Supplement to

PHARMACEUTICAL ENGINEERING

2009

Facility of the Year Awards
CATEGORY WINNERS

Facility of the Year Awards
CATEGORY WINNERS

ENGINEERING PHARMACEUTICAL INNOVATION

ISPE

www.ISPE.org

Table of Contents

Cover Photographs

Photos courtesy of Aseptic Technologies, Centocor Biologics Ireland, Centocor R&D Schaffhausen, hameln pharma, Orchid Chemicals & Pharmaceuticals, and Roche Pharma Biotech Production Basel

ISPE HEADQUARTERS
3109 W. Dr. Martin Luther King Jr. Blvd.
Suite 250
Tampa, Florida 33607 USA
Tel +1-813-960-2105
Fax +1-813-264-2816

ISPE ASIA PACIFIC OFFICE
73 Bukit Timah Road
#04-01 Rex House
Singapore 229832
Tel +65-6496-5502
Fax +65-6336-6449

ISPE CHINA OFFICE
Suite 2302, Wise Logic International Center
No. 66 North Shan Xi Road
Shanghai 200041, China
Tel +86-21-5116-0265
Fax +86-21-5116-0260

ISPE EUROPEAN OFFICE
Avenue de Tervueren, 300
1150 Brussels, Belgium
Tel +32-2-743-4422
Fax +32-2-743-1550

www.ISPE.org

ISPE
ENGINEERING PHARMACEUTICAL INNOVATION

Supplement to
PHARMACEUTICAL ENGINEERING®

2009 Facility of the Year Awards CATEGORY WINNERS

Articles

Daldrop + Dr. Ing. Huber congratulates Hameln Pharmaceuticals and Roche Pharma on their "Facility of the Year Award 2009"

2009 Facility of the Year Awards CATEGORY WINNER Operational Excellence • Supplier

2009 Facility of the Year Awards CATEGORY WINNER Project Execution • Supplier

Daldrop + Dr. Ing. Huber planned and built the entire cleanroom technique of the award winning building infrastructure Hameln Pharmaceutical Neurosterile Production Plant and Roche MAB Building 95 using the SHELMEQ® system. Conventional cleanroom building procedure is for the floors, walls and ceilings to be designed by architects and the building services by consulting engineers. The revolutionary SHELMEQ® system by Daldrop + Dr. Ing. Huber handles both the physical infrastructure as well as the cleanroom conditions out of one hand thus eliminating possible interface disturbances.

Daldrop+Dr. Ing. Huber
Daldropstraße 1
72666 Neckartailfingen
Germany

Phone: +49 7127 18 03-0
Telefax: +49 7127 38 39

varipro@daldrop.com
www.daldrop.com

2009 Facility of the Year Awards Program Reaches New Heights

Now in its fifth year, it is not an exaggeration to say that the Facility of the Year Awards (FOYA) program reached new heights in 2009. Along with garnering increased industry visibility – having been covered by an ever-increasing number of international and industry publications – the FOYA program also has solicited submissions from the best and brightest from around the world. Submissions during the past five years have been received from more than 20 different countries and territories. This year alone, the program received submissions from innovative facilities built in Belgium, France, India, Italy, Ireland, England, Germany, Japan, the Netherlands, Spain, Switzerland, and the United States.

Co-sponsored by ISPE, INTERPHEX, and *Pharmaceutical Processing* magazine, the awards program effectively spotlights the accomplishments, shared commitment, and dedication of individuals in companies worldwide to innovate and advance pharmaceutical manufacturing technology for the benefit of all global consumers. The 2009 Category Winners, as well as each of the submitters, literally and brilliantly embody this sentiment.

Aseptic Technologies: Filling and laser re-sealing in capping area of workshop.

Aseptic Technologies – determined to resolve the incidents of product contamination that are reported in the industry each year – developed the innovative, new Crystal® Closed Vial technology for aseptic filling of injectable products. Taking its solution one step further, the company installed the associated equipment in its own Gembloux facility as a way to help clients obtain stability data without accepting the financial risk of implementing the new technology themselves. Taking such a unique approach to a critical industry issue and tackling the complexities of vial component preparation was not only ingenious, but also will help patients worldwide.

Centocor Biologics Ireland: Facility to capture rainwater from roofs within a grey water recovery system for future use in sanitary and ancillary process applications.

Centocor Biologics Ireland went to extraordinary lengths to ensure that its BioCork facility in County Cork met or exceeded standards for energy-efficiency and sustainability with the utilization of a biomass boiler, an advanced membrane waste water treatment facility, recycled rainwater capabilities, and extensive landscaping that mitigated the visual impact of such a large facility in a largely residential area. Not only is the facility 40% more energy-efficient than internal benchmarks, but it was also one of the safest large projects ever built in Ireland.

Facility integration was the objective for **Centocor R&D Schaffhausen** as it smoothly incorporated its new fill finish pilot plant into its existing Schaffhausen campus with a fast-track approach that allowed the talented project staff to complete the facility within 30 months. The F2P2 project contributes significant advances to the pharmaceutical manufacturing industry by creating a unique solution for a multi-product, multi-format R&D clinical fill finish

Centocor R&D Schaffhausen: Syringes being transported to the sterilization tunnel.

facility in a strategic location on an existing site.

The planning of **hameln pharma**'s streamlined 9200-square-meter sterile production facility began in March 2006 with lean production concepts leading the way. The standardization of rooms, equipment, inventory, production resources, and processes throughout design and construction led to a successful project completion in only 25 months, significant increases in employee productivity, and the efficiency of hameln's entire production process.

hameln pharma: Filling and closing of vials, Class A/B. These fixed gloves used for interventions together with a continuous airflow from Class A to the outside of the room and doors with safety locks ensure an extremely clean environment.

When **Orchid Chemicals & Pharmaceuticals** began to create a new facility with modern and flexible cGMP aspects to manufacture internationally acceptable products, its staff knew that new technologies would be necessary; and they met the bold challenge successfully. With the high degree of facility automation, innovative energy conservation measures, and one of the first cGMP operational systems for bulk API handling in India, Orchid has become a model for other organizations building facilities in the region.

Orchid Chemicals & Pharmaceuticals: Production blocks are well integrated.

Finally, the project team at **Roche Pharma Biotech Production Basel** shined while delivering an ultra fast-track, completely unique, vertical MAB facility on the site of a former chemical plant in the middle of a busy Basel residential area. Every aspect of this project had to be flawlessly executed to accommodate the many challenges of the site, location, and facility design. The result was a skillfully orchestrated project delivered six weeks ahead of an already aggressive schedule.

Roche Pharma Biotech Production Basel: Space between structures max. 25 feet.

Each of the impressive submissions was reviewed by an independent, blue-ribbon judging panel of global representatives from the pharmaceutical design, construction, and manufacturing sectors. The judging panel was comprised of professionals who have hailed from and participated in pharmaceutical facility construction projects throughout the world.

The following are the members of 2009 Facility of the Year Awards Judging Panel:

- **Andy Skibo, Judging Panel Chair** – Senior Vice President Global Engineering and Facilities, MedImmune
- **Jim Breen** – Vice President Project Management, Johnson & Johnson
- **Chaz Calitri** – Senior Director Global Engineering, Pfizer
- **Brian H. Lange, P.E.** – Director of Engineering, Merck & Co. Inc.
- **Geoff Monk** – Vice President Global Engineering Services, Schering-Plough
- **Jon Reed** – Vice President Corporate Engineering, Genentech
- **Ron Trudeau** – Vice President Facilities Engineering, Baxter Healthcare
- **Shinichi Osada** – General Manger, Hitachi Plant Technologies, Ltd.

"The judging panel was truly impressed with the quality of this year's submissions, as well as the depth and breadth of each organization's innovative solutions for pharmaceutical manufacturing challenges," said Robert P. Best, ISPE President and CEO. "It seems that each year the most talented minds in the industry raise the bar for quality, creativity, and ingenuity… which will ultimately benefit people worldwide," said Best.

For more information about the Facility of the Year global annual awards program, visit www.facilityoftheyear.org.

Aseptic Technologies

Crystal Clear Aseptic Filling

Introduction

To address the complexities inherent in conventional glass vial filling processes that can increase the risk of contamination to sterile products, and ultimately to patients, Aseptic Technologies developed the new Crystal® Closed Vial technology for aseptic filling of injectable products.

To showcase this new technology to potential clients, Aseptic Technologies, a developer and manufacturer of aseptic production equipment for the pharmaceutical and biotech industries, built the **GMP Manufacturing Site for Aseptic Filling** in Gembloux, Belgium – winner of the **2009 Facility of the Year Award (FOYA) for Equipment Innovation**.

Facing Challenges with Innovation

Aseptic processing in general has long been considered by many in the pharmaceutical industry to present unique and difficult challenges.

The conventional glass vial filling operation in a cleanroom has reached a high level of complexity to ensure safe processing. Vials and stoppers need to be prepared prior to filling, which consists of WFI washing and sterilization either with steam (stoppers) or in depyrogenation tunnel (vials). High speed stoppering and aluminum cap crimping generate many short stops.

Human activities required to execute the process significantly increase the risk of contamination. It is estimated that personnel represents the highest risk of contamination due to either the presence of contaminants on operating personnel or due to mistakes made during sanitization and operations[1].

To address these challenges, Aseptic Technologies, a subsidiary of Glaxo SmithKline Biologicals, developed the new Crystal Closed Vial technology for aseptic filling of injectable products. Since this technology was completely new, in March 2005, the company decided to install the first Crystal Closed Vial Filling Line (CVFL) in a new facility and operate it as a contract manufacturing organization offering filling of stability batches for clients who wish to investigate the stability of their product inside a Crystal® vial.

Filling line in the filling room.

In 16 months, Aseptic Technologies constructed the GMP Manufacturing Site for Aseptic Filling in Gembloux, Belgium. The site is composed of two buildings: AT01, which is dedicated to offices, meeting rooms, and workshops and AT02, which includes a workshop, offices, and the filling facility.

The 400 m² filling suite includes all the necessary equipment to perform aseptic filling. The operations performed in the suite are:

- Raw Materials – reception and storage
- Material Preparation – a washing room with double door autoclave is dedicated to the preparation of the filling needle and the tubing attached to it.
- Filling – a Class 100,000/Grade C/ISO 8 cleanroom is equipped with a CVFL with a capacity of 1,500 vials/hour. This line is able to handle batches from a few thousands up to 20,000 vials per batch.
- Downstream Processing – all downstream processing (particle inspection, labeling, and packaging) are manually performed because Aseptic Technologies target small batch filling, such as stability and initial clinical batches.
- Quality Control Laboratory – the few in-process quality control operations are performed inside the laboratory.

The Technology

The closed vial technology is based on a vial provided with the stopper in place. The vial manufacturing process has been optimized to ensure that the vial is clean inside and sterile by use of cleanroom production and sterilization by gamma-irradiation. This specific manufacturing process generates ready-to-fill containers, eliminating washing, sterilization, and depyrogenation

Aseptic Technologies

Category Winner – Equipment Innovation

Project: GMP Manufacturing Site for Aseptic Filling
Location: Gembloux, Belgium
Size: 4,306 sq. ft. (400 sq. m.) filling suite, 8,611 sq. ft. (800 sq. m.) other
Total Project Cost: US $4.98 million
Duration of Construction: 16 months

– the most complex filling steps of conventional open vials.

The filling is done by means of a needle piercing the stopper and dispensing the liquid. After needle withdrawal, the puncture trace is immediately resealed with a laser to restore the closure integrity.[2]

The Vial

The closed vial is a container composed of five elements:

- Vial Body – Cyclo-Olefin Co-polymer (COC) is used to produce vial bodies. This plastic was selected because of its excellent barrier and transparency properties, making it one of the most renowned plastics for containers in the pharmaceutical industry. Two different technologies are used to produce vial bodies: injection molding for small vials and injection blow molding process for larger ones.
- Stopper – made of a specific ThermoPlastic Elastomer (TPE) able to absorb laser energy and to melt when temperature exceeds 133°. This melting property is used to reseal the needle puncture trace to restore the closure integrity.
- Top Ring – secures the closure integrity of the assembly of the vial body and the stopper with non-return right angle snap fits.
- Bottom Ring – ensures good stability of the vial and firm holding during piercing and needle withdrawal.
- Cap – polyethylene cap, equipped with a circular rib pressing on the stopper surface, has the property to protect the piercing area by keeping it in a Class 100/Grade A/ISO 5 environment until use by the health professional. This specific characteristic avoids the contamination of the stopper surface after filling and during vial storage and transportation.

Continued on page 8.

Why Our Project Should Win

The following is an excerpt from Aseptic Technologies' submission, stating, in their own words, the top reasons why their project should win the 2009 Facility of the Year Award:

- First facility implementing the innovative Crystal® Closed Vial technology aiming to improve the quality for patients
- Simple operating environment with elimination or dramatic simplification of the major sources of complexity for classical aseptic filling facilities
- Inexpensive installation with very limited capital resources to be injected in the project
- Fast implementation with less than two years from management decision up to final inspection by authorities
- Strong attention and support from global regulatory authorities as illustrated by interest from both the US FDA and EMEA

Notes from the Judging Panel – What Impressed Them

Equipment is very innovative. They have an interesting concept for quality improvement of vial filling.

Not only is the material and design of the vial innovative, but so is its manufacturing process, according to Aseptic Technologies. To ensure cleanness and sterility, the vials are molded and stoppered by robots in a cleanroom Class 100/Grade A/ISO 5 and then sterilized by gamma-irradiation. The manufacturing of the vials comprises the following steps:

- The vial bodies and the stoppers are molded at the same time in two molds installed in a cleanroom Class 100/Grade A/ISO 5.
- Immediately after mold opening, two robot arms pick the vial body and stopper and bring them in front of each other. The assembly is performed by simple pressure of the two elements. This assembly creates closed vials with Class 100/Grade A/ISO 5 air inside.
- The vials are then transferred by one of the robot arms to an adjacent cleanroom Class 100,000/Grade C/ISO 8 where the addition of top and bottom rings are performed by a full automatic machine. All assembly steps are automatically controlled to eliminate the vials with one of the elements missing or misplaced.
- After packaging, the complete pallet is gamma-irradiated at a minimum dose of 25 kGray.

This process provides vials with extremely high quality in terms of stability and both particle and endotoxin contamination. Therefore, any additional step, such as washing and depyrogenation, are deemed unnecessary and the vials are provided ready-to-fill.

The Filling Line

The filling of the vial is performed on a dedicated filling line equipped with specific technologies. The complete filling process, from delivered vials to filled and capped vials, comprises five steps:

1. Loading – the operator loads the vials from polyethylene boxes using semi-automatic opening equipment. Therefore, the risk of contamination by the operator is strongly minimized.
2. Top Surface Sterilization – as the loading is still manual, the sterility of the stopper surface can be jeopardized by human error. Therefore, an e-beam (beta-irradiation or electron beam at 25 kGray) is used to re-sterilize the most critical surface – the stopper surface which will be in contact with the filling needle during piercing. After the e-beam, the vials directly enter a barrier that maintains a Class 100/Grade A/ISO 5 environment during all filling operations.
3. Filling – a 13-gauge needle with a pencil point and two exits with 30º angle pierces the stopper, dispenses the volume of liquid, and comes out by lifting. The needle was designed specifically to 1. eliminate a coring effect in the stopper and to minimize the generation of particles during piercing, 2. dispense the liquid smoothly to avoid damages for sensitive products (e.g., proteins) during filling, and 3. properly cut the TPE to ensure optimal laser resealing. The side wall of the needle is equipped with four groves to vent overpressure generated during filling.
4. Laser Resealing – to fully restore the closure integrity, the resealing of the pierced stopper is performed by a laser dispensing 6.5 W/s. This laser shot increases the temperature of the stopper surface up to 165ºC to melt the material which then fuses and restores closure integrity as it cools. The melted stopper material fully recovers its initial characteristics in terms of elasticity and resistance. By using a low energy laser, the energy is absorbed on the top surface of the stopper and does not reach the product. This is achieved by adjusting the laser wavelength and the absorption characteristics of the TPE. Product safety was confirmed; temperature inside the vial was measured and no change was recorded in the liquid after a laser shot.
5. Capping – using plastic caps with the snap fit technology, capping is easily performed without need for crimping.

The first two steps are performed under a laminar airflow delimited by soft walls. The last three steps are made in a Closed Vial Filling System (CVFS) with access only through gloves and rapid transfer ports. As the doors can not be open and direct access is forbidden for operators, a high quality of Class 100/Grade A/ISO 5 environment is permanently ensured. Isolators and closed RABS can be used for classical products, but become mandatory to protect the operator from contamination by specific products, such as cytotoxics, bio-hazard, and radioactive products.

Key Advantages of the Technology

When comparing conventional glass vial technologies to the closed vial technologies, key advantages can be identified.

Better Sterility Assurance Level and Reduced Particle Presence

The most important advantage is an increase in quality for the patient, observed for both sterility assurance level and particle presence.

A higher sterility assurance level is obtained through the concept of always keeping the vial closed. This reduces the risk of a contaminant penetrating the container. In the conventional glass vial filling process, opened vials and free stoppers can be exposed up to a few hours, for example, when large batches of stoppers are used. Regarding particle presence, the full process with the closed vial generates a very limited amount of particles, twice less compared to glass vial filling processes.

Another advantage for the patient is a newly designed capping technology. The entire stopper surface is protected by a circular rib, located on the inner face of the cap, which creates additional closure integrity.

Crystal® clinical line in workshop before delivery.

Simplified Filling Operations

Several glass filling equipment become obsolete with the closed vial technology, including:

- The washing stations for both vial bodies and stoppers are unnecessary.
- Because of the absence of washing, consequently there is no need for Water For Injection (WFI) on the filling line, eliminating a major source of expense, validation work, and risk of batch reject.
- The sterilization tunnel, with its high consumption of energy and difficulties for validation, is eliminated.
- The stoppering station, a source of frequent short stops, is replaced by the laser resealing station.
- The capping station, using simple snap fit technology, is simplified and more productive compared to the crimping station used for the aluminum cap.

The e-beam sterilization and laser resealing stations are two new technologies added to the closed vial filling process that are not on the conventional glass filling line. These technologies have been designed to ensure full compliance with the most advanced current Good Manufacturing Practices (cGMPs), such as Process Analytical Technology (PAT). A filling line can be installed in a building just equipped with electricity. WFI is only needed to prepare the filling equipment in the washing room and to autoclave the needle assembly.

Key Project Participants

Architect: Somville, Presciutti, and Partners, Fleurus, Belgium
Construction Managers: Christian Vandecasserie, Director, and Françoise Delhalle, Responsible Pharmacist, both of Aseptic Technologies, Gembloux, Belgium
Main/General Contractor: Cobelba, Naninne, Belgium
Piping and HVAC Subcontractor: D-FI, Sprimont, Belgium
Automation and Control Supplier: Honeywell, Diegem, Belgium
WFI Generator Supplier: Millipore, Brussels, Belgium
Autoclave Supplier: Steritec, Brussels, Belgium

Secured Supply Chain and Easier Handling

There are advantages linked to the innovative design of the vial, improving the supply chain until injection of the product. The vial body, made of COC, is resistant to shocks and can not be easily broken, conferring a higher safety assurance for the operators, practitioners, and nurses, especially when potent products are used. In addition, the stopper was designed to have a large and flexible piercing area and to favor the complete collection of the liquid by avoiding recess areas.

The design of the vial also allows online coding by either RFID chip installation or laser coding before any operator has access to the vials.

Reduced Capital and Operating Expenses

In terms of total cost of operation, filling in the closed vial was evaluated to be more cost-effective than filling in glass vials, in particular for expensive products, according to Aseptic Technologies. The following considerations were gathered in an evaluation Aseptic Technologies conducted with several companies:

- Using sterile and ready-to-fill vials adds a significant cost increase compared to classical components of glass vials which need to be cleaned and sterilized.
- However, capital expenses and one-shot expenses are reduced because of simplified equipment, reduction of cleanroom size, and reduction of resources and time allocated to validation.
- Operating expenses are reduced because of reduction of residual volume, reduction of vial breakage, and lower utility consumption.

Conclusion

Determined to resolve the incidents of product contamination that are reported in the industry each year, Aseptic Technologies developed the innovative, new Crystal® Closed Vial technology for aseptic filling of injectable products. Taking its solution one step further, the company installed the associated equipment in its own Gembloux facility as a way to help clients obtain stability data without accepting the financial risk of implementing the new technology themselves. Taking such a unique approach to a critical industry issue and tackling the complexities of vial component preparation will help patients worldwide.

References

1. Akers, James E. and James P. Agalloco, "The Akers-Agalloco Method," *Pharmaceutical Technology,* 2 November 2005, Volume 29, Issue 11.

2. Thilly, Jacques, Doris Conrad, and Christian Vandecasserie, "Aseptic Filling of Closed, Ready to Fill Containers," *Pharmaceutical Engineering,* March/April 2006, Volume 26, Number 2.

3. Verjans, Benoît, "A New Technology for Aseptic Filling of Injectable Drugs," *Controlled Environments,* October 2007.

Centocor Biologics Ireland

The Value of Sustainability

Introduction

To provide additional manufacturing capacity for two promising new drugs in their pipeline, Centocor Biologics Ireland embarked on a project to build a new cell culture and purification site in Ringaskiddy, County Cork, Ireland.

This complex project, dubbed BioCork, underwent careful and integrated planning, resulting in a facility that was completed ahead of schedule, under budget, and exceeds capability requirements in all areas, especially in the sustainability category. **BioCork** is the winner of the **2009 Facility of the Year Award (FOYA) for Sustainability**.

Search Yields Greener Pastures

In 2001, Centocor, which develops and produces biopharmaceuticals to treat autoimmune diseases, started looking at options to provide additional manufacturing capacity for two promising new drugs in their pipeline, CNTO 148 and 1275. Centocor's existing manufacturing sites were built-out so it was necessary to consider a greenfield site.

In June 2004, after three years of study, Centocor approved funding to establish BioCork. Constructed in two years, BioCork includes four buildings, 264,000 square feet of manufacturing, utilities, warehouse, and lab/office space spread over a 100-acre greenfield site. BioCork is expected to provide manufacturing capacity for 180 kg-per-year of biologic API.

Sustainability by Design

It was important to Centocor that the BioCork project be consistent with the company's values, which demand safety of personnel during construction and operation, involvement with the surrounding community, compliance with all regulatory requirements, and minimal impact on the environment.

Rather than add sustainability features to the project after the blueprints were drawn, this criteria was an integral part of BioCork's design, construction, and operation. The result: a plant that is 40% more energy efficient than internal benchmark biotech facilities and a 97% reduction in the carbon footprint versus fossil fuel.

Centocor Biologics Ireland

Category Winner – Sustainability

Project: BioCork
Location: Ringaskiddy, County Cork, Ireland
Size: 264,000 sq. ft. (24,526 sq. m.)
Total Project Cost: $586 million
Duration of Construction: 24 months

Aerial view showing landforms surrounding plant on east and south.

The following are key sustainability features at BioCork:

- Based on 2007 and 2008 operational data, BioCork's efficient design required 3.92 MMBTU/meter²/year to operate its 24,391 m² facility versus the average of 6.49 MMBTU/meter²/year needed at other Centocor biotech facilities.
- BioCork contracts its electricity from a company that provides wind power generation and operates a biomass fuel boiler. As a result, the facility has a carbon emission of about 250 tons per year compared to 8,415 tons per year using fossil-fuel derived electricity and burned fossil fuel for heat and steam.
- Twenty-two tons of nutrients per year are prevented from being discharged to Cork Harbor. An advanced membrane bioreactor wastewater treatment plant is designed to remove 11.6 tons per year of nitrogen and 10.5 tons per year of phosphorus, in addition to conventional pollutants, such as biological oxygen and suspended solids, before discharging the water into Cork Harbor. Removal of nitrogen and phosphorus reduces the plant's impact on algae growth in the harbor, designated as eutrophic sensitive waters.
- All construction and operating materials and wastes were recycled where possible.
- Facility captures rainwater from roofs within a grey water recovery system for future use in sanitary and ancillary process applications, e.g., boiler makeup water and flushing toilets.
- Highest efficiency (90%) Reverse Osmosis units to minimize water wasted.
- Sophisticated rainwater and runoff containment, monitoring, and diversion system protect Cork Harbor from BioCork activities.

Continued on page 12.

PM+CRB Congratulates Centocor BioCork

Winner of the Facility of the Year Award for Sustainability

2009
Facility of the Year Awards
CATEGORY WINNER
Sustainability • Supplier

"Environmental sustainability is a major challenge today and this award is a reflection of the dedication by Centocor and the PM+CRB project team to creating a world class manufacturing facility that also breaks new ground in sustainable design".

Lee Emel, Biotech Director, CRB

"We're delighted for both Centocor Biologics Ireland and the PM+CRB team that BioCork has been recognised with this award. Centocor and the design team worked hard to produce a sustainable facility, both in terms of its design and its operating efficiency and effectiveness".

Pat McGrath, CEO, PM Group

PM+CRB Project Services

- Site Evaluation, Masterplanning and Permitting
- Architecture and Engineering Design
- Procurement
- Construction Management
- Commissioning and Qualification

A Global Alliance of Real Results

C O N T A C T
USA: Gary Reichelt +1 919 852 5400
Europe: Liam Foley +353 21 4358922
Asia: Fintan Cassidy +65 6513 1000

www.pmgroup.eu
www.crbusa.com

PM GROUP + CRB CONSULTING ENGINEERS, INC.

PM+CRB is a worldwide alliance between PM Group and CRB Consulting Engineers. We provide a full range of project delivery services to the biopharma sector. With combined resources of over 2,200 personnel in 21 offices globally, we provide customer teams that are 'on the ground' in the United States, Europe and Asia.

- Energy efficient Variable Frequency Drives (VFD) on air handling units, chillers, pumps, and compressors.
- Lighting is controlled by occupancy sensors throughout the site.
- Eighty percent recirculation of air within cleanroom air-handling units.

Why Our Project Should Win

The following is an excerpt from Centocor Biologics Ireland's submission, stating, in their own words, the top reasons why their project should win the 2009 Facility of the Year Award:

- Sustainability – sustainability is an integral part of BioCork's design, construction, and operation. The cumulative effect of these efforts will ensure significantly less energy and water usage than comparable facilities with less waste leaving the site.
- Project Execution – the entire BioCork Team focused on meeting the overall project objectives using an integrated approach to project execution that enabled this project to reflect Centocor's values, including contractor and operator safety; involvement in the community; compliance with all regulatory requirements; minimizing impact on the environment, exceeding performance requirements, and completing qualification ahead of schedule and under budget.
- Facility Integration – by including user input for all aspects of the project from concept through completion, the BioCork project closely reflects user's technical and aesthetic requirements. Features such as sufficient staging area for clean and dirty equipment, the ability to do almost all routine maintenance outside the cleanrooms, and the incorporation of ergonomics into selection of equipment and room layouts are all included as requested by the users. The workers can appreciate the spectacular natural setting of Cork Harbor with views from process, laboratory, and public spaces.
- Exceeded Capability, Schedule, and Budget Goals – through use of integrated budgeting and scheduling coupled with full user participation, this complex project was completed ahead of schedule, under budget, and exceeded capability requirements. BioCork allows Centocor to reliably supply patients with life saving and life enhancing drugs.
- Safety – through a coordinated and concerted effort, this site has achieved an exceptional safety record and developed a strong safety culture. Construction is a hazardous process. A project the size and complexity of BioCork, with more than 350,000 days worked, has countless opportunities for accident and injury. Through careful preparation, communication, and implementation of safety planning, BioCork is one of the safest large projects ever built in Ireland.

Biomass boiler fueled woodchip from sustainable forests.

- Gas-fired boilers are designed for biodiesel as an alternative fuel source.
- Recently commissioned biomass (woodchip) boiler will reduce the overall site CO_2 footprint by 3396 tons at maximum output (compared to natural gas).
- Wood used for the woodchip biomass boiler is sourced from renewable sustainable forests certified under the Forest Stewardship Program.
- Southerly alignment of the administration and laboratory areas facilitate passive solar heating.
- Groundwater monitoring wells and protection program monitors and protects groundwater resources in the locally important aquifer beneath the site.
- Applied energy management software monitors, trends, and manages energy utilization for improved energy efficiency, cost control, and reduction in carbon footprint.
- Innovative radiant cooling system and AHU heat wheels for office areas.
- Boiler stacks fitted with flue gas economizers.
- Cumulative impact of conservation techniques reduces boiler gas consumption by 60% and chiller electrical consumption by 30%.

Considerate Neighbors

An environmental impact study was completed as part of the design process and an environmental impact statement was submitted to the Environmental Protection Agency. This considered the following impacts in detail: human; landscape and

Continued on page 14.

Coming from a multi discipline engineering background ProsCon is ideally placed to meet your Control System and Sustainability requirements.

ProsCon offer a comprehensive range of services to meet your facilities needs:

- **Control Systems** – PLC, DCS, SCADA, Batch
- **MES** – EBR, Historian, OEE, Material Tracking, EMI, Weigh & Dispense
- **Energy Management** – Energy Audits, M&T, Process Optimisation, Energy Reduction Projects
- **Sustainability** – Distillation, Solvent Recovery, Bio-Fuel Recovery
- **Process Design & Modular Build**

Contact: salesteam@proscon.com

www.proscon.com

LISTEN.
THINK.
SOLVE.®

ProsCon

2009 Facility of the Year Awards CATEGORY WINNER

Allen-Bradley • Rockwell Software

Rockwell Automation

Notes from the Judging Panel – What Impressed Them

The sustainability features, including traffic mitigation; offsetting carbon emissions; working with the community to mitigate visual impact; planting 70,000 trees; carbon footprint being reduced due to wind generated power; biomass facility; and rain capture ability, all noteworthy. They really utilized the strengths of the region. The logistics of working on the site were difficult, construction in/out and labor in/out was a challenge. The two-lane road in/out was a challenge and staging the trades was difficult for a project this size in this region. Good mix of local technology and overseas technology.

visual; roads and traffic; soils, geology, and hydrology; flora and fauna; noise and vibration; water and effluent; air quality and climatic factors; waste management; material assets; archaeology; architecture; cultural heritage; and sustainability.

As a result of this process and consultation with residents in the area, it became apparent that the key concerns, beyond compliance with existing regulations, were the impact on traffic and the visual impact of constructing the plant.

Traffic impact was mitigated by instituting a Commuter Management Plan to reduce the impact of traffic during construction when the maximum number of people would be entering and exiting the site. The project also involved extensive landscaping, including planting 70,000 trees to mitigate visual impact of the plant.

It's All About Integration

Alongside its values, integrated planning, integrated project execution, and integrated teams, were essential parts of BioCork's platform.

Integrated Project Execution

A project of BioCork's magnitude is often managed as distinct phases of engineering, procurement, construction, commissioning, qualification, and operation with different owner and vendor teams responsible for planning and executing those phases. Miscommunication and disconnects between phases can lead to schedule and budget problems and the need for significant corrective work at the end of the project.

The BioCork strategy was to integrate the teams, management techniques, and values across different phases and disciplines in order to proceed smoothly and efficiently from original concept to operable plant.

Integrated Teams

Teams were integrated to minimize the number of handoffs from team-to-team by having key members participate in multiple phases, including:

- Even before the permanent users were hired, a team of highly experienced temporary users were recruited from other Centocor plants to represent the user perspective during early design.
- Permanent users were hired early on and participated in design reviews, construction quality walks, and as hands-on members of the commissioning teams.
- Centocor's lead engineers were full time "system owners" from concept design through commissioning ensuring continuity.
- A number of design engineers played lead roles on the FAT teams, field engineering support teams, and the commissioning teams.
- Key people from the construction management team were involved from early design through the end of commissioning.
- Quality personnel were heavily involved in reviewing construction and commissioning progress.

Media prep skid.

Integrated Planning

It is common for large projects such as BioCork to meet schedule and budget objectives on one or more aspects of the project, but fail to meet overall schedule and budget. Delays occur when one critical activity does not complete as required for the overall schedule and opportunities are lost when subsequent activities are not ready to capitalize on early success. BioCork's aggressive planning was a major contributor to the project's overall success.

BioCork's master schedule was unique in that it included owner activities to the same level of detail compared to more traditional engineering and construction activities. Progress against each area of the master schedule was reviewed weekly and the entire schedule was updated monthly. In order to capitalize on good progress, early dates were planned and then the schedule was adjusted if they had not been met.

BioCork's budget also tracked all aspects of the project in great detail. Due to the "open book" style of contracting, the

Concludes on page 16.

owner had access to the details of the engineer's and contractor's expenditures on a continuous basis. This minimized surprises for expenditures that slipped between the cracks.

Safety First

BioCork is one of the safest large projects ever built in Ireland. The BioCork's team credits this to careful preparation, communication, and implementation of safety planning.

A tiered safety management system was in place for the duration of the project. Each contract company had a safety officer. The main contractor had a Project Safety Team that managed all the day-to-day aspects of project safety. The client safety personnel then reviewed overall project safety systems and outcomes.

All those working on site were required to complete site specific safety induction training and one-day off-site FAS Safe Training (National Construction Safety Training). Owner personnel visiting the site were held to the same standards as contractor personnel.

The contractor conducted regular toolbox talks (safety briefings) and multiple daily internal audits while the client conducted weekly safety audits. An external consultant conducted bi-weekly safety audits. Each audit produced action items and work was stopped if action items were not addressed in a timely fashion. Safety metrics for each contractor/sub contractor were measured and published on a monthly basis and improvement plans were developed for contractors scoring below a set limit. Overall accident free hours were set, and when achieved, the site was closed early and a celebration with prizes held.

As a result of these efforts and the cooperation of those working on the site, the following results were achieved:

Walkable ceilings minimize traffic in cleanrooms.

- With more than 4,000 contract personnel involved in the construction of the facility over a two and a half year period and with more than 830 people on site at peak, 1,052,997 consecutive hours were worked without injury and only five lost workday cases were experienced over a total of 2,865,012 hours worked with no serious injuries.
- The Lost Time Incident Rate (LTIR) = 0.35 (industry average for 2005 was 2.2).
- Received National Irish Safety Organization award for construction safety.

Conclusion

Centocor Biologics Ireland went to extraordinary lengths to ensure that its BioCork facility in County Cork met or exceeded standards for energy-efficiency and sustainability with the utilization of a biomass boiler, an advanced membrane waste water treatment facility, recycled rainwater capabilities, and extensive landscaping that mitigated the visual impact of such a large facility in a largely residential area. Not only is the facility 40% more energy-efficient than internal benchmarks, but it was also one of the safest large projects ever built in Ireland.

Key Project Participants

Architect/Engineer: The PM Group, Blackrock, Cork, Ireland *(See ad on page 11)*

Designer/Architect/Engineer: CRB Consulting Engineers, Inc., Plymouth Meeting, Pennsylvania, USA *(See ad on page 11)*

Construction and Main/General Manager: John Sisk and Son Ltd., Capwell Works, Cork, Ireland *(See ad on page 15)*

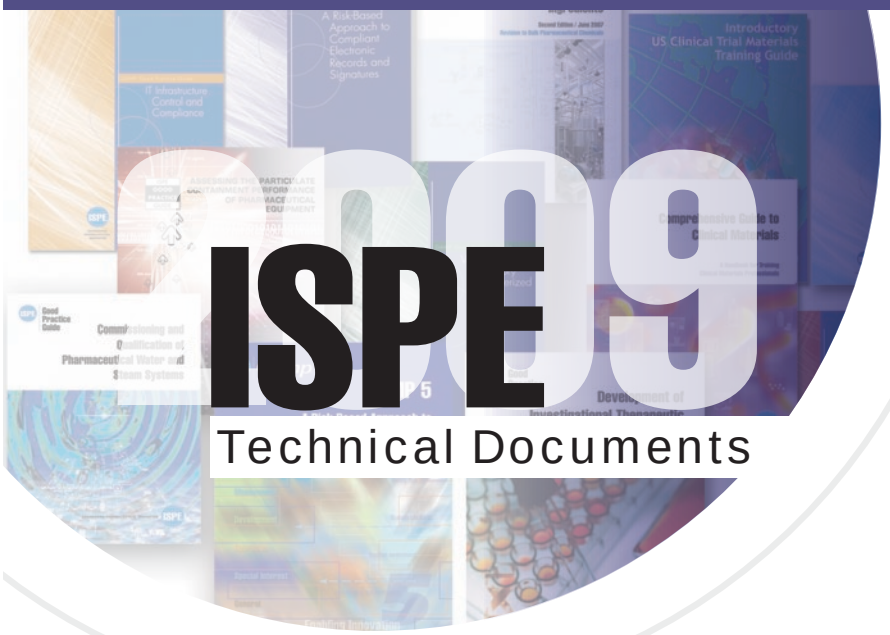
Piping Subcontractor: Mercury Engineering, Foxrock, Dublin 18, Ireland

HVAC Subcontractor: Rockwell Construction Ltd., Cork, Ireland

Automation and Control Supplier: ProsCon, Cork, Ireland *(See ad on page 13)*

Major Equipment Suppliers:

- Emerson Process Management Ltd., Cheshire, UK
- Fedegari Autoclavi SpA, Albzzano (PV), Italy
- Flow Technology Ltd., Cork, Ireland
- GE Healthcare UK Ltd., Bucks, UK
- Getinge-La Calhene, Cambridge, UK
- Gilroy Automation Ltd., Cork, Ireland
- Kells Stainless Ltd., County Meath, Ireland *(See ad on page 14)*
- SkidTeck Ltd., Cork, Ireland
- Schneider Electric Ireland, County Kidare, Ireland
- Techniserv Inc., Berwick, Pennsylvania, USA
- York International Ltd., Essex, UK



Stay on the Cutting Edge with ISPE Technical Documents and Publications

ISPE offers the tools and resources necessary to keep you up-to-date with industry changes, while keeping your production costs low.

ISPE GAMP® Reflecting current regulatory expectations and good practices, the *GAMP® 5* Guide and *GAMP®* Good Practice Guide series help narrow the interpretation of regulatory standards for improved compliance, quality, efficiency, and cost reductions.

ISPE Good Practice Guide ISPE *Good Practice Guides* (GPGs) provide information on a particular topic area while explaining underlying technical principles and suggest multiple solutions where several outcomes may be possible.

ISPE Baseline® PHARMACEUTICAL ENGINEERING GUIDE ISPE's *Baseline® Guides* offer practical answers to challenges facing facility designers while providing an understanding of products and processes.

ISPE GMP Institute GMP products and publications make good business sense and help meet regulatory requirements.

Electronic licenses are now available.
Contact Gloria Hall at ghall@ispe.org for more information.

ENGINEERING PHARMACEUTICAL INNOVATION ISPE

For more information on these or other ISPE technical documents and publications, visit www.ISPE.org/publications today!

Centocor R&D Schaffhausen

Superior Integration Shortens Bridge from R&D to Commercial

Introduction

Recognizing the need for more capacity and capabilities in their existing fill finish facility to meet the future needs of its expanding product pipeline, Centocor Research and Development built the **F2P2 R&D Fill Finish Hub**.

This new fill finish pilot plant facility, located on Centocor's Schaffhausen, Switzerland campus, is the winner of the **2009 Facility of the Year Award (FOYA) for Facility Integration**. The plant demonstrates excellence in integration with existing facilities on campus and exceptional integration of facility and equipment designs, all contributing to an efficient and flexible operation.

Mission: Ease Process Comparability and Scale-Up

Centocor Inc., a subsidiary of Johnson and Johnson, is a leader in monoclonal antibody production and technology, using research and biomanufacturing to deliver biomedicines for immunological and oncological disorders. The company has created therapies for the treatment of people suffering from gastroenterologic, rheumatologic, and dermatologic diseases and brought drugs to market that effectively treat Crohn's disease, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, ulcerative colitis, and psoriasis.

In Schaffhausen, Centocor R&D is a division of Cilag AG and is responsible for fill finish operations and analytical testing of clinical supplies for technology transfer activities and for marketed product support to commercial plants.

The new 670 sq. m. R&D fill finish plant produces biological drug product for early- and late-stage clinical trials and also plays a key role in the transfer of fill finish operations into a commercial plant, also located on the Schaffhausen campus. With its capability for compounding and final formulation, vial and syringe filling, and lyophilization, F2P2 is a highly integrated facility that provides flexibility for new product development and clinical manufacturing, as well as an efficient operational platform. The plant offers a state-of-the-art technology portfolio that mirrors the set-up of commercial facilities to ease process comparability and scale-up.

Centocor R&D Schaffhausen

Category Winner – Facility Integration

Project: F2P2 R&D Fill Finish Hub
Location: Schaffhausen, Switzerland
Size: 7,219 sq. ft. (670 sq. m.)
Total Project Cost: $24.9 million
Duration of Construction: 21 months

View of the CIP/SIP compounding work stations.

Campus Integration

Although challenging to design, the facility was built in a way that maximizes interactions with other key groups such as Quality Assurance (QA), Quality Control (QC), and commercial manufacturing.

The facility had to be integrated into an existing building and connected to the facility entry to the adjacent QC building. Additionally, the facility shell had to be expandable to three additional floors that were level with the production floors of the adjacent Commercial building, which houses parenteral manufacturing.

Centocor considered this condensed arrangement the most feasible way to segregate R&D and commercial plants, while benefiting from synergies in campus infrastructure and from key support functions located in the QC building, such as QA QC labs and R&D offices.

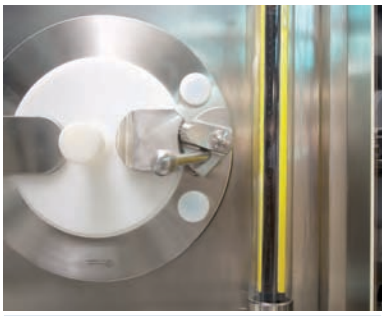
Based on these requirements, the available space to integrate the entire production facility as well as the required building services was limited to 670 sq. m. with a clearance height of only 4.10 m. Another 300 sq. m. of technical area to be shared with operations were available in the basement of the building.

Integration of Facility and Equipment Designs

The new facility provides three cleanrooms: two Restricted

Continued on page 20.

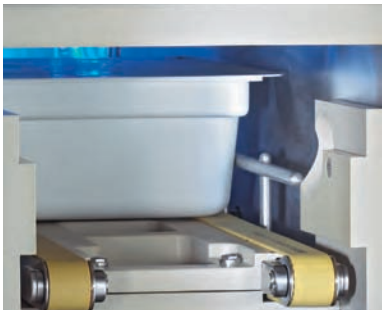
METALL+PLASTIC
Cleanroom Technology




Congratulations to centocor

We are proud to have been part of your team.
It was great working with you.




METALL+PLASTIC is a global leader in the design, manufacture, installation and validation of Isolators, E-Beam Tunnels, VHP® Transfer Chambers and Gastight Doors.

2009
Facility of the Year Awards
CATEGORY WINNER
Facility Integration • Supplier

Germany

METALL+PLASTIC GmbH
Bodmaner Straße 2
78315 Radolfzell-Stahringen
Phone +49 (0) 77 38-92 80-0
e-mail info@metall-plastic.de

USA

METALL+PLASTIC INC.
1222 West Golf Road
Libertyville, IL 60048
Phone +1-847-247 1112
Mobile +1-847-219 5443
e-mail j.vogel@metall-plastic.de

www.metall-plastic.de

Notes from the Judging Panel – What Impressed Them

Integration was exceptional with existing facility. They are doing some innovative things with process control. Expanding floors for future growth was a plus. It was a challenging work site. There were noise restrictions because of the residential area nearby. This is a nice solid project in a tricky area.

Access Barrier Systems (RABS)-based cleanrooms and one classical cleanroom, the latter designed for manual filling or manufacturing/assembly processes of combination products.

Room layouts were designed to maximize use of space. A common support area services both vial and syringe suites. Each filling suite can be isolated from the other areas by means of hermetically sealed doors and dedicated HVAC units, thereby permitting concurrent operations.

Since there were space limitations for material storage, a new concept of a rotating multi-shelf storage cabinet was introduced. This simplifies logistics and material storage in a controlled environment and is a central part of the material preparation area.

Facility mockup study. The layout details are drawn on a cover laid over top the finished epoxy floor.

A Vaporized Hydrogen Peroxide (VHP) pass-through chamber was built as an integrated part of the cleanrooms to connect the material preparation area with a B-grade corridor. This feature supports the transfer of heat sensitive, decontaminated material and equipment into the aseptic core. The VHP chamber is equipped with airtight doors on both sides. The chamber has H_2O_2 sensors for personnel protection. A short decontamination cycle time (qualified for a 6 log bioburden reduction) of no more than two hours supports a fast changeover.

Process comparability between R&D and commercial was one of the key design criterions for incorporating stainless steel

compounding and filtration tanks. As a result, the pooling, compounding, and filtration equipment had to be designed to account for batch volumes covering a range of 1-65 L. A multipurpose, flexible concept based on modular components was chosen for the filling lines.

The vial filling line is a customized, multi-format equipment which allows the processing of a broad spectrum of vial sizes, including standard glass components as well as pre-sterilized vial formats based on cyclo-olefine polymers. A continuous manufacturing process based on inline washing, depyrogenation, filling, and capping was incorporated to permit an efficient operation. Filling technology was designed for rotary piston pumps as well as peristaltic pumps to account for shear sensitive formulations. A scale ratio of factor three to four from lab (0.6 sq. m.) to pilot and to commercial (25 sq. m.) provides good comparability and reproducibility of lyophilization cycle performance. Capping is designed to occur under aseptic conditions, as proposed under EMEA regulations.

A unique hybrid concept was chosen for the syringe filling line to allow maximum flexibility for syringe processing. The bulk syringe line serves as the backbone of this hybrid system and is fitted with several mobile modules to process pre-siliconized, pre-sterilized Ready-to-Fill (RtF) syringes in tubs. This unique approach allows development of baked-on siliconization technology for bulk syringes, while other syringe formats or materials (plastic, pre-coated) can be processed on the same line via the RtF extension. After filling, the syringes are collected on a

Why Our Project Should Win

The following is an excerpt from Centocor R&D Schaffhausen's submission, stating, in their own words, the top reasons why their project should win the 2009 Facility of the Year Award:

- Creating a unique solution for a multiproduct, multi-format R&D clinical fill finish facility well integrated into an existing campus and has the possibility for expansion by adding floors above the existing structure
- Demonstrating superior integration of facility and equipment designs that provide maximum flexibility with high levels of sterility assurance (RABS and VHP decontamination concept) and an efficient operation
- Demonstrating the use of several important design methodologies, such as air flow simulations, facility mockups for equipment, layout, and process FMEAs
- Demonstrating innovative design of vial and syringe equipment that offers multiple format options for greater flexibility
- Providing a high level of equipment and process comparability for a lean scale-up and technology transfer process between R&D and commercial operations

Continued on page 22.

re-trayer equipped with empty trays. Another special flexibility feature of this hybrid syringe line allows for a mobile cartridge filler to be connected to the depyrogenation tunnel outlet.

Both filling lines are equipped with two filling stations and nitrogen overlay features. Current technical filling capacity is at approximately 4,000 units/hour for the largest format (30 ml) to be processed.

Innovation in Process Controls

Process excellence tools were applied during the initial design of the facility to analyze and streamline the production process. This analysis in the early design phase had a major impact on the specification of the equipment. As a result, process steps on the time-critical path could be identified and optimized by introducing automated process steps. For example, a process simulation revealed that the substitution of the manual disinfection process by a fully automated VHP-cleanroom decontamination is a clear benefit to the overall batch processing time.

A number of features enable the facility to be run efficiently and with a limited staff. Automation of process equipment, data acquisition, and documentation retrieval all contribute to this. A single automation architecture for all process equipment and utilities simplifies running the various systems. Automated data collection is used. For example, facility environment sensors are networked to a central server, allowing for real-time data collection from cleanrooms and data access from the office areas. A plant historian system enables data sharing throughout Centocor's worldwide enterprise. SOPs and technical documentation for equipment handling are accessible

Cleanroom operator opening the cabinet containing sterlized frames for the freeze dryer.

Concludes on page 24.

Watch ISPE.org for details.

Brussels Conference on Enhanced Competitiveness - Sustainable Achievements
30 March-2 April 2009, Brussels, Belgium

HVAC: Good Practice and Innovations, *GAMP® 5*, 21 CFR Part 11 and the EU GMP Annex 11, critical utilities, continuous process and process intensification, manufacturing excellence and R&D laboratories, and containment and calibration training courses

India Affiliate Meeting Featuring PQLI®
13-14 April 2009, Mumbai, India

Japan Affiliate Annual Meeting Including PQLI®
16-17 April 2009, Tokyo, Japan

Held in Funabari, Tokyo.

Washington Conference: Engineering Regulatory Compliance
1-4 June 2009, Washington, D.C., USA

PQLI, barrier isolation technology, packaging challenges, GAMP Good Practice Guides on VPCS Ver. 2 and Calibration Management Ver. 2, C&Q, global supply chain security and anticounterfeiting, applied risk management, renovation project challenges, and training courses on *GAMP 5* and GMPs

Strasbourg Conference: Quality - Knowledge Through Science
28 September-1 October 2009, Strasbourg, France

Barrier isolation innovation updates and new case studies, investigational products, *GAMP 5* operational aspects, containment, disposables, PQLI, and C&Q

Live Webinar: GAMP Hot Topic Series *GAMP 5* Approach to Compliant End-user Applications
25 March, 11.00 EDT, 09.00 PDT, 16.00 GMT, 17.00 CET

End-user systems, risks related to end-user systems, risk management approach, and approaches to compliance

Chicago Classroom Training
11-14 May 2009, Chicago, Illinois, USA

GAMP 5, water, HVAC, biotechnology, C&Q, Q7a, and technology transfer for finished dosage forms

Madrid Classroom Training
18-21 May 2009, Madrid, Spain

GAMP 5, water, technology transfer for API, HVAC, C&Q, and PAT

Philadelphia Classroom Training
5-8 October 2009, Philadelphia, Pennsylvania, USA

HVAC, *GAMP 5*, sterile products, water, C&Q, oral solid dosage, and clinical materials

Dublin Classroom Training
Fall 2009, Dublin, Ireland

Water, *GAMP 5*, Q7A, basic C&Q, biopharmaceutical manufacturing processes, and PAT

ISPE 2009 Annual Meeting
8-11 November 2009 • San Diego, California, USA

Eleven session tracks: product development, facilities and equipment, information systems, supply chain management, production systems, regulatory compliance, quality systems, project management, investigational products, suppliers, and survival-focused.

Sponsorship and Exhibit Opportunities Available

ENGINEERING PHARMACEUTICAL INNOVATION ISPE

Key Project Participants

Architect: PMB Bau AG, Schaffhausen, Switzerland
Designers/Architects/Engineers:
- Advens AG (Bickel & Bachofen AG), Winterthur, Switzerland *(See ad on page 21)*
- NNE Pharmaplan, Bad Homburg, Germany *(See ad on page 25)*

Construction Manager: Danny van Dyck, Beerse, Belgium
Piping Subcontractor: Zeta AG, Wangen, Switzerland
HVAC Subcontractor: Axima AG, Winterthur, Switzerland
Automation and Control Suppliers:
- Etavis Installation AG, Zürich, Switzerland
- Retel Neuhausen AG, Neuhausen, Switzerland

Major Equipment Suppliers:
- Belimed AG, Ballwil, Switzerland
- HOF Sonderanlagenbau GmbH, Lohra, Germany *(See ad on page 20)*
- Optima Group Pharma, Schwäbisch Hall, Germany *(See ad on page 22)*
- Metall + Plastic GmbH, Radofzell, Germany *(See ad on page 19)*

online via operator panels in the cleanrooms.

The F2P2 is supported by a state-of-the-art analytical laboratory for both routine operations as well as a particulate analysis laboratory, which contains equipment for microanalysis using methods based on infrared, X-ray, and mass spectroscopy. In collaboration with the particulate analysis lab, a facility specific particulate database was developed. All materials used during construction, qualification, and validation of the facility, as well as material used for the daily operations (e.g., gowning material, agents for sanitization and disinfection) were characterized and entered into an analytical database to trace back foreign matter identified during visual inspection of drug product. During manufacturing, the fill finish process in F2P2 is monitored by means of turbidity and Microflow Digital Imaging (MDI) measurement.

Conclusion

Through superior integration, the F2P2 efficiently bridges development to commercial operations. Using the facility,

Glove ports for the syringe line that is integrated into the cleanroom wall; human machine interface (HMI) displays process and environmental data for operators inside the cleanroom.

Centocor representatives said their staff has demonstrated on-time delivery of clinical supplies in more than six batch runs. In addition, a high level of comparability between R&D and commercial fill finish process, equipment, and scale have facilitated technology transfer and scalability from pilot to commercial scale. The facility has allowed Centocor to expand its new product pipeline and to bring new drug candidates quickly into clinical trials.

View from the visitor corridor of the washer and depyrogenation tunnel located in the C-grade area.

more than engineering

…leads to **exceptional** facilities

Client: **Centocor Research & Development**
Where: **Schaffhausen, Switzerland**
When: **October 2004 – March 2008**
What: **New R&D fill finish pilot plant**
Service: **Layout Development, Process/Equipment Design and Installation/Commissioning Management**

2009 Facility of the Year Award Winner – Facility Integration

Client: **Hameln Pharma**
Where: **Hameln, Germany**
When: **March 2006 – April 2008**
What: **New sterile production plant**
Service: **Review and rework of Conceptual Design, Basic Design, Process Engineering and Qualification**

2009 Facility of the Year Award Winner – Operational Excellence

Client: **Novo Nordisk A/S**
Where: **Hillerød, Denmark**
When: **May 2001 – November 2002**
What: **Facility for the life saving drug NovoSeven®**
Service: **Design and construction. Finished in 18 months by use of modular engineering**

2005 Facility of the Year Award Winner

NNE Pharmaplan is the world's leading engineering and consulting company focused exclusively on the pharma and biotech industries. NNE Pharmaplan employs more than 1500 people at over 20 locations around the world.

nne pharmaplan®

nnepharmaplan.com

hameln pharma

Every Step Counts Toward Operational Excellence

Introduction

Three years ago, hameln pharma embarked on a mission to build a factory that would significantly increase their production capacity in the area of parenteral contract manufacturing, create expansion possibilities for their company, and ensure reliable compliance with international regulatory standards.

This category winner successfully completed their mission with the construction of the **New Sterile Facility** in Hamelin, Germany. Winner of the **2009 Facility of the Year Award for Operational Excellence**, the facility was tailor-designed and constructed by Koppenhöfer + Partner GmbH to maximize the efficiency of every step of the sterile production process.

A Family of Experts in Parenteral Medicines

Experts in parenteral medicines, hameln pharma is part of the hameln group, a family-owned and -operated group of companies whose core business has been the development, production, and distribution of pharmaceuticals with a focus on parenteral medicines for more than 50 years.

The company specializes in the contract manufacturing of parenteral medicines predominately used in hospitals and intensive care in more than 70 markets worldwide. The company has more than 350 employees skilled and experienced in dealing with products, such as narcotics, suspensions, and oily solutions – from the initial weighing for preparation and filling, up through the packaging of 1 mL to 50 mL ampoules or 2 mL to 250 mL vials.

In an existing facility located at hameln group's headquarters in Hamelin, Germany, the staff of hameln pharma currently processes about 350 products on the bulk products level, aseptic or terminally sterilized. The new 9,200 sq. m. sterile production plant integrates all process steps required for the production and filling of parenteral products, while the subsequent processes of visual inspection through final packaging remain in the existing building.

hameln pharma

Category Winner – Operational Excellence

Project: New Sterile Facility
Location: Hamelin, Germany
Size: 99,028 sq. ft. (9,200 sq. m.)
Total Project Cost: $44.5 million
Duration of Construction: 13 months

Setting the machines up in a u-shape reduces the space required in the highest cleanroom class and increases the employees' productivity.

As Lean as Can Be

Lean production concepts were consistently implemented throughout the design and construction of the new facility.

The work areas within the sterile production plant were arranged using a materials flow simulation to prevent any form of waste of capacities, personnel, and materials movement, resources, area, or time. These simulations provided the construction prerequisites for an optimized, efficient process, which is demonstrated in the facility's ratio of 63% effective area to gross area. With the aid of integrated locks and hatches, materials are always transferred by the shortest route from one production step to the next.

The arrangement of the cleanroom classes to each other and a consistent lock design ensure that employees only need to cover short distances and go through as few clothing changes

Material locks in the wall ensure short ways for the transfer of samples and documentation to the analytical department.

as possible, saving time and improving safety significantly. The consistent standardization of rooms, equipment, inventory, production resources, and processes increases employee productivity as well as the efficiency of the entire production process since employees are able to continuously orient themselves and work in a quick and organized manner.

Lean production principles also were implemented in the arrangement of the filling systems. The U-shaped structure of the systems reduces the footprint in the highest cleanroom class and increases productivity. Both the loading of glass containers and the removal of the filled and sealed ampoules and vials are done in a Class D room by one and the same employee, who does not have to move between different cleanrooms. The complete monitoring of the actual filling process is done by another employee who remains in the neighboring Class B cleanroom. Less movement in the cleanroom means reduced risk of contamination.

A pharmaceutical cleanroom ceiling that is 100% accessible – meaning that it can be walked on everywhere – allows the exchange, installation, and maintenance of basic technical equipment, such as lamps and filter units, from above the ceiling, keeping production undisturbed. The arrangement of the cleanrooms to each other and separate corridors with integrated maintenance doors and segmented ventilation circuits allows maintenance and repairs to also be carried out on individual filling lines without interrupting production.

Annex 1 Compliant

According to Annex 1, continuous particulate monitoring compliant with standards for cleanroom classes A and B was installed during construction. Airborne germ measurements at critical points in the Class A area are also monitored by an automated system. With the remodeling of Annex 1, the capping for all vial lines will be done in cleanroom Class A as an aseptic process with sterilized caps, physically separated from stoppering and filling.

Managing Operations with 5-S

Short routes, reduced intermediate storage, and optimized materials flow reflect

Notes from the Judging Panel – What Impressed Them

The process that this company goes through to make sterile products, how they do their business, and how all elements fit together from the corporate, employee, operational, etc., standpoints, and the tying of everything together is exceptional. The project cites being up to date on all new Annex 1 regulations. The pricing is fairly low for what they built. This facility has taken so many processes and tied them together.

Continued on page 28.

Key Project Participants

Project Director: Dr. Simone Dahlmanns, hameln pharmaceuticals gmbh, Hamelin, Germany
Designer/Architect/Engineer: Peter Fischer, Koppenhöfer + Partner GmbH, Office for Industrial Planning, Stuttgart, Germany *(See ad on page 28)*
Construction Manager: Ulrich Baumann, IKB Immobilien Management, Düsseldorf, Germany
Main/General Contractor: Adam Abel, ARGE Pharmabau, Neckartailfingen, Germany
HVAC Subcontractors:
- Adam Abel, Daldrop + Dr. Ing. Huber, Neckartailfingen, Germany *(See ad on page 3)*
- Christian Hage, IP – Innovatives Planen GmbH, Neckartailfingen, Germany

Automation and Control Supplier: Gerhard Neuberger, Neuberger Gebäudeautomation GmbH 7 Co. KG, Rothenburg, Germany
Major Equipment Suppliers:
- Robert Bosch GmbH (Bosch Packaging Technology), Crailsheim, Germany *(See ad on page 29)*
- Belimed Deutschland GmbH, Mühlheim am Inn, Germany
- Letzner Pharmawasseraufbereitung GmbH, Hückeswagen, Germany *(See ad on page 31)*
- Pharmatec GmbH, Dresden, Germany
- NNE Pharmaplan, Bad Homburg, Germany *(See ad on page 25)*
- Carpus Prozess Experten GmbH, Hattersheim, Germany

the entire production layout. To take that a step further, on the operational level, the 5-S method is used to improve overall processing times. This management method consists of:

- Separate and Scrap
- Straighten
- Scrub
- Standardize and Spread
- Systemize

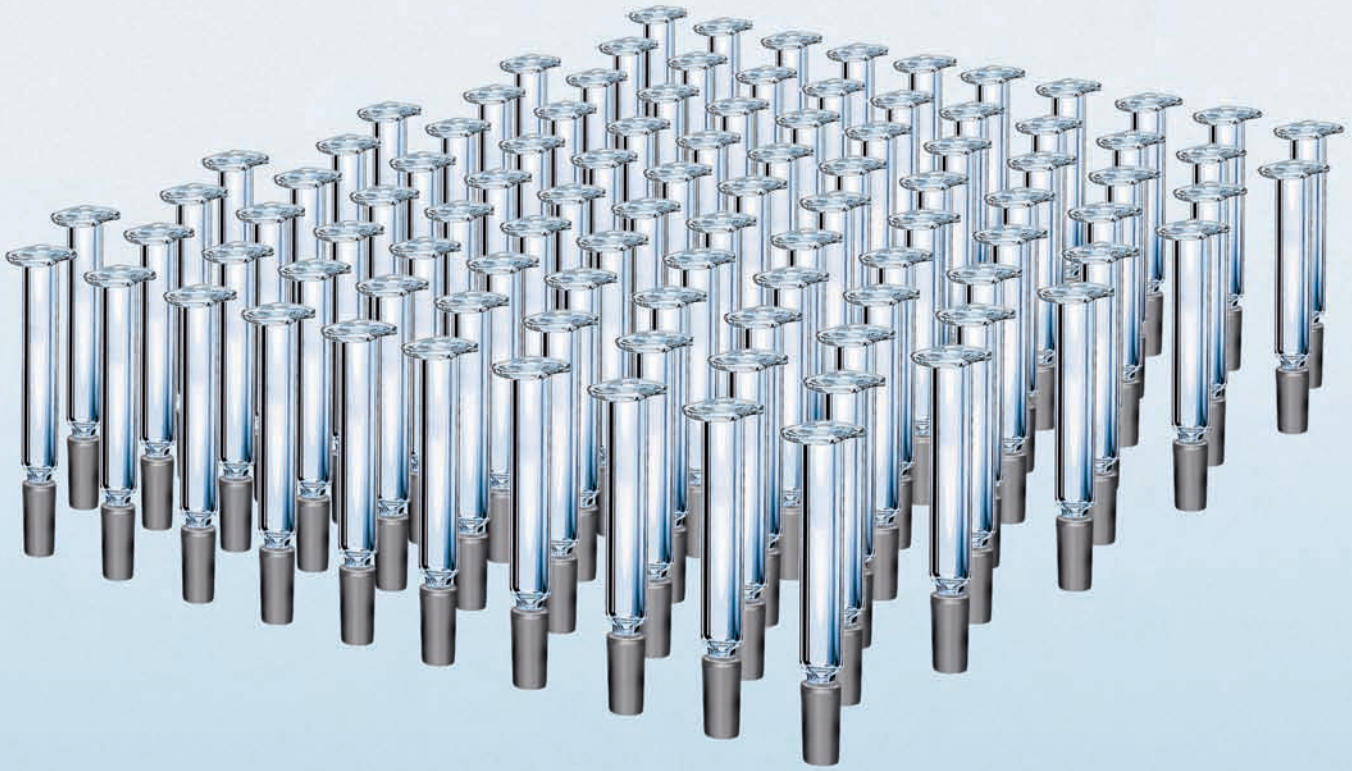
For hameln pharma, the 5-S method ensures safe, clean workstations; avoids time wasted searching for resources and work equipment; allows for the early and timely detection of defects and maintenance requirements, avoiding downtime; reduces the cleaning effort; and improves ergonomics in the workplace.

With the assignment and concentration of individual products on suitable production lines, the complete product pass, from start through filling and finally to packaging, is performed in a flow of movement leading to an optimal utilization of capacities at maximum productivity.

A system of coordinated equipment, transportation, and storage activities for the cleaning and sterilization of format parts ensures a cyclical process that avoids any type of waste. During the entire cleaning process, the format parts remain on one and the same cart on which they occupy the ideal and always identical position depending on their subsequent use. The format parts carts have the dimensions they need to be able

Concludes on page 30.

Bosch. Nested syringe filling
like you have never seen before.



ACHEMA 11 – 15 May 2009

Visit us in hall 3.1 at booth F2-J11

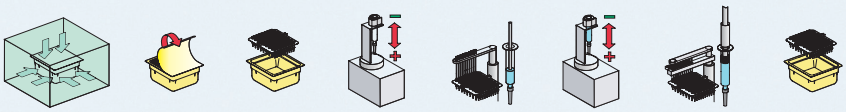
Messe Frankfurt, Frankfurt am Main, Germany

We look forward to seeing you!

Bosch is well known for filling and packaging of vials, ampoules, cartridges and bulk syringes. It is with this extensive knowledge and experience that Bosch now introduces a new product line designed specifically for nested syringes. With quality and innovation in mind, Bosch is introducing a complete portfolio of nested syringe filling and packaging equipment. You can expect all of the same great quality, efficiency, high performance and support as Bosch offers with its other equipment.

BOSCH

Invented for life



Robert Bosch GmbH
Pharma Liquid
Phone: +49 79 51 40 21 | Fax: +49 79 51 40 22 58
packaging@bosch.com | www.boschpackaging.com

Why Our Project Should Win

The following is an excerpt from hameln pharma's submission, stating, in their own words, the top reasons why their project should win the 2009 Facility of the Year Award:

- Form follows function – a facility that perfectly combines functionality and aesthetics, offering conditions that promote both efficiency and well-being, while still remaining flexible enough to react to varied requirements was the vision and governing principle of the tailor-made layout of this multipurpose building. The entire cleanroom concept, the configurations of the filling lines and the processes themselves have been designed and implemented to support functionality. This also facilitates the handling of a broad variety of container formats, batch sizes, potencies, formulations, and product types. Suitable areas for a growing number of potent APIs were built which allow their handling without risk of cross-contamination or health risk to staff.
- Operational excellence – from the facility layout and process design to the start of production, the pro-ject included all the aspects necessary for supporting modern, lean production. Reduced interim storage and optimized material and personnel flow along short paths characterize the entire production layout. The set-up of the work areas follows the logical structure of the process itself, and all equipment is installed in such a way that it supports an efficient process run. Processes were simulated in advance to ensure a set-up which allows standardized movements to increase efficiency and speed and reduce the risk of interference.
- Upgrade to existing technology – critical processes such as the cleaning and sterilization of equipment, such as product containers, were automated by implementing systems able to control processes fully automatically without any of the involved equipment being automatic. This reduces the staff time required for cleaning and sterilization tasks significantly and increases the reliability of the production processes.
- Unique solution virtually eliminates regulatory impact on product transfer from the existing facility to the new one – a consistent risk-based approach according to ISPE and ICH guidelines was applied for the qualification and validation concept as a winning, low-cost strategy. This reduced the cost for all qualification and validation activities to a mere 6% of the total investment. The overall strategy of defining a "best case scenario" helped to nearly eliminate all regulatory impact thus, the cost for any potential product transfer. This scenario was supported by successfully reasoning that the new facility is "the same facility" and by proving that the new environment, utilities, equipment, and processes have no negative impact on either product quality or stability. This strategy was accepted by the health authorities and by more than 90% of all customers, which meant that 95% of all products could be transferred without incurring additional work and cost.

to go into the small parts washing machine as well as the pass-through autoclaves. Once the parts are cleaned and sterilized, the entire cart, including the format parts, are reintroduced into the actual production process. At his or her work station, the employee finds the individual format parts in the position on the cart with which he or she is familiar, and then puts them back in the same place after use so that the completely filled format parts cart is again prepared for cleaning and then the cycle can begin again. Studied processes accelerate productivity, while a standardized and efficiently organized cleaning process prevents time wasted due to searching for work equipment and then arranging and organizing it in the production process.

Ready for the Future

To be able to operate a plant offering maximal production flexibility, hameln pharma buildings, facilities, and processes are standardized as much as possible. The building itself is a grid that can be expanded as needed on a modular and scalable basis; therefore, it was designed for future expansion in both spatial and technological terms.

To fulfill this requirement, the walls are set on four equal floor sections and are not embedded in the floor, which consists of 100% seamless pharmaceutical grade terrazzo. Wall fixtures, such as tool cabinets, are standardized and integrated flush with the walls. The filling rooms in the facility are all constructed identically and allow a standardized and therefore secure operation, and production preparation activities also are organized as uniformly as possible to enable smooth and efficient production.

This standard solution has made the facility into an efficient, flexible, and manageable production operation while, at the same time, future products can be established in the shortest possible time, even new and innovative customer projects. This saves both the contract manufacturer and the customer significant effort and cost.

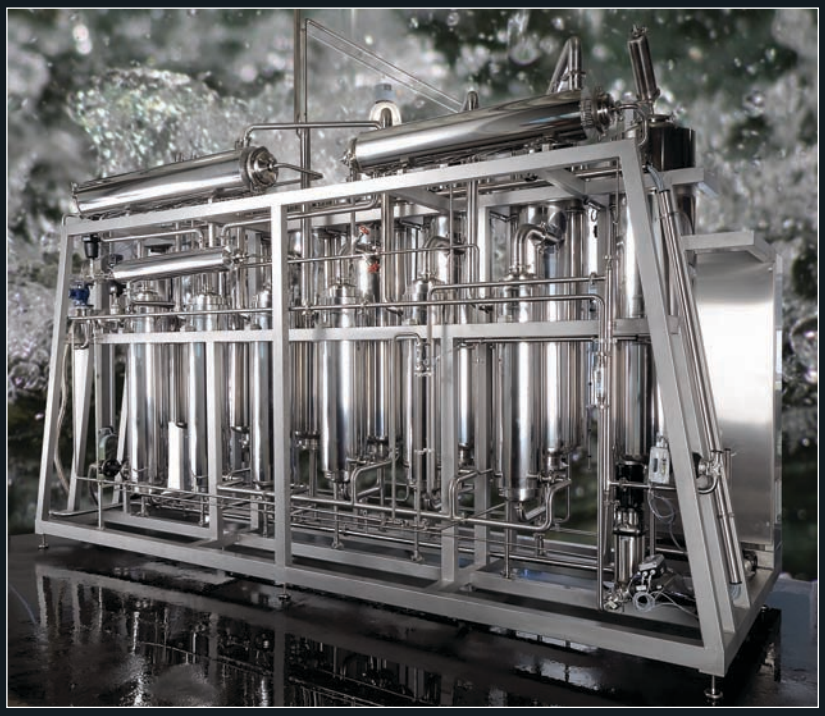
Conclusion

The planning of this streamlined plant began in March 2006. Only 25 months later, hameln pharma was able to put a highly innovative and flexible production facility into operation. The layout of the facility is tailored to optimally support the production process, maximizing efficiency. To achieve this, all process steps were simulated in advance and defined so that each movement can be completed efficiently in a standardized manner.

With an eye on future development, the new production building is designed so that it can be flexibly adapted to future requirements and needs with regard to both space and technology.

Intelligent solution including:

Antirouging and energy recovery !



Letzner Pharmawasseraufbereitung GmbH
Robert-Koch-Str. 1 · D-42499 Hückeswagen · Tel: +49 (0) 21 92/83 88 3 · Fax: +49 (0) 21 92/92 17 33 · www.letzner.de

2009
Facility of the Year Awards
CATEGORY WINNER
Operational Excellence -Supplier

LETZNER
Pharmawasseraufbereitung

Orchid Chemicals & Pharmaceuticals

A Model Facility for the Pharmaceutical Industry in the Region

Introduction

When Orchid Chemicals & Pharmaceuticals constructed their new **Carbapenem Production Facility** in Aurangabad, India, they also created a facility that would serve as a beacon for others in the region.

Winner of the **2009 Facility of the Year Award for Regional Excellence**, Orchid's new facility houses one of the first cGMP operational systems for bulk API handling in India and features a high degree of automation and innovative energy conservation measures – concepts that contribute to their goal to produce quality products in a safe, consistent, and environmentally sound manner.

Making Room for the Future

Based in Chennai (Madras), India, Orchid Chemicals & Pharmaceuticals Ltd. manufactures and sells APIs with a niche position in cephalosporin antibiotics. According to Orchid, they are the largest cephalosporin manufacturer and exporter from India.

To accommodate the growing number of development products and promote the application of new technologies, Orchid decided to create a new facility at their existing manufacturing site in Aurangabad, India, with modern and flexible cGMP aspects to manufacture internationally acceptable products.

A central goal of Orchid was to integrate all major intermediates and finished API product facilities with safe working areas and promote optimal communication and seamless cooperation across the relevant disciplines. They wanted an independent, safe facility with maximum flexibility for the handling of a broad diversity of product types and batch sizes. Most challenging was safeguarding all operations in a multi-product facility and avoiding cross-contamination.

Orchid's solution for this variety of requirements was to construct a new facility with relevant separate buildings. The new facility contains state-of-the-art process equipment, laboratories, cGMP facilities, and office areas. Both the building layout and concept for technical support systems allow easy adoption to future needs and the implementation of new technologies.

Orchid Chemicals & Pharmaceuticals

Category Winner – Regional Excellence

Project: Carbapenem Production Facilities
Location: Aurangabad, India
Size: 107,642 sq. ft. (10,000 sq. m.)
Total Project Cost: $35.72 million
Duration of Construction: 14.5 months

The Carbapenem Blueprint

The new facility is located in Aurangabad, India, 400 kilometers away from Mumbai, in an industrial zone where companies manufacture electronic devises, automobiles, chemicals, and pharmaceuticals.

Orchid's Aurangabad site includes three major manufacturing sections for: 1. non-penicillin non-cephalosporin APIs, 2. penicillin APIs, and 3. carbapenem APIs.

The Carbapenem Production Facility project consists of four major well-integrated production blocks, (Intermediate/API/Sterile/Hydrogenation) each with dedicated service and production areas. All critical operations are contained in cleanrooms and advanced technical systems are used in all sections of manufacturing.

The Carbapenem Production Facility is divided as explained below:

- Intermediate block – Key Starting Material (KSM) is charged here and intermediates are manufactured.
- API block – Intermediates are used in the API plant to produce non-sterile product.
- Hydrogenation block – The reactor and associated systems are designed to carry out high pressure reaction. The equipment is designed for 35 kg/cm2 design pressure. The high speed agitator is designed for gas induction and is magnetically coupled with drive to avoid any leakage during high pressure reaction.

The reactor has a catalyst filtration system, sampling system, hydrogen and nitrogen gas manifold. The reactor is

Horizontal scrubbing system.

installed in a separate bay surrounded by a blast proof concrete wall toward the plant area and open to the atmosphere on the other side to avoid the effect of an accident. The reactor is equipped with all safety systems, such as a safety valve, rupture disc, knock out pot, instrumentation, and safety interlocks. Seven layers of safety are provided to ensure the highest level of safety for the asset, person, and product. Fire doors are also provided.

The majority of the plant is open from all sides to facilitate easy dispersion of hydrogen gas in case of any leakage and to minimize an explosion effect due to a confined area in case of an emergency. This layout also provides a better working environment for personnel.

- Sterile block – non-sterile products are taken to this facility to produce sterile APIs.
- Solvent recovery plant including tank farm
- Effluent treatment block
- Fire hydrant water tank and pumping station
- Infrastructure facilities such as utilities, transformer

Conserving Energy and Reducing Costs

Orchid took several measures to conserve energy and reduce manufacturing costs during facility design, including the following:

Vacuum System

The facility features a dry vacuum system instead of a conventional vacuum system to maintain a consistent level of vacuum throughout the process, enhance process safety and productivity, and to avoid the use of water resources, sustaining a clean environment. Pumps are designed with PFA coating to work with any corrosive fluid. All supportive systems, such as instrumentation/electrical/mechanical, are developed and installed in-house to improve process and environmental safety. The vacuum level is monitored constantly through the DCS, assuring almost no backflow in case of a power failure or mechanical breakdown of the system. A series of filters are provided to save the environment.

Horizontal Scrubbing System

The facility also features horizontal scrubbing systems instead of conventional vertical scrubbing systems. The result is a reduction in electrical consumption by 30%, a reduction of load on the floor by 50%, and better efficiency of scrubbing because of an effective cross flow pattern. According to Orchid, this type of system, designed and installed by Orchid, has become a boon for the pharmaceutical industry to use such a system to handle a huge quantity of lean gases with less investment and operating cost.

Ultrasonic Technology for Crystallization Process

Orchid uses ultrasonic energy for the crystallization of their complex products. Ultrasonic wave is a form of energy which when applied, allows chemical reactions to take place in its presence. The ultrasound produces cavitations in the liquid, which effectively act like millions of micro

Continued on page 34.

stirrers, increasing the effective surface area. The cavitations produced also increase local pressure and local temperature by several hundred degrees in the vicinity of the bubble collapse. This not only reduces reaction time, but also helps carry out many reactions which normally require high temperature and pressure. Using this technology, crystallization time is reduced from 40 to 4.5 hours, and results in better product quality. Crystallization time reduction is variable based on product.

Secondary Steam Generation from Evaporator System

Orchid uses an evaporation system for the treatment of high pollutant effluent generated from various processes. The secondary steam generated from the evaporation system is utilized as low pressure steam in manufacturing areas. This has saved much thermal energy (reduced load on steam boiler, hence reduction in furnace oil consumption) and related emissions.

Agitated Filter Dryer

To overcome the inability to recover the product "heel" left from using traditional filter/dryers and pan dryers, Orchid installed an agitated Nustche Filter Dryer with a gas knife system. This innovative technique was first implemented and commissioned at Orchid's new facility. The gas knife system includes a series of nitrogen nozzles located on one side of the S-blade agitator. Nitrogen is delivered down through the shaft and ported to the nitrogen nozzles. A specially designed rotary joint and shaft allows nitrogen to be ported to the agitator hub.

Why Our Project Should Win

The following is an excerpt from Orchid Chemicals & Pharmaceuticals' submission, stating, in their own words, the top reasons why their project should win the 2009 Facility of the Year Award:

- Building concept – being a multiproduct facility, it consists of physically well separated manufacturing blocks, each having its own dedicated service area and production area. A strategy was devised to guarantee the shortest supply and disposal routes. All critical operations are as much as possible contained in cleanrooms and advanced technical systems are used in all sections of manufacturing.
- Technical concept – HVAC units with separate technical areas for repair and maintenance allow cost effective and sustainable building operations. The degree of automation is completely high novel. The facility features operational ease, improved safety and process integrity, consistency in production through automation. Continuous monitoring of process parameters, control, and measuring of parameters produce consistent high quality products.
- Equipment innovation and systems – fully contained powder handling and processing equipments were developed and implemented. We believe this is the first cGMP operational system for bulk API handling in India. Automated SIP sterilization system for sterile process equipments were developed, implemented, and successfully validated. Agitated Nutsche Filter Dryer has gas knife provision and hydraulically operated locking arrangements. Equipment planning was done to increase productivity if required in the future, and flexibility was designed in to accommodate future needs, if any.
- Commitment toward environment and safety – human safety is a core organizational value and it is a condition of employment for each Orchidian. Orchid safety systems are strengthened by DuPont and Orchid aims to become one of the world's safest organizations in the next two years. We have a "zero discharge facility." This concept is a dream for many industries of our kind in India. We are treated as a role model in environmental safety by various organizations and local regulatory agencies, increasing our social responsibility and boosting our confidence to innovate new systems. All new processes underwent a risk assessment study by competent persons before commercial production.
- Energy efficient system – Orchid has always strived hard in the field of energy conservation. Several measures to conserve energy and to reduce associated costs were taken during facility design:
  - High level automation to precisely control process parameters, e.g., vacuum distillation, batch distillation, batch monitoring, automation of process equipments like the reactor, centrifuge, driers, HVAC units, utilities, etc.
  - 30% less power consumption by horizontal scrubbing system than conventional scrubbing system for the same application
  - Less power consumption by dry vacuum systems than conventional system
  - Installation of energy efficient multistage evaporator with least steam (0.1 kg/kg of effluent) and lowest power consumption
  - Installation of energy efficient water cooled refrigeration systems
  - Installation of energy efficient compact fluorescent lamps
  - Effective systems such as automated nitrogen blanketing for centrifuges, flash steam recovery, secondary steam generation from evaporator, etc., to save loss of utilities, which saves energy
  - Designing optimum sizes of cleanrooms by selecting innovated process equipments like peeler centrifuges, combination of operations in one unit, etc.
  - Providing modular supportive systems as per requirements than centralized common systems, hence utilization as per demand to save energy
  - Dedicated energy conservation team on site

Notes from the Judging Panel – What Impressed Them

Their timeline and safety record were very good, especially considering the location. This project was well-executed and the first to use certain technologies in India. They brought in a lot of technology in a place where it's difficult to do so. The challenges and how they overcame them are appreciated. They were able to increase their productivity all with local expertise.

This mechanism provides an effective removal of product heel and resulting benefits, such as increase in productivity, less manual handling of sterile product, drastic reduction in leftover quantity of product.

Nitrogen Blanketing System for Centrifuges

Orchid and their supplier together developed a nitrogen blanketing system for centrifuges. This system consists of a series of pressure reducing valves to obtain required pressure and back pressure regulated valves at vent to hold specified nitrogen inside the centrifuge basket for inertisation purposes. Pressure switches are provided to monitor the nitrogen pressures which are interlinked to a control system.

This blanketing system provides the following advantages:

- Ensure proper inert atmosphere in the centrifuge for safety.
- Avoids the loss of nitrogen, thereby reducing nitrogen consumption by 90%, saving much energy.
- Since the system is closed, it avoids solvent loss to the atmosphere thereby saving the environment from pollution.
- Ensures consistent product quality and less human exposure and operator interference.

Key Project Participants

Architect: R.V. Dalvi & Associates, Mumbai – Maharashtra, India
Designer/Architect/Engineer: Projects Dept., Orchid Chemicals & Pharmaceuticals, Aurangabad, India
Construction Manager: Projects Dept., Orchid Chemicals & Pharmaceuticals, Aurangabad, India
Main/General Contractor: Hexagon Constructions, Hyderabad – Andhra Pradesh, India
Piping Subcontractor: Metro Engineers, Ankleshwar – Gujarat, India
HVAC Subcontractors:
- Aarco Engineering Projects Pvt. Ltd., Mumbai – Maharashtra, India
- M&W Zander Facility Engineering, Mumbai – Maharashtra, India

Automation and Control Suppliers:
- Emerson Process Management, Mumbai – Maharashtra, India
- Honeywell Automation India, Pune, India

Major Equipment Suppliers:
- Apurva Buildcare Technologies, Mumbai – Maharashtra, India
- Fedegari Autoclavi SpA, Albuzzano, Italy
- Gardner Denver Schopfheim GmbH, Germany
- Integrated Cleanroom Technologies, Hyderabad – Andhra Pradesh, India *(See ad on page 33)*
- JR Fibreglass Industries Pvt. Ltd., Mumbai – Maharashtra, India
- Kleen Enviro Systems Pvt. Ltd., Pune – Maharashtra, India
- MRC Systems FZE, Dubai, United Arab Emirates
- Novindustra AG, Sissach, Switzerland
- Rosenmund VTA AG, Liestal, Switzerland
- Sartorius India Group, Bangalore – Karnataka, India
- Stilmas, Milano, Italy
- TECNinox Srl, Parma, Italy

Automated operations in cleanrooms to avoid product exposure.

High Level of Automation

The new facility features a high level of automation to precisely control process parameters, e.g., vacuum distillation, batch distillation, batch monitoring, and automation of process equipment, such as the reactor, centrifuge, driers, and utilities. All equipment is automated with a Distributed Control System (DCS) and Programmable Logical Controllers (PLCs) – technological tools commonly available on the market, but unique in API manufacturing, according to Orchid.

Orchid claims to be the first Indian bulk API manufacturer to implement a DCS for batch process. Reactors' utilities such as air, -10 Deg, -40 Deg, +10 Deg, and nitrogen are controlled by a DCS to maintain accurate process parameters. In addition, some of the reactors are equipped with Variable Frequency Drive (VFD) as per application based on process requirements.

For Orchid, a DCS not only offers operational ease, but also helps reduce batch time, and in turn, helps conserve energy.

Conclusion

When Orchid Chemicals & Pharmaceuticals began to create a new facility with modern and flexible cGMP aspects to manufacture internationally acceptable products, its staff knew that new technologies would be necessary; and they met the bold challenge successfully. With the high degree of facility automation, innovative energy conservation measures, and one of the first cGMP operational systems for bulk API handling in India, Orchid has become a model for other organizations building facilities in the region.

Roche Pharma Biotech Production Basel

Skillful Orchestration of a Complex Project

Introduction

To provide additional production capacity for the API of Avastin®, a successful new treatment medication in the fight against cancer, Roche Pharma Biotech Production Basel built the **MAB Building 95** in Basel, Switzerland.

Winner of the **2009 Facility of the Year Award for Project Execution**, this ultra fast track project was delivered in the middle of a busy residential area of Basel. The small and unique footprint of this Monoclonal Anti Bodies (MAB) facility and complex construction site logistics tested the ingenuity of the project team at every turn.

Center of a Transformation

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. At its headquarters, Roche operates a second European Center of Excellence for Biotechnology, in parallel to the Biologics IV center in Penzberg, Germany – a project that won the 2008 Facility of the Year Award for Project Execution.

The Basel site is being transformed from its traditional chemicals and pharmaceuticals production background to a center of excellence for biologics and pharmaceuticals. Roche representatives say the MAB 95 building is the nucleus for this future.

Erected on the plot of a former chemical production plant, the new building stands 40 meters tall with eight floors above ground and two floors underground. The multiproduct facility allows simultaneous production of two different products. It comprises 6 × 12.5 m^3 fermentation capacity plus two down stream processing lines for purification, and associated utilities, laboratories, and offices.

Construction Outside of the Box

The confines of the site – in a residential area in the middle of Basel city – restricted the size of the construction plot to 60 by 30 meters with no available lay-down area. Construction staff occupied a project office located on an elevated platform over the main public roadway.

Placing a vessel in the pit under the future main entrance.

To reduce congestion in and around the already tight project site, cutting-edge communication technology was applied whenever possible, in the day-to-day running of the project. Extensive use was made of video conferencing, documentation was exchanged via the Internet prior to joint reviews, site access was restricted to key personnel, and all project participants were encouraged to conduct as much communication as possible through electronic media. This allowed a large reduction in travel time and cost.

Space restrictions forced the project team to develop a "just in time" logistics program for both equipment manufacturing and site logistics.

Key elements of this approach to a biotech project were:

- The complete 100% 3D CAD modeling of process and utility pipe work
- The remote, off-site workshop, delivering "just in time" manufactured equipment and piping spools built precisely to the 3D CAD isometric drawings
- A very detailed construction schedule, broken down to daily delivery and work packages with aligned progress monitoring
- The extensive pre-commissioning FAT program at supplier's workshop
- Full integration of suppliers into team scheduling, synchronized timing, and delivery routes

A Vertical Submarine

The confines of the site forced the project team to take a new approach toward the building concept and layout, often described

Continued on page 38.

Roche Pharma Biotech Production Basel

Category Winner – Project Execution

Project: MAB Building 95
Location: Basel, Switzerland
Size: 209,896 sq. ft. (19,500 sq. m.)
Total Project Cost: $370 million
Duration of Construction: 19 months

Teamwork is the key to success.

And a great way to win awards.

Linde-KCA-Dresden congratulates Roche on winning the Facility of the Year Award 2009 for its new MAB facility in Basel! As the main contractor for the engineering of the plant, Linde-KCA-Dresden is honored to have been involved in the successful design and execution of this highly complex project.

Linde-KCA-Dresden serves clients from its main office in Dresden, the office for the Basel region in Lörrach and further offices in many countries around the world, including Russia, India, the UAE, Saudia Arabia, the USA, Brazil and China.

Linde-KCA-Dresden is a world-leading company in the planning and construction of biotechnological, pharmaceutical, chemical and gas plants. Our biotechnological/pharmaceutical spectrum includes plants for:

- → Pharmaceutical (Red) Biotechnology
- → Chemical active pharmaceutical ingredients
- → Fractionation of blood plasma
- → Pharmaceutical finished dosage forms
- → Industrial (White) Biotechnology
- → Fine chemicals
- → Food additives

Linde-KCA-Dresden GmbH
Bodenbacher Strasse 80, 01277 Dresden, Germany
Phone +49.(0)3 51.250-35 12, Fax +49.(0)3 51.250-48 00, lkca.biotech@linde-kca.com, www.linde-kca.com

as a vertical submarine.

The production process clearly dictated equipment arrangement which the architecture had to balance against the overall aesthetics of the building and its environment.

Utilizing a top down process flow resulted in the tank farm with all media and buffer tanks located on the second top floor. This makes MAB Building 95 the only production building with liquid storage 35 m above ground. This unique layout, providing liquid flow under gravity (with support from pressurized nitrogen when necessary) works well and saved many pumps – beneficial for the facility's sustainability, investment costs, and maintenance effort and costs, said representatives from Roche.

Strategy through Scheduling

Since the facility had to be arranged vertically and all systems are fully integrated (piping as well as automation), the normal option of sequential completion proved to be too slow when modeled in the schedule. This forced the project team to develop the strategy and tactics necessary to complete the whole facility as a single entity, i.e., work on everything in parallel. This extremely aggressive schedule dominated the project execution strategy.

High emphasis was placed on very detailed planning and scheduling of tasks. Great attention was focused on weekly progress reviews where the achieved physical progress for all disciplines was audited and corrective actions were agreed upon if any schedule slippage was identified. This meticulous planning, scheduling, and execution of the plan was another critical success factor of the ultra fast track project management methodology.

The resources and tools required to plan at this depth were provided in all phases of the project. A primary focus for the project team was the synchronization of the interfaces between phases. This assured seamless workflow not only in the distinct project phases, but also through these interface periods. This removed the productivity reduction often seen during funding period activities when a project team is focused on securing funding for the next project phase. These techniques produced the following results:

- The first DCS – controlled fermentation run (October 2006) was running in the installed equipment 33 months after the start of concept design.
- Handover of the building (May 2007) was six weeks ahead of the original ultra fast track schedule.

To achieve this, many activities were run in parallel and multiple acceleration programs were employed:

- After the project start in July 2004, the building's basic design was accelerated to apply earlier for a construction permit, typically a lengthy process due to the site location in a residential zone.
- Demolition of existing building started immediately with excavation work starting two months later.

Continued on page 40.

Bayer AG
Pfizer
Lek Pharmaceuticals
GlaxoSmith Kline
Smithkline Beecham Pharmaceuticals
BRI
BASF AG
Interbio
Sandoz
ARC International
Eden-Waren
TMI
Miles, Inc.
Biotechnikum
EuroCetus
Sclavo SpA
Pasteur Merieux Connaught
Gist-Brocades
Südzucker AG
Lonza AG
Genzyme Biochemicals
Lignozym
EBEWE Pharma GmbH
Lonza Biotec s.r.o.
AKZO Intervet International BV
Amgen, Inc.
Ciba-Geigy
Antibioticos
Werthenstein Chemie AG
Bio-Intermediair BV
Lederle, Inc.
Shanghai United Institute of Cell Biology
Rauch Fruchtsäfte GmbH & Co
Bio-Intermediair, Inc.
Fluka
Pharmaplan Deutschland GmbH
Medarex, Inc.
Wyeth Lederle
Snamprogetti Biotecnologie
Instituto Nacional de Higiene
Cerestar Deutschland GmbH
Astra Zenaca
Novartis Pharma AG
Tecnogen S.C.p.A.
LG Chem
Universiti Teknologi Malaysia
Sanofi-Aventis
DSM Biologics
Biotechnology General
Acambis, Inc.
Allergan Pharmaceuticals, Inc.
Strathmann Biotech
Wockhardt Ltd.
Kyowa Hakko Kogyo Co. Ltd.
Laboratorios Hipra, S.A.
Regeneron Pharmaceuticals, Inc.
Avecia Ltd.
Laboratoires Serono SA
Cerbios-Pharma SA
GPO
Biovitrum AB
BT Biotech Pharmaceuticals Co. Ltd.
CP Guojian Pharmaceutical Co. Ltd.
Celltrion, Inc.
Dongbao Enterprise Group Co. Ltd.
Suzhou Landing Biopharmaceutical Co. Ltd.
Zhejiang Hisun Pharmaceutical Co. Ltd.
Daiichi Suntory Pharma Co. Ltd.
Dr. Reddy's Laboratories Ltd.
Serum Insitute of India Ltd.
Center of Molecular Immunology
Phyton Biotech GmbH
Panacea Biotec Ltd.
Sacco S.r.l.
Novo Nordisk A/S
Allergopharma Joachim Ganzer KG
Rentschler Biotechnologie GmbH
F. Hoffmann-La Roche
Serono France S.A.
Chengdu Institute of Biological Products
China Biotech Wuhan Institute of Biological Products

Bio XXL

Bioengineering AG – large-scale bioreactor projects.

Congratulations to Roche, the Facility of the Year Award Winner for Project Execution!

We are proud to be part of it!

BIOENGINEERING

Bioengineering AG, 8636 Wald, Switzerland
Tel. +41 (0)55 256 81 11, Fax +41 (0)55 256 82 56
Bioengineering, Inc., Waltham, MA 02451, USA
info@bioengineering.ch, www.bioengineering.ch

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 2009 Facility of the Year Award:

- Exemplary project management and leadership, excellence in project procurement, expediting, and quality control
  - Empowering and integrating the whole project team of service providers, suppliers, trade contractors, architects, designers, engineers, and Roche
  - Integration of 24 different nationalities and languages, recruited Europe wide, into a unified, motivated team
  - Great team-spirit and outstanding focus on ultimate project goal
  - Implementation of innovative design and execution strategies as well as novel project management methodologies to achieve ambitious project goals
  - Sophisticated expediting including extensive progress and quality control at the suppliers' workshops (also for the automation package) to ensure timely delivery of high quality packages
  - "Just in time" delivery of equipment and materials to the construction site in pre-determined time slots
- Excellence in execution of an Ultra Fast Track project
  - Excellent task planning and resource management allowing seamless workflow and motivating the workforce to increase effort
  - Delivering a high quality, architecturally unique but space constrained facility six weeks ahead of a fast track schedule
  - 100% tested functionality (process, building, automation) and qualification reports approved at the time of handover
  - Project 9% below cost budget (which had no provisions for fast track actions)
- Excellence in facility integration
  - Unique as being the only biotech production facility with vertical layout and having a tank farm on top, making most possible use of gravity flow
  - Unique in combining the functionality and requirements of a biotech production facility with inner-city, unique, and state-of-the-art architecture with full glass curtain wall façade
- A true 100% 3D CAD Building Information Model (BIM) model and a unique approach of integration of the modeling with the project schedule
  - Each item in the facility 3D CAD model was linked to an activity in the project schedule.
- Excellence in construction management
  - Very early integration of CM into project team, working on constructability analysis and administering trade contracting
  - Establish construction site with no usable space on the ground
  - Establishing highly sophisticated construction schedule, synchronizing interfaces to design and engineering, equipment and materials delivery, spool piece pre-manufacturing and coordinating the trades on site
  - Organize and coordinate trades and workforce on construction site (at peak time 500 workers) to assure uninterrupted workflow and under the pressure of constant competition for space to work
  - Daily physical progress monitoring with weekly reporting

- Procurement for the building shell trade contractor and the other major building trades started immediately to facilitate an early construction start.
- An extensive procurement program based on competitive bidding was coordinated with the Biologics IV project in Penzberg.
- Exhaustive acceleration program during detail design mainly for piping isometrics, HVAC ducting, and electrical wiring supported an early start of mechanical installations.
- A sophisticated building construction schedule secured six weeks for a basement floor and three weeks for a super structure floor.
- Infrastructure mechanical installation in the basement began while the concrete for the above ground floors had yet to be poured.
- Acceleration program for piping and HVAC installation
- Since all mechanical systems were interconnected, commissioning, start-up, and qualification of utilities and process units were performed in sequence.
- The start-up team was staffed as much as possible with future production crews.
- Introduction of technical batches (non-qualified runs under production conditions) during start-up allowed for early detection of flaws and reduced time for remedial work.

Teamwork at its Best

High ethical standards were set for project management and leadership. The primary areas of focus were on:

- teamwork and team motivation
- engagement and empowerment of team members
- building an environment of integrity and trust in the team
- working together with contractors and suppliers in a spirit of open team partnership

"No blame, fix the problem," was an overriding principle that led Roche's integrated project team. The contracting strategy based on reimbursable cost contracts with prime contractors and incentive schemes supported this environment.

A Roche philosophy is to take ownership and actively manage project risks instead of delegating them. In this project, the

Concludes on page 42.

sartorius stedim biotech

Congratulations to Roche

Winner of the "Facility of the Year" Category Award for Project Execution

As a long-term project partner and key supplier to Roche, we would like to congratulate you on achieving this splendid award.

We at Sartorius Stedim Biotech take pride in working with our customers to achieve one common goal: the best and most innovative solution for their process.

There's more to it than just supplying products. We work side by side with our partners right from the early development stages and on up along the entire process chain. We understand that every process is unique and calls for a custom-tailored solution.

Take our efficient virus clearance concept, for instance. Our orthogonal platform comprises technologies like:

- UVivatec® for virus inactivation by exposure to UV-C light
- Virosart® nanofilters for virus removal through size exclusion
- Sartobind® for virus adsorption by membrane chromatography

Find the winner: uniquely tailored solutions throughout your entire process.

Sartorius Stedim Biotech
USA +1.800.368.7178
Europe +49.551.308.0

www.sartorius-stedim.com
turning science into solutions

Notes from the Judging Panel – What Impressed Them

This is the sister project to last year's winning project in the same category, but this one is in Basel. It was well coordinated for such a complex project in a very busy area. It sits right in the middle of a residential area with no onsite storage. They had to truck in materials over 10 miles. It is a vertical MAB facility, which is unique in the industry. Because of lack of space, an elevated office above Basel's street traffic was constructed for project management staff. Very innovative for the space they had to work with.

benefits of this philosophy were proven. Support was provided by all parts of the Roche organization and their experts as critical issues surfaced or interfaces were to be managed. The project was able to call for additional support anytime and was given priority. Peer reviews for design and project management were carried out by colleagues from the worldwide Roche engineering network.

Much effort was invested in project definition (e.g., user requirements) and project execution planning during project initiation, where organizational setup, roles, responsibilities, and execution strategies were defined to support achievement of project goals. Best practice engineering processes were applied in all disciplines.

Current project control best practices are standard processes in Roche and are successfully applied in all Roche projects. Special efforts were made on controlling the scheduling of critical path items and on the enabling of early commissioning of 100% completed systems. Together with focused acceleration programs, these were the most important planning measures for schedule reduction.

Sophisticated resource planning including the application of different shift-models ensured staffing levels, avoidance of work overload, especially on the user side and automation, and enabled recruitment of the plant operatives to be complete early in the project.

Since the production group had to be established from scratch by recruiting knowledgeable operators, some of whom were new to biotechnology and without specific experience, intensive training programs were established. In cooperation with the Zürich College in Wädenswil, training was provided in theoretical background, and experience with large scale production was shared by colleagues from Roche Penzberg and Genentech.

Test runs under production conditions.

Key Project Participants

Owner: Roche Biotech Basel
Engineering: Roche Pharma Global Engineering and Roche Basel site Engineering
Designer/Architect/Engineer: Herzog & deMeuron, Basel, Switzerland
Construction Manager: Bovis Lend Lease, Munich, Germany (liquidated)
Main/General Contractor: Linde – KCA, Dresden, Germany *(See ad on page 37)*
Piping Subcontractor: MCE, Salzburg, Austria
HVAC Subcontractor: Axima, Basel, Switzerland
Automation and Control Supplier: Siemens Swiss, Zürich, Switzerland
Major Equipment Suppliers:

- ABB Secheron, Baden-Dättwil, Switzerland
- ABB Swiss, Baden-Dättwil, Switzerland
- Alfa Laval, Tumba, Sweden
- Apaco, Grellingen, Switzerland
- Balzaretti & Frey, Udligenswil, Switzerland
- Bioengineering, Wald, Switzerland *(See ad on page 39)*
- Calorifer, Elgg, Switzerland
- GEA Dissel, Niedersachsen, Germany
- Gecma, Kerpen, Germany
- Gemü, Ingelfingen, Germany *(See ad on page 38)*
- Glatt, Wiesbaden, Germany
- Karasek, Gloggnitz-Stuppach, Austria
- Mavag, Neunkirch, Switzerland
- Millipore, Molsheim, France
- Pall, Dreieich, Germany
- Pharmatec, Wiesbaden, Germany
- Ramseyer, Flamatt, Switzerland
- Renggli, Rotkreuz, Switzerland
- Sartorius, Goettingen, Germany *(See ad on page 41)*
- Sauter, Basel, Switzerland
- Stedim, Fribourg, Switzerland
- Zeta, Graz, Austria

Conclusion

Delivering an ultra fast track biotechnology facility is a huge challenge for a project manager by itself. To combine this challenge with the added dimension of a restricted site footprint, city center construction logistics, residential neighborhood, and a star architect with strong views on design and material selection called for innovative project management techniques. The project team at Roche Pharma Biotech Production Basel shined while delivering an ultra fast-track, completely unique, vertical MAB facility. Every aspect of this project had to be flawlessly executed to accommodate the many challenges of the site, location, and facility design. The result was a skillfully orchestrated project delivered six weeks ahead of an already aggressive schedule.

Need Knowledge? No Budget for Travel?

No Problem.

ISPE Online Learning delivers critical knowledge
and training to you anytime, anywhere,
and at a price to fit your budget.

Go to www.ISPE.org/onlinelearning
for a complete list of Web-based learning opportunities
or call ISPE Member Services at tel: +1-813-960-2105.

ISPE
ENGINEERING
PHARMACEUTICAL
INNOVATION

GlaxoSmithKline Manufacturing

Advancing the Aseptic Powder Filling Process

Introduction

GlaxoSmithKline's (GSK) Italian operations have been based in Verona, Italy since 1932 and the region has become a center of excellence for the production of sterile cephalosporin powder products.

Knowing that the greatest risk to sterile processes is the possibility of people contaminating the product, GSK decided to create the necessary conditions for its production process to take place without people being present in critical areas. The decision resulted in the revamping of their Verona **Aseptic Powder Filling Facility 4** – the **2009 Facility of the Year Award Honorable Mention**.

Filling the Need for a Better Process

At GSK's Verona site, production of bulk sterile vials is carried out in a dedicated building, designed to work as four fully independent filling lines. In each line, the vials are washed in an automatic washing machine and thermally treated by dry heat in a unidirectional flow depyrogenation tunnel. The sterile vials are automatically filled and plugged inside the cleanroom. The closed vials are transported by a belt protected by a unidirectional air flow toward the over-sealing stations located adjacent to the filling room. After application of the over-seal, the vials move on to the inspection station where each vial is inspected visually and laser marked on the neck with the identification data. After marking, the vials are packed in a cardboard tray, ready for further packing operations.

In 2006, GSK's production line number four was radically restructured and modernized. On the basis of the experience gained during previous projects, Verona tried to define and implement the best possible application of the concept of Restricted Access Barrier System (RABS) to protect the vials being filled with antibiotic powder. Application of RABS avoids the operator coming into direct contact with critical areas of the process.

The aseptic filling of powder requires a challenging approach, compared to the aseptic filling of liquid. While RABS and CIP/SIP to point of fill is readily applicable to the liquid filling process, the technology associated with powder filling is rather outdated and requires significant manual aseptic assembling of the equipment components. Powder filling is a completely different matter, involving frequent format changes, consistent ingress of materials (i.e., plugs, API), and a facility with traditional cleanroom design and services. These considerations make isolator technology simply not affordable, said GSK representatives.

Aseptic powder filling facility.

GSK needed a process that would assure a proper protection for set-up, routine operations, and materials transfer, while maintaining all of the experience gained in traditional cleanrooms. The Aseptic Powder Filling Facility 4 would be the project that would satisfy their protection needs and consequently take aseptic production to a higher level.

Creating an Innovative Template

The target of the project was to implement technological and operating solutions to assure, in the long term, a state-of-the-art process suitable for the antibiotic business as an alternative to isolator technology. This included an innovative approach to equipment, environment, handling, and storage that is unique in the industry. GSK effectively created a template for aseptic powder filling and designed several elements specifically for this project to make the process reliable and repeatable.

The revamp of GSK's Aseptic Powder Filling Facility 4 was completed in March 2007. The main features of the new facility are:

- Product contact machine parts pre-assembled before sterilization

Concludes on page 46.

GlaxoSmithKline Manufacturing

Honorable Mention

Project: Revamping of Aseptic Powder Filling Facility 4
Location: Verona, Italy
Size: 150,695 sq. ft. (14,000 sq. m.) – Filling Facility Floor Area
Total Project Cost: $6.3 million
Duration of Construction: 4 months

Genetically modified technology

MAC • Modular Aseptic Compact System

Incorporating a vial washer, depyrogenating tunnel, filling, stoppering and alu-capping **into a single compact integrated system** for liquid, lyo or powder, with RABS or Isolator **in 20% of the space**.

IMA LIFE S.r.l.
mktg.filling@ima.it • www.ima.it

IMA NORTH AMERICA, INC.
sales@imausa.net • www.imanorthamerica.com • www.ima.it

IMA LIFE
Aseptic Processing & Filling Solutions

VIAL LOADING • WASHING • DEPYROGENATING • FILLING • FREEZE-DRYING • STOPPERING • CAPPING

Notes from the Judging Panel – What Impressed Them

Very innovative technologies for handling powder. They overcame a lot of challenges with aseptic powder filling in a really unique way. They found a way to template the process so that they can repeat it the same way every time, which is very practical and reliable. They designed several elements specifically for this project to make the process repeatable. Haven't seen anything like this in the industry.

- Semiautomatic setup completed using glove ports
- Grade A continuity
- Routine operations performed using glove ports
- Enhanced protection of operators from API
- Increased line performances
- In-line particle counting monitoring

As in the traditional cleanroom process, the production begins in the aseptic area with the preparation of the filling machine. To avoid manually assembling the numerous pre-sterilized components of the machine, exposing them to the risk of contamination, they are pre-assembled on a single plate before sterilization. The plate, with the pieces pre-connected and arranged in the definitive configuration, is supported by a special chassis enabling it to be transported and coupled to the machine. The chassis, complete with the plate and all the pre-assembled pieces, is sterilized in the autoclave as a single unit. Once sterilized, the parts in contact with the product, the components and closures, are transported to the point of use by means of a special trolley with protective barriers.

Today, each sterile component is assembled in the filling machine using automatic systems and devices. Assembly is completed without any direct contact between the operators and the sterilized components. The operator remains on the other side of the barrier, keeping him away from critical objects, thus improving the safety of the production.

To ensure sterility of sterile product contact parts, equipment, and closures while traveling from the autoclave to their point of use, a Barrier Protected Trolley (BPT) is used. The trolley has been designed to ensure that contained items have a constant flow of unidirectional grade A air sweeping over their surfaces and out from the cabinet without entrainment or entrapment of air from the external environment air under static and dynamic conditions. The BPT runs on rails, facilitating the operator on repeatable routes.

The project was developed by the GSK site engineering team, working in strong partnership with the supplier of the filling machine (IMA) for the modifications to the machine's core and assessing the innovative solution on protoypes.

Key Project Participants

Designer/Architect/Engineer: GSK Manufacturing Verona staff
Construction Manager: GSK Manufacturing Verona staff
HVAC Subcontractor: STERIL manufacturing division, Milano, Italy
Major Equipment Supplier: IMA Life, Bologna, Italy
(See ad on page 45)

Core of the aseptic area.

Conclusion

After the release in production, the continuous support of the site engineering team allowed an impressive performance improvement and the development of new solutions in material handling.

With talent, skill, and motivation from the Verona work group and supplier IMA, a step forward has been taken in guaranteeing the sterility of the aseptic powder filling process. The Verona factory is now able to provide patients with an even safer product.

Transfer on rails of the chassis at the end of the campaign (without BPT).

ISPE would like to thank the following companies for their generous advertising support which made this Supplement possible.

Advertiser's Index

The Facility of the Year Award is sponsored by:

ISPE
ENGINEERING PHARMACEUTICAL INNOVATION

INTERPHEX2009™
Conference & Exhibition

Pharmaceutical Processing

FACILITY OF THE YEAR SUPPLEMENT STAFF

Publications

Editor and Director of Publications
Gloria N. Hall

Publications Manager
Lynda D. Goldbach

Technical Writer
Rochelle Runas

Publications Coordinator
Amy Lecceardone

Sales

Director of International Sales
David J. Hall

Sales Coordinator
Valerie Adams

European Sales Manager
Christine Sainvil

Marketing Communications

Communications Manager
Marni Schribman

www.facilityoftheyear.org

2010

Facility of the Year Awards

Awarded by ISPE, INTERPHEX, Pharmaceutical Processing

Facility of the Year Awards
2010 Call for Entries

The Facility of the Year Awards are an annual program that recognizes state-of-the-art pharmaceutical manufacturing projects that utilize new and innovative technologies to both improve the quality of the project and to reduce the costs of producing high-quality medicines. The Awards program is unique because it provides a platform for the pharmaceutical manufacturing industry to showcase its new products and accomplishments in facility design, construction, and operation.

The program, its Category Winners, and the Facility of the Year Award Overall Winner will receive high-profile attention and media coverage from ISPE, INTERPHEX, and *Pharmaceutical Processing* magazine.

Belgium. Canada. France. Germany. India. Ireland. Italy. Japan. Singapore. Spain. Sweden. Switzerland. United Kingdom. United States.

Companies from around the world have already submitted their state-of-the-art facilities to participate in the Facility of the Year Awards program, and we'd love to hear from you. ISPE, INTERPHEX, and *Pharmaceutical Processing* magazine are looking to highlight projects that demonstrate global leadership by showcasing cutting-edge engineering, innovative new technology, or advanced applications of existing technology.

Don't let your company pass up this outstanding opportunity to showcase its new or renovated facility!

For additional information about the Awards program and submission procedures, visit www.facilityoftheyear.org.

ISPE
ENGINEERING PHARMACEUTICAL INNOVATION

INTERPHEX™

Pharmaceutical Processing

www.facilityoftheyear.org