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Facility of the Year Awards

OVERALL WINNER

2008
Facility of the Year Awards
OVERALL WINNER

Pfizer Manufacturing Deutschland GmbH

ENGINEERING PHARMACEUTICAL INNOVATION

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Overall Winner – 2008 Facility of the Year Award

Pfizer Manufacturing Deutschland GmbH

Containing a New Era in Pharmaceutical Manufacturing

by Rochelle Runas, ISPE Technical Writer

A few years ago Pfizer Manufacturing Deutschland GmbH in Illertissen, Germany began working on the answer to the question: Can we push a button once to start the process and several hours later – without any human intervention – receive film coated tablets?

The answer materialized in 2007 in the form of an elegant, futuristic facility housing one of the most intelligent pharmaceutical production plants in the industry. The facility, named the New Containment (NEWCON) Facility for Oral Solid Dosage, is this year's Overall Winner of the 2008 Facility of the Year Award.

NEWCON exterior view.

NEWCON turned unconventional processing concepts – including the single-room concept, high automation requiring no operator interface, and PAT applications – into a safe and efficient manufacturing reality for the production of the smoking cessation product Chantix®.

In an era where industry faces cost and time pressures and changing market demands, Facility of the Year Award judges viewed NEWCON's achievements as innovative, resourceful, and pioneering, not only in containment production, but in the entire field of pharmaceutical manufacturing.

Pfizer Manufacturing Deutschland GmbH

Overall Winner (and Category Winner in Process Innovation)

Project: New Containment Facility for Oral Solid Dosage (NEWCON)
Location: Illertissen, Germany
Architect: PhC PharmaConsult, Heidelberg
Consultant: PhC PharmaConsult, Heidelberg
Construction Manager/Project Manager: Hans Sägmüller, Pfizer Illertissen
Size: 83,958 sq. ft. (7,800 sq. m.)
Cost: US $55 million (39 million Euros)
Product: Chantix®/Champix®
Key Project Participants:

Axima	Glatt	Koppenhoefer and Partner
Comecer	IMA	Rotan
GE Fanuc	Imtech	Servolift
Gerteis		

A Market-Driven Decision

In 2005, Pfizer Manufacturing Deutschland GmbH in Illertissen, Germany was provided with a preliminary sales forecast projecting a rising demand for Chantix® (European product name: Champix®), a smoking cessation product with the active pharmaceutical ingredient varenicline, which helps adults quit smoking by reducing smoking cessation withdrawal symptoms and the craving for cigarettes.

Pfizer manufactures varenicline in Little Island, Ireland, and at the time was conducting secondary production (tablets) at Pfizer Illertissen's pilot containment facility, Illertissen Containment (ICON).

"It became crystal clear that our existing

pilot containment facility would not be in the position to support the lifecycle of this product and was never intended to," said Holger Weyhers, PhD, Director of Production, Pfizer Manufacturing Deutschland GmbH.

Driven by the urgent need for greater production capacity, in 2005, Pfizer Illertissen embarked on the design for the NEWCON project. Time pressure was further intensified by the successful launch of Chantix® in the US the following year, pushing up the project completion date by six months. Nevertheless, the 7,800 sq. m. facility was completed in late 2007 after a construction period of just 25 months.

Pioneers in Containment Manufacturing

Pfizer Illertissen, which specializes in the oral solid dosage form production of highly potent compounds involving complex containment requirements, was already breaking new ground in containment manufacturing at its ICON pilot facility.

During the first planning phase of ICON, Pfizer Illertissen was faced with a challenge that is increasing in frequency in the pharmaceutical industry: many newly discovered pharmaceutical actives from research are highly potent, requiring extraordinary measures to protect the production staff and the environment.

Instead of opting for the usual spatial isolation of individual process stages and using conventional, physically demanding protective suits with external supply, ICON designers developed a single-room concept in which all contained production equipment was located in a single high containment module and largely automated.

The safe inward and outward transportation of the substances and products are ensured by vacuum systems and split-valve containment technologies. Inside the production area, laser-controlled, driverless transport vehicles move the containers with the materials to the weighing and granulation area, to the tablet press, and to the coaters.

All process stages are controlled and monitored from a separate control center so that employees do not come into contact with any dust that might be generated during the tablet production run.

This novel containment concept was put into operation in ICON in 2003 and served as the prototype for the NEWCON project. "We already had established the design and operational principles for containment manufacturing," said Weyhers. "We simply kept what was good."

Lessons in Automation

While the initial focus of NEWCON's design was on operator safety, the road to that goal also led planners to improving the operational efficiency attained in ICON.

While largely automated, at ICON, the operator needs to trigger the next process sequence. "Operators need to go to their personal computer and program specific directions into the system," said Georg Bernhard, Director, Right-First-Time, Pfizer Global Manufacturing. "For example, 'pick up the bin from location A and bring it to location B.' Once that transfer is finalized, then you program in, 'mix for nine minutes, etc.'"

At NEWCON, the process is completely automated. "We had

Single containment module.

"Driven by the urgent need for greater production capacity, in 2005, Pfizer Illertissen embarked on the design for the NEWCON project.

...the 7,800 sq. m. facility was completed in late 2007 after a construction period of just 25 months."

AGV transport to a unit operation.

all the logic of the sequence," said Bernhard. "You push the button, everything starts on its own, and at the end you have the tablet. Operators supervise the entire process from a control center. This frees operators up from this kind of work."

One area is which automation did not work as well was in the weighing and dispensing of micronized API. "Micronized API causes problems with commercial off-the-shelf equipment," said Bernhard. "Maybe it needed to be coarse. But to build a solution would have taken too long. We tried feeders, different solutions, and in the end opted for a manual process for this part in NEWCON."

Notes from the Judging Panel – What Impressed Them

This project used the ICH concepts of Design Space as the basis for a unique approach to process innovation. PAT applications were installed at key process steps to support adaptive process control. A single containment module houses all process equipment for the production of the dosage form. All internal containment transport is handled by an automated laser AGV system. Material transport is also integrated into the AGV system. The installation has achieved a Design Exposure Limit that does not require the use of PPE, as the automation level is designed for no operator interface.

While automation was a significant aspect of the NEWCON project, Weyhers recommends not over-engineering. "Avoid being trapped in automation. I'm a fan of operators being able to intervene if they have to. If something goes wrong, you have the opportunity at least to switch to a manual mode. Otherwise, you're in deep trouble."

A dual operator interface was implemented with the main portion at the control center and a second interface at line in case of at worse events so that operators are in a position to do something directly with the equipment, said Weyhers.

Improvements in PAT

Process Analytical Technology (PAT) applications also were improved upon with the goal of aggressively moving toward real-time release for the product. "We are very proud of the PAT improvements," said Bernhard.

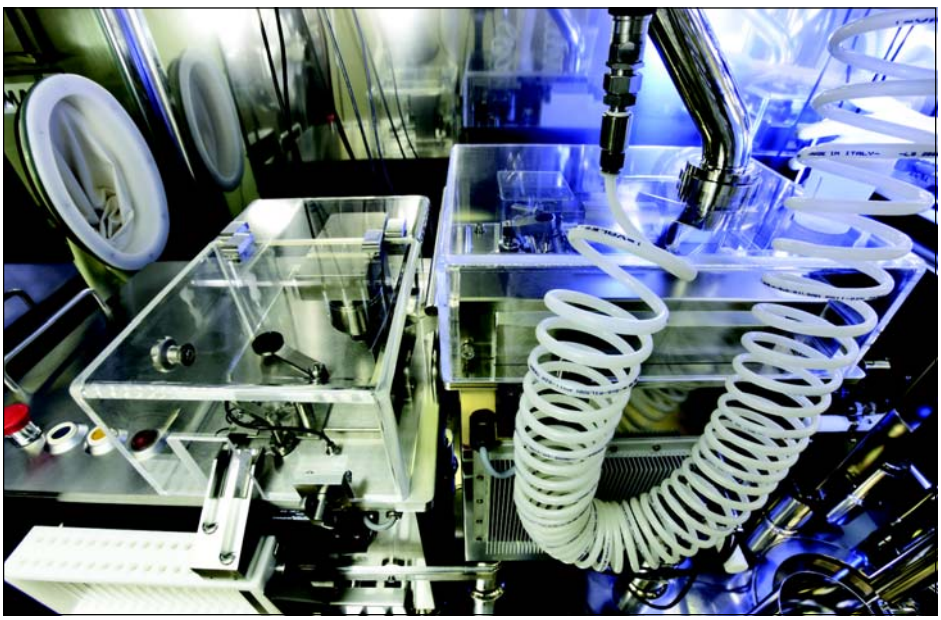
In the mixing and granulation process, Near Infra-Red (NIR) spectroscopy is used to check whether the mixture is homogeneous and the active substance is present in equal doses in all the tablets. Not only is the data used to verify the quality of the product, but it has the potential to shorten blending cycles.

For the tablet press, a special device was developed to extract coarse directly from the press in order to measure tablet potency. The vision is for this continuous online analysis to replace the time consuming, manual HPLC testing in the future, and to allow staff to respond swiftly in the event of faults or irregularities. Pfizer Illertissen is currently gathering data and plans to file this PAT application with the authorities by the end of this year, Weyhers said.

Lean Concepts Optimize Throughput

The concepts of lean manufacturing also were applied to identify bottlenecking and potential improvements. With model simulation software, NEWCON production processes were illustrated virtually and optimized.

"We wanted to achieve line balance, meaning the focus is to equally load the major unit operations of compounding, core compression, and film coating," said Weyhers. "Our findings had an impact on equipment size and selection, and this was done up front."



PAT technology.

Compression operation (incl. PAT application).

The NEWCON team of experts was able to achieve synchronized unit operations. As soon as the first process stage is completed, the next batch is brought in, so that up to three batches can be produced in parallel. This semi-continuous production sequence has resulted in a significant increase in output compared with ICON. NEWCON has a capacity of a billion tablets per year in three-shift operations round the clock and five days a week.

With the implementation of principles of lean manufacturing, Bernhard said they were able to reduce the operator level by 66 percent, which corresponds to an increase in efficiency of 300 percent. Together, with an increase in the batch size, there also was a reduction in the production costs by 42 percent, compared with ICON.

Streamlining C&Q

The philosophy of improving and streamlining NEWCON's design also was applied to NEWCON's Commissioning and Qualification (C&Q) approach.

"If we used the conventional approach of 'the more the better,' we simply would have missed the timeline. We had to come up with something different," said Weyhers.

"We have a saying within Pfizer Global Manufacturing: Shamelessly steal good ideas. We simply made use of the ISPE GAMP® 4 Guide."

"Based on risk assessment, we categorized our systems into Direct, Impact, and Non-Impact systems and this really helped to funnel down the overall validation approach and unburden the organization," said Weyhers. "We managed to shift the major chunk of the workload toward the vendors."

"At the end of the day, it's the product that counts," said Bernhard. "The equipment and facility serve one purpose, and that's to produce a good, safe, quality product for the patient. We focused on what was important, and I'm happy that this logical approach is becoming more and more prevalent in the industry."

Crazy Can Lead to Pioneering

The vision for NEWCON started a few years ago with a team of experts asking crazy questions and answering with 'why not?' said Bernhard.

Today NEWCON provides pioneering ideas for the future, not only in containment production, but for the entire field of pharmaceutical manufacturing, said Bernhard.

"It is certainly plausible that the degree of automation that Pfizer Illertissen has achieved in NEWCON will be standard for the pharmaceutical sector in one or two decades," said Bernhard. "And it is just as likely that the fully-automated containment technology will then be used not only for highly potent substances, but also in other areas of pharmaceutical manufacturing. For example, perhaps the single-room concept can be applied to a packaging line."

"These days, with cost pressures, decreasing direct labor costs, and market challenges, automation should be considered in facility design in order to be competitive in this industry."

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2008 Facility of the Year Awards CATEGORY WINNER Process Innovation • Supplier

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Comecer representatives will be at the ISPE Annual Meeting in Boca Raton, Florida, 26-29 October, Table #623

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