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for the process industries

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Expertise for the pharma industry

Cover story
A micro "factory of the future" with Siemens technology

Case study
Digitalization advances personalized therapies

Solution
Simatic IT eBR for operational excellence

“Flexibility and modularity are the current trends in the pharmaceutical industry.”

Siemens AG

Dear readers,

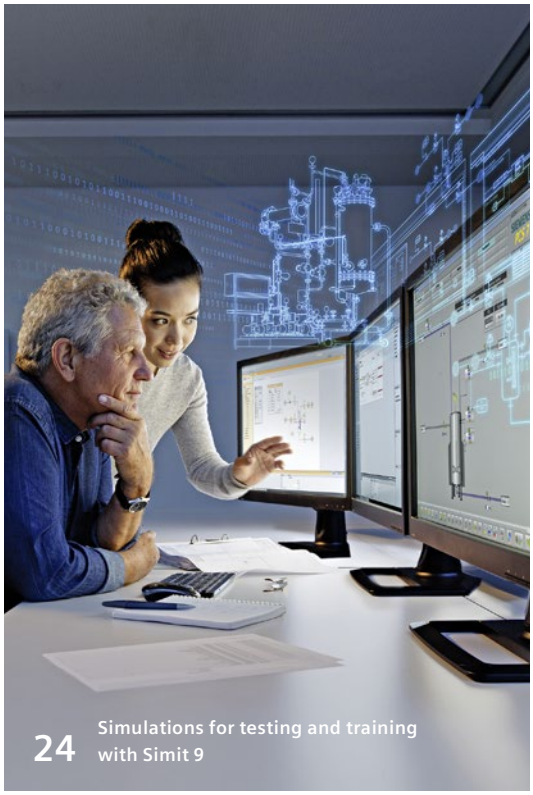
When one looks at the current trends in the field of pharmaceutical production, two terms stand out: flexibility and modularity. Almost all the major pharmaceutical companies have embarked on one or more projects that deal with the introduction of technologies with these characteristics. Flexibility and modularity can help manufacturers harmonize active pharmaceutical ingredients more closely with patient requirements or move production to the locations where the medicines are needed, and they also contribute to improved capacity planning based on actual demand – all important factors for sustainable success in the pharmaceutical industry.

As a longtime partner to the pharmaceutical industry, Siemens is continually developing its portfolio of products and solutions so that our pharmaceutical customers can benefit from digitalization and strengthen their competitive positions – whether through integrated engineering, simulation, or cloud-based solutions.

Today, pharmaceutical companies are using Simatic IT eBR for electronic batch documentation to help prove their product quality with significantly lower costs and to optimize their processes more easily. BioNTech, for example, relies on our innovations for the manufacture of an individualized cancer vaccine, using our manufacturing execution system and our extensive process and pharmaceutical expertise to design 100% digital, flexible production processes. In our cover story, you will learn how GSK benefits from our innovative products and pharmaceutical expertise in a strategic partnership. These are just two of the examples showing how modern technologies contribute to assuring the safety and availability of pharmaceuticals – today and in the future.

Dr. Hartmut Klocker
Vice President Business Segment Pharma
Siemens AG

Sergey Nivens - Fotolia



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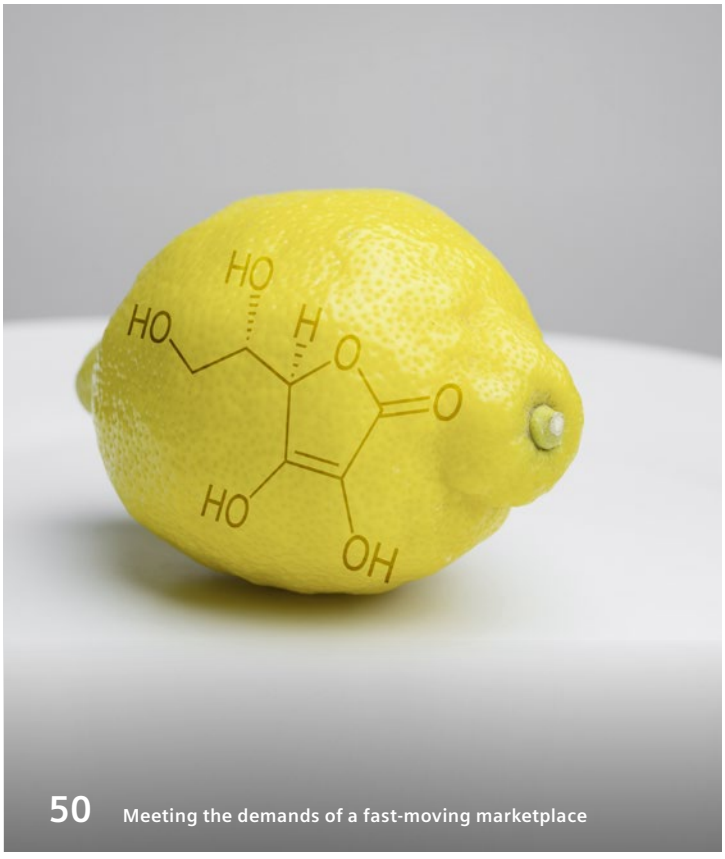

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The art of the possible

Next to its main campus in Stevenage, England, GSK has set the course for the future of pharmaceutical manufacturing: the IIM Digitisation Lab.

GSK / Tim Pope

Enter the unit and a narrow, dark corridor leads to an open space in a refurbished warehouse, revealing an artfully decorated facility with large screens and cubicles where teams of people are busily analyzing data. It looks a bit like Google meets life science, with a bit of Hollywood added in for effect, and it is nothing less than the future of pharmaceutical manufacturing. "We wanted to build a facility we can point to and show the art of the possible," says Patrick Hyett, who heads GSK's IIM digitisation project.

The building that houses the IIM Digitisation Lab project was intentionally designed by Hyett and his team to create the impression that this place is different. He says, "This is meant to resemble more a start-up firm than a branch of a global healthcare company. What we do here is aimed at rapidly seeking, incubating, and driving innovation in many areas of pharmaceutical manufacturing: we want to change the way people look at making pharmaceutical products and how they go about product development and new product introduction, as well as how they operate production facilities. We wanted to start from an empty space and take a new approach rather than take an existing space and add tools over the top of it, so that we could force people to take a new look at things."


GSK /Tim Pope

Making change apparent

This change is very visible in the facility's changing room. In this space operators don overshoes, gowns, gloves, safety glasses, and hairnets before entering the clean room area within a small production unit for oral solid-dosage drugs. This routine activity usually controlled by training personnel on standard operating procedures has been transformed through interactive technologies that guide the operator through the process and provide visual and digital confirmation that each piece is donned correctly. This changes the way people think about gowning from something routine to something that is correct and standard every time. It is the kind of total rethinking of how things are done that lies at the heart of the center.

A micro "factory of the future"

In the space beyond that changing room, the IIM facility currently boasts a complete production unit for a continuous direct-compression oral solid-dosage manufacturing line, a very typical pharmaceutical process. Though comparatively simple, the facility has all the system components required for design and development, tech transfer, and new formulated product introduction.

»We will continue to call on our partners, including Siemens, for future strategic collaboration, and I am looking forward to seeing what else they will bring to this project.«

Patrick Hyett,
IIM Digitisation Lab Director, GSK

GSK / Tim Pope

IIM Digitisation Lab

The idea behind the IIM Digitisation Lab is to show the art of the possible in a working pharmaceutical manufacturing facility to help stakeholders experience the opportunities presented by automation, manufacturing execution systems, analytics, and informatics. The facility aims to demonstrate how state-of-the-art systems and technologies can be used and combined in a manufacturing environment to help the pharmaceutical industry exploit the potential of digitisation, ultimately contributing to GSK's goal of improving access to medication for patients all over the world.

"This is where we want to trigger another change in mind-set," says Hyett. "In a pharmaceutical manufacturing facility, systems can be exploited to help manage operations, target operational efficiency, improve quality and compliance in the plant, and develop reliable and robust manufacturing processes for a new product. With the IIM facility, we use a range of technologies to integrate the data that are generated along the product lifecycle with the context in which they are generated, record and assemble these data automatically, and present them as meaningful information. Then we can make use of the data to improve the various processes. We can use data in the design phase to drive lineage more efficiently and build confidence in experiments, which will potentially reduce time to market as we make informed decisions based on data almost in real time. On the manufacturing floor, we can drive and build models on a unit level to optimize or adapt a process for related products, or we can develop sophisticated models for specific products. This modeling capability gives us the means to continuously test and improve all processes."

Combining expertise

What sounds easy on paper, however, requires quite a business change, as Hyett explains: "The IIM team needed expertise in many technical areas – development and production business processes, process automation, manufacturing execution systems, IT, and data science – in order to convert what is available in terms of new technology into a solution that would address our business challenges."

For example, one issue involved operator acceptance: "As an engineer, and especially as an automation engineer, what you think is essential information on a screen often is not what an operator needs or expects. So getting feedback from manufacturing practitioners was extremely important for us, and we have completely redesigned the user interface and what our electronic batch records look like on display systems. The core workflow engine remained, but the operation and representation of the system is all new and focuses on showing the operator only the information required to complete the current manufacturing step and to maintain situational awareness of upcoming events." ›

GSK / Tim Pope

»As game-changing technology innovations are transforming other industries, a mechanism for rapid assessment of these innovations in our business is essential. Real business impact can be achieved when you bring the right technology to bear on a functional need.«

Patrick Hyett

GSK / Tim Pope

More than just a set of clever technologies

Hyett emphasizes that while the visible technology is eye-catching, there is a serious strategy behind the approach: "When we came up with the plan for the IIM proof of concept, we wanted to demonstrate that with state-of-the-art technology, we could help exploit the potential of digitisation for GSK and address many of our manufacturing challenges. It is very difficult to point to a reference facility in pharma where there is truly an end-to-end digitised model that can act as a role model for a network of manufacturing sites. While most people understand that a well-designed digital system architecture can help improve many aspects of our business, such as operational efficiency, product robustness, and regulatory confidence, we needed to make the required transition real to people – including having a working production unit – so they could experience physically what can be achieved and also em-

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brace the changes and challenges associated with it. That's why we built this facility."

The technologies in the center are designed to provide systems that enable context-rich data acquisition and control; enforcement of sample, experiment, and batch genealogy; electronic workflow execution (e.g., elimination of paper records); and data virtualization and integration, enabling data use without manual intervention. Rather than enhance existing tools to perform these functions, the center reached out to innovators in other industries and found a new generation of tools that could help transform pharma.

Turning data into information

While the advanced models are still being developed for pharma, the center has reached out to partners like Siemens, which have helped integrate data and context in other areas with readily available solutions for data acquisition and control, manufacturing execution systems, production scheduling, and workflow execution. "One of the key learnings we gained during this project – and where the collaboration with Siemens has proven very valuable – was how we can make the data available on different levels of our organization. Ensuring ease of data use and information for management is key, and having Siemens' industry expertise has really helped our journey to achieve this," says Hyett.

Smart space

In this manufacturing "smart space," created by aligning people, technology, and data, the focus is on the abstraction and presentation of data for the operators, streamlining their situational awareness during the manufacturing process and allowing the manufacturing room itself to be an equal participant in the creation of medicines, alongside the human operators themselves. Acting as a true smart space, the room identifies situations and statuses that humans cannot see or perceive at a glance, like the performance of an equipment train, stopping the process of manufacturing before mistakes are made. This then frees up humans to do what they do best: managing by exception, drawing inferences, and using their senses and intuition to make data-driven decisions.

Interactive screens and advanced communications systems are used to enable access to intuition from remote parties. "As game-changing technology innovations are transforming other industries, a mechanism for rapid assessment of these innovations in our business is essential. Real business impact can be achieved when you bring the right technology to bear on a functional need," says Hyett. "We can get to the point where we can enable remotely located staff to work together within a manufacturing operation using high-fidelity video, screen sharing, and a secure remote user interface for shared operation control. This technology enables new forms of batch context – voice and video – and in turn the possibility of online checks and proactive 'during-execution' online quality support or technical support."

This concept extends beyond the manufacturing room. In the corridor outside, display systems present a real-time picture of the manufacturing process under way at configurable levels of detail, ranging from a plantwide overview to operating instructions for tableting to trending of process parameters shown against a predictive model. In addition, the location and status of all people, equipment, and materials in the facility are available from radio-frequency identification (RFID) sensing and are used to determine the

Value added by Siemens technology

- Process control with Simatic PCS 7
- Performance analysis with Comos XHQ
- Production scheduling with Preactor
- Electronic batch records created and managed with Simatic IT eBR

GSK / Tim Pope

The IIM Digitisation Lab is located in a refurbished warehouse – an artfully decorated facility with large screens and cubicles where teams of people are busily analyzing data

status of rooms within the facility – whether actively manufacturing, awaiting an intervention, or complete and awaiting cleaning.

Building the center

The team came up with completely new ideas in many other areas as well, also working with specialist companies in some cases. "We brought in people from the computer gaming industry, user experience designers, and IT and automation experts, and in certain areas we built our own solutions from scratch," says Hyett. "At the same time, we needed to keep the solution as simple as possible and keep the number of applications to a minimum for delivering the desired functionality – IIM has to be manageable in an industrialization context, after all."

When selecting partners for the project, Hyett and his team were especially looking for one thing: willingness to collaborate and learn in an open innovation set-up. "Partners like Siemens, who is also a strategic partner of GSK in manufacturing automation and thus a preferred automation supplier for GSK production and R&D sites worldwide, were brought in," says Hyett. "They clearly recognized that, together with us, they could shape and expand their offering for the pharmaceutical industry – and this collaborative spirit is what distinguishes a strategic partner from a (preferred) supplier. Additionally, they brought in added value in terms of cross-industry know-how. When you aim to design a data-driven business process, as we do with IIM, you need extended modeling capabilities. Siemens has some advanced predictive modeling solutions for other industries, for example, models designed to streamline maintenance for wind turbines, and we might be able to adapt these for our own modeling solutions."

The road ahead

The project team rapidly designed, built, and implemented the IIM facility, and the center is now being used to accelerate technology adoption within GSK. The IIM team is already busy with the next steps: establishing software- and system-neutral requirements as a prerequisite for strategic industrialization, working on point solutions for prioritized tasks for manufacturing sites, and refining solutions so they can be deployed as a fully digitised manufacturing process in capital investment projects. "We will continue to call on our partners, including Siemens, for future strategic collaboration, and I am looking forward to seeing what else they will bring to this project," says Hyett. For him, IIM has already been a trigger for a mind-set shift, and not just for manufacturing: "It's not just about technology – what is equally important is the human aspect. We have put an incredible amount of effort into creating the data architecture, but we want to road test the facility with formulation scientists, operators, schedulers, quality assurance, and many other specialists to ensure that our solutions are really giving people the information they need to do their job and make timely and informed decisions with the minimum of effort. The ability to interact with advanced technology in a simple form really makes a compelling argument. This is something that I have learned from this project: you are not just designing a machine or a control system; you are creating a user experience as well – and winning users over to your purpose is just as important as meeting the technical specifications."

The IIM team has obviously been very successful at that. "We have excellent feedback from key stakeholders within GSK who are as thrilled by our achievements as we are. So much is possible already. All you have to do is be creative and make use of the technology that is out there," Hyett says. ■

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GSK / Tim Pope

Sergey Nivens - Fotolia

Targeting cancer

With its personalized vaccine, BioNTech is a pioneer in the battle against cancer. To enable the active pharmaceutical ingredient (API) to be produced faster and in large quantities, the company has installed an entirely paperless manufacturing system featuring Simatic IT eBR and Preactor.

BioNTech AG

»The production of the Ivac Mutanome individualized vaccine is based on a standardized process that enables the creation of tailored products that vary widely in their composition.«

Prof. Dr. Ugur Sahin,
CEO, BioNTech AG

The development of personalized therapies was long considered a daring experiment, entailing major challenges – not just scientifically, but also in terms of production costs and time. In recent years, however, new developments in the field of oncology have shown that personalized therapies might well be able to revolutionize cancer treatment in the foreseeable future.

Personalized therapy at an affordable cost

BioNTech AG in Mainz, Germany, works on tailored medications, developing new-style, personalized immunotherapies against cancer and other serious illnesses. To this end, the biotech company is pushing ahead with its Ivac (Individualized Vaccines Against Cancer) Mutanome platform to make personalized cancer therapies available rapidly and at an affordable cost.

BioNTech CEO Ugur Sahin explains: "The production of the Ivac Mutanome individualized vaccine is based on a standardized process that enables the creation of tailored products that vary widely in their composition according to individual patient characteristics." This is initiating a paradigm shift in clinical development: the focus is no longer on the end product as such, but rather on the overall production process of medications tailored to individual patients. This approach also entails new conceptional, regulatory, technological, and clinical challenges. Immunotherapy using Ivac Mutanome is based on decrypting the individual mutation patterns of tumors in each individual cancer patient. The appropriate synthetic RNA vaccines are then produced, matched precisely to the mutation profile for each patient.

Experienced digitalization partner

To test and verify the efficacy of these new-style therapies in extensive study programs, two key prerequisites must be met: first, the production of the personalized vaccines needs to be accelerated, and second, the vaccines must be made available in larger quantities. Running production processes in parallel and speeding them up can achieve higher capacity. Paperless manufacturing is essential to this process. Since 2015, in its efforts to optimize production time and costs, BioNTech has been drawing on Siemens' extensive experience in digitalization to establish a fully automated, paperless, digital manufacturing process. Sahin says, "We aim to be in a position to provide hundreds of thousands of patients with personalized medications within less than

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five years. That will require the development and convergence of innovations in a range of different advanced technologies, such as big data, artificial intelligence, and fully automated analytics and production lines. The various components will in the future be fully digitalized and will collaborate with each other within interconnected processes. We believe Siemens has the necessary know-how to provide us with optimal support in attaining our goals." BioNTech also greatly appreciates Siemens' extensive portfolio and large workforce, which enable it to handle even such major projects quickly and reliably.

High quality thanks to automation

The Simatic IT eBR and Preactor manufacturing execution system (MES) are used to implement paperless manufacturing. As a result, the necessary information can be retrieved from all production processes and subsequently analyzed, archived, and applied to generate reports. This creates "regulated" flexibility, which is an essential element of state-of-the-art pharmaceutical manufacturing. The solution almost entirely eliminates time-consuming manual actions – whether in the lab, in production, in logistics, or in quality assurance. Full automation enables personnel to be deployed in an optimal way, process steps to be executed correctly, and releases to be issued as and when required. This is important in terms of the quality of documentation, and thus for compliance with all internal and regulatory requirements.

Unified process

Because the production of Ivac Mutanome vaccines takes several weeks and involves a sequence of process steps, precise operational planning is essential. The unified MES solution comprising Simatic IT eBR and Preactor links two separate operating locations into a single continuous process – from production planning to analysis to the finished personalized medication in lot size 1. Siemens successfully ran a concept study beforehand and subsequently drafted the functional specifications in the blueprint phase. The company's comprehensive process and pharmaceutical know-how, combined with the deployment of an experienced project team with high-caliber experts, proved ideal. The contract also includes the factory acceptance test (FAT) and site acceptance test (SAT), as well as the production of qualification documents.

Pioneering role as a challenge

With its pioneering role in research, clinical testing, and manufacturing, BioNTech is well on its way to revolutionizing the treatment of cancer through personalized mRNA-based immunotherapies. "Our pioneering work routinely throws up challenges that we have never before encountered, which means we must continually come up with new ideas and methods in order to find appropriate solutions," states Sahin. Thanks to the global presence of Siemens and the commitment of an international team, all the preconditions for implementation of BioNTech's planned global production rollout were met. The first market approval of the new vaccine is scheduled for the year 2021. ■

BioNTech AG, Mainz

BioNTech is a holding company with several subsidiaries combining all the technology platforms and competencies for research, clinical development, and marketing under a single umbrella. The subsidiaries specialize in different, complementary biopharmaceutical and diagnostic platforms and in the manufacture of medications for human use.

The company's strategy is to devise new technologies and converge innovations in order to develop and market personalized treatment approaches offering unique medical potential. As a result, BioNTech has in recent years taken on a pioneering role in the field of personalized cancer vaccines. Because every cancer case exhibits differing features, an average of only 15% to 30% of cancer patients with advanced tumors benefit from commonly available drug treatments.

Treatment tailored to the individual cancer and patient is expected to deliver much higher therapeutic success and improve chances of a cure.

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Boehringer Ingelheim

Taking the long view

A new production plant for pharmaceutical active pharmaceutical ingredients (APIs) and their precursors has been in operation at Boehringer Ingelheim's largest research and development facility in Biberach, Germany, since December 2014. The technical center, known as Technikum K 62, is the result of an intensive project successfully implemented across multiple phases.

The quantities of pharmaceutical APIs required to develop new drugs to the licensing stage are rising steadily. In early research phases, just a few milligrams of a substance are often sufficient. For more advanced toxicological and pharmaceutical testing, quantity requirements rapidly increase to tens or hundreds of kilograms.

The largest research and development facility within Boehringer Ingelheim's global network, in the town of Biberach in southwest Germany, is where most of the corporation's in-house development is carried out.

New innovative technical center

In 2011, to be able to provide adequate quantities of newly developed drugs for clinical studies and the continually increasing numbers of patients they involve, Boehringer Ingelheim began planning a new technical center, with an investment budget of some €50 million, to replace the existing building. The new pilot plant was planned to produce pharmaceutical APIs in quantities from 10 to 100 kg. The project team put forward a number of additional ideas to extend the facility's service life over the long term in a project presentation at the Siemens Competence Center Pharma in Karlsruhe, Germany. These included the virtualization of client and server applications and the use of Profinet for both the plant bus and fieldbus.

Three-level plant design

In contrast to those of a mass-production facility, the technical center's operations are characterized by continually changing synthesis reactions, products, and processing methods. So the plant design did not focus on optimizing the production processes of specific APIs; rather, the installed equipment had to offer maximum flexibility in order to produce a wide variety of different APIs and intermediate products.

The plant design incorporated three production levels: two reactor levels and an isolation area. The top reactor level also needed to incorporate hydration reactors. The entire planning process was implemented in line with cGMP (current Good Manufacturing Practice). To interlink the reactors as flexibly as possible, the reactor rooms were arranged in a cascade configuration. The physical separation of production areas enables the simultaneous, contamination-free production of multiple APIs.

The original system design was continuously enhanced throughout the project by Siemens Solution Partner on/off engineering gmbh and by Siemens itself, adapting the system to the needs and wishes of the operator. The project team presented Simatic Batch, Profinet, Scalance, and Maintenance Station based on the functions of the latest version of Simatic PCS 7 and answered customer questions in the course of meetings. Implementation of the project by on/off engineering gmbh began in late 2012.

Implementation with the latest products

The high degree of flexibility provided by on/off allowed for some adaptations during implementation of the systems, so as to incorporate the latest products from the Siemens portfolio as appropriate. For example, the originally planned Simatic S7-400 CPUs, types 414-3 and 414-H, were replaced on short notice with the new Simatic PCS 7 CPU 410-5H controller.

Operators were impressed by the extensive but integrated hardware package, with high-end memory, communication, and computing performance, as well as scalability. A total of 11 new controllers were deployed, including two configured as a redundant automation system. Complemented by additional Simatic PCS 7 components including redundant Batch, OS, maintenance, and engineering servers; two engineering clients; a Process Historian server; and a total of 26 Batch–client–licensed OS clients, the overall system won over the operator right from the initial partial acceptance testing, thanks to its wide-ranging options and, above all, its usability.

Boehringer Ingelheim

The new Boehringer Ingelheim facility for the production of pharmaceutical agents is adapted to the operator's needs

Boehringer Ingelheim

The Technikum K 62 facility in Biberach, Germany, offers more than 2,700 square meters of floor space

Configuration in a virtual environment

Implementing the complete system in a virtual environment posed a particular challenge and represents a highlight of the project. Five ESXi hosts were deployed for the purpose, with an additional one on cold standby. This project represents the first time that this configuration has been implemented in a Simatic PCS 7 environment. The technical expertise and experience of on/off engineering gmbh were beneficial in achieving this. A redundant fieldbus was implemented to boost availability based on MRP (Media Redundancy Protocol) and system redundancy. The Advanced Engineering System was used to implement high-quality programs in a timely and cost-effective manner. Use of the Advanced Process Library in conjunction with qualified control module type (CMT) modules from on/off ensured a high level of standardization as well as cGMP-compliant implementation. The operator was provided with a step-by-step introduction to the extensive possibilities offered by the system. This included, for example, the implementation of a manual level for direct control of the batch phases from the visualization unit. The benefits in terms of day-to-day operations and the reproducibility of workflows were already apparent to the operator in this phase.

Successful together

The new technical center has been up and running since December 2014. The 2,700-square-meter site houses synthesis labs, where processes are transferred from laboratory to pilot plant scale, and the complex pilot plants in which the newly developed pharmaceutical APIs are produced.

For all the project stakeholders – the customer, the Solution Partner, and the system supplier – the aim was quite simple: to complete the project successfully together. And that worked very well. On completion of the project, Siemens provided Boehringer Ingelheim with a support contact from Simatic Systems Support Process Automation beyond the standard level of service in order to ensure ongoing assistance in all technical matters. Another key factor in the project's success was the increasingly strong collaboration between the project team and the head office during the period from January to October 2013. During that time, the team monitored specific issues within the project and drew up an action plan. This resulted in detailed specifications for the configuration of the ESXi servers as a visualization platform and for on-site support for the initial installation of all software components. Simatic Batch workshops are held to answer specific questions, assess the experience gained to date, and agree on further optimization measures.

Not least, on/off and Siemens also help minimize risk in connection with the adoption of new functionality. For example, before the commissioning, the operator wanted to update to Simatic PCS 7 Version 8.1 in order to selectively load individual continuous function chart (CFC) diagrams. Thanks to detailed update planning involving all stakeholders, this aim was achieved.

Investment in the future

At the launch, Dr. Fridtjof Traulsen, head of corporate division development, asserted, "Regulatory requirements relating to the development and licensing of innovative pharmaceuticals are continually increasing. The new technical center will assure supplies of APIs to the preclinical development stages and clinical studies over the years ahead." Professor Dr. Andreas Barner, the former chairman of the board of managing directors of Boehringer Ingelheim, said in summary, "The new technical center is an investment in the future for Boehringer Ingelheim." ■

onoff-group.de

on/off engineering gmbh was established in Hannover in 1988 to provide automation engineering services independent of specific products and systems, and the company has since grown into a leading service provider in the field of process automation. It is a certified Siemens Solution Partner for the pharmaceutical industry. The company is DIN ISO 9001 certified and provides services in accordance with cGMP or GAMP 5 standards. Thanks to the on/off group's active membership in the Siemens Solution Partner network and its other cooperation agreements, staff are kept constantly up-to-date with the latest technical developments.

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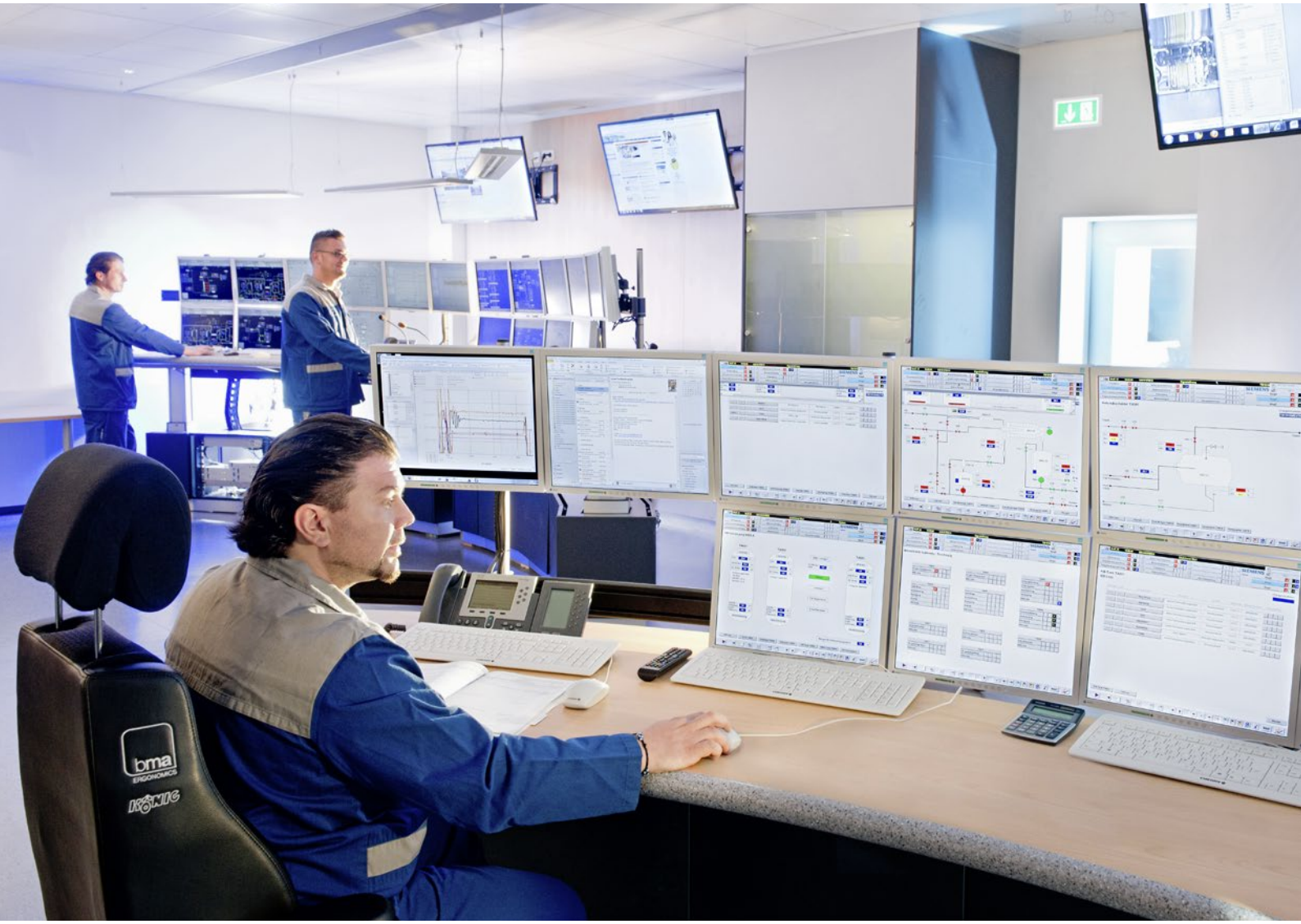
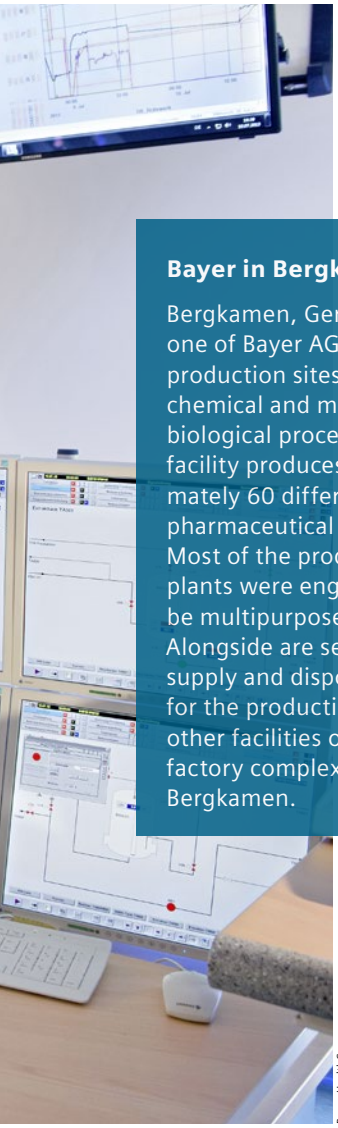
Successful project road map

An upgrade to a pharma facility in Bergkamen, Germany, has a timetable like the ones you find in road or rail construction. The planning and implementation of the process control technology migration for a total of six Bayer Pharma AG plants in Bergkamen will take eight years. Siemens is the strategic partner supporting the project as part of a migration alliance.



The production plants are monitored from the control center

Bayer's Bergkamen, Germany, facility encompasses a good 110 hectares of land – plenty of space for the production of active pharmaceutical ingredients (APIs) in a wide variety of treatment and application fields from radiocontrast substances to hormones for "the pill." Around one-tenth of the corporation's total revenues are generated from the products manufactured here, making Bergkamen an important Bayer AG's API production site. In Bergkamen, farsightedness and clear vision are not only necessary for the creation of new APIs; they also play a major role in one of the more ambitious projects Bayer Bergkamen has tackled in recent years. Gerd Schmidtke, who, along with Christoph Krampe, is responsible for the migration projects in Bergkamen, describes the challenges: "We are bringing the process control technology in a total of six production plants up to the technological state of the art and, in the process, are applying the most extensively standardized solution possible in all of them. From the first project in 2013 to the last migration, we are following an eight-year road map for migrating each individual plant. There are not many long-term projects that have to be planned in such detail and provide the opportunity to set the course of the production department's future at the same time."



Bayer HealthCare

Bayer in Bergkamen

Bergkamen, Germany, is one of Bayer AG's key production sites. Using chemical and microbiological processes, the facility produces approximately 60 different active pharmaceutical ingredients. Most of the production plants were engineered to be multipurpose systems. Alongside are several supply and disposal plants for the production halls and other facilities of the entire factory complex in Bergkamen.

On the way to digitalization

As well as modernizing its process control technology, Bayer is implementing several new concepts to lay a foundation for digitalizing and integrating the processes. Virtualized systems enable the optimal use of system resources: Process Historian will make it easy to quickly and consistently access process data for plant analysis and performance optimization, and with Simatic IT eBR, Bayer is preparing for the conversion to electronic batch documentation. As Krampe says to sum up the situation, "We have a lot to do!" To ensure a smooth project implementation, the parties responsible at Bayer voted in favor of a long-term strategic partnership for all of the migrations, selecting Siemens as their partner.

Currently, two operative teams are working to transfer the existing recipe controls – some of which have been in operation for more than 20 years – to Simatic PCS 7 and Simatic Batch, implement the new functions, and commission all the new systems. The road map they are following is extremely tight. In the process, the project teams from Siemens have been able to fall back on a pool of established knowledge. Some of the members have known the plants in Bergkamen inside and out for years. "We work together very closely and constructively so that we can systematically treat most of the themes on the operative level," Krampe says. "Thanks to the migration alliance, we have the security that Siemens will support us not only with its on-site teams, but also with experts from Cologne and Karlsruhe, which are Siemens' key locations for process control technology in Germany. It has been three years since the first project, and we already see that the synergies and learning effects are ›

The migration project at a glance

In cooperation with Siemens, Bayer AG will equip six production plants with new process control technology by 2021. Ultimately, around 30,000 measuring points with approximately 50,000 I/Os will be migrated to Simatic PCS 7. In the process, Siemens will use the Open AS platform for tool-supported migration, virtual systems, and simulation tools. The goal is to implement a standardized solution that provides a high level of investment security across the entire site. The solution includes the following components:

- Simatic PCS 7 with AS410 controllers in F and H versions, Simatic ET 200M/ET 200iSP I/O systems, and Siwarex U and FTA weighing technology
- Simatic Batch and Process Historian/Information Server
- Simatic IT eBR
- Software standards based on Advanced Process Library (APL) with SFC types
- Simatic PDM
- Asset management
- Simatic Management Console (SMC)

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there as anticipated – at our company and Siemens. We have achieved one of the project's crucial KPIs [key performance indicators]: reducing the engineering costs from project to project. And of course the direct channels at the site create an open project climate in which all the people involved are acting in concert."

Consistency creates synergies

Krampe lists synergies and lean processes as two significant reasons for the migration alliance, and not only on the technical level: "Of course you can implement a project like this in sections, with different partners. However, you should not underestimate the commercial and technical costs involved – the specifications and scopes of delivery/performance would have to be negotiated separately for each subproject because each one would be calculated separately. Now we can more or less select services and costs as project modules. This makes purchasing and project planning much easier." Schmidtke explains another benefit: a partner – as in this case – also supports the level of system standardization that Bayer wants to attain in the course of the migration. "Modern process control systems are very powerful tools. We decided that to the greatest extent possible, we would like to have one platform for all the plants and processes so we can service the technology to the technological depth required as economically as possible. Siemens supports this approach with a comprehensive solution within which we can apply different systems and components. At the same time, we use Siemens' knowledge to ensure that the standards are implemented well and the project planning for the same tasks is the same across all the plants – an important criterion in view of system maintenance and modernization in the future." One instrument Siemens uses to support standardization is the tool-supported migration of existing project planning via the Open AS platform. This saves the project teams engineering time and also ensures uniform, consistently high programming quality. This level of standardization also has advantages for the validation to which the systems in Bergkamen are subjected, which ensures that all the projects can be implemented consistently.

Ideal basis for optimization

Other migration projects within the Bayer corporation have already demonstrated the efficacy of long-term collaboration with Siemens. "We were able to take over some of the existing specifications and contractual modules – which simplified the project launch phase," says Schmidtke. However, this project differs from earlier projects in that, as a pharmaceutical operation, Bergkamen's production is subject to Good Manufacturing Practice regulations. "This is why we audited Siemens in Cologne as a project partner," he adds.

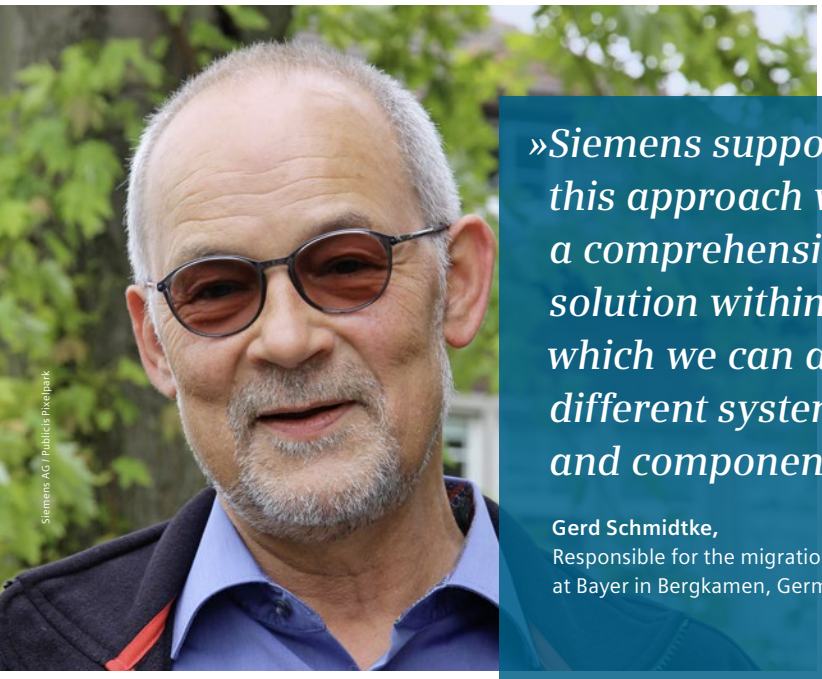
From a technical viewpoint, what makes Bergkamen unique is that the parties responsible decided to virtualize the automation solution. The IT department at Bayer supplied the virtual machines and Siemens implemented the corresponding software. As a result, the project team can thoroughly test the automation software. This enables team members to minimize the commissioning costs with the associated adverse effects on production and adhere to the tight migration schedule. "We have been receiving completely positive feedback from production – in my case, that means I don't hear much," says Krampe with a wink. "If something wasn't functioning properly, I would find out immediately. After all, production has top priority."

"The migration also creates the opportunity to establish the existing processes on a modern basis," adds Schmidtke. "With Process Historian and electronic batch documentation, we now have the op-

Siemens AG / Publicis Pixelpark

»We have achieved one of the project's key KPIs: reducing the engineering costs from project to project.«

Christoph Krampe,
Responsible for the migration projects at Bayer in Bergkamen, Germany



»Siemens supports this approach with a comprehensive solution within which we can apply different systems and components.«

Gerd Schmidtke,
Responsible for the migration projects at Bayer in Bergkamen, Germany

tion to properly document and analyze process data more easily than before. On the one hand, we now satisfy the requirements of the responsible authorities. On the other, we can safeguard the stability and performance of our processes more efficiently and continue to improve them. This means the migration project is also contributing to operational excellence at the site."

Electronic batch documentation with Simatic IT eBR will also help relieve the operators in the control center. According to Krampe, "Currently, recording the batch documentation takes up a major portion of our working hours. In the future, the employees in the operating station will have more time to monitor the process and optimize operations – and this will surely make a positive contribution to the plants' productivity and efficiency."

Step by step to the goal

Right now, the first plant is being equipped with Simatic IT eBR and the next ones are in the pipeline. "I think we will quickly see that it has paid to invest in this area. We now have the tools to easily optimize activities such as maintenance and asset management based on real, robust plant data," says Krampe. The system switch has encouraged Schmidtke to think differently: "Until a few years ago, the idea was that the automation solution should run for as long as the plant did – in our case, that could be up to 30 years. From the viewpoint of production and validation, this concept is understandable, but the result would be a nonhomogeneous system landscape that is very difficult to maintain. With our modernization and standardization project, we now have a strategy for the ongoing maintenance of the control systems for the entire lifecycle with predictable intervals for updates and hardware modernization. It is helping us make an important contribution to investment protection and plant availability." That is why Schmidtke feels so positive about the results of the migration alliance. ■

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Virtualization and simulation

To design the process control technology modernization project to run as smoothly as possible and with a minimum of downtime, the project teams in Bergkamen, Germany, used virtual systems. They virtualized the entire Simatic PCS 7 system, including the controller, operator stations, and batch server. A test using Simit VC (virtual controller) was run on the migrated formula structure before commissioning. The project team was thus able to verify in advance whether the existing formulas would be migrated to the new system without errors. This type of secure environment also allows one to test the required adjustments to the batch control system. Such an approach provides a means to verify programming quality and functionality. And afterward, the actual system commissioning process will take much less time.

In the next step, the entire process – from human-machine interface (HMI) and automation to the process signals and the actual production process – will be simulated. The simulator will use the original HMI and automation. Simit will also simulate the automation and production processes. And the simulation solutions can even be used to train operators. This way, Bayer in Bergkamen can design the production, maintenance, and modernization of its plants more effectively.

↗ **siemens.com/simit**

Simulating instead of trialing

Getting to market faster and responding more flexibly to market changes are the challenges faced by today's process industry. A simulation software platform that combines process simulation and operator training provides an efficient solution.

Simulation is key to creating more efficient processes in the engineering and commissioning of production lines. Simulation technologies can be used right from the planning phase to detect any errors in the production plant, and especially in the automation. It is even possible to train staff in advance so that everyone knows what to do when production starts.

When a system is automated with Simatic PCS 7, Simit is the simulation program of choice. It has proved its worth in more than 500 applications to date. Many large chemical and pharmaceutical companies now even specify that testing and commissioning must be carried out using Simit.

With Simit, Siemens offers a unified software platform for automation project testing and training. It not only supports the virtual commissioning of systems, machines, and processes but at the same time also creates a realistic training environment for plant operators. The latest generation of the software, Simit 9, features a graphical user interface (GUI) as an intuitive front end, aiding quick set-up of simulation projects and enabling efficient learning processes directly at the workstation.

Planning certainty right from the beginning

Inconsistent data and workflows very often pose a major challenge when implementing automation projects. Process simulation greatly reduces risk in commissioning, because any problems or weaknesses can be identified and eliminated in advance. An interface between Simit 9 and the Simatic PCS 7 process control system integrates all the key planning, engineering, and automation data, as well as all libraries of functional components, into the simulation process. There are also interfaces with the Comos plant management software.

This seamless integration into the Simatic PCS 7 infrastructure greatly speeds up the engineering process. And even complex automation projects can be implemented within a much tighter time window than was previously conceivable.

Training in a real environment

Another key factor in achieving an efficient start to production is the training of the staff who will later be responsible for trouble-free operation of the plant. For this, Simit 9 offers a realistic training environment in which a wide variety of different operating scenarios can be simulated long before online production starts. The simulation program uses the automation system's actual operator screens and enables staff to familiarize themselves with all aspects of the plant and its functions.

This functionality likewise ensures that work can be carried out simultaneously, thus saving time. It reduces the resource requirements for commissioning and the start of production. It also reduces risk for the operating personnel, especially in the initial phase, and is a key factor in bringing perfect-quality products to market faster.

Incorporating the complete lifecycle

The simulation of new or changed processes not only speeds up engineering procedures leading up to the start of production. It also means that experience can be gathered right from the early phases and incorporated

from the beginning into the process sequence. And it enables the specification of plant data that otherwise might need to be collated later while production is running. Thus, Simit 9 also supports the targeted acquisition and documentation of production-related know-how.

Simit 9 is currently the only simulation software for automation systems offering such a wealth of functionality. As an integral part of the Simatic PCS 7 environment, it is a valuable tool in helping companies in the process industry to bring their products to market faster, with consistently high quality. ■

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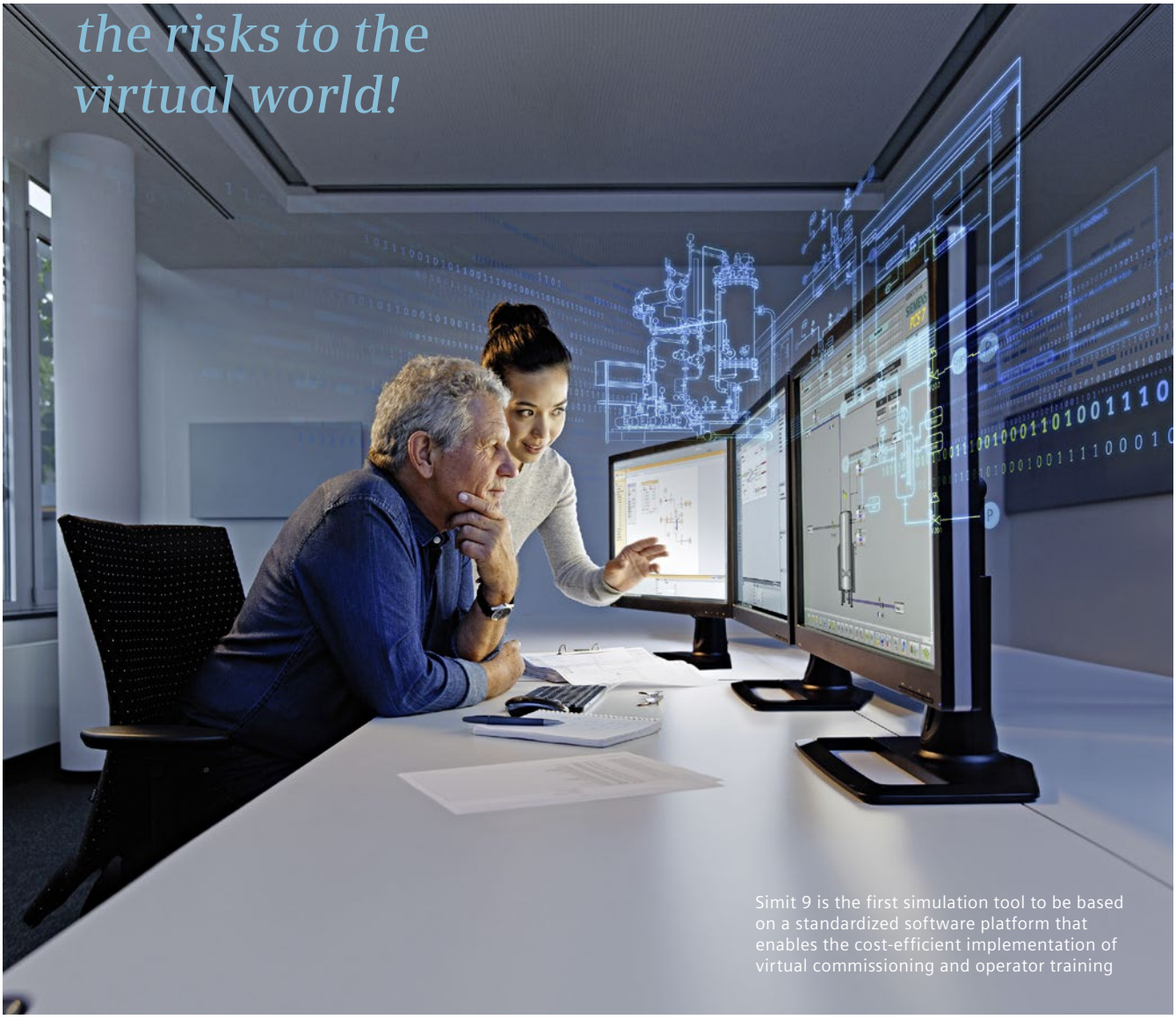
There is no reset button in life – Simit 9 transfers the risks to the virtual world!



Simit 9 is the first simulation tool to be based on a standardized software platform that enables the cost-efficient implementation of virtual commissioning and operator training

Marc Dietenmeier

Virtualization on the march

On a new-build project at the B. Braun AG facility in Berlin, ZETA Automation opted for a virtualized platform featuring the Simatic PCS 7 process control system with Simatic Batch. The service-friendly automation and IT system enabled the production plant to be put into operation more rapidly and efficiently than with alternative systems. The solution has shortened plant shutdown times and reduced lifecycle costs.

Leading medical technology and pharmaceutical manufacturer B. Braun AG, based in Melsungen, Germany, has commissioned a new production plant at its Berlin site. Following the initial development phase, the 4,600-square-meter facility now produces sterile injection solutions and packages them in plastic ampules. The project was completed rapidly – just 18 months from award of contract to final acceptance. That short time window also posed a major challenge for ZETA Automation, which handled the complete automation package for the formulation plant. The contract covered plant design, selection and installation of the hardware and software components, equipping the control cabinets, hardware and software engineering, electrical installation, and commissioning and qualification.

Integrated recipe control

To automate injection solution production, ZETA chose the Simatic Batch V8.0 software package for the Simatic PCS 7 process control system, safe in the knowledge that it would deliver consistent batch quality. The process control system conforms to the requirements of FDA 21 CFR Part 11. The integrated recipe control means that the automation system does not need to be modified in the event of changes to the recipe – the control recipes run in Simatic Batch. User-specific production reports are implemented by the standard report designer of the Simatic Batch system. Authorized users are able to export individual recipes, trend data, and audit trail and alarm data, and the batch recipes created by the user can be saved, copied, and reused for new batch recipes.

In terms of hardware, the plant was equipped with a central main control cabinet for the automation systems and high-performance Siemens frequency converters, with server racks for the Simatic PCS 7 infrastructure, virtualized on two hosts, as well as with on-site enclosures for the distributed I/O system. Simatic Batch is operated via multiple thin clients with touch functionality housed in a stainless steel cabinet in the clean room process area.

Fast and efficient project execution

The process control system is based on a virtualized computer system, which not only offers sufficient re-

The integrated, service-friendly system aids work processes and speeds up the implementation of software changes

serves for later plant expansions but, thanks to its performance, also represents a future-proof investment. For this virtualized system platform, ZETA recommended that the B. Braun project team use Simatic Virtualization as a Service (SiVaaS).

ZETA was able to complete the project smoothly and successfully, thanks to the state-of-the-art virtualized computer platform, which enabled the key elements to be executed on schedule and within budget. Those key elements included, in particular, the drafting of function specifications based on process descriptions and piping and instrumentation diagrams developed by ZETA, writing of the Simatic PCS 7 application software in conformance to GAMP 5 and S88, installation of a batch management system with formulation mode, and development of custom trend and production reports. For Björn Stolle, project manager at ZETA Automation, the outstanding teamwork with the customer was key: "The collaboration with B. Braun was handled optimally, with successful solutions being developed on a joint basis. B. Braun operators were available to us at all times during the commissioning phase, enabling us to complete the project efficiently and successfully." A major benefit for B. Braun in terms of the project execution was that ZETA offers both process know-how and expertise in automation. This meant that process sequences could be incorporated quickly and, above all, safely into the Simatic Batch PCS 7 software project.

Benefits of virtualization at a glance

- 20% to 25% energy saving thanks to virtual hosts with lower power consumption than physical servers
- Higher availability of computer systems thanks to the hardware redundancy of the hosts and the automatic load distribution of the virtual servers
- Optimized computer performance
- Lower cost of plant expansion because the virtualized Simatic PCS 7 system does not need to be migrated within the plant application
- 30% to 40% lower lifecycle costs for the control system, with an average machine and plant service life of 10 to 15 years

Thomas Rosenthal

Decreased plant shutdown time

ZETA consciously chose SiVaaS because it meant the benefits of Siemens support were available right from the project phase. And B. Braun also benefited, because SiVaaS assures customers of professional service and fast supply of replacement parts. All the members of the project team, from both B. Braun and ZETA, agreed that ZETA's choice of hardware and software systems was exactly right. The continuity and service-friendliness it offered, combined with a significant easing of the workload and shorter plant shutdown times, were key factors in the success of the new production plant. The continuous function chart (CFC) / sequential function chart (SFC) structures configured within the Simatic PCS 7 system mean that any software changes can be implemented more rapidly than with conventional Supervisory Control and Data Acquisition (SCADA) systems, resulting in roughly 30% less shutdown time.

The certified Siemens Automation Drives Solution Partner is well respected in the production plant automation market for the pharmaceutical, biotech, and food industries. ■

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Trust your data

Data integrity is essential for safeguarding the quality of pharmaceutical products, protecting the health of patients, and implementing Good Manufacturing Practice (GMP). Siemens products have an emphasis on secure data. This is shown by the example of Sipat, a Siemens product for Process Analytical Technology (PAT) solutions.

Since 2013, the US Food and Drug Administration (FDA) and European authorities have increasingly enforced guidelines on data integrity, that is, the validity of data and their relationships. Following these guidelines is now more important than ever due to the digitalization of manufacturing processes, which is generating more and more data. Classically, data are being obtained and stored on paper, where established rules apply. However, with a growing use of electronic systems for batch and process records, GMP-relevant data are often purely digital and also require a different approach to ensuring data integrity. Companies often struggle with implementing suitable measures, as is demonstrated by a rise in FDA warning letters and EMA noncompliance reports in recent years. In addition to being a legal requirement, data integrity is vital because if any data are incorrect or inconsistent they can jeopardize product quality and the safety of patients. The transition of data from paper-based to digital systems has also required new rules and technology to ensure data integrity and to counter threats such as human input errors, missing raw data, uncontrolled alterations without audit trails, invalidated data entries, and inadequate archiving.

A digital approach to data integrity

Several guidances deal with ensuring data integrity for electronic systems. For example, in March 2015 the UK's Medicines and Healthcare

products Regulatory Agency (MHRA) issued a guidance document on how to design systems to assure data quality and integrity. In this document, the agency gave several examples of elements needed for an appropriate system design: access control on the recording station, controlled user rights management, automated data capture from devices, and the ability to access raw data for inspection and control of values. During the validation and operational phase the following aspects need to be considered: type of data recording, backup and restore procedures, definition and verification of all interfaces, audit trail, archiving concept, and user management, as well as deviation management and change control.

State-of-the-art automation and data management systems will typically provide the required features and can make a vital contribution to data integrity when deployed correctly. For example, one area of application where large amounts of data are generated is Process Analytical Technology (PAT), whereby multivariate process data are interpreted with the help of advanced models. The consequence is that a lot of data are generated that need to be collected from different sources, aggregated, monitored, calculated, and integra-ted into Advanced Process Control loops. Full integration of data integrity principles is a must in such a complex PAT data management landscape.

Safeguarding compliance and quality

The Siemens PAT software Sipat was developed from the start to comply with data integrity requirements. Sipat is highly scalable and modular, with a full range of tools for controlling access, backing up and restoring, and running audit trails to track and improve performance. Sipat's user management controls ensure that only authorized individuals or groups have access. This includes controlling access to a certain level, from a specific country, and to data for particular plants.

All activities are then tracked with detailed audit trails, which can be visualized for each element and added to reports. To protect against the risk of electronic signatures being falsified, Sipat adds additional identifiers, including a company chip card or an identification code, as well as comments on why an electronic signature was added. For backup and restore functions, Sipat automatically saves a year's data online, and these data are synchronized with an archive database holding data for up to 10 years. These databases are routinely backed up for fast disaster recovery.

Data integrity done right

As Sipat demonstrates, pharmaceutical manufacturers can ensure the accuracy, integrity, availability, and legibility of documents with the right systems and solutions. Suitable concepts help to establish, control, monitor, and record all activities that directly or indirectly impact all aspects of the quality of medicinal products, ensuring not only data integrity but also product and patient safety. ■

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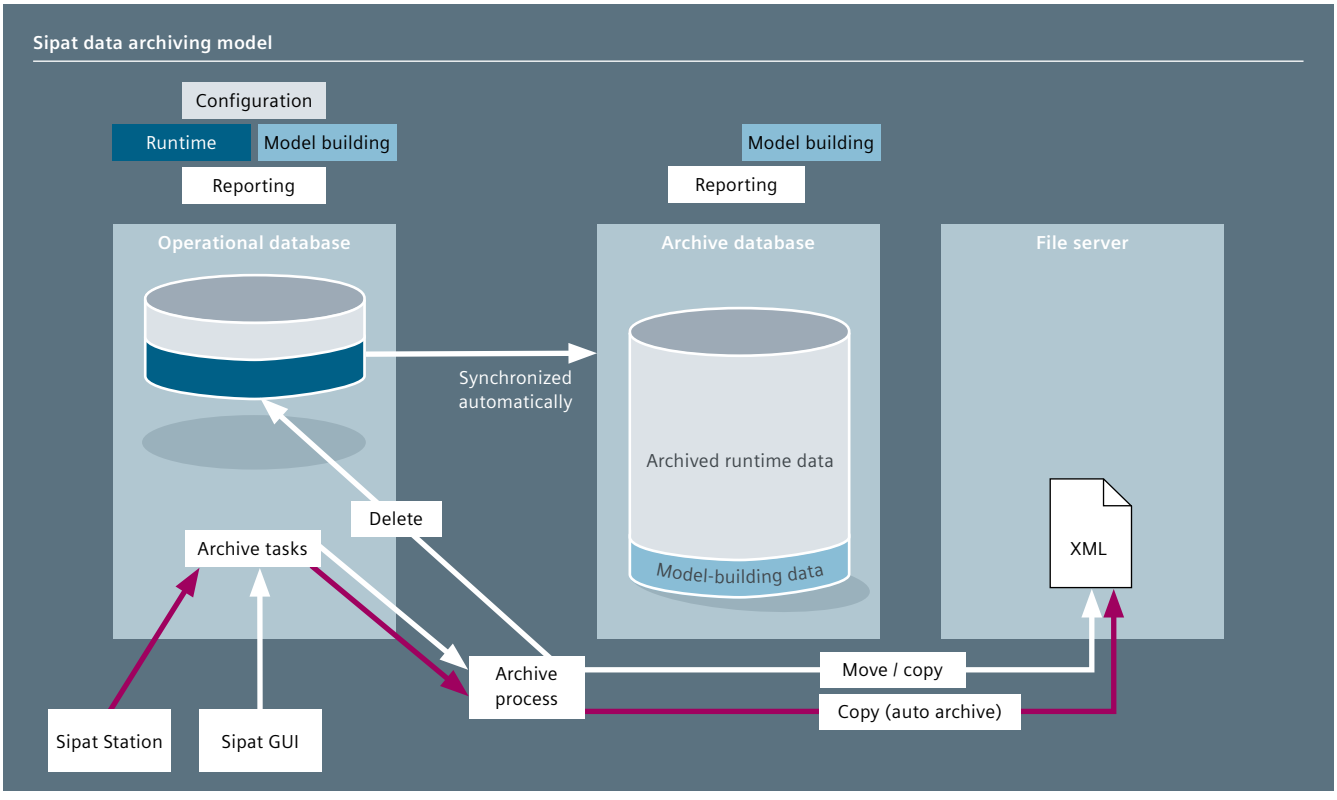

Making bacteria feel good

The respiratory quotient is a key indicator for the control of fermentation processes. A new technique for the high-precision measurement of oxygen consumption and carbon dioxide emissions allows for the creation of conditions in the fermenter that ensure optimal cell growth.

Biogenic APIs are a growing trend in the pharmaceutical industry. Production of these APIs involves fermentation processes that run in special reactors. In these fermenters, optimal conditions are created for yeast cells, animal cells, or bacteria, for example, enabling the cells to grow and reproduce as quickly as possible. Fermenters must be controlled in order to achieve optimal cell growth and thus maximize API yield. This control requires detailed knowledge of the fermentation process itself. And there are also other key indicators that enable the process to be continuously monitored and integrated into an automatic process control loop.

Respiratory quotient as a growth indicator

One such indicator, the respiratory quotient (RQ), is used in biopharmaceuticals to evidence optimal cell metabolism. The quotient expresses the ratio of the amount of carbon dioxide (CO_2) given off in a certain period of time (the carbon dioxide emission rate, or CER) to the amount of oxygen (O_2) absorbed from the air and consumed in the same period (the oxygen uptake rate, or OUR). In simplified terms, it can be said that this quotient is an indicator of the well-being of the microorganisms in the fermenter. If the RQ is in the wrong range, the cells are not com-

Siemens AG

The Siprocess GA700 analyzer, in conjunction with the Ultramat 7 and Oxymat 7 analysis modules, precisely records both the oxygen absorbed from the air and the amount of carbon dioxide emitted

Siddharth Siva

Fermentation processes can be monitored in a targeted manner based on specific measurement variables

A physical-difference measurement between the fermenter's intake and exhaust air enables the actual oxygen consumption and carbon dioxide emissions to be calculated very precisely.

fortable and produce less API. Even minor fluctuations in the oxygen concentration can slow the metabolism, or even cause cells to die. So to maximize API production, the fermenter must be controlled in such a way that the RQ is always within the optimal range.

Miscalculation inevitable

To determine the current RQ, the CO_2 and O_2 concentrations inside the fermenter are simply measured. Sensors are located in the plant's exhaust gas stream for this purpose. They provide the process computer with the data, which are then used for continuous calculation of the indicator. It is the standard method currently used to control practically all fermentation processes in the pharmaceutical industry.

The devil is in the details, however. The measuring equipment typically used covers the complete measuring range from 0% to 25%. But this relatively wide span routinely returns significant measurement error, even when precision measuring equipment is used. This can create problems, because even the tiniest measurement error can lead to inadequate results – especially in relation to animal cells. The consequence is that the fermentation process is incorrectly controlled, so the conditions for optimal cell metabolism are not attained.

The solution would be more precise measurement of the O_2 concentration in the fermenter, but that is hardly possible with the current method of measuring only the exhaust gas.

Measurement error effectively eliminated

Siemens has devised a solution that eliminates the inherent inadequacies of the conventional O_2 and CO_2 measurements. It not only involves measuring the concentration of the two substances in the exhaust air but also includes the intake air in the fermenter in the calculation. A physical-difference measurement enables the actual O_2 consumption and CO_2 emissions produced by the fermentation process to be calculated very precisely. This means that for the first time the actual behavior of the fermenter is recorded without the measurement result being corrupted by fluctuations in the intake air, for example. Differing dew points in the intake and exhaust air can also no longer lead to measurement errors.

Smarter, more precise, more reliable

At the heart of the new measurement system is the Siprocess GA700 analyzer in conjunction with the Ultramat 7 and Oxymat 7 analysis modules. Siemens' proprietary paramagnetic alternating pressure technique is used to measure the O_2. It is currently the fastest-working extractive CO_2 analysis technique, delivering exact results even with the smallest measurement volumes. The OUR and CER can be determined more precisely by the new method, thus indicating the actual conversion rate and metabolic activity.

The method is characterized by strict linearity and permits O_2 measurement in a minimal range from 0.0% to 0.5%. This narrow measurement span results in a much lower measurement error tolerance and thus enables consumption measurements of a previously unmatched precision.

The hardware is highly service-friendly in design. For example, a defective analyzer can be very easily replaced in live operation, assuring high levels of availability of the measuring equipment. Additionally, an automatic switching system enables any number of fermenters to be linked to create a single measuring system.

Consequently, the well-being of the microorganisms is assured under all conditions, resulting in maximum cell growth. ■

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Sanofi

Insulin production in Frankfurt-Höchst, an important part of the European research network and the largest integrated production and assembly site in the Sanofi Group

Flexible cooperation at Christmas time

People who must take insulin depend on a continuous supply. For that reason, one of the world's largest manufacturers of human insulin agreed to only a very short plant shutdown while its old control system was being converted from Simatic S5 to the current version of the process control system Simatic PCS 7.

With more than 100,000 employees, Sanofi is one of the largest pharmaceutical companies in the world. At the Sanofi-Aventis Deutschland GmbH headquarters in Frankfurt, Germany, alone there are 8,400 employees. Located in the Höchst Industrial Park on the banks of the Main River, it is Sanofi's largest production and manufacturing facility. The site also houses a key research center that is part of Sanofi's worldwide research network. From the logistics section of the extensive company premises, drugs produced in Höchst are shipped to 86 countries.

Sanofi's focal areas are drugs for the treatment of diabetes, cancer, and cardiovascular and thyroid diseases. In addition, the company provides a wide range of drugs under the name Zentiva. Sanofi also has over-the-counter drugs, vaccinations, and veterinary medicine products in its portfolio.

Modernization of a proven plant

Sanofi operates several plants for the biotechnological production and manufacturing of human insulin in Höchst as well. The insulin solution and suspensions that fill the insulin cartridges for pens are produced in preparation plants. A batch process is used to create compounds of human insulin, water, and other additives.

The entire production process takes place inside a completely en-

cased system. The key steps in the process are dissolving, adjusting the pH value, mixing, and filtering. The plant also contains equipment required for insulin purification and sterilization. As part of a manufacturing plant modernization, Siemens received the order to replace the existing Simatic S5 automation system with a new, state-of-the-art solution. To do so, Siemens would need to convert the entire process control system to Simatic PCS 7 in conjunction with Simatic Batch.

Such a control system replacement is possible only during plant shutdown. Siemens had to keep the cessation of activities as brief as possible, because Sanofi wanted to retain its ability to supply as agreed.

Open-heart surgery

For Dr. Helmut Uhl, the project was the equivalent of "open-heart surgery." Uhl is head of insulin manufacturing at the Frankfurt-Höchst site. He was aware of the extreme conditions under which the automation system upgrade had to take place. Of course the project had to satisfy the Good Manufacturing Practice (GMP) requirements applicable to the pharmaceutical industry and also adhere to an exact schedule.

»Together with Simatic Batch, the Simatic PCS 7 process control system facilitates efficient batch process planning, control, and logging.«

Dr. Helmut Uhl, Head of Insulin Production Frankfurt
Sanofi-Aventis Deutschland GmbH

Siemens implemented the project itself in the period from June 2014 to February 2015. The plant downtime required for assembly, functional testing, start-up, and production testing was limited to the Christmas holiday in 2014. After that break, the plant would have to resume production as normal.

Batch process with extra benefits

When teamed up with Simatic Batch, the Simatic PCS 7 process control system facilitates efficient batch process planning, control, and logging. It takes into consideration the GMP production conditions, required quality assurance, and connection to the Prodis system in accordance with IP 21.

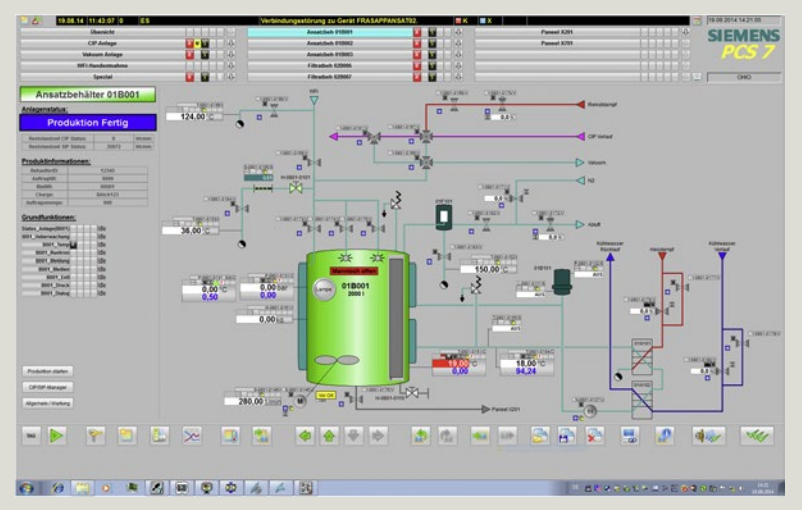
The production processes are controlled with the help of formulas stored in the system. Simatic Batch creates the formulas and uses them to control the plant. Any manual operation sequences required are embedded as operator dialogs and implemented via WinCC terminals in the plant. Adding materials or entering analysis data, for example, are manual operations.

All of the process and operating data are recorded and documented on a batch-specific basis and can be printed out in the form of a batch log. Simatic Batch also provides a comprehensive range of fully automated batch management functions.

Successful cooperation among experts

In addition to creating the user software, the Siemens service package included planning and supplying the required hardware. Tasks such as loop checks, factory and site acceptance tests, system operator training sessions, and start-up with subsequent production supervision for restarting production were also part of the package.

The project was implemented on schedule under the existing, extremely time-sensitive conditions – the successful result of close collaboration between Sanofi and Siemens. All of the parties involved demonstrated extraordinary flexibility – even agreeing to work overtime and Christmas and New Year's shifts. ■



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Formulas stored in the process control system control the production process, and any manual operations required are embedded in the relevant formula elements as operator dialogs

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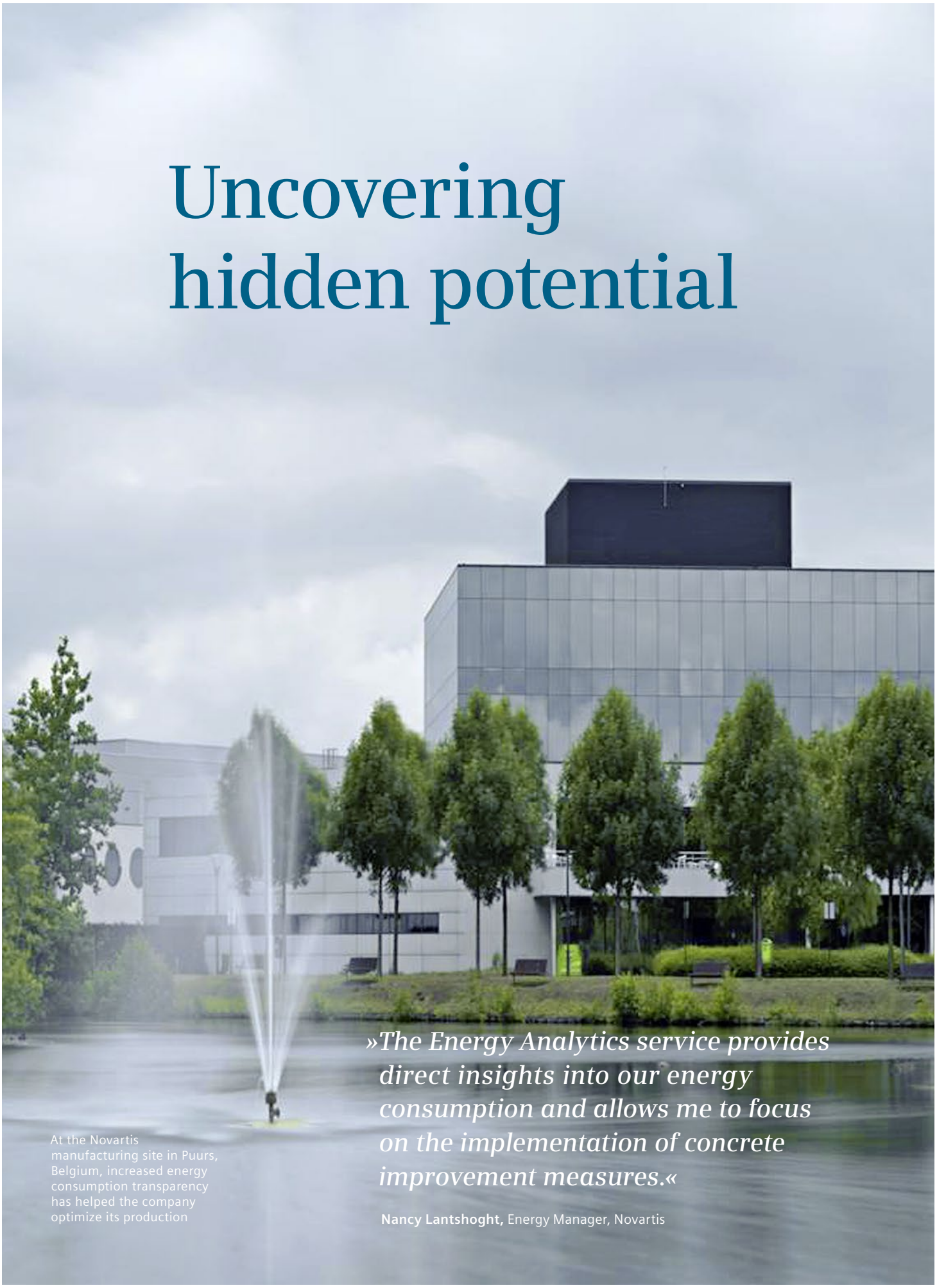
Uncovering hidden potential



»The Energy Analytics service provides direct insights into our energy consumption and allows me to focus on the implementation of concrete improvement measures.«

Nancy Lantshoght, Energy Manager, Novartis

At the Novartis manufacturing site in Puurs, Belgium, increased energy consumption transparency has helped the company optimize its production

Siemens AG / Novartis

In Belgium, the implementation of effective energy data management has helped a pharmaceutical company improve its energy consumption transparency and uncover a hidden potential for savings – resulting in greater efficiency, lower costs, and an optimized production environment.

The Puurs manufacturing site, the second-largest division of Novartis, is a global leader in eye care. The ophthalmologic company offers a wide range of surgical, pharmaceutical, and vision care products to treat various eye diseases and conditions. Development of these products requires an aseptic environment, and to maintain this environment, the clean rooms require energy-intensive systems for water treatment; heating, ventilation, and air conditioning (HVAC); and steam pressure sterilization. To improve the transparency of the energy usage associated with these systems, Novartis embarked on a strategic partnership with Siemens by entering into a long-term Energy Analytics service agreement.

Identifying opportunities

Because Energy Analytics is a managed service, Siemens takes on the responsibility for storing and analyzing data. At Novartis' manufacturing site in Puurs, Belgium, this was particularly beneficial because it allowed operators to focus their time and efforts on the actual implementation of energy-efficiency measures. Customized reports sum up the results of the data analysis provided by Energy Analytics. These reports are based on data from more than 400 measuring points spread across energy-consuming utilities involved in the production processes. Nancy Lantshoght, Novartis' energy manager at the facility, has a great deal of experience in the area of energy efficiency. With the help of Energy Analytics, she now has a way to identify further opportunity for energy optimization thanks to direct insights into energy consumption, thus allowing for continuous improvement of facility operations.

Tailored operations

Siemens has assembled a range of energy data management functions and analytical tools into four separate Energy Analytics options, all of which are then tailored to the unique requirements of the given customer's operations. As an Energy Analytics Platinum customer, Lantshoght has access to the worldwide network of energy consultants at the Siemens Operation Center. These consultants propose potential improvements to increase energy efficiency, which are then reviewed and verified by Novartis to determine feasibility.

Siemens developed the Energy Analytics Platinum for users like Novartis whose highest priority is maximizing the transparency of their energy data. Effective reports on key energy figures, analyses at the machine level, and consumption reduction projects have helped operators increase the energy efficiency of their production plants and standardize energy data management processes. At the same time, the service also lays the groundwork for ISO 50001 certification.

Immediate results

The strategic partnership with Siemens allowed Novartis to invest valuable capital into optimization measures right from the start. Initial measures were implemented shortly after the site was connected to the Operation Center. One of the first projects examined the control scheme of two compressors used in the production process. As a result of the analysis, the Siemens consultants recommended an optimized control scheme that reduced the energy consumption of the compressors by approximately 12%.

Novartis was able to optimize the production plant only a few months after implementing Energy Analytics, and the company is now on target to achieve its energy efficiency goals. Novartis Puurs' submission of this project for the 2014 Novartis HSE & Business Continuity Award is a testament to the success of the collaboration with Siemens. ■

Siemens AG

Project facts

Siemens helps increase the transparency of energy consumption and improve the energy efficiency of clean rooms through a set of tailored services:

- Energy Analytics as a managed service
- Access to a worldwide network of experts for ongoing consultation to improve energy efficiency
- Definition of KPIs based on initial analyses of facilities and assets
- Energy reports based on data from more than 400 measuring points

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From cell to organ

The creation of a new organ from a patient's own cells as a means of curing serious illness and injury remains a vision for the future. A research group in Würzburg has developed systems that might make that vision a reality more rapidly.

At the University of Würzburg's Department of Tissue Engineering and Regenerative Medicine, headed by Professor Heike Walles, a number of teams are investigating how new tissue – and even complete organs – can be generated from human cells. One of the aims of this work is to produce implants that will help patients with serious illnesses and injuries. What sounds like something from a sci-fi movie can already be seen in action in one of the institute's labs: small incubators hold special reactors in which the tissue – such as for a lung – can mature within a controlled environment.

This research work is not only interesting from a biochemical and medical perspective. For the tissue – and thus the organ – to develop and adapt to its subsequent function or environment, it must be provided with additional stimuli during the incubation period. This may mean mechanical stresses such as pressure fluctuations based on simulated blood circulation or breathing, or physical or chemical stimuli, which the researchers introduce into the bioreactor by way of various media and nutrient solutions. The bioreactor and cell model are being developed together in Würzburg – first by in silico modeling on the computer and subsequently as actual bioreactors with the relevant control systems. As Dr.-Ing. Jan Hansmann, head of the department's Electronic Tissue Interfaces research group, explains, "This enables us to control the pumps, motors, and sensors in the incubator correctly so we can optimally stimulate the biological processes."

Integrated automation solution for research

For the automation of the incubators and bioreactors, Hansmann's team is relying on its own know-how and on tried and tested technology from Siemens. Each incubator is equipped with a Simatic HMI Comfort Panel, via which the researchers can retrieve and analyze data and control the systems in the incubator. The control system is a Simatic ET 200 distributed I/O system with a dedicated CPU. There are currently 15 of the systems in the lab, with more planned.

The staff uses the TIA Portal engineering framework to configure the panels and control system. Hansmann describes the benefits: "The system is very simple and easy to understand. In our lab we have to

Siemens AG/W.Geyer

»The system is very simple and easy to understand.«

Dr.-Ing. Jan Hansmann, Head of Electronic Tissue Interfaces Research Group, Department of Tissue Engineering and Regenerative Medicine, University of Würzburg

Siemens AG/W.Geyer

Simatic Comfort Panels ensure that the researchers are able to easily control the processes in the incubator

integrate many individual units into an integrated architecture. The flexibility of TIA Portal enables us to upgrade our equipment step by step, while at the same time providing a unified system with a consistent look and feel for the lab staff." The ease of handling results in 50% less effort and expense compared with the engineering system the lab previously used. Siemens provides the staff with special training to help them carry out the automation tasks. Hansmann cites the modular design as an additional advantage: "We can very easily utilize preexisting modules and operator screens based on TIA Portal's library concept." The incubators can also be very easily connected to the IT environment, enabling experiment data to be stored on a central server for subsequent evaluation and analysis on a PC. Automatic backup is activated at the click of a button, and the Comfort Panel saves all the essential operating data to a Simatic HMI memory card.

Automated solutions for test systems

The researchers in the Department of Tissue Engineering and Regenerative Medicine have big plans. Their work on so-called vascularized tissue (tissue equipped with blood vessels) has attracted a great deal of attention, and not just in scientific circles. Hansmann describes one of the major successes of tissue engineering in Würzburg: "Working with the University Hospital and the Robert Bosch Hospital, we recently produced a complete section of a human windpipe in the bioreactor and successfully implanted it into a very seriously ill patient as part of a 'compassionate use' program." In fact, no other research group in the world has to date produced such a complex biological implant.

The scientist sees great demand for automated solutions in the production of test systems to aid research into disease and the development of new drugs: "We have already developed a first production line for artificial human skin, capable of producing batches with as many as 5,000 test systems. We are doing this work in conjunction with the Fraunhofer Institute for Interfacial Engineering and Biotechnology here in Würzburg, seeking to drive applications of our research in the pharmaceutical and cosmetics industries."

Automated production of these skin models enables the researchers to more quickly investigate cell interactions following injury, or the effects of substances on and in the skin, and also aids substance screening. The legally mandated validation studies are currently being conducted to enable skin model testing to be used as an alternative to animal testing.

Promising future for regenerative therapies

The tissue engineers in Würzburg will soon have even more facilities at their disposal to enhance their work. Nearby, construction is currently under way on the Fraunhofer "Regenerative Therapies for Oncology and Musculoskeletal Diseases" Translational Center – a center for the development of new materials and their biologization, and for the advancement of cell-based regenerative therapies in medical applications. The center will address the entire value chain of regenerative therapies, from product development to the licensing of medical products, biologized medical products, and cell grafts. Team leader Hansmann says, "At the Translational Center we are also relying on efficient Siemens technology through the TIA Portal engineering framework and the Simatic HMI panels, which I am sure will lay the groundwork for the future success of regenerative therapies." He continues, "It is very important to have the appropriate high-performance automated bioreactor systems for the production process, so that the many products currently in development – some of which are about to enter clinical testing – can actually be produced." ■

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A strong relationship

A Texas-based manufacturer of cleanroom PODs asked for an experienced global partner to implement a robust and scalable automation solution that would help the company create a GMP facility out of an existing warehouse, as well as improve its worldwide pharmaceutical production operations.

G-CON Manufacturing Inc. designs, produces, and installs prefabricated, autonomous cleanrooms, known as PODs. G-CON's extensive cleanroom POD portfolio covers both large- and small-scale requirements, from laboratory environments to personalized medicine and production process platforms.

In 2015, G-CON was selected to build a multi-POD ISO Class 7 formulation and filling suite for the University of Tennessee Health Science Center (UTHSC). The purpose of the new facility was to expand the capabilities of the UTHSC Plough Center for Sterile Drug Delivery, which is currently used for process development and analytical and stability studies, as well as hands-on training in aseptic processing and sterilization techniques.

G-CON

G-CON cleanroom PODs for large- and small-scale requirements ensure that any products produced in the facility will be done at the highest cGMP quality standards

Siemens AG

The automation panel with a 15-inch HMI is one of the automation-related products for the project from Siemens

The building, a former warehouse, was purchased by UTHSC about five years ago and will serve as a state-of-the-art facility for manufacturing drugs and training students and professionals from the pharmaceutical industry and government regulatory agencies in pharmaceutical production. It required a highly robust, reliable, and scalable automation system in order to meet both customer needs and the climate control requirements for a current Good Manufacturing Practice (cGMP) facility. To achieve this, G-CON partnered with Siemens to implement an integrated software solution – a decision that would prove critical to the success of the overall project.

A reliable and robust solution

G-CON's POD cleanroom units stand out from traditional cleanroom structures due to their ease of scalability, their mobility, and the ability to repurpose the POD once the production process reaches the end of its lifecycle. The POD suite provides approximately 1,800 square feet of cleanroom space at the facility and incorporates areas for component preparation, compounding/formulation, filling, and lyophilization for use in the manufacturing of clinical and small-scale products. An additional POD provides approximately 760 square feet of cleanroom space for the development and manufacture of semisolid products.

Siemens was the single-source provider of automation-related products for the project, supplying a total of six panels on one programmable logic controller (PLC) rack with multiple remote I/O devices. Siemens also delivered an automation panel with a 15-inch HMI. All communication is carried out via Profinet, including communicating with Sinamics G120P drives for air handlers, pressurization, and cascades. Siemens implemented a ring topology with Scalance switches for redundancy, along with an uninterruptible power supply (UPS), which ensures uptime for the system. AWC Inc. provided all the programming for the PLCs and drives.

Real-world results

AWC used TIA Portal to develop HMI screens while building out the I/O system. By leveraging the portal, the project team was able to significantly reduce programming and engineering time. The integrated solution from Siemens also offers long-term benefits because the library structure is built for future projects, which will further improve engineering efficiency.

AWC supported the factory acceptance test (FAT) with a local team that included both programmers and project managers. The team completed all functional testing at G-CON's facility in College Station, Texas, and it will be supporting G-CON at the client facility during the site acceptance test (SAT), which is scheduled for summer 2016. The documentation generated can be used for installation qualification / operational qualification (IQ/OQ).

Future success

The new Plough Center for Sterile Drug Delivery has allowed UTHSC to strengthen its national and international position as a pharmaceutical manufacturer. Siemens support and lifecycle expertise during the development of the solution played a critical role in the success of the project. The relationship with Siemens enabled G-CON to offer competitive prices, expand its applications to end users, and use the integrated solution from UTHSC to improve production operations at other facilities across the globe. ■

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Baxter Oncology GmbH

Coordinated to perfection

In the field of pharmaceutical production, stringent clean room standards apply. At a new Baxter Oncology GmbH production site in Halle Westfalen, Germany, all the building technology for ventilation, air pressure, temperature, and humidity was automated for the first time using Simatic PCS 7.

Baxter is a company with international operations and a workforce of 50,000 in more than 100 countries worldwide. Baxter products can be found in almost every clinic and health center and in patients' homes. These products include dialysis treatments, cytostatic drugs, artificial nutrition, biomaterials for surgery, and anesthetics.

Baxter acquired its Oncology Division from ASTA Werke at the turn of the millennium. With production sites in Halle and Bielefeld, the company has made a name for itself through its cancer medicines, and it primarily produces preparations for the treatment of breast and colon cancer and non-Hodgkin's lymphoma. Today, it ranks among the world's leading manufacturers of cytotoxic drugs.

At the Halle location, Baxter Bio-Pharma Solutions (BPS) received the 2016 Facility of the Year Award from the International Society for Pharmaceutical Engineering (ISPE) for its consistent application of operational excellence and its end-to-end lean manufacturing principles implemented for process, personnel, material, and waste flows. In Halle, Baxter Oncology GmbH, which added a new production area in 2014, also operates a filling plant for small-batch pharmaceutical production.

Complete building technology from one source

Baxter commissioned Siemens to install all the building technology for the plant, including the necessary utility supply systems. In addition to heating, ventilation, and air conditioning (HVAC), this also included the distribution of hot and cold water as well as the cooling water supply for the freeze dryer used in production.

Baxter wanted to use its employees' existing know-how with Simatic PCS 7 and therefore insisted that the building technology for the new area be controlled via the familiar, tried and tested automation system. This was intended to ensure that technical problems could be resolved very quickly and without outside help – a crucial criterion in the pharmaceutical environment, where production facilities operate under clean room conditions.

The Baxter Group is a company with international operations and a workforce of

50,000

in more than

100 countries

Baxter Oncology GmbH

The facility used to control room conditions is operated by Baxter employees via the familiar automation system

Climate-controlled conditions within tight tolerances

Varying and precisely defined clean room conditions must be guaranteed for each production area. Thus, the task is to maintain ambient room pressure, temperature, and humidity within certain limits. Adherence to these levels must also be documented through the building automation system and consequently be verifiable at all times.

The overpressure levels in the building are crucial in this respect. They must meet the criteria of the required clean room category and cannot fall below these levels under any circumstances. This is the only way to ensure that no external particles penetrate the clean room. A failure of the ventilation system would inevitably lead to a drop in the required air pressure. The clean room conditions would consequently no longer be guaranteed, resulting in a very costly revalidation of the production facilities.

Special requirements met

HVAC projects with automation via Simatic PCS 7 tend to represent exceptional cases. The task in this project therefore was to take into account a number of special features and make specific adjustments. For example, a number of expansions had to be made to the Advanced Process Library (APL) and the Industry Library in order to adapt the control of the volumetric flow controllers, valves, and filter/fan units to Baxter's requirements. In addition, the project team adapted module symbols and faceplates to an HVAC system and developed some modules from scratch.

Another special challenge was the separate regulation of room conditions for the different rooms. In addition, more than 100 filter/fan units needed to be connected via Modbus TCP. These units produce a laminar airflow and are used in the production areas in which clean room category A is a stipulated requirement.

The special features of this project included the establishment of a decontamination air lock, the type and size of which had never before been created. The air lock is needed for the sterilization of the bottles and containers used in production and requires a special control to immediately detect the leakage of harmful gases.

The building technology in the new production areas at Baxter Oncology in Halle has now been in operation for more than a year without any critical situations or even malfunctions arising.

This success is thanks not least to the close collaboration between the Siemens specialists and Baxter's application engineers. ■

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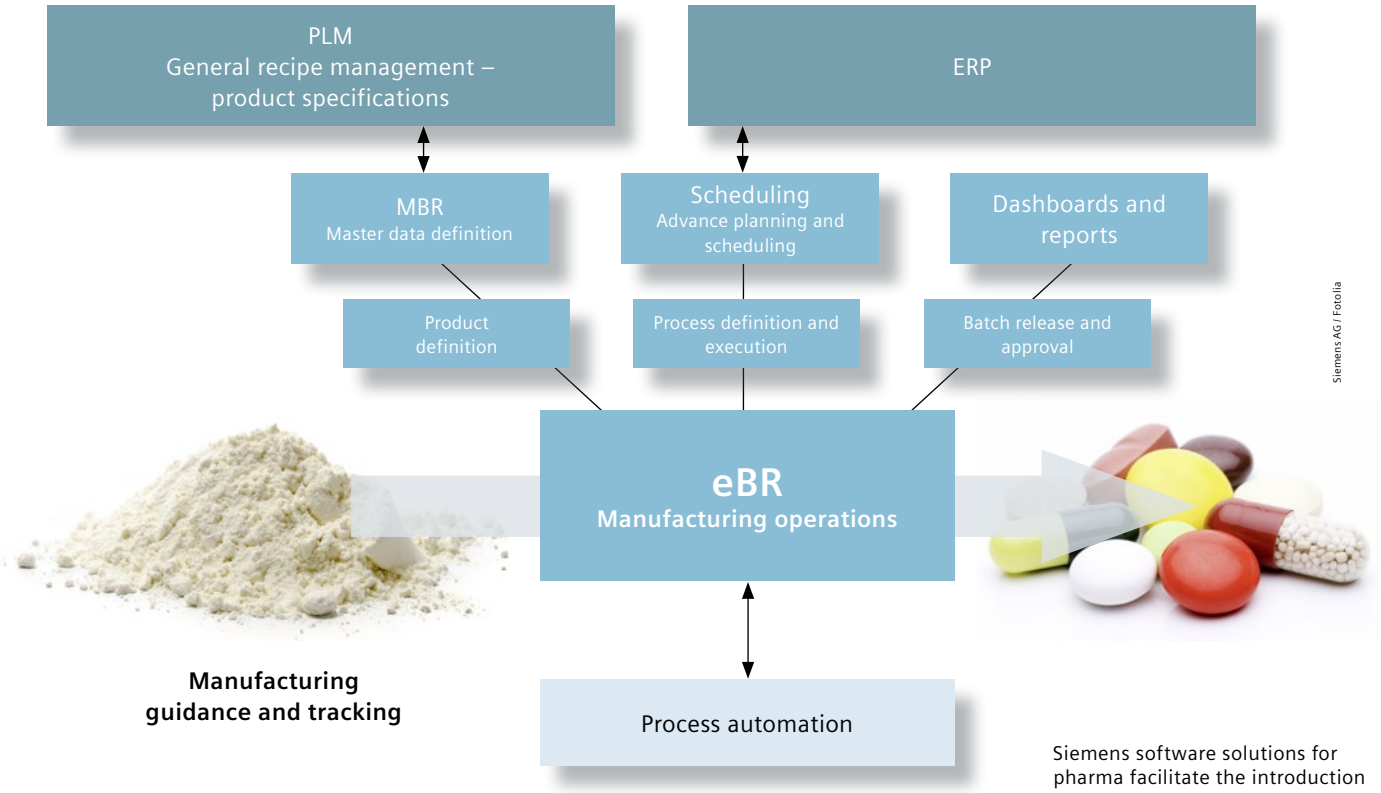
Electronic excellence

Electronic batch records can help improve pharmaceutical processes, maintain high product quality, and reduce risk. The new version of Simatic IT eBR supports the implementation and management of electronic batch recording in all phases of the batch lifecycle.



Siemens software solutions for pharma facilitate the introduction of new products

In a paper-based environment, creating and maintaining master batch records (MBRs) involves huge effort. During production, manual entry is subject to human error, information can be duplicated because of multiple systems, and it takes a lot of time to gather and input all relevant data. The review and reconciliation of this information is also time-consuming.

Standardization in the definition of the different manufacturing processes is even more difficult because information is not always centralized. Analysis of the key performance indicators of executed batch records is possible only after the labor-intensive reentry of data from disparate systems.

Streamlining management of master batch records

In contrast, electronic master batch record management with a manufacturing execution system (MES) is based on master batch record templates that are subject to automatic version management. Master batch record / electronic batch record (MBR/eBR) systems provide the ability to create standardized processes or subprocesses and facilitate their maintenance and validation.

These systems provide a framework for setting up and generating an empty eBR form for data collection during production. Then the required production parameters are distributed to the relevant systems for execution. The MES then

automatically synchronizes and collects all batch-related information into an eBR.

This approach provides error reduction and prevention as well as data centralization for further analysis.

An integrated solution for paperless manufacturing

For several years, Simatic IT eBR has been successfully applied in MBR and eBR management. Step by step, the solution follows the lifecycle of the batch record, taking advantage of the wide range of out-of-the-box MES functionalities, such as order management, tracking and tracing of materials, and equipment management.

To further simplify the implementation and operation of an eBR solution, the latest version of Simatic IT eBR features a web-based MBR module. This facilitates the management of key process parameters and offers native integration with the Simatic solution in the automation layer. With the new MBR module, users can easily acquire definitions for critical process parameters (CPPs) and critical quality parameters (CQPs). These are configured directly in the system or sourced from enterprise resource planning (ERP), product lifecycle management (PLM), or general recipe systems. Together with product and process recipe definitions, these key parameters can then be used to create a comprehensive description of the batch record. This helps reduce engineering time and significantly accelerates the introduction of new products. The native integration between Simatic IT eBR and Simatic PCS 7 helps streamline the entire batch record lifecycle from design to execution and review.

During the design phase, Simatic IT eBR provides users the ability to browse batch recipes and directly use eBR-relevant critical parameters that are defined in the batch system. Users can define the set points and threshold values for automatic and manual process actions based on MBR data. The integration of the MES and the distributed control system (DCS) enables the capabilities of each system to be used in one environment: a robust and powerful batch engine in the DCS for complex low-level S88.01 recipes, and an intuitive and easy-to-use tool in the MES to design processes and implement parametric MBRs according to S95 standards. The recipe information is available directly in the MES tool, and designing MBRs is greatly simplified.

During production execution, every key process parameter defined in the MBR is enforced in the eBR execution. Manual operations are guided with electronic work instructions; automated operations are controlled by the DCS; and every resource used across the process is verified, tracked, and traced. Quality testing (in-line, at-line, and off-line sampling) is completely integrated during the execution of the process. Alarms and alerts are recorded in the MES and can be configured to trigger corrective or preventive actions. In addition, the system will aggregate charts and reports as part of the eBR, which is based on real-time data and can be accessed anytime.

In the review phase, this solution enables the electronic release of the batch by exception. In addition, the integrated manufacturing intelligence tool allows review and comparison of batch data to identify potential for improvement, thus supporting operational excellence initiatives.

Key benefits

- Paperless process
- Reduction of development effort in integrating MES and DCS
- Ability to develop standardized libraries of process operations
- Single point of review for all batch-relevant information

Proven yet innovative

Simatic IT eBR draws on Siemens' more than 30 years of system and solution expertise in the pharmaceutical industry. It is fully compliant with Good Manufacturing Practice (GMP) and US Food and Drug Administration (FDA) regulations and provides a lean and scalable solution for truly paperless manufacturing. ■

Siemens AG

Integration of MES task list into HMI screen

↗ **siemens.com/pharma**

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Running smooth

Regardless of a project's size, managing documentation is always a challenge, whether due to the number of documents or the need for reliable data to prevent flaws in the project. By automating the document handling procedures in its Large Drives engineering business, Siemens in Brazil achieved substantial time savings.

The Operation & Engineering Center for Solutions in Brazil provides integrated engineering services to companies that manage pulp and paper projects. Until 2012, the documentation for all the projects was managed manually, requiring a significant amount of time and effort from personnel to generate document transmittals and update lists.

Knowing that the market already provided tools that could help with documentation management, the department decided to move to enterprise content management (ECM) software.

Open architecture and seamless integration

After an extensive search for a tool that would best fit the project requirements, the project team selected Comos PQM (Project Quality Management) software as the best possible solution. In addition to its open architecture, Comos PQM allows for integration between document management and engineering. Overall, it represented the option that would best fit the needs of the department. The Comos PQM document management system ensures more structured project documentation, and the solution works with both documents that are generated by the software and external ones. Examples of the latter include the descriptions, calculations, drawings, and correspondence that are found in every project in a variety of file formats. The external documents are assigned to the relevant database objects instead of being stored in folder structures. In addition, the solution offers version and revision management. For every document, the history, author, test stages, responsibilities, and so on can be displayed. This all ensures greater traceability and transparency. The implemented test-and-release procedure not only simplifies the work: when the project is handed over, the customer also receives consistent, up-to-date documentation.

Siemens Brazil

»With Comos, we were able to adapt the software to our process and our requirements. This was essential for the success of the implementation.«

Mário Ricardo de Marco,
Comos Administrator at Siemens engineering segment PD LD OEC

Rolling out the solution

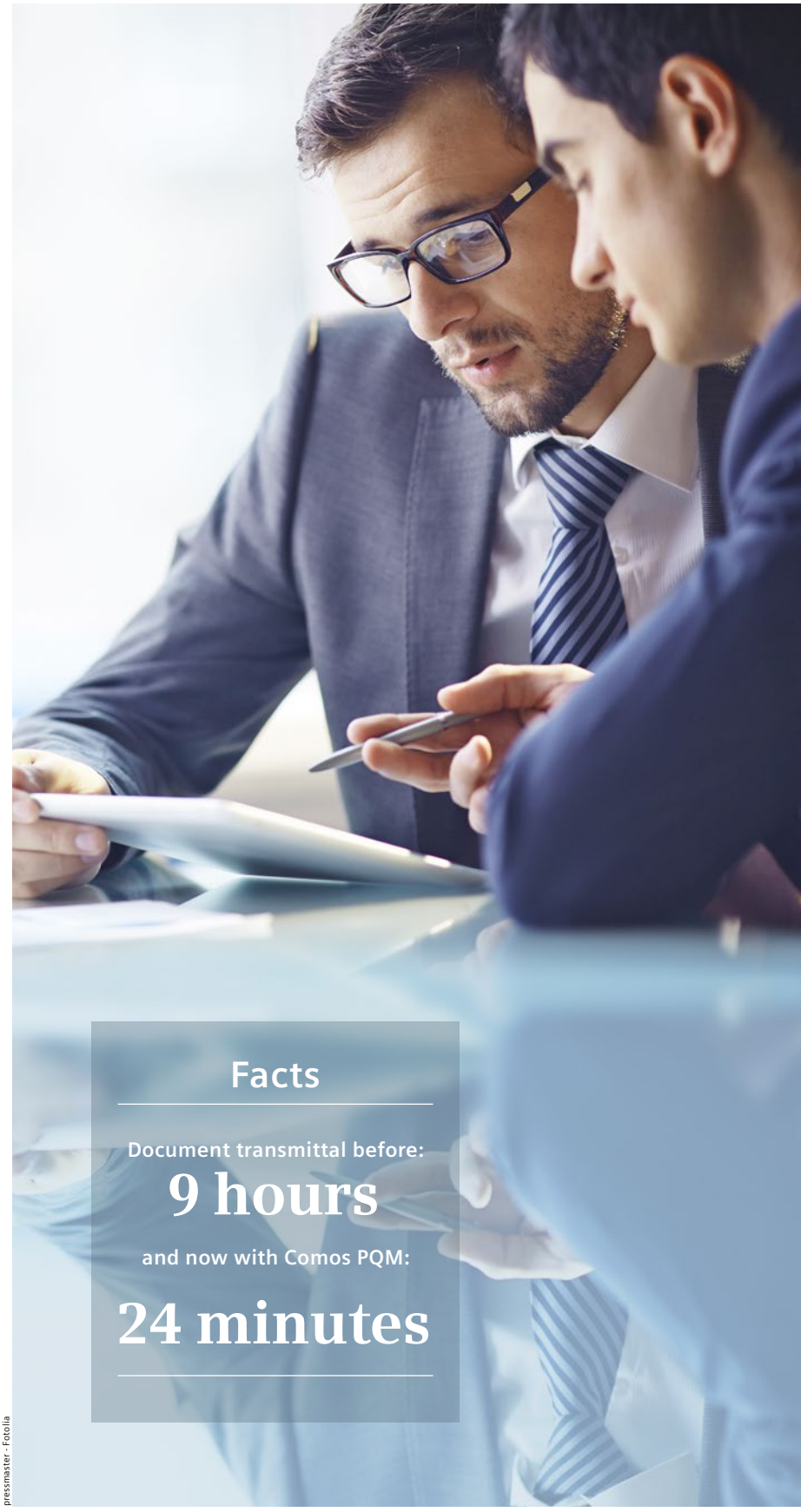
After the initial decision to use Comos, the team broadened the project specifications to also include the requirements of other business areas at Siemens involved in the process, such as Oil & Gas, Marine, and Process Automation. This required standardization of procedures and documents, and the project teams worked together to develop a solution. Thus, Comos also helped define and improve internal processes. The teams were able to produce quality work with less effort, leading to improved overall team and business performance. The implementation took place over the course of a year.

Currently, there are more than 30 active projects in Comos, and all new projects are being executed solely in it. Projects developed prior

to the Comos implementation were migrated during a whole year and now all projects are in the software. The software customization was successful, and performance has exceeded expectations. Now, all documentation processes are automated and standardized, the time required for document management has decreased, and productivity has increased. The productivity gains brought by the software are noticeable to all involved and are actually measurable.

Impressive savings

To quantify the time savings, the team decided to measure and compare some procedures carried out before and after the Comos PQM implementation. The measures have shown gains of more than 90% in productivity, generating substantial time and cost savings. Among the significant benefits, one outstanding example is the reduced time required to create a document transmittal. Before, a transmittal with five documents took about 30 minutes to be concluded. Now, with Comos PQM, the process for the same number of documents is accomplished automatically within 7 minutes, by just dragging and dropping the documentation. ■



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Comos PQM allows for integration between documentation management and engineering to increase productivity

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A cleaner process

Offering high-quality, standardized, and flexible equipment requires close cooperation between original equipment manufacturers (OEMs) and suppliers. A Belgian company is a leading example of how OEMs can take advantage of such relationships to maximize benefits for the customer.

A strong team: Sitrans F M MAG 6000 with Sitrans P compact and Sitrans TS300 for precise measurements of flow, pressure, and temperature ...

... and the pressure transmitter Sitrans P D S III in endurance tests

For more than 50 years, the Belgian company Packo Inox has produced high-quality stainless steel systems for food and pharmaceutical manufacturing. In addition to milk cooling tanks, pasteurizers, and mobile and stationary cleaning-in-place (CIP) systems, the company supplies complete process lines. Its equipment is used in processes where high hygienic standards are essential, and its products are designed to be cleaned in position to eliminate any bacteria and to comply with strict hygiene guidelines. Packo Inox develops products that strike a balance between standardization and customization: standardization so they can be used in other systems and applications, and customization to meet special customer requirements. However, the challenges of the market are varied and constantly changing, so the company is always looking to innovate its products, systems, and solutions. Packo Inox selects its components and suppliers very carefully to fulfill this goal.

OEM solution partners

Packo Inox has used equipment from Siemens for many years, including automation, HMI, monitoring, power supply, and instrumentation components for fully integrated solutions. In addition to its extensive portfolio, Siemens

»We are working more and more with international customers. This means that we need partners and suppliers who also work globally and can help us at the installation site – which is precisely where Siemens comes in.«

Ove De Backer,
Industry Business Unit Manager, Packo Inox

supports Packo Inox with its in-depth understanding of OEMs and their challenges.

Packo Inox requires a wide range of products that are able to withstand harsh industrial conditions and that can be integrated into larger systems. Siemens makes integration easier by providing scannable EAN codes that give access to a component's technical data. This helps reduce design, manufacturing, and repair costs.

"The ease of integration makes it possible to quickly design and engineer projects, including smooth commissioning of our CIP units. This means faster commissioning, and our customers profit from a shorter time to market," says Karel Maeyens, project manager at Packo Inox.

Quicker and cleaner results

Packo Inox's CIP systems play a crucial role in achieving exceptional hygiene standards. They can automatically clean tanks, pipes, heat exchangers, and mixing systems without these components needing to be moved. This improves efficiency, reduces cleaning times, and decreases the quantity of chemicals used.

The company's CIP systems also constantly monitor and regulate pressure, temperature, and other parameters. The instruments used for measuring these processes include the Sitrans F M MAG 6000, Sitrans P Compact, and Sitrans TS300, all of which can withstand high temperatures and aggressive cleaning agents to provide many years of reliable performance.

Packo Inox's industry business unit manager, Ove De Backer, says, "We appreciate the robustness and stability of Siemens devices. Our customers want to have a secure business 24/7 that extends over many years of operation."

The components of success

Packo Inox's automated CIP system runs through several steps: water in the prestage, hot detergent, hot water or steam in the main cycle, cold water, possibly disinfectant, and again water for rinsing. All these liquids must be pumped through at prescribed times, cleaning agents dosed correctly, and dirty liquids pumped out at the end. Siemens automation components handle all these tasks, in conjunction with continuous monitoring and operational control.

In addition to the CIP systems, Packo Inox equips its dosing units, storage tanks, and subsystems with Siemens components. These enable Packo Inox to benefit from simpler integration and efficient engineering, and Siemens' global support network helps the company implement its systems for food and pharmaceutical manufacturers worldwide. ■

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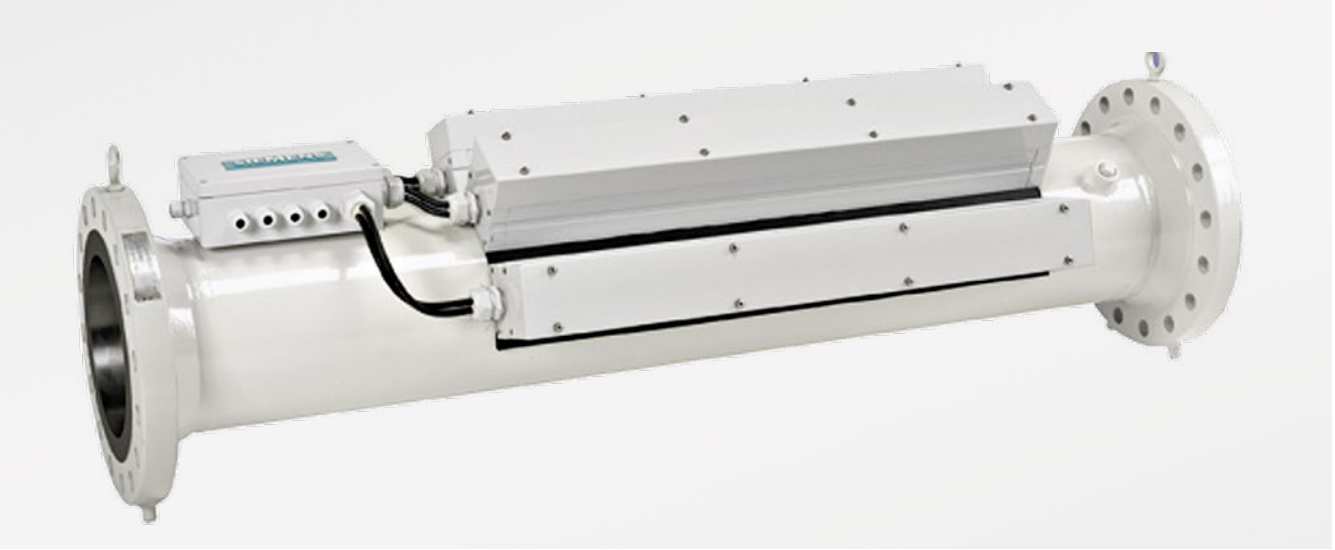

Siemens AG

The Sitrans FUT1010 ultrasonic flowmeter is available in dual, three-, and four-channel configurations and also for gas measurement

An ultrasonic advantage

At a fertilizer plant in Russia, the use of ultrasonic flow technology helped an operator improve flow measurement accuracy, reduce maintenance, and significantly improve the company's bottom line.

The Russian plant yields nearly 1.1 million tons of solid ammonium nitrate per year for fertilizer through a production process that involves deriving hydrogen (a primary component of ammonium) from natural gas feedstock. The facility must measure the flow of gas through the pipeline after receiving it from the supplier, both to ensure that the agreed-upon amount of gas has been delivered and to optimize the overall production process.

Overcoming limitations

Until recently, the operator had been relying on two orifice plates for these measurements. But because the plates were in regular contact with the flowing medium, they required periodic cleaning. The turndown ratio was also quite low, limiting the range of flow rates that could be monitored accurately.

Taking these factors into account, the plant operator knew it was time to replace the orifice plates with a different, higher-performing flow measurement technology. The project team first considered one supplier's inline ultrasonic flowmeter due to its high degree of accuracy. However, upon realizing that inline flowmeters require sensor cleaning in order to function optimally, the company began examining other options. The operator decided to install the Sitrans FUT1010 ultrasonic flowmeter from Siemens and immediately noticed a number of benefits.

Across-the-board savings

After putting the Sitrans FUT1010 into operation, the plant instantly saw a 1% increase in the accuracy of the calculated flow rate compared with that of the gas supplier's orifice plate – translating into several thousand dollars in savings per day. The flowmeter features the unique TransLoc system, which mounts clamp-on transducers to the outside of the pipe. Thanks to this external configuration, the transducers require very little cleaning, which resulted in reduced maintenance and downtime at the plant.

The meter's whole-bore configuration, which prevents pressure drop, helped achieve further cost savings by reducing the amount of electricity needed to pump gas through the pipeline. The high turndown ratio also allowed for consistent performance despite the varying rates of natural gas flow.

A sound investment

The Sitrans FUT1010 has now been incorporated into the facility's natural gas pipeline for some time, and the customer remains extremely satisfied with its performance. The plant operator plans to purchase a second meter in the near future to further optimize the production of ammonia-based fertilizer and boost the company's bottom line. ■

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Addressing accuracy

When it comes to transmitting process variables, 4–20 mA technology is by far the most popular method. However, in applications in which measuring accuracy is mission-critical, the use of a digital fieldbus such as Profibus, Profinet, or Foundation Fieldbus may be the better option.

Holcim Zementwerk

An example of technology for measuring levels in extreme conditions: the Sitrans LR560 on top of a cement silo

First introduced in the 1950s as a revolutionary technology, 4–20 mA offers a number of benefits, including ease of use, low cost, resistance to electrical noise, and immunity to line losses. However, it also has limitations and pitfalls – perhaps the most notable of which is loss of accuracy. Although it is generally accepted that the validity of a signal degrades with 4–20 mA, many individuals disregard, or at least fail to recognize, the extent of the degradation. All field devices today use digital technology. This means that 4–20 mA devices must convert the internal digital value into an analog value to transmit it, and then convert it back to digital at the controller. During the signal conversion and transmission, a number of errors can occur that affect accuracy. The accuracy of 4–20 mA devices may also be impaired – unnoticed – by environmental factors such as water ingress.

Experiment demonstrates effects

Water ingress can result from aging seals or accidental mishandling of instrument lids, which is not uncommon in real-life process plants. In an experiment performed by Siemens, rainwater that had been sitting in a wheelbarrow for a period of time to imitate natural pollution was poured into a 4–20 mA device while it was performing level measurement. Before the water was added, the device was measuring 16.23 mA. Shortly after the water was added, the measuring level rose to 18.55 mA – representing a 14.5% change in value. When the same experiment was performed with a Profibus PA device, the ingress of water had no visible effect on the process variable or on the network. It is only over time that network errors occur. However, even in this case, the process variable is still transmitted with full accuracy and the end user knows what is going on – Profibus PA never silently reduces accuracy the way 4–20 mA can.

New insights gained

In general, the problems and pitfalls of 4–20 mA technology are rarely discussed – with most operators failing to recognize just how significant the loss of accuracy associated with such devices can be. This loss is not an issue with digital fieldbuses such as Profibus, Profinet, or Foundation Fieldbus, and in applications in which measuring accuracy is paramount, they will likely be the more suitable option. ■

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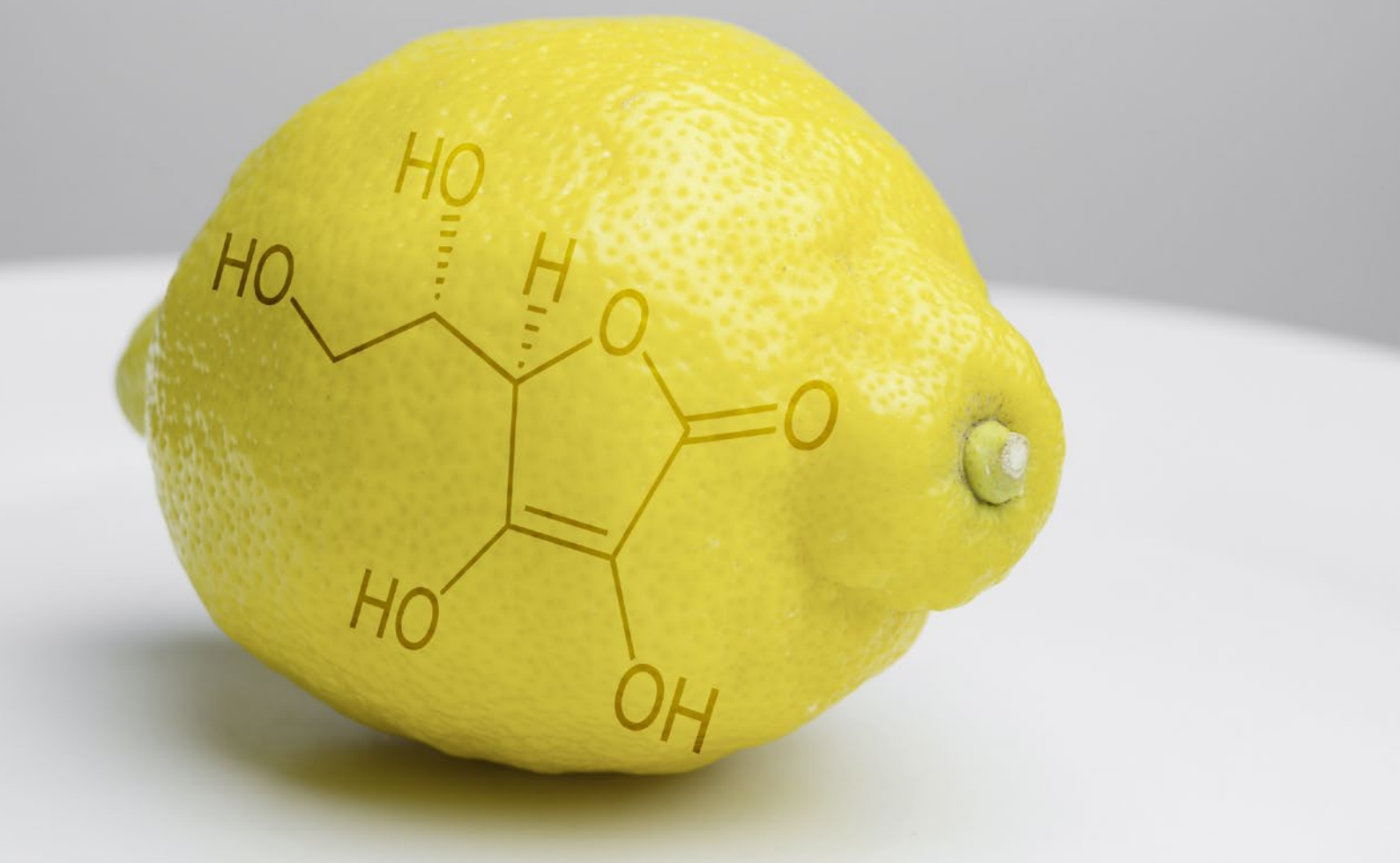
Pioneers of change

Founded in 1902 as the Dutch State Mines coal mining company, DSM diversified into petrochemicals and industrial chemicals in the 1950s and over the last decade has transformed into a life science and materials science company.



»Nutrition is becoming increasingly important in China and consumer demand is therefore rising. DSM has introduced China to the vitamin industry and we are now a leading global vitamin maker.«

Helen Jiang, DSM Large Capital Project Department China Hub Manager

Today DSM is pioneering changes to meet the demands of a fast-moving marketplace. We spoke with Helen Jiang, capex manager of DSM, about the company's role in the highly competitive Chinese market and about the key areas of innovation that will help DSM consolidate its strengths.

DSM could be regarded as a pioneer of change in the Chinese market. Can you tell us how DSM stays ahead in this challenging environment?
Helen Jiang: DSM has a strong history in China, and one that we want to build on. China is the largest consumer market in the world, so it is a very important market for us. Consumer behavior is constantly developing, however, so in order to meet the changing demands of our customers, we need to continually expand our product and service offerings. Our transformation into a life science and materials science company has enabled us to direct our focus toward nutrition, where we see a huge opportunity for growth. Nutrition is becoming increasingly important in China and consumer demand is therefore rising. Following our recent acquisition of Jiangshan Pharmaceutical, a Hong Kong–based company producing vitamin C, DSM has introduced China to the vitamin industry and we are now a leading global vitamin maker.

The Chinese market is currently undergoing a process of change. What do you think has sparked this process and what trends are emerging?
Helen Jiang: The changes in the market have been a result of continuous capital investment in China, despite the fact that the world economy is on a slight downturn. DSM, for example, currently has 14 joint ventures, 19 fully owned enterprises, and five fully owned sales offices in China. I mentioned before that China has the largest consumer population in the world, and this is bringing about increased competition. When it comes to DSM's vitamin business, for example, our biggest competition lies in the Chinese market, rather than in Europe: we see China as our innovation center for technology. Companies like DSM are seeking new opportunities to stay ahead in this fast-moving marketplace. At the same time, consumer behavior and mind-sets are changing, so the need for smart products and continued innovation is key.

You mention the need for innovation. How is DSM's strategy changing to meet the evolving demands of the Chinese market?
Helen Jiang: Following years of acquisition, our focus is now on driving sales to bring about higher EBITDA (earnings before interest, tax, depreciation, and amortization) and ROCE (return on capital employed). This aim is outlined in our new 2018 strategy, which is driving profitable growth and concentrates on high-growth economies, innovation, and sustainability. To achieve this, we need smart products and operational excellence. This is where we look to our suppliers for support.

In what ways can suppliers help DSM drive its strategy forward?
Helen Jiang: We need the in-depth, specialist knowledge of our suppliers to help us improve production at existing DSM plants by looking at how they can work more efficiently and seeing where value can be added to extract the highest ROI. Of course, our suppliers' strategy must align with that of DSM and the Chinese market, too. The focus needs to be on local production and specialist knowledge to ensure high quality. At the same time, we need a partner that can create flexible solutions to address our challenges. Let me give an example: the vitamin C plant. In order to satisfy the growing demand for vitamin C in China, we worked with Siemens to implement an integrated control solution that would provide us with a great deal of operational data and thereby enable us to optimize production and achieve significant cost savings.

Digitalization and Industrie 4.0 are key trends right now. How is DSM moving forward in these areas?
Helen Jiang: These trends already have a strong presence in Europe. We see them as the next step in optimizing efficiency and production processes and thereby staying ahead of rapidly changing market trends in China. Of course, implementing these measures takes time, and processes must be adapted to the Chinese market. Siemens' local knowledge combined with its expertise in digitalization can help us improve daily operations at our plants so we can work more efficiently. For example, Siemens' extensive integrated portfolio for industrial automation products, including TIA Portal and Comos, enables us to integrate automation into our design processes, which provides significant energy savings. Having an experienced partner that offers advanced technological know-how can help us spur innovation where we need it and ultimately allow us to stay ahead of the change process.

Ms. Jiang, thank you for speaking with us. ■

DSM

Helen Jiang has more than 15 years' capex project experience in the chemical, infrastructure, and mining industries. She has led local teams in the implementation of quality greenfield and brownfield capex projects that meet high safety standards and support DSM China's business development.

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Going global

For chemical plants, upgrading from manual control to an integrated IT infrastructure is essential to keep up with customer demands and ensure profitability. A German chemical company understands this well. The implementation of an upgrade at one of its plants served as a pilot project prior to the rollout of a standardized automation solution that helped improve company operations worldwide.

The Chemetall Group is a manufacturer of advanced specialty chemicals used for surface treatment in aerospace and automotive applications. In 2002, the company upgraded from a manual process at its plant in Langelsheim, Germany, to one that completely integrates the manufacturing execution system (MES) into the process and feeds data to SAP. The upgrade would serve as a pilot for a standardized solution that could be supported by the company on a global basis. Considering all Chemetall's requirements and business goals, ATS Automation's Process Automation Solutions affiliate designed a solution based on the Simatic family of products.

First taste of automation

Before the project was implemented, personnel were required to manually operate the plant's 30 reactors. Operators pushed buttons to start and stop mixing motors. All dosing and level measurements were manual as well. Ensuring accurate dosage was very challenging, cycle times varied, and data entries were not consistent. The need to resolve these problems was the immediate reason for the upgrade; however, the transition to an integrated IT infrastructure would also serve as a pilot project for a global rollout.

The project was completed in phases, the first of which involved introducing bar-code scanners that allowed operators to identify materials. The operators downloaded production orders into Batch enterprise resource planning (ERP), which fed information back to the Simatic PCS 7 process control system. The new solution also introduced tables for material tracking and picking systems, as well as for lot reporting and batch history.

Improving supply chain efficiency

Over the years that followed, the plant owners focused on maximizing supply chain flexibility. However, in 2008, with Batch ERP no longer supported, Process Automation Solutions was once again tasked with upgrading the control infrastructure. The main part of the project focused on replacing the existing Batch/MES components with a standardized solution based on Simatic Batch and Simatic IT V6.4.

An important part of the Simatic IT platform was its Production Suite, which links the ERP system with the Simatic PCS 7 process control system. It gave Chemetall operators real-time plant performance visibility on a level that increased the efficiency of the overall supply chain. Production Suite also handled the plant's production management and execution, coordinated the systems with other plants, standardized production across the entire enterprise, and kept manufacturing processes aligned with supply chain activities. Additionally, it provided complete material genealogy and full backward or forward traceability for regulatory compliance, as well as material management and plant performance analysis for production cost optimization.

Results bring worldwide rollout

After the successful upgrade of the Langelsheim plant, the company installed a nearly identical Simatic automation system at a Chemetall greenfield site in Jackson, Michigan, in 2011. The engineering time associated with installation was shortened by roughly 30%–35%; the project was originally scheduled to take nine months but took only six. The engineering time improved because recipes were automatically handled and there was no need to manually create batches.

The results of the pilot project and the US rollout met Chemetall's expectations. Productivity at the Langelsheim plant increased by 15% as a result of Simatic IT's integrated data handling and automatic consumption reporting to SAP. Warehouse stock was reduced by 20% after moving from build-to-stock (BTS) to build-to-order (BTO) production. In addition, customer satisfaction improved due to the increase in quality, consistency, and timeliness of delivery, which improved by 15%.

A foundation for future success

Today, Chemetall has standardized with Simatic IT globally. It is the standard interface for Simatic

products, but third-party programmable logic controllers (PLCs) and other components can be integrated as well. The company has more than 20 production sites worldwide. There are ongoing projects in several countries to further harmonize the company's process automation. The rollout is well under way, and Siemens' global presence combined with Process Automation Solutions' engineering force creates a perfect foundation for future success. ■

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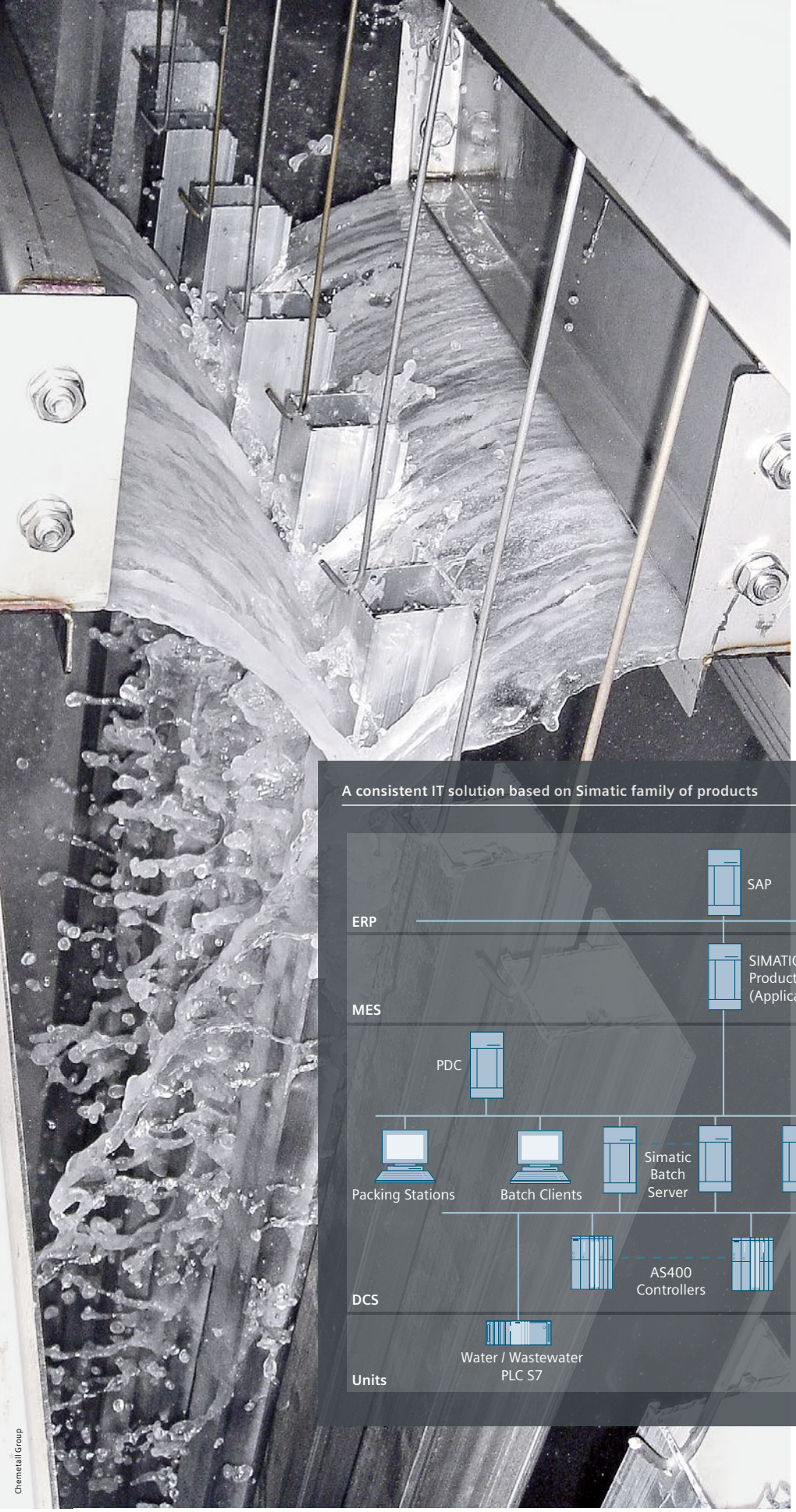

Chemetall Group

Chromium-free pretreatment of aluminum with specialty chemicals from Chemetall

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