi AppTec Biopharmaceuticals Co., Ltd. The Forefront of Single Use Manufacturing in Biopharmaceuticals

Introduction

WuXi AppTec Biopharmaceuticals Co., Ltd. is a leading biopharmaceutical contract manufacturing organization with operations in China and the United States. WuXi AppTec Biopharmaceuticals Co., Ltd. was established as a first-class technology platform for pharmaceutical products in May 2010 and designed to meet US FDA, EMA, and China CFDA current GMP requirements. As a research-driven, customer focused company, WuXi AppTec provides domestic and international pharmaceutical companies with “one-stop-shop” services for monoclonal antibodies, vaccines, recombinant proteins, biological drugs, or other biological medicinal products. WuXi AppTec’s services are designed to assist its global partners in shortening



Exterior view.

WuXi AppTec Biopharmaceuticals Co., Ltd.

Honorable Mention – Equipment Innovation

Project: Fully Single Use mAB Production Facility

Location: Wuxi City, China

Project Mission: to be the first biologics manufacturing facility in China using 100% single use technology and meet cGMP standards of the US, EU and China.

Size: 8,000 sq. m. (86,111 sq. ft.)

Duration of Construction: 18 months

the cycle time and lowering the cost of drug products.

Construction on the new Fully Single mAB Production Facility began in October 2010 and is located in the Biopharmaceutical Research and Development Outsourcing Service Center in Marshan Area, Wuxi City, PR of China. Their recently completed flexible cGMP bulk cell culture production facility has been recognized for Process Innovation and is the recipient of an Honorable Mention award as part of the ISPE 2014 Facility of the Year Awards. This facility, consisting of two parallel upstream cell culture bioreactor lines with flexible working volumes of 50 L through 2,000 L bioreactors and one downstream purification production line is the most advanced facility built in the PR of China.

Strategy Milestones in Biopharmaceutical Manufacturing

WuXi’s Fully Single mAB Production Facility is a company milestone in providing a comprehensive, fully integrated service platform for its biopharmaceutical customers. Another key

milestone for WuXi was to incorporate production flexibility in order to comply with a variety of very high process design requirements for individual drug candidates. As a contract manufacturing organization in Asia, WuXi recognized the importance of an evolving response to a rapid and drastically changing manufacturing perspective in biopharmaceuticals. A new industry challenge is presented in the demand for high productivity at a manageable cost ratio. This is particularly true for China where enterprise purchasing power is limited compared to other global areas.

“ WuXi understands that single use technology requires not only rigid adherence to normal cGMP manufacturing practices, but an extensive control of vendor supplied material, all the way back to resin source. The plant itself is built to the highest Western world biopharmaceutical standards for cGMP commercial production.

– FOYA Judges

Saving capital investment and operational costs, shortening time to market, and matching the overall regulation of cGMP are the rationale and driving forces for the application of single use equipment and technologies. To increase productivity, WuXi improved titers to several g L⁻¹ reducing fermenter volumes (also the entire production chain) and allowed economic production in the range of 200 to 2000 L. The permanent decreasing bioreactor volumes is an advantage of new and highly innovative single use technologies used to reduce the complexity and cost of goods. This innovative method provides an opportunity for the entire biopharmaceutical industry to lower downtime, decrease cross contamination, and shorten validation time.

Maximum Levels of Efficiency

WuXi's new facility is one of the first global plants using nearly 100% single use materials while meeting the GMP standards, not only in China, but also in the United States

Why Our Project Should Win

The following is an excerpt from WuXi's submission, stating in their own words, the top reasons why their project should win the 2014 Facility of the Year Award:

- Nearly 100% single-use bio-equipment covered whole biopharmaceutical manufacturing processes from media/solution preparation, cell cultivation, purification to freeze and storage
- By far, the largest single use bioreactor scale used for monoclonal antibody drug products in Asia Pacific region
- Faster product/process change over and higher efficiency
- More flexible and convenient process design responding to any new project demands
- Higher level of safety and limit cross-contamination to a minimum level
- Reduce investment costs and labor cost

and Europe. Maximum flexibility of the new state-of-the-art disposable technologies along the process chain enables GMP production of biologic drug substance manufacturing from preclinical to clinical phases.

To reach a maximum level of efficiency and economic utilization, three upstream process lines at the scale of 500 L, 1000 L, and 2000 L fermenter volumes were linked to one downstream process line which operated individually at each production



Cell culture 50 L / 200 L / 1000 L bioreactor line.



Pre-virus purification line.

scale. The individual and specific composition of single use equipment along the downstream process enabled WuXi operations flexibility and opportunities for reactive manufacturing. All equipment in direct contact with products are single use, which greatly reduces the product change time and lowers the risk of cross-contamination between different production lots. Therefore, WuXi was able to create a revolutionary and trend setting production line and produce client products safely with consistent high quality.



Post-virus purification line.

Prepared to Serve

WuXi's Fully Single mAB Production Facility adaptations and progressions led to becoming a highly innovative, single use process, state-of-the-art CMO manufacturing plant exceedingly prepared to serve the Asian, as well as the international biopharmaceutical market. The entire process chain is comprised of:

- Highly innovative platforms
- Multiple flexible upstream and downstream technologies
- Single use bioreactors from flask to 2000 L scale
- Controlled freeze and thaw process allowing intermediate storage of drug substance

“This facility marks another milestone in WuXi's strategy to provide a comprehensive, fully integrated service platform for its biopharmaceutical customers.

– WuXi AppTec

The fact that the world of single use technology has become a reality is evident in WuXi's equipment installation which includes various multi-integrated systems. As a result of Fully Single mAB Production Facility, WuXi has shown how a production line can allow for rapid development and flexible reaction either on scale or with varied process design under cGMP guidelines while remaining economically competitive. WuXi has shown that individual process variations can be successful without the need for intensive time or cost commitment especially when setting up procedures and revalidation efforts. Single-use technologies are the most significant feature of WuXi AppTec's philosophy. Single-use systems do not need CIP/SIP or performance of an extensive cleaning validation for product or process change-over. This means no demand on the CIP/SIP systems or associated water and steam

honorable mention


WuXi AppTec Biopharmaceuticals Co., Ltd.



QC P&C laboratory.

requirements dramatically lowering utility and labor costs. The application of single-use technology also greatly shortens the equipment installation and commissioning time, reduces the investment cost, and enabled WuXi AppTec Biopharmaceuticals to finalize the equipment installation commissioning and to complete the start-up process in just less than four months.

Conclusion

WuXi's Fully Single mAB Production Facility is a flexible cGMP bulk cell culture production facility that was recognized for process innovation. This facility, consisting of two parallel upstream cell culture bioreactor lines with flexible working volumes of 50 L through 2,000 L bioreactors and one downstream purification production line is the most advanced such facility built in the PR of China. Facility processes focused use of single use technology from media/solution preparation through bioreactors to final purification. While such an approach has just recently been implemented in the Western world on a large plant scale, this end-to-end use of single use technology is an innovative step for any first time production facility. From design oversight by NNE, through project team operating under a "one team" culture, the design and construction details align with the most stringent expectations that any biopharmaceutical manufacturer would expect in regions with 20 years of experience in this industry. 

Key Project Participants

Designer/Architect: Sino Pharmengin Corporation
Engineer: NNE Pharmaplan (See ad on page 28)
Construction Manager: Chen Ze
Piping Subcontractor: Winatech Engineering
HVAC Subcontractor: Shanghai Songhua Air Purification Equipment Co., Ltd.
Automation and Control Supplier: Sartorius Stedim Systems GmbH (See ad on page 47)
Equipment Suppliers: Sartorius Stedim Systems GmbH (See ad on page 47) and GE Healthcare

Creating Fluid Solutions

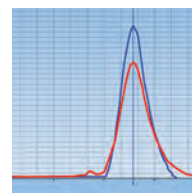
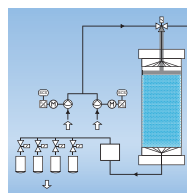
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FOYA – A Truly Global Awards Program

Over the past 10 years, ISPE has set out to recognize global leadership in pharmaceutical manufacturing. The annual Facility of the Year Awards (FOYA) program showcases cutting edge engineering, innovative technology, and the latest in operational excellence.

Submissions from around the world represent state-of-the-art projects that improve manufacturing and quality of drug products and medicinal therapies. By bringing together such a magnitude of experiences and ideas, a synergetic manufacturing culture is built upon the willingness to present and demonstrate

developments in an ever-changing industry.

The unique Facility of the Year Awards program showcases a true global representation of pharmaceutical advancements. The collective accomplishments in facility design, construction, and operation provide an unparalleled resource to the cutting-edge of an industry. FOYA recognizes the shared commitment and dedication of individuals worldwide to benefit the health of all global consumers.

Over the years, projects have been submitted from many different countries and companies have been named

Category Winners for innovation within specific areas of pharmaceutical manufacturing. FOYA truly brings together a world of knowledge promoting the collaborative culture necessary to assure continuous improvement and the upmost quality in medicinal products.

2013 Facility of the Year Category Awards Winners

- **Biogen Idec**, winner of the Facility of the Year Award for Facility Integration for its Flexible Volume Manufacturing Project in RTP, NC, USA

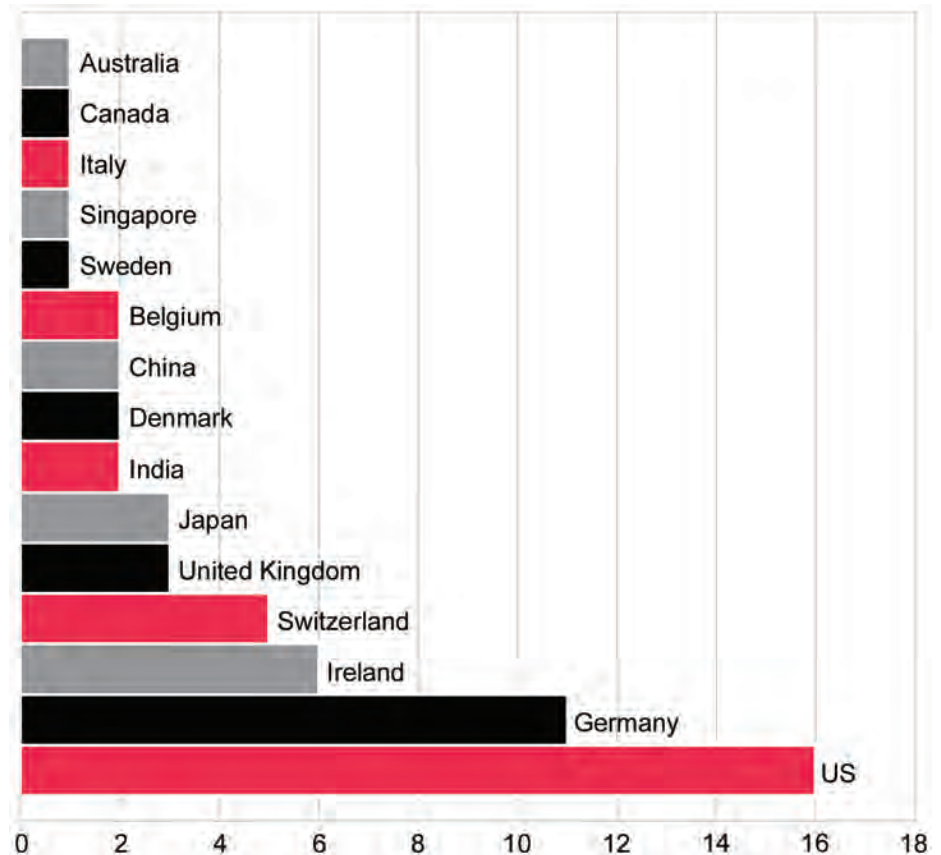
2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Canada (1)	Belgium (1)	Belgium (1)	Australia (2)	Belgium (1)	Canada (1)	China (2)	Belgium (1)	China (1)	Australia (1)
Denmark (2)	Germany (2)	Germany (2)	Germany (3)	France (2)	Costa Rica (1)	Germany (2)	Canada (1)	France (1)	Bulgaria (1)
Finland (1)	India (3)	India (3)	India (2)	Germany (1)	France (2)	India (1)	France (1)	Germany (3)	Canada (1)
Brazil (1)	Ireland (2)	Ireland (2)	Ireland (1)	India (3)	Ireland (3)	Japan (1)	Germany (2)	India (5)	China (2)
France (1)	Japan (3)	Japan (3)	Japan (2)	Ireland (3)	Italy (1)	Puerto Rico (1)	India (3)	Ireland (2)	France (1)
Japan (3)	UK (1)	UK (1)	Puerto Rico (1)	Italy (3)	Japan (1)	Serbia (1)	Ireland (2)	Italy (5)	Germany (1)
Mexico (1)	US (2)	US (2)	US (8)	Japan (2)	Malaysia (1)	South Korea (1)	Italy (3)	Singapore (1)	India (3)
Poland (1)				Netherlands (1)	Singapore (1)	Sweden (1)	Singapore (1)	Switzerland (2)	Ireland (1)
Puerto Rico (1)				Spain (1)	Sweden (1)	Switzerland (2)	US (6)	UK (1)	Japan (1)
Singapore (2)				Switzerland (2)	Switzerland (1)	Turkey (1)		US (10)	Puerto Rico (2)
Spain (1)				UK (2)	UK (2)	UK (2)			Saudi Arabia (1)
UK (2)				US (8)	US (6)	US (11)			South Korea (1)
US (11)									Switzerland (2)
									UK (2)
									US (7)

Number of submissions by country.

- **F. Hoffmann – La Roche Ltd.**, winner of the Facility of the Year Award for its TR&D – Building in Basel, Switzerland
- **MedImmune**, winner of the Facility of the Year Award for its UK Automation Upgrade Project in Speke, Liverpool, United Kingdom
- **Merck & Co., Ltd.**, winner of the Facility of the Year Award for its Vaccine and Biologics Sterile (VBSF) Project in County Carlow, Ireland
- **Morphotek, Inc.**, winner of the Facility of the Year Award for its Pilot Plant in Ambler, PA, USA
- **Novartis Vaccines and Diagnostics**, winner (**Overall Winner**) of the Facility of the Year Award for its U.S. Flu Cell Culture Facility in Holly Springs, NC, USA

2012 Facility of the Year Category Awards Winners

- **Chiesi Farmaceutici S.p.A.**, winner of the Facility of the Year Award for Sustainability for its Chiesi Farmaceutici Research and Development Centre facility in Parma, Italy
- **Eisai Pharmatechnology & Manufacturing Pvt. Ltd.**, winner of the Facility of the Year Award for Project Execution for its Eisai Knowledge Centre facility in Andhra Pradesh, India
- **Merck & Co., Inc.**, winner (**Overall Winner**) of the Facility of the Year Award for Facility Integration for its Merck Vaccine Bulk Manufacturing Facility (VBF) Program of Projects in Durham, North Carolina USA
- **Rentschler Biotechnologie GmbH**, winner of the Facility of the Year Award for Equipment Innovation for its REX III manufacturing facility in Laupheim, Germany
- **Roche Diagnostics GmbH**, winner of the Facility of the Year Award for Operational Excellence for its TP Expand project in Penzberg, Germany



Number of category winners by country.

- **National Institute for Bioprocessing Research and Training (NIBRT)**, winner of the Facility of the Year Award Special Recognition for Novel Collaboration for its New Greenfield facility in Dublin, Ireland

2011 Facility of the Year Category Awards Winners

- **F. Hoffmann – La Roche Ltd.**, winner of the Facility of the Year Award for Process Innovation for its “MyDose” Clinical Supply facility in Kaiseraugst, Switzerland
- **MedImmune, LLC**, winner (**Overall Winner**) of the Facility of the Year Award for Project Execution for its Frederick Manufacturing Center (FMC) Expansion facility in Frederick, Maryland, USA
- **Merck and Co., Inc.**, winner of the Facility of the Year Award for Facility

Integration for its Global Clinical Supplies Manufacturing, Packaging and Warehouse expansion project in Summit, New Jersey, USA

- **Novartis Vaccines and Diagnostics GmbH**, winner of the Facility of the Year Award for Equipment Innovation for its “MARS Project” (Marburg Site) facility in Marburg, Germany
- **Pfizer Health AB**, winner of the Facility of the Year Award for Operational Excellence for its Project Pegasus – Bio 7 Manufacturing facility in Strängnäs, Sweden
- **Pfizer Manufacturing Deutschland GmbH**, winner of the Facility of the Year Award for Sustainability for its SPRING & E-MAP (Strategic Plant Restructuring & Energy Master Plan) project in Freiburg, Germany
- **Shire HGT**, Facility of the Year

Award Honorable Mention for its Project Atlas, Building 400 facility in Lexington, Massachusetts, USA.

2010 Facility of the Year Category Awards Winners

- **Biogen Idec**, winner of the Facility of the Year Award for Operational Excellence for its facility in Research Triangle Park, North Carolina, USA
- **Genentech**, winner (**Overall Winner**) of the Facility of the Year Award for Project Execution for its facility in Tuas, Singapore
- **MannKind Corporation**, winner of the Facility of the Year Award for both Equipment Innovation and Process Innovation for its facility in Connecticut, USA
- **Pfizer Biotechnology Ireland**, winner of the Facility of the Year Award for Sustainability for its facility in County Cork, Ireland
- **Pfizer Ireland Pharmaceuticals**, winner of the Facility of the Year Award for Facility Integration for its facility in Dublin, Ireland

2009 Facility of the Year Category Awards Winners

- **Aseptic Technologies**, located in Gembloux, Belgium, winner of the Facility of the Year Award for Equipment Innovation
- **Centocor Biologics Ireland**, located in Ringaskiddy, Cork, Ireland, winner of the Facility of the Year Award for Sustainability
- **Centocor R&D Schaffhausen**, located in Schaffhausen, Switzerland, winner of the Facility of the Year Award for Facility Integration
- **hameln pharma**, located in Hameln, Germany, winner of the Facility of the Year Award for Operational Excellence
- **Orchid Chemicals & Pharmaceuticals**, located in Aurangabad, India, winner of the Facility of the Year Award for Regional Excellence
- **Roche Pharma Biotech Production Basel**, located in Basel, Swit-

zerland, winner (**Overall Winner**) of the Facility of the Year Award for Project Execution

2008 Facility of the Year Category Awards Winners

- **Boehringer Ingelheim Pharma GmbH & Co. KG**, located in Biberach, Germany, winner of the Facility of the Year Award for Facility Integration
- **Bristol-Myers Squibb**, located in New Brunswick, New Jersey, USA, winner of the Facility of the Year Award for Equipment Innovation
- **IDT Biologika GmbH**, located in Dessau-Rosslau, Germany, winner of the Facility of the Year Award for Operational Excellence
- **Pfizer Manufacturing Deutschland GmbH**, located in Illertissen, Germany, winner (**Overall Winner**) of the Facility of the Year Award for Process Innovation
- **F. Hoffmann La Roche AG**, located in Basel, Switzerland, winner of the Facility of the Year Award for Project Execution

2007 Facility of the Year Category Awards Winners

- **Cook Pharmica, LLC**, located in Bloomington, Indiana, USA, selected as winner of the Facility of the Year Award for Facility Integration
- **Genentech**, located in Oceanside, California, USA, selected as winner (**Overall Winner**) of the Facility of the Year Award for Project Execution
- **Shanghai Roche Pharmaceuticals, Limited**, located in Shanghai, China, selected as winner of the Facility of the Year Award for Project Execution Regional Excellence
- **Taiyo Pharmaceutical Industry Co., Ltd.**, located in Takayama City, Japan, selected as winner of the Facility of the Year Award for Equipment Innovation
- **Vetter Pharma-Fertigung GmbH & Co. KG**, located in Ravensburg, Germany, selected as win-

ner of the Facility of the Year Award for Process Innovation

2006 Facility of the Year Awards Finalists

- **AstraZeneca's** facility in Macclesfield, UK was chosen for its Large Scale Laboratory (LSL) Project
- **Baxter BioPharma Solutions'** Bloomington, Indiana, USA facility was selected as a finalist for its Phase IV Vial and Syringe Filling project (**Overall Winner**)
- **Daiichi Asubio Pharma Co., Ltd.** facility of Tokyo, Japan, has been chosen for its NBP (New Bio Plant) project
- **Janssen Pharmaceutica** was nominated for its Facility: Small Volume Area in Geel, Belgium.
- **Wyeth Pharmaceuticals** was named for The Wyeth BioPharma Campus at Grange Castle project located in Dublin, Ireland
- **Biolex Therapeutics'** facility located in Pittsboro, North Carolina, USA has been selected for special merit recognition for its Pittsboro Phase II Facility Expansion project

2005 Facility of the Year Awards Finalists

- **Alkermes, Inc.** of Cambridge, Massachusetts was chosen for its Brickyard Square manufacturing site
- **Apotex, Inc.** of Winnipeg, Manitoba, Canada received a nomination for an expansion to its Etobicoke, Ontario manufacturing facility
- **KOWA Company Ltd.** of Nagoya, Japan was named a finalist for a new addition to its manufacturing plant for oral solid dosage products
- **Lundbeck Pharmaceuticals Ltd.** of Copenhagen, Denmark, was chosen for its new manufacturing facility at Seal Sands, Middlesbrough, United Kingdom
- **Novo Nordisk A/S** was selected as a finalist for its new manufacturing plant in Hillerød, Denmark (**Overall Winner**) 



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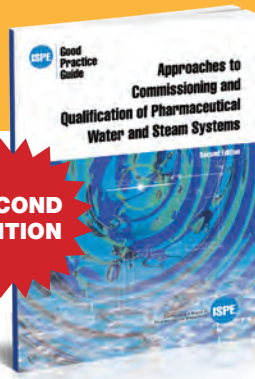
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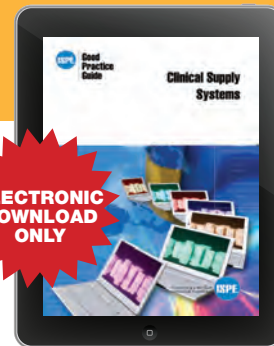
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