GlaxoSmithKline, GEA Pharma Systems, and Siemens are currently developing a solution for tablet making that will redefine drug manufacturing.

Dr. Thomas Tauchnitz, Sanofi-Aventis Germany, speaks about the first pilot project for the integration of Comos and Simatic PCS 7.

Simatic PCS 7 supports consistent, transparent communication right down to the field device, regardless whether it is linked by Profibus or Foundation Fieldbus H1.

Cover

Pharmaceutical Industry
4 Changing the Clock Speed
Continuous Manufacturing
8 Pharma 2020
Pharmaceutical Industry Trends
10 “We Are Moving in the Right Direction”
Integration of Comos and Simatic PCS 7
14 Research for Real-Time Release
Process Analytical Technology in Freeze-Drying Processes
16 More Efficiency, Assured Quality
Validation
18 Serialization Package
pester pac automation, Germany
19 Combating Counterfeit Medicines
EFPIA, Sweden
19 The Start of a Long-Term Relationship
Julphar, United Arab Emirates
20 The Best Medicine
Sanofi Pasteur, France
22 Chinese Flu Shots
Sanofi Pasteur, China
25 Quality Chain
Shandong Shinva Medical Instrument Co. Ltd, China
26 Energy-Efficient Production
Gansons Ltd., India

Technology

Process Instrumentation
28 Micro Flow, Maximum Functionality
Merck KGaA, Germany

Manufacturing Execution System
30 Certified Transparency
Johnson Matthey, Germany

Process Control
32 Perfect Alignment
Foundation Fieldbus and Simatic PCS 7

Industry

Chemical Industry
34 A Clean Start
BASF Coatings, Germany

In Brief
36

Dialogue
39
Dear Readers:

The pharmaceutical industry is the third-largest industrial sector in the UK, employing over 70,000 people. In terms of manufacturing specifically, the UK sector is extremely strong. But we can see some key challenges faced by pharmaceutical companies in the UK: the pharmaceutical manufacturing sector has among the lowest scores in terms of key performance indicators (KPIs) such as productivity, stock turns, and machine utilization. For example, the latter lies at 15 percent in the UK pharmaceutical industry, while in other sectors such as food and beverage and automotive it is above 90 percent. Stock turns in UK pharmaceutical manufacturing are approximately 3 to 5 times per year, compared to 30 in automotive.

These statistics, however, also speak loudly for keeping manufacturing in the UK. If we can successfully raise these KPIs to benchmark levels, the UK will be able to boast the best pharma manufacturing sector in the world.

This is exactly the objective of Siemens: to work with the UK manufacturing industry to massively improve operational efficiencies. Better use of automation, innovation, and management information systems is key to this. Historically, the pharma industry has been very conservative in adopting innovation, and we want to help change this and encourage faster adoption.

This is why we see the project for continuous tableting with GSK and GEA Pharma Systems (see article on page 4) as very exciting. It adopts all the latest innovation and will dramatically improve productivity, stock turns, time to market, and several other KPIs. With our experience in this sector and our product portfolio, we are able to support the pharmaceutical industry with groundbreaking projects. We consider this a better strategy to keep manufacturing in the country.

Additionally, this issue of process news presents an outlook on the future of pharma. We work with our customers in the pharmaceutical industry and research institutions such as the University of Ghent to continually improve our offerings for the pharmaceutical industry and to help our customers all over the world improve their process performance and quality – for example, for Sanofi Pasteur in China and for Julphar in the United Arab Emirates.

I hope that we can give you some valuable ideas and that you enjoy the read!

Yours,
From concept to results in record time: the new continuous manufacturing test plant delivered the first tablets in February 2010 – after only six months of planning and design.
Changing the Clock Speed

In a joint project, GlaxoSmithKline, GEA Pharma Systems, and Siemens are currently developing a solution for tablet making that will redefine drug manufacturing. The new system will enable continuous manufacturing and is an innovative alternative to traditional batch processes.

Continuous manufacturing has been on the agenda of pharmaceutical companies and their suppliers for quite some time. But some visionary people, along with a highly motivated and dedicated team, were needed to make this vision reality. It all came together in a project called SPRINT (Secondary Process Intensification). The project is funded by the British Technology Strategy Board as an initiative aimed at helping the UK pharmaceutical industry maintain worldwide competitiveness in pharmaceutical manufacturing. A consortium that includes GlaxoSmithKline, GEA, and Siemens Ltd. was formed to push continuous processing and improve pharmaceutical manufacturing efficiency in the UK in response to competition from emerging markets.

Secondary manufacturing processes typically suffer from low equipment utilization and are labor intensive and based on a process setup that requires extensive release procedures.

This is particularly true of oral solids dosage (OSD) manufacturing, which is characterized by high inventory requirements (including “work in progress”), long changeover times, disconnected processes, high process losses, and low asset utilization. Additionally, the product quality is ascertained in postproduction analysis, which means that it can take as long as two months for a batch to be released.

A high-speed project

The project partners GSK, GEA, and Siemens jointly accepted the challenge to provide a proof of feasibility (PoF) for a continuous manufacturing unit with real-time-release capability. The PoF was initiated in August 2009 and completed in early 2010. “The key challenge of this project was the timeline,” explains Jan Vugts, managing director at GEA. “Normally these types of projects take a long time in the pharmaceutical industry. But GSK was determined to get fast results, so we implemented a very lean feasibility approach. There was a high level of commitment by all participating companies, who were prepared to jump over their own shadows, work together very closely, and find practical agreements. We knew that we needed each other; there was no room for going our separate ways.

“Another important aspect was that all three companies are global companies and were able to bring in knowledge from different areas. GEA brought in people from the US, the UK, and Belgium; Siemens was able to do the same; and GSK, of course, contributed its knowledge from around the globe. Together we wanted to drive this innovation and bring the continuous manufacturing technology to the next level. It was not just a matter of granulating the powder and making a tablet, but more importantly generating the information that goes with the tablet to enable real-time release of the finished product.”

An integrated solution

A key factor in the PoF was a suitable Process Analytical Technology (PAT) and automation solution, and Siemens could provide such a system with Sipat. Frank Roche, GSK project leader, explains: “A project like this takes a lot of trust in your partners. We relied on Siemens’ and GEA’s know-how. The Siemens technology has improved tremendously within the last three years. Today it is the most integrated solution on the market, and we are impressed by the completeness of the technology. We wanted to use Sipat, the Siemens PAT solution, as it had already proved to be the right solution in different projects at GSK.”

Projects like this take a lot of trust in your partners. We relied on Siemens’ and GEA’s know-how.

Dr. Frank Roche, Project Leader, GSK

The test plant that was set up for the PoF consists of equipment for granulation, drying, milling, blending, and compression. The automation solution consists of two Simatic S7-300 controllers. One CPU controls the granulation, drying, milling, and blending processes, and the tablet press from GEA Courtoy is controlled by the second S7-300. The signals in the field are collected via Simatic ET 200 systems, and
**Simatic WinCC is used as the line visualization system. The Sipat software collects and evaluates quality- and performance-related process parameters in the process steps, such as loss on drying or particle size distribution. These parameters are transmitted to the Simatic IT manufacturing execution system (MES) for real-time-release reporting. The real-time-release reports are generated via the Simatic IT Report Manager and provide drill-down functionality down to individual parameters.**

**„Having a strong partner like Siemens, who is willing to invest and combine forces, is very important for us in a project of this dimension,” explains Vugts. “We have been using Siemens products for many years, but this was the first time we had implemented Sipat, the Siemens PAT software. And from our point of view, the Sipat software platform really is the most evolved and the most integrated system on the market. There is a clear intent by GEA Pharma Systems to work more closely together with Siemens in this area. We are currently in intensive discussions with Siemens to bring the control part into the continuous tableting demo unit that we are installing in the new clean room of our Center of Excellence here at Wommelgem.”**

**We are very enthusiastic about what we achieved. In fact, the results exceeded our expectations.»**

Jan Vugts, Managing Director, GEA

**A tenfold reduction in footprint compared to traditional batch process equipment: the continuous tablet making unit can be easily fitted into a regular room**

**Proven results in record time**

In February 2010, after just six months, the GEA test plant in Wommelgem was producing tablets reliably, continuously, and with excellent quality. The most striking benefit of the plant is its much smaller footprint (10 times less than conventional batch units), which minimizes investment in clean-room space and saves tremendous amounts of energy in maintaining clean conditions.

Vugts confirms: “We are very enthusiastic about what we achieved. In fact, the results exceeded our expectations. It was an exciting journey and the results are very convincing, not only to GSK but also to other customers. Suddenly we can see the future. Like Siemens, we have been working on continuous manufacturing already for a couple of years. Now we have been able to remove the barriers, and so today we can see this new technology picking up speed.”
We were able to prove that with continuous manufacturing you can reduce the process development time tremendously. It took us less than two weeks to develop a process for a new tablet. And there are countless other applications in which continuous manufacturing is advantageous. It is cheaper to build and to operate. The real-time release enabled by in-process quality control alone makes a strong case. The amount of quality information that is available now on each tablet is huge. Up to now we knew that a batch was good, but now we can say every tablet is good. We have taken a big step toward the future, and there are many customers who are waiting for this new technology.

Both the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have been following this project with great interest. At the 1st Continuous Manufacturing Symposium in the United States in March, the FDA recognized the value of continuous manufacturing and is now working to raise the level of awareness of this technology among its review staff.

Next steps

With the PoF complete, GSK is determined to bring this new technology into GSK’s real-world manufacturing. Jim Fox, head of the GSK center of innovation, says, “We now have a strong case for commercialization.” In the meantime, GEA and Siemens will improve and harden the real-time-release process for industrial application. The second challenge will be to get the real-time-release strategy formalized and ready for approval by the regulatory bodies. After that, says Vugts, “our next step is to implement it in to a production unit.

“The new approach to drug manufacturing has reached the pharmaceutical industry at a critical time,” continues Vugts. “We are currently faced with a crisis in the industry, and there is a lot of rethinking going on. There is a slowdown in investments in Western Europe and the United States, while the demands from the Asian markets in particular are increasing. Continuous manufacturing is well accepted in other industries and now is gradually getting accepted in the pharmaceutical market. It is an important development that will enable us to have a sustainable business basis and sustainable growth in the future – the benefits are enormous.”

This assessment is shared by GSK as well, according to Fox: GSK will “change the clock speed” of drug manufacturing.

Continuous manufacturing: the key benefits

By introducing continuous manufacturing capabilities in drug manufacturing, experts say that the pharmaceutical industry can significantly improve its processes. Some of the main benefits are as follows:

- Increased equipment efficiency
- Savings in space, construction, and energy
- Time-based process: scalability improvement
- Better process understanding
- Reduction of raw material and energy usage
- Reduction of scrap, waste, and rework
- Reduction of human interference (lower costs, improved safety)

For the specific process step of drying and tablet making, the international engineering, construction, and project management contractor and power equipment supplier Foster Wheeler expects that continuous manufacturing will result in:

- 65% lower building volume
- 60% lower capital cost
- 85% less waste
- 60% less manpower
- Less solvents and process inventories, so process safety is improved

“We now have a strong case for commercialization.”

Jim Fox, Head of Center of Innovation, GSK

Contact

www.siemens.com/pharma
ivo.backx@siemens.com

For the specific process step of drying and tablet making, the international engineering, construction, and project management contractor and power equipment supplier Foster Wheeler expects that continuous manufacturing will result in:

- 65% lower building volume
- 60% lower capital cost
- 85% less waste
- 60% less manpower
- Less solvents and process inventories, so process safety is improved

“...the benefits are enormous.”
Pharmaceutical industry trends

Pharma 2020

A recent study by PricewaterhouseCoopers (PwC) examined the future of pharma and revealed essential technological and IT strategies. Developments in manufacturing, research and development (R&D), and IT will shape the future of pharma, as Ingrid Maes of PwC elaborates.

According to PwC, one of the major steps pharmaceutical companies need to take is to create better connectivity between different parts of their value chains. “Much technological architecture is in the form of separate stand-alone systems – one for one part of R&D, another for another part, a quite different one for manufacturing, and so on. This is becoming unsustainable and will be completely so by 2020,” says Maes.

Embracing innovation

“Technological and IT changes are critical if companies are to embrace the full potential of the FDA’s cGMP (US Food and Drug Administration’s current Good Manufacturing Practice) and new validation guidelines,” Maes says. “They are equally critical to reduce drug development times. Technological innovation can radically reduce costs by minimizing waste. Investments such as quality by design (QbD), Process Analytical Technology (PAT), and product lifecycle management and knowledge management tools are ways companies can prepare for live licensing while addressing the pressures of today. “Such investments can help companies deliver more flexible manufacturing, reduce costs, respond to regulations, and bridge the gap between R&D and manufacturing – and thus reduce development times and business risks,” she says.

Areas of improvement

The PwC Pharma 2020 study provides some examples of possible areas for improvement. One focus is on using product and process lifecycle management systems. By introducing such systems, pharmaceutical companies can improve their responsiveness to new regulatory and official initiatives. These include the publication of the FDA process validation draft guidance, the International Society for Pharmaceutical Engineering (ISPE) PQ LI (product quality lifecycle implementation), live licensing submissions based on e-CTD (electronic Common Technical Document), and the ASTM E55 continuous quality verification standard.

Another area of improvement identified in the study is achieving built-in quality through PAT. QbD in R&D reduces process development, upscaling, and technology transfer time, while PAT in the plant delivers greater productivity at lower costs. “Many pharma companies have been slow to implement PAT. When they do, they implement it in a narrow way rather than realizing its full potential. PAT/QbD lets companies move from 70 to 90 percent yields to near zero wastage,” says Maes.

Specific recommendations

“There are two essential building blocks: first, fast transfer from R&D to manufacturing, and second, linking feedback from patients directly to the development and manufacturing process,” says Maes. Many of these changes cannot wait. Regulators are now requesting insight on produced batch information. Data information systems need to be configured to allow safe and efficient data exchange with authorities and clients.

What is Pharma 2020?

The PwC Pharma 2020 series of reports paints a challenging and compelling vision of the pharmaceutical industry:

» All medicines receiving approval will be approved on a real-time basis, with live licenses contingent on extensive in-life testing, including trials in patient subpopulations.
» Pharma products will become more diverse.
» Technologies for manufacturing will become more complex.
» Many agencies will share safety and efficacy data to create a broader picture of how medicines perform.
In the other direction, feedback from clients and suppliers offers opportunities for product improvement. Internet portals and customer relationship management (CRM) systems must be developed to capture this feedback.

**Judging the best technological moves**

Many companies seek to implement change but do so in ways that do not maximize benefits. To better accommodate the forces that will shape the future of pharma, road maps should cover 5 to 10 years. In the short term, companies will upgrade facilities to lower manufacturing costs, increase safety and quality, comply with new regulations, and so on. These upgrades can include more automation, integration of equipment and systems, and new technologies. In the medium term, companies will increasingly replace batch manufacturing and “after the event” product testing with automated and integrated continuous manufacturing. This will allow manufacturing on a smaller footprint. And finally, in the long term, more personalized medicines could increase manufacturing and supply chain complexity. A larger variety of products will require greater flexibility in production and closer integration along the whole pharmaceutical chain. 

»These are the two essential building blocks: first, fast transfer from R&D to manufacturing, and second, linking feedback from patients directly to the development and manufacturing process. «

Ingrid Maes, PricewaterhouseCoopers
Cover Pharmaceutical Industry
“We Are Moving in the Right Direction”

“And it’s a good thing we’ve made a start,” says Dr. Thomas Tauchnitz, head of engineering of the Technology Process Group at the Frankfurt pharmaceuticals site of Sanofi-Aventis Germany, regarding the first pilot project for the integration of Comos and Simatic PCS 7. We spoke to him about results and his expectations.

Dr. Tauchnitz, you published an article back in 2005 that propagated the concept of integrated engineering for process technology and automation. The article ended with a reference to tools that could enable such integration at that time but that had not yet been used to implement it. What was your aim back then?

Tauchnitz: The reason was the current situation that existed at our company here in Frankfurt five years ago. You could say that there were irreconcilable differences between the process engineering and design and the implementation of the corresponding functions in the control system, although even then I believed that both worlds could be “happily married.” I therefore wanted this article to be understood as an appeal to our partners on the system supplier side to tackle this problem. We were already in negotiations with some providers. Then Siemens bought Innotec, whose Comos engineering software we had been using for years. That was the signal for me: our idea could now be realized.

What happened next?

Tauchnitz: The first pilot project was initiated in mid-2009. We had chosen a small but typical plant for pharmaceutical production – a preparation tank with a volume of 3,000 liters. We wanted to take a step in the direction of integration with this pilot project, and we were successful – although I must stress that we are still far from reaching our final goal even after the completion of this first pilot project.

Is this not a rather disappointing result?

Tauchnitz: Not at all. We knew we had a long way to go. The important thing is that we have made a start. Now we are working with Siemens to develop the integration further. We are working on important items that have not yet been implemented at the moment: the automatic creation of the equipment modules for PCS 7 and the bidirectionality of the automatic data exchange. The last item especially is important for us as an operator. We have also gained important knowledge about why process engineers and control technology specialists sometimes have difficulty understanding each other, and we will use this knowledge in the future.

Does that mean the collaboration will continue?

Tauchnitz: Certainly. In the next project we will structure the plant during the functional planning of the process technology so that it is easier to reuse the software. I think Siemens has also learned that company-wide standardization of the equipment modules in process technology is not possible and not useful either. This will certainly be considered in the further development of the interfaces and...
Sanofi-Aventis and Siemens recently implemented the first application of integrated engineering of process control and process functions. The pilot project was a preparation tank with a capacity of 3,000 liters for the pharmaceutical production plant in H600 on the Frankfurt-Höchst industrial estate. This plant is small and compact, but it also includes many typical units and processes, which made it suitable for a proof of concept of integrated engineering. The preparation tank contains a total of 10 equipment modules.

The functions are controlled by the Simatic PCS 7 process control system. A Simatic PCS 7 Box RTX system that communicates with the distributed Simatic ET 200M I/O systems, a Simocode motion control system, and a Simovert frequency converter are used as hardware. The measuring points in the plant are linked primarily via Profibus PA.

From the typical to the function sequence

The appropriate Sanofi-Aventis Comos typicals formed the basis for the engineering. These typicals were ported to the corresponding continuous function chart (CFC) typicals in Simatic PCS 7. The project team used the plan-in-plan method. Every typical has the same name in Comos and in PCS 7 and has the same inputs and outputs. It is therefore immediately identifiable as a Sanofi-Aventis typical in every representation – which is important for good acceptance. In the pilot project, this step needed a few manual interventions. However, data were also transmitted automatically in parallel via the Simatic PCS 7 VXM-based interface. In addition, changes that arose in the course of the project were also made to the PCS 7 system during on-site commissioning and then transferred in the opposite direction to Comos.

Doesn’t this close collaboration make you too dependent on one supplier?

Tauchnitz: Dependency has very negative connotations. Comos is fixed for us as the engineering software for functional planning. That is not so much dependency as standardization. And for the control technology we will continue to choose the system that best meets our requirements in the future. Because the engineering in Comos is manufacturer-neutral, I do not expect any serious technical problems.

And how do you assess Siemens’ plans to integrate an appropriate interface for exchanging engineering data in Simatic PCS 7 and Comos?

Tauchnitz: This integration is important because it is the only way to maintain the interface, in my opinion. We will have a different Comos version and a different version of PCS 7 in 5 or 20 years. And it must still be possible to make changes to the plant in both systems and to create a uniform state of documentation. An integrated interface is important.
During the work on the real plant in Frankfurt, a team at Siemens in Karlsruhe also worked on a shadow system to further develop the functions for the bidirectional data transfer of engineering data between Comos and PCS 7.

From the concept to the plant

The entire project was carried out by the project teams in Karlsruhe and Frankfurt. First Siemens transferred the Sanofi-Aventis Comos PT typicals to PCS 7, and the system structure from the Comos PT environment was transferred to the appropriate hardware configuration in Simatic PCS 7 with tool support. Almost simultaneously, the measuring point instances from Comos PT were converted into Simatic PCS 7 CFC instances with tool support, and the equipment modules created in Comos PT were converted into PCS 7 sequential function chart (SFC) instances, partly with the aid of automatic tools and partly manually, and the application software for the plant operation was created. The software was tested at Siemens at the end of July 2009, and the factory acceptance test for the software took place at Sanofi-Aventis at the beginning of August. The systems were installed in Frankfurt in mid-August so that commissioning and validation could commence on August 17, 2009.

Successful completion

Thanks to the partly automatic data transmission, the software engineering was completed much faster than expected. In the meantime, the functionality of the interface between Comos PT and PCS 7 was developed further so that subsequent projects will benefit from the experience gained in the course of this proof of concept.
University of Ghent, Belgium

Research for Real-Time Release

A recently initiated collaborative effort between Siemens and the University of Ghent (UGhent) aims to help pharmaceutical companies gain greater efficiency and control in their freeze-drying processes through the use of Process Analytical Technology (PAT) tools.

Freeze-drying (lyophilization) is an important part of the manufacturing process of many pharmaceuticals, especially in the fast-growing area of biotech production. Through lyophilization, the pharmaceutical product becomes more stable, acquiring a greater tolerance to various transport and storage conditions, a wider temperature tolerance, and a longer shelf life.

Enhancing product quality and stability

Freeze-drying is a complex, multistep process that is critical for end quality. However, in the manufacturing environments of today, the only information being monitored during lyophilization is process data on the parameters of the freeze-dryer, not what is actually happening with the product itself. The result is that any degeneration of the product during the process can only be identified and rectified by postprocess sampling and analysis.

Understanding and continuously monitoring what is taking place within the product during the actual freeze-drying process not only can ensure that product quality is maintained, but can also provide optimal management of the process. This approach also facilitates real-time release of the product directly after lyophilization. For this reason, research has been under way for some time to establish suitable analytical methods and the corresponding software tools to enable in-process quality monitoring and control.

Several process analyzers have been developed that allow in-line and real-time determination of the...
freeze-drying step end points; these include thermocouples, manometric temperature measurements, and the use of vapor pressure methods. However, these systems are based primarily on the continuous monitoring of the product temperature, the water vapor content, or pressure changes inside the freeze-dryer chamber. These existing techniques are also mostly indirect and often disturb the normal freeze-drying procedure. They do not allow monitoring of all critical process aspects, do not improve understanding of the product behavior during the process, and/or cannot characterize the intermediate- and end-product quality parameters, which are essential for real-time product release.

A novel approach

In the collaboration between UGhent and Siemens, some new and innovative analytical technologies have been implemented. The researchers at UGhent use Raman and near-infrared (NIR) analyzers that avoid the previous drawbacks and give a much fuller picture of the process inside the product. The UGhent approach has gained an understanding of the freeze-drying process by using a number of complementary PAT tools.

This approach uses in-line and noninvasive Raman and NIR spectroscopic tools to provide simultaneous information about process-step end points, product behavior, and characteristics. This enables the critical process parameters of the product to be fully monitored during lyophilization. Water and ice produce very weak signals in Raman spectra but very strong absorption signals in NIR spectra, so NIR spectroscopy is excellent for in-line and real-time end-point detection of the drying phases. The UGhent approach is also evaluating several batch modeling methods that allow early-warning detection if the process moves in an unwanted direction. Such early-warning detection is vital for continuous process control and real-time product release.

The next step toward real-time release

The UGhent approach has initially not been executed in real time, as the data are collected after the process has finished. Building on this work, Siemens has proposed a solution for real-time monitoring and real-time product release by combining the analytical systems with the Sipat software and linking analyzers and PAT tools into one single system architecture. Sipat makes it possible to collect analytical data in real time and use it with additional process data in a model that gives continuous predictions on the quality of the batch. Most importantly, it enables companies to have a control strategy that delivers Advanced Process Control and to achieve robust, Right First Time manufacturing. With Sipat it is possible to act while the process is running to correct a batch if any parameters are going wrong. Instead of having end-of-process testing, in which some product is lost or even a whole batch if quality turns out not to be correct, manufacturers can be confident that the integrity of the product has been maintained throughout lyophilization. Together, Siemens and UGhent are working with manufacturers that are interested in deploying this PAT technology and combining it with Sipat to achieve real-time release in their own freeze-drying processes. This would represent a major step change in this crucial stage in pharmaceutical and biotech production.
More Efficiency, Assured Quality

In collaboration with a well-known pharmaceutical company, Siemens Industry Software GmbH & Co. KG and Josteit & Krüger Consulting GmbH have developed a software solution that supports the validation process. The software enables higher transparency, validation at any stage of the process, and considerable time savings.

Considering the stringent regulatory requirements applying not only to the pharmaceutical industry but to many other industrial sectors, the validation process is undoubtedly a crucial factor in quality assurance. Currently, many companies still rely on nonintegrated – and sometimes paper-based – solutions for validation, qualification, and documentation. Especially in the pharmaceutical industry, with product development cycles of up to 10 years or more, this approach involves a high risk of error. Updates are often not incorporated into the documentation. The earlier in the specification phase these updates were made, the more difficult it is to retrace who made which changes when and whether the relevant data are still valid. This is particularly true of the subsequent testing phase.

Transparency ensures higher data and product quality

Against this backdrop, Siemens Industry Software has developed a software solution that supports the validation process. Higher transparency, improved risk management, structured internal workflows, efficient process monitoring with automated check routines, transparent representation of errors, and
optimum traceability of updates – all these are factors enabling time and cost savings, and thus enhancing profitability and competitiveness. Project phases are shortened, sources of error are eliminated, and the approach to regulatory compliance is streamlined. These factors can be utilized to establish “active CIP management.”

**Genuine lifecycle management also with regard to validation**

Validation must not be neglected once the product is approved and marketable; the product must remain valid. This requires continuous, efficient, and reproducible validation across the complete lifecycle. The new software solution from Siemens Industry Software guarantees validity at any point in time – from front-end engineering and design to the maintenance phase. The goal is the efficient parallelization of previously serial workflows. A defined handover with clearly defined signature regulations (using eSign and eStamp) makes sure that only verified, valid data will be transferred to subsequent processes. The functional scope of the solution is focused on the items that are risk-relevant and thus impact product quality.

**Future-proof through collective expertise**

Validation with Comos is a software solution tailored to market demands and developed with a view to bringing the fields of engineering, operations, and compliance closer together. Thanks to collaboration with customers and industry experts, the requirements imposed by the regulatory authorities have been complemented with practical expertise.

“Future-proofness is and always has been an essential criterion in product development at Siemens Industry Software,” says Alexander Mankel, director of international sales and business development at Siemens Industry Software. “This is why the Comos solution is already based on the envisaged harmonization of statutory requirements in the pharmaceutical sector (ICH guidelines). Like all Comos products, the new solution is fully object-oriented, too. Comos enhances efficiency in the validation process and makes a decisive contribution to quality assurance.”

**Optimum adaptation to customer requirements**

The high standardization level of the Comos validation tool permits rapid implementation in the validated environment. After implementation at the customer’s facility and the entering of customer legacy data, the software can be adapted to the validation master plan established by the customer. The customer is thus offered a validation instrument optimally geared to both in-house workflows and official regulations.

The novel solution serves to improve existing structures established in a company or to freshly develop efficient new structures and to define the relevant workflows.

Throughout the validation process, Comos offers valuable support for project and qualification management, documentation and maintenance, role concepts and responsibility matrix, and quality assessment and GMP analysis, as well as status management from the design to the handover phase. This solution turns the vision of a future-proof qualification and validation approach into reality.

---

<table>
<thead>
<tr>
<th>Process Level</th>
<th>Yesterday</th>
<th>Today</th>
<th>Comos</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>serial</td>
<td>serial, shortened by tools</td>
<td>parallel</td>
</tr>
<tr>
<td>Level</td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
</tr>
<tr>
<td>Process</td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
</tr>
<tr>
<td>Lab-Scale</td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
</tr>
<tr>
<td>Pilot-Scale</td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
</tr>
<tr>
<td>Product-Scale</td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
<td><img src="https://example.com/diagram.png" alt="Diagram" /></td>
</tr>
</tbody>
</table>

Further optimization potential of individual tools is widely exhausted.

---

**info contact**

www.comos.com

evelyne.kadel@comos.com
A bundle of serialized drug packages

Serialization@Siemens

- All hardware and software as well as consulting, analysis, and project management for the creation of a serialization solution for pharmaceutical packaging
- Rollout support: installation and integration, joint testing, and start of operation
- Quick and customer-oriented worldwide support and implementation of sales and marketing initiatives

The German company pester pac automation has been setting standards in packaging machinery for the pharmaceutical and cosmetic industries for over 40 years. pester pac provides innovative machinery for foil and carton packaging as well as for pallets. Each day, more than 7,000 pester plants and lines help multinational corporations be more productive. In light of the technical challenges and the IT expertise required, pester pac automation chose Siemens as its partner and IT service provider in the development of a comprehensive serialization solution that will increase security and transparency within the global supply chain for customers in the pharmaceutical industry.

Unique ID
Serialization involves assigning a unique coded serial number to any salable unit, enabling the unique identification of such a unit within the supply chain. Pharmaceutical products thus obtain an electronic pedigree that allows them to be monitored and documented without interruption. For the pester pac automation serialization project, Siemens has implemented the Siemens AutoID Connector (SAC) serialization solution in an end-of-line packaging system. The solution includes a powerful system that writes, reads, and processes 2-D data matrix codes. The SAC contains databases to store the data and aggregates data for export to third-party systems. It also parses and stores data coming from third-party systems and provides all user interfaces such as reports, monitoring, and production order and user management windows. Additionally, industry-specific functions were introduced for quality control, support of manual packaging processes, management of serial numbers, and tracking. The Siemens solution also controls and monitors the hardware installed, such as cameras and printers.

Proven systems
Pester provides industry-proven and well-established packaging machinery that is combined with the fully integrated Siemens serialization solution. With the Siemens solution, compliance with legal and corporate requirements for tracking and tracing of pharmaceutical products is assured. A further benefit of the serialization solution is the safeguarding of consumers’ health through enhanced security against counterfeiting. Siemens also provides complete integration into the pharmaceutical company’s enterprise resource planning (ERP) system.

info contact
www.it-solutions.siemens.com
juergen.manz@siemens.com
EFPIA, Sweden

Combating Counterfeit Medicines

The European Federation of Pharmaceutical Industries and Associations (EFPIA) has launched a pilot project that includes the testing of a coding and identification solution in Sweden. Siemens is supplying the information and communications technology. This solution enables counterfeit products to be reliably identified at all times and monitors the movement of medicines throughout the entire supply chain. The EFPIA’s new coding and identification solution is based on a 2-D data matrix bar code with a unique serial number that can be easily generated and printed on the packaging by the manufacturer. A scanner is used to read the code and pass it to a verification system that checks that the pack with that serial number has not been dispensed before. When a pharmacist scans the pack, if it is already marked in the database as dispensed, an alert is triggered and the pharmacist is made aware of the possibility that the pack may be counterfeit. Pharmacy staff can then take the necessary precautions and immediately launch an investigation. If this pilot project is successful, EFPIA will present it to the EU authorities for replication in the other EU countries and so create a uniform platform for key players in the European pharmaceutical industry in the fight against counterfeit medicines.

Julphar, United Arab Emirates

The Start of a Long-Term Relationship

Gulf Pharmaceutical Industry (Julphar), one of the largest pharmaceutical companies in the Middle East, has signed a €4 million contract with Siemens for the design and implementation of Simatic PCS 7 for the company’s new human insulin plant in Ras Al Khaimah, UAE. Siemens will supply the process control system, including all project management, engineering, and validation services for the entire project lifecycle, from the user requirement specification to the functional design specification to installation and commissioning. Siemens’ first-class biopharmaceuticals knowledge and experience, in combination with innovative automation products and solutions, were the main reasons that Julphar decided for Siemens.

The contract was signed in the Julphar headquarters on May 16 by Dr. Ayman Sahli, Julphar’s general manager. Both companies are looking forward to the ongoing mutually beneficial collaboration. According to Dr. Ayman, it is the start of a long-term relationship, initially focused on successfully completing what Julphar considers to be one of its most strategic projects during recent years. In its 30 years, Julphar has managed to achieve great success by following the latest regulations in the pharmaceutical industry and maintaining the highest level of quality in all products. Julphar has more than 180 products in the market and distributes them in more than 40 countries.
Sanofi Pasteur, the vaccines division of the Sanofi-Aventis Group, is a world leader in vaccine manufacturing. The company produces vaccines protecting against 20 infectious diseases and manufactures over 1.6 billion doses per year across 10 production sites.

Vaccine production is a complex and lengthy process. It can take up to 22 months to produce a vaccine, and strict process and quality controls must be applied at every stage. The objective of Sanofi Pasteur is to meet public health needs with a reliable supply of vaccines in response to global demand. In order to improve quality and regulatory compliance while accelerating cycle times and improving effectiveness, Sanofi Pasteur decided to implement a manufacturing execution system (MES).

**Response to public health needs**

In vaccine manufacturing, it is essential to be responsive to public health needs. In the event of an epidemic, vaccine production must be geared up to tackle the outbreak by rapidly producing a large quantity of doses effective against the infection. At Sanofi Pasteur, the quality teams working closely with the heads of industrial operations determined that an MES would provide the required responsiveness through tight control of manufacturing processes. Following a review of available MES software, Sanofi Pasteur selected XFP, an independent software
Sanofi Pasteur's vaccine production philosophy is to manage globally and implement locally. Consequently, the company decided to install XFP at selected Sanofi Pasteur sites in France and the United States.

The aim of Sanofi Pasteur in implementing an MES strategy was to move from its paper-based control record system to an electronic master batch record process with electronic work instructions. The ultimate goal of deploying XFP is to achieve a completely paperless manufacturing process with electronic batch release.

A biological manufacturing process
Vaccine production is a complex biological process. Skilled operators and scientists undertake the majority of the operations, including the culture of living cells, bacterial fermentation, and the purification and attenuation of the live vaccine. Each production facility is an isolated sterile unit operating under clean-room conditions. Because public vaccination programs involve administering to large numbers of people, everything possible must be done to prevent any undesirable effects of the drugs. To ensure the safety and quality of the vaccines, a highly stringent regime of inspections, quality audits, and lot traceability controls encompasses the complete production process. With a paper-based production data system, maintaining these quality controls can be a cumbersome and time-consuming process.

Process excellence
XFP MES software is optimized for life science applications. It reduces paper use, guides the operators through the production processes, collects production data, and provides consolidated batch records with full traceability. Guiding the operators, whether they are running manual or automated processes, ensures consistency and repeatability. Vaccine production requires the gathering and processing of huge volumes of data for process control and quality assurance – up to 10,000 data points per batch. XFP software automates this process and provides real-time visibility of any process deviation, something quite impossible with manual, paper-based systems.

The deployment of XFP enabled Sanofi Pasteur to replace manual recording of production data with automated electronic batch records, with all the associated benefits. This gave Sanofi Pasteur the means to achieve the highest levels of quality, efficiency, and regulatory compliance in its production sites worldwide.
Chinese Flu Shots

New Sanofi Pasteur factory in Shenzhen brings French company experience in vaccine production to China.

Beautiful – but potentially deadly: a human influenza virus
The threat of a swine flu pandemic over the 2009–10 winter appears to have passed, fortunately, but new virulent influenza strains are almost certain to emerge in the future. According to the World Health Organization (WHO), influenza epidemics are thought to result in between three and five million cases of severe illness, leading to 300,000 to 500,000 deaths annually. An influenza pandemic can develop when an especially virulent and infectious virus emerges for which there is no preexisting immunity. Such pandemics are capable of producing much higher levels of mortality. The development of effective vaccines is one of the major achievements of medical science, and the deployment of these vaccines has saved countless lives.

The production and use of influenza vaccines up to now has been largely concentrated in developed Western countries. Immunization levels in Europe and North America range between 20 percent and 40 percent but are only 2 percent in China. Despite this, there is a true growing demand for vaccines in China, including influenza vaccines, when at the same time the Chinese authorities have been reemphasizing the role and benefit of prevention as a concept. As a trusted partner of the Chinese health authorities, grounded in more than 10 years of collaboration, Sanofi Pasteur naturally strengthened its commitment to Chinese public health, with a €70 million investment in a top-of-the-line vaccine production unit in Shenzhen, China.

When it comes fully on stream in 2012, the new vaccine facility, in the Long Gang district of Shenzhen, will produce 25 million doses annually for the Chinese market with the capacity to double production as needs in China grow. A key element of the design of the plant will be the capability to rapidly switch production from seasonal to pandemic influenza vaccine in the event of a pandemic emergency’s being declared. Sanofi Pasteur is the vaccines division of the Paris-listed Sanofi-Aventis Group, a leading global pharmaceutical company. Sanofi Pasteur is a world leader in the research, development, and manufacture of influenza vaccines and contributes to pandemic preparedness projects worldwide. When Sanofi Pasteur launched the vaccine production project in 2007, it turned to Siemens Industrial Automation to implement the information systems and process controls within the facility. In introducing high-technology vaccine production outside Europe and North America, Sanofi Pasteur viewed this project as a flagship project. The success of the scheme will be vital.

Vaccine production
The production of an influenza vaccine starts with the culture of WHO-recommended viral strains using chicken eggs. The antigens (substances in the vaccine that stimulate production of seroprotective antibodies in the human body) obtained from the splitting of the viral strains are isolated and purified in a bulk and blending facility, then made into doses using a filling and packaging unit. To ensure that there is no contamination of the plant’s surroundings, all wastewater must be purified to international standards for surface water. Sanofi Pasteur has already established a production base in Shenzhen, having built a filling and packaging unit in 1996. The unit packages active ingredients imported from France. The new factory will contain incubation and clarification units for manufacturing the active ingredients locally and a dedicated wastewater treatment plant.

The implementation of process controls to incubate live organisms and produce vaccines to clinical standards requires both knowledge of pharmaceutical regulations and practical experience. Siemens possesses both and has a track record with the

> The proposed solution from Siemens matched our requirement. Only minor modifications were made on-site during commissioning.«

Jacky Cheramy, Director of Process Engineering, International Sites and External Manufacturing, Sanofi Pasteur

Sanofi-Aventis Group, having worked previously with the Animal Health Division. A key element of this project is knowledge transfer from France to China. Already having an established presence in China, Siemens committed to support Sanofi Pasteur and to provide training of the local Sanofi engineers up to the level at which they could assume responsibility for the production tools.

The process automation package had to be implemented as a fast-track project to allow sufficient time for the exhaustive qualification phase before full production is scheduled to begin in 2012.
Siemens initially developed the project in France together with its solution partner, Ekium, before transfer of the project to China. Good communication with Sanofi Pasteur in China was a key factor in delivering the project on time. Siemens Industrial Automation Ltd. Shanghai (SIAS) was responsible for the engineering and implementation of the process automation package. Another key factor in the smooth execution of this project was the good coordination between the SIAS team in Shanghai and the Siemens process automation experts in France.

Water treatment
The Shenzhen environmental bureau set stringent limits for the contaminant levels in wastewater, in accordance with international environmental quality standards for surface water (GB 3838-2002 category V). The production of trial batches of vaccine could not begin without these environmental standards being met, so it was critical that the design and installation of the wastewater treatment plant be completed on time. The Siemens Water Technologies office in Shanghai worked proactively with Sanofi Pasteur in the analysis of the target specifications. At this stage, Sanofi Pasteur was grappling with the problem that in the early stages of production, the organic loading of the plant would be only one-sixth of that assumed in the environmental impact assessment. The wastewater treatment equipment would be heavily underused during this early phase. Siemens Water Technologies came up with an economical solution whereby sufficient equipment would be put in place to cover the initial loading and the later addition of an upflow anaerobic sludge bed would increase the plant’s capacity by a factor of six.

In February 2009 Sanofi Pasteur awarded the wastewater treatment unit contract to Siemens Water Technologies and Engineering (Tianjin) Company. The turnkey package included the design, construction, and commissioning of the plant to the required environmental quality standards. Siemens moved quickly, and all equipment was delivered to the site by late June. Unfortunately, construction of the buildings was delayed through the summer because of heavy and continuous rainfall. Siemens was unable to start installation of the subsidiary systems such as control systems, sludge dewatering, and chemical dosing until early October, just five weeks before the first trial batch of vaccine was scheduled for production. To meet the deadline, Siemens came up with innovative solutions such as carrying out static and kinetic commissioning simultaneously to save time. With these measures, the commissioning program was completed on time, and by the end of November the treated effluent chemical oxygen demand fell below the specification requirement of 40 milligrams per liter.

Process architecture
The architecture employs Simatic S7-300 programmable controllers with MP377 intelligent HMI touchscreen control and information panels linked via ET 200S distributed I/O systems. Both Profibus and Ethernet networks are employed. Siemens’ experience with the Simatic S7-300 in related medical and food production applications made it a natural choice for this project. The S7-317/2 is a recent addition to Siemens’ S7-300 programmable controller family. With an installed base of hundreds of thousands of units across the globe, the S7-300 has established itself as an industry workhorse since its introduction in 1994. The new S7-317 supports simultaneous connections to distributed I/O devices, peer control devices, supervisory systems, and the business world using a combination of Profibus and Profinet.

A partner in emerging economies
In undertaking this project at Shenzhen, Siemens completed a fast-track project on time, including full compliance with tough local environmental regulations. The success of the project was due in no small part to the presence in Shanghai of Siemens water treatment specialists who came up with innovative solutions to problems created by the local monsoon environment. The Siemens specialists will continue to work with Sanofi Pasteur at Shenzhen in the ongoing pilot production and qualification programs to bring the plant fully on stream by 2012.

Siemens is committed to the support of developing nations and emerging economies throughout the world. Access to technical expertise from Siemens has enabled the foundation and germination of pilot projects in third-world countries in advance of their readiness for full industrial implementation. Following the good collaboration and experience gained in this project, Sanofi Pasteur has gone on to award Siemens the system automation/controls contract for its new influenza vaccine plant in Mexico.
When Sanofi Pasteur embarked on the construction of its new vaccine production plant in Shenzhen, the company was determined to use local Chinese OEM suppliers wherever possible. One caveat was that for Sanofi Pasteur to qualify its plant to international pharmaceutical standards, all the component elements in the production process would have to qualify. Sanofi Pasteur needed to be sure of a complete quality chain with no missing links.

The Shandong Shinva Medical Instrument Co. Ltd. (Shinva) is one example of an OEM that has succeeded in the qualification process with Sanofi Pasteur. Shinva is a Shanghai Stock Exchange–listed company, employs 2,500 people, and has a 65-year history of producing medical instruments. It is now the leading supplier of sterilization and medical devices in Asia. Much of Shinva’s output is sold in mainland China, but a growing number of sales are exported to the developing areas of the world, including Asia, Africa, and South America. A very important and growing element of Shinva’s domestic business is sales to multinational pharmaceutical companies building new production facilities in China.

During the planning of its Shenzhen vaccine plant, Sanofi Pasteur invited Shinva to tender for the supply of decontamination units, subject to qualification to EU/US quality standards. The tender was accepted, and Siemens came into the loop to work with Shinva on quality compliance.

Bridge of knowledge
Siemens became a technical bridge between Sanofi Pasteur and Shinva. With its detailed knowledge of the production process for the new vaccine plant, Siemens provided training to Shinva to ensure seamless integration of the Shinva equipment into Sanofi’s production line. Siemens’ Chinese-speaking engineers worked with Shinva on Good Manufacturing Practice documentation, specification and testing, programming, and commissioning to EU and US quality standards and regulations.

To raise the quality levels in its factories, Shinva made changes to its production processes, including the installation of new process control systems supplied by Siemens. The decontamination units ordered by Sanofi Pasteur were supplied on schedule and integrated into the new vaccine facility without any problems. Shinva has now gone on to develop new business with other multinational pharmaceutical companies in China.

Shinva sees Siemens as a key partner in developing its business. According to Yang Zhaoxu, managing director, “Siemens has an extensive service network all over the country, with qualified, Chinese-speaking engineers able to act instantly on our call for support, and this adds to the value of Siemens for the Shinva business.”

»Collaboration with a global supplier that combines strong local presence with international experience and support capabilities clearly pays off.«
Yang Zhaoxu, Managing Director, Shandong Shinva Medical Instrument Co. Ltd.
Gansons Ltd., headquartered in Thane, India, was founded in 1947 with the vision of manufacturing world-class equipment. Since then, Gansons has evolved into one of the leading manufacturers of process equipment. Gansons conceives, designs, and provides technical solutions, especially for pharmaceutical manufacturing. Major products in this segment are automatic tablet-coating machines, Nauta mixers, high-speed mixers, and granulators. Gansons supplies machines to almost all major pharmaceutical companies in India. Gansons also has customers in the United States, Europe, North Africa, and Southeast Asia. Throughout its history, Gansons has been committed to innovation. “We are continuously developing novel solutions to meet ever-stricter quality guidelines and to better serve our customers in India and worldwide,” says Mr. Ashis Banerjee, managing director of Gansons.

An elegant solution
Tablet coaters are a key offering of Gansons for the pharmaceutical industry, and the company makes a broad variety of versions and designs. The core of a table coater is a perforated rotating drum mounted at an angle. As the drum rotates, the tablets are mixed by angled baffles and flowing air in the drum. As the drum turns, tablets are lifted and turned from the sides into the center, exposing each tablet surface to an even amount of coating.

Liquid spray coating is dried onto the tablets by heated air drawn through the tablet bed from an inlet fan. The regulated airflow provides controlled drying and extracting rates, and also keeps the drum air pressure slightly negative relative to the room, providing a completely isolated process atmosphere.
for the operator. The coating pan in a tablet coater rotates at a very slow speed to ensure even and smooth coating of tablets. The required high reduction in the speed was typically achieved with a gear unit, traditionally using a worm gear unit or bull gear. These designs, however, had a high power loss and necessitated large machines, and they were prone to overheating. This, in turn, caused oil seal failure and leakage, particularly unacceptable in the pharmaceutical industry due to the hygiene requirements for manufacturing.

To address these challenges, Siemens offered helical-bevel (helical bevel) gear units with a very high-speed reduction ratio, which are 40 percent more efficient than the prevailing system. A helical-bevel gear is a toothed gear in angular design. The input side is provided with a motor flange or a free input shaft, and the output side is provided with a free shaft end or a hollow shaft. Helical-bevel gears are fitted with flanges of various sizes. Reciprocating tools cut them. The Siemens solution achieved the desired machine speed with a single gear unit. Due to its higher efficiency, the motor size was reduced, reducing wattage and allowing the machine to be much more compact, so it can even be integrated into the machine body. Assembly of these gear units is also very simple.

Providing more benefits than requested
Gansons manufactures various types and sizes of tablet-coating machines, and the company has standardized on Siemens’ gear units due to their value to the end user and to their environmental friendliness. The innovative Siemens units are more energy efficient than conventional designs. Gansons was able to demonstrate the improved energy efficiency of the new design through measurements. Additionally, there are even more benefits to the new design: a lower noise level (important for operator workplace regulations) and very good thermal conduction, which is also important for workplace comfort, as well as HVAC requirements. Since the gear units are easy to install and commission, Gansons has been able to drastically reduce machine lead times, allowing faster time to market for customers who are upgrading or expanding their production.

Gansons customers also benefit from low maintenance requirements. “We never had a single complaint after sales, and we had no complaints on-site – we wouldn’t even know what a complaint for those gear units could be,” says Banarjee. “The quality is always perfect, so we do not have to perform quality tests on the gear units as they are always delivered in the same excellent quality!”

Helical-bevel gear units at Gansons

- Gansons was looking to innovate its tablet coaters by employing an energy-efficient and maintenance-free solution for the rotating drum, which is a core mechanical part of the machine
- Siemens provided its compact, energy-efficient gear unit, which is less noisy, has favorable thermal conduction, and offers unparalleled operational reliability combined with increased power capacity
- The simple and straightforward installation arrangement for the gear unit has drastically reduced project lead times

The compact design of the gear units enables novel machine designs that feature reduced footprint

info contact
www.siemens.com/pharma pharma.india@siemens.com
For more than 300 years, Merck has developed a global presence in pharmaceuticals and chemistry. Merck is the world leader in liquid crystals for flat screens, and its chemical business includes industrial pigments, biotech, cosmetics, and drug production.

Hans Muntermann, Merck’s renowned automation expert in microreaction technology, operates at the cutting edge of the newest automated microreaction systems (MRS). In MRS, flow channels are on the millimeter scale, in components of polymer, ceramic, glass, or metal.

When Merck needed to measure flow on a groundbreaking millimeter-scale line, the company looked to Siemens to provide a highly compact flowmeter, with excellent results.

On the verge of commercial breakthrough, MRS is hot news in the chemistry world. The advantages of MRS include improved safety, the ability to control material flow with high precision, the ability to add or remove heat rapidly, and more intense reactions between liquid and gaseous reactants in multiphase processes.

A flowmeter to meet MRS standards
It is enormously important that MRS instrumentation have very high accuracy, versatility, flexibility, and maximum compatibility with an automated control
system. Siemens and Merck have partnered for years to achieve these goals. Merck began experimenting with Coriolis flowmeter technology over 15 years ago and now uses Coriolis in MRS mass flow metering. Merck helped develop the new Siflow FC070 Coriolis mass flow transmitter, the first flow transmitter for direct integration into the Simatic rack.

In 2006, the Merck automation development group incorporated the Siflow FC070 into 1.5-millimeter-diameter MRS process lines, with outstanding results. The flowmeter consists of a compact Sitrans FC 2100 sensor on the process lines, and a remote FC070 transmitter in the programmable logic controller (PLC) rack. Siemens optimized the sensor for compactness, truncating the housing to fit into Merck’s tight MRS space constraints. An important feature of the customized sensor housing is that it minimizes heat loss. Even slight heat losses significantly affect processes when the operation is on such a small scale.

Seamless integration

Easy to install, commission, and run, the FC070 transmitter is built on the Simatic platform, so it communicates easily not only with Simatic automation systems but also with Simatic Manager, Simatic PCS 7, and Simatic PDM. After the simple snap-on installation, the transmitter self-configures and speaks the same language as the rest of the automation system.

Because the FC070 integrates seamlessly into the automation system, it provides relevant and reliable feedback. The uniform system architecture and communication enabled by Totally Integrated Automation facilitate the smooth integration of all process control systems into one aligned solution. The diagnostic features of the FC070 are valuable for managing MRS. Users receive the operational information and self-diagnostics that are essential for predictive maintenance. The easy-to-use self-test feature helps users identify and plan solutions for process problems in the automated systems.

In addition, this Coriolis mass flowmeter is extremely reliable, with high accuracy and repeatability. With no moving parts, it is virtually maintenance-free, so the MRS team can focus on research.

Measuring versatility

The capacity to monitor multiple variables, particularly density, in parallel with the mass flow rate is a high priority for Muntermann, and the FC070 provides this. The FC070 also has other features, such as totalizers and advanced batch. Using these multiple capacities allows instrumentation to be minimized – a great advantage in the miniaturized world of MRS.

Preparing for tomorrow’s MRS

Merck is confident that Siemens mass flow instrumentation, and in particular the Siflow FC070, can meet the challenge of commercializing MRS. The FC070 can number up or scale up MRS processes, demonstrating superior repeatability and a high turndown ratio. Muntermann believes that Siemens Coriolis instrumentation will form a cornerstone of Merck’s new gaseous MRS processes. The versatile FC070 is well suited to the coming challenges: it is designed for measuring both gas and liquid and is compatible with any fluid, including highly aggressive, nonconductive chemicals.

Merck uses the Siflow FC070 Coriolis flowmeter in its microreaction systems

Advantages of Siflow FC070

- Measures gas or liquid
- Is virtually maintenance-free
- Is compact, with multiple functionality
- Minimizes heat loss with sensor housing
- Provides predictive diagnostics through embedded intelligence
- Features simple installation and ability to self-configure
- Monitors multiple variables in parallel with mass flow rate
- Can number up or scale up MRS processes

Merck uses the Siflow FC070 Coriolis flowmeter in its microreaction systems
Johnson Matthey, Germany

Certified Transparency

Johnson Matthey gives its performance a double boost: with the Simatic IT manufacturing execution system (MES), the company improves process safety as well as productivity and makes employees’ jobs easier.

Johnson Matthey is a global leader in manufacturing selective catalytic reduction (SCR) converters for heavy goods vehicles. The company operates an ultramodern manufacturing plant for catalytic disk and honeycomb converters in the German town of Redwitz. Production must comply with strict guidelines from both official regulatory authorities and customers, such as the ISO TS 16949 for automotive suppliers, and must be completely documented and traceable, as this is a prerequisite for ISO certification.

Standard system instead of individual solutions
To optimize production, Johnson Matthey already had an MES in place, but in October 2007 the company decided to replace it with a new, platform-based system. The company required an MES platform that would be highly configurable, increase operational safety and productivity, and guarantee absolute traceability. Johnson Matthey’s chief concern was high stability during use, together with high availability.
The order was won by the Bayreuth software company Xavo AG, which is a longtime certified Siemens Solution Partner with many years’ experience with the Simatic IT MES. “We opted for Simatic IT because we are certain of its technical suitability. It is an excellent platform that can be readily configured to meet almost any customer requirement. A further important consideration was that Siemens, the global leader in automation technology, provides backup service covering system maintenance and development,” explained Hans-Jürgen Postler, project manager at Xavo.

The size and complexity of the module production was a particular challenge. Several different processes run simultaneously around the clock, and up to 40 users have parallel access to the system. User guidance must support widely different tasks. The transparency of the processes must always be guaranteed, even when users are on the move with PDAs in the plant. Additionally, an enormous volume of data – generated by the complete traceability of all components – needs to be managed. Moreover, devices and systems with different file formats must be integrated for the individual processing steps.

**Integrated and open for extensions**

Conversion to the new MES was performed in stages, with the implementation phases oriented to the material flow through production. In the first phase (weighing, mixing, and kneading), the technology engineers needed to optimize the composition of the materials in such a manner that the required specifications were achieved. The process for this was modeled using the Simatic IT Production Suite. The Product Definition Manager took on the task of recipe management with its complex calculations of recipe parameters. The conversion was automatically documented, without the requirement for manual logging of offset versions. The second and third phases included straining, extruding, and calcination. The Simatic IT Material Manager maintains the product characteristics and administers the batches and individual components throughout the entire process. This includes management of pallets and frames as well as complete, seamless tracing. The modules are identified by means of a data matrix code that is applied during extrusion. Data handling is extremely simple: once the pallets are driven into the furnace, a laser captures the label and the assignment is coded. Should the module code become unreadable for any reason, the system reliably prevents the assignment of a replacement code, and the component must be rejected. This is a significant contribution to improved operational safety.

The interface to the robots has also already been implemented for the conclusion of production phases in sawing, measuring, sorting, and packaging. In the final control stage, the system is also impressive in its display of the remarkable data volumes it can process: 25 measurement values relevant to quality are captured and processed within one second, on a per module basis.

**Xavo AG Enterprise IT Solutions**

Xavo AG, a certified Siemens Solution Partner Automation, implements custom-made MES solutions based on Simatic IT. The focus is on production as well as support for research, development, and laboratory automation.

**Headquarters:**
Meistersingerstr. 2
95444 Bayreuth
Germany

**Contact:**
Tel.: +49 (0)921/787779-0
Fax: +49 (0)921/787779-29
E-mail: info@xavo.com
Web: www.xavo.com

**Positive results**

The new MES has significantly increased transparency in production and has also been well received by employees. The decisive factor is the improved clarity that has been achieved without cumbersome logging activities. As a result, the established team of Johnson Matthey and Xavo is already planning the implementation of Simatic IT in production planning as well.

»The benefits of the system are far from being fully exhausted. We still see a great deal of potential, right up to full integration of production with the SAP system.«

Hans-Jürgen Postler, Project Manager, Xavo AG
Simatic PCS 7 supports consistent, transparent communication right down to the field device, regardless whether it is linked by Profibus or Foundation Fieldbus H1.

The functionality, performance capability, and flexibility of Simatic PCS 7 have been extended continuously since the process control system was first launched on the market. An important feature of PCS 7 from the beginning was that the system is based on open industrial standards and uses standard automation components. This means that the process industry also benefits from all the advantages of Totally Integrated Automation. On the process level, PCS 7 relies on Profibus as a communication standard. With Profibus, large data volumes can be transferred reliably and efficiently, fail-safe signals can be transmitted with standard communication on one bus system, and I/O systems can be linked in the process via the intrinsically safe Profibus. Profibus also supports extensive diagnostic and asset management functions and therefore enables efficient and highly available communication.

**A bridge between two systems**

The Simatic PCS 7 process control system, as of V7.1 SP2, now also allows the smooth integration of Profibus PA and Foundation Fieldbus and therefore enables the free selection of connected fieldbus instrumentation. Profibus PA and Foundation Fieldbus benefit equally from the master Profibus architecture. As with PA Link, a new FF Link allows the smooth integration of Foundation Fieldbus H1 networks into the Simatic PCS 7 process control system. The equally new FDC 157 field device coupler links the field devices. Existing Foundation Fieldbus networks can thus be easily integrated into the Simatic PCS 7 architecture. By opening up to Foundation Fieldbus H1, Simatic PCS 7 also makes Totally Integrated Automation available to this fieldbus environment. Foundation Fieldbus devices can be parameterized, configured, and monitored in the same way as Profibus PA and HART devices. This

---

**Foundation Fieldbus Link**

- Smooth integration of Foundation Fieldbus H1 into Simatic PCS 7
- Linking of field devices by FDC 157 field device coupler
- Central parameterization and configuration
- Integration into Simatic PCS 7 Asset Management
- No additional software or third-party components required
- Scalable redundancy concept for maximum availability
- Central and distributed system configuration
creates consistent transparency throughout the entire automation system and the technical infrastructure, allowing the implementation of proactive concepts and total asset management.

Active in the field
The individual field devices are linked to the fieldbus by active field distributors. Although the possibilities for making changes during operation are very restricted in conventional fieldbus installations, users can connect I/O devices easily and safely with the fieldbus main line via the active field distributors in ongoing operation. The active field distributors have short-circuit-proof stub cable connections. In case of a wire break or short circuit on the main line, an intelligent logic device automatically ensures isolation of the defective subsegments, including automatic bus termination. The main line can also be extended or shortened during operation, and extendable fieldbus ring topology can be set up for greater availability. Unused free interface points do not need to be planned because a segment can be extended for additional field devices at any time by installing other field distributors. In this way, the user benefits from much higher system availability because ongoing operation no longer needs to be interrupted for maintenance or expansion measures.

Intrinsically safe in the Ex area
The new AFDis active field distributor with integrated field barrier is a special type of field distributor. It limits the power for the connected field devices and therefore provides an intrinsically safe power supply for the explosion-risk areas of Zones 1 (21) and 2 (22). The explosion protection can be certified according to the FISCO model without the need for complex calculations. An integrated fieldbus repeater reproduces the communication signals between the main cable and the stub cable and therefore ensures a high signal quality, free of undesirable feedback.

AFDis active field distributor
- Intrinsically safe power supply for up to 6 field devices in the Ex area
- Certification of explosion protection according to FISCO
- Automatic bus termination and isolation of defective subsegments
- Opening of the main line in Zone 2 without fire certificate
- Integrated fieldbus repeater for greater robustness and greater-quantity frameworks and network expansion
- Short-circuit-proof stub cable with intelligent debounce logic
BASF Coatings, Germany

A Clean Start

BASF Coatings in Münster-Hiltrup, Germany, has one of only two plants in Europe in which the process containers for paint production can be cleaned. Therefore, nothing could be allowed to go wrong during the modernization of one of the two plants with Simatic PCS 7.

At first glance, the container-cleaning facility of BASF Coatings in Münster-Hiltrup appears to be only one of many utilities on the site. But it has a very central and crucial function within BASF Coatings. Approximately 200 production containers are cleaned in this unit every day. The containers are made of stainless steel and usually have a volume of between 500 liters and 1 cubic meter. They come not only from Münster-Hiltrup but also from other sites – and production depends on clean containers.

Living plant with a past
The Siemens Solution Partner Bormann+Reinhold (B+R) was contracted to modernize the process automation of this production-critical plant at BASF Coatings, a project that was unique in many respects.

The container-cleaning unit consists of a washing line with several washing cabins in which the containers are cleaned with automatic brushes. The conditions are extremely harsh, and therefore there are
harry any possibilities for viewing the process directly. Only two small viewing windows allow a look inside the cleaning unit.

The automation of the plant was based on Simatic S5 controllers with separately wired fail-safe systems. In the course of its lifecycle, the plant had been extended and revised several times. BASF’s plan was to totally convert this plant to new control and safety technology. Because the production containers can only be cleaned in advance and stored for a few days, only five working days and the following weekend were available for the complete conversion, including installation and commissioning. In addition, the emergency stop signals that were previously separately hardware wired had to be integrated into the fail-safe PCS 7 automation with the safety matrix.

Process simulation speeds up implementation

“Under such demanding conditions, the completion of this project was really only possible with the help of the Simit simulation tool,” Helmut Reinhold, CEO of B+R, reports. First B+R had to create a process image, which was no easy task in view of the existing process automation situation. “The BASF Coatings staff in the plant helped us collect all the necessary information. This collaboration is typical of the BASF Coatings employees, who offer their expertise in the course of such projects and therefore contribute greatly to rapid implementation,” explains Anette Hoppe-Öchtering, who worked for B+R on the project to modernize the container-cleaning plant.

The information for the process image was created based on the operation of the real plant. The result was a simulated process environment – with more than 60 Simocode modules for the brushes, motors, and drives in the washing line – that served as a basis and model for the planning of the new automation solution. B+R needed about three weeks in total to set up the simulation environment and most of another three weeks for programming and testing of the new Simatic PCS 7 system. Because of the extremely rapid switching processes necessary for controlling the plant, especially for processing the fail-safe functions, a highly efficient AS/400 FH automation system is used as the core of the control system on the hardware side.

Rapid implementation with concise specifications

Then it was time for the actual system upgrade. BASF Coatings had already cleaned as many containers as possible in advance and filled the container store prior to the conversion, in order to have a certain stock of clean process containers. Based on the test with the Simit tool, B+R was already able to ensure that the programming was working properly and without errors before installation. Therefore, only the normal tuning work had to be done on-site, and the time for the implementation could be reduced considerably. The good collaboration with the BASF Coatings team was also decisive in this critical project phase. “Despite all our preparations, we would never have been able to complete the project so well and so quickly without the excellent local support,” says Hoppe-Öchtering.

Modern automation with integrated documentation

The result was impressive: the plant resumed operation as scheduled, and the conversion had practically no effect on ongoing production. Ever since, BASF Coatings has been operating a highly modern, well-documented container-cleaning plant with integrated safety technology and modern, efficient hardware. The new process control system also supports the evaluation of plant performance: the PM Quality tool records performance-relevant data for the container cleaning per container and per shift. These data allow optimization of the processes in the container-cleaning plant and therefore help ensure that the optimum number of cleaned containers is available for production at all times.
**Sitrain for Totally Integrated Automation**

*Fit in Process Automation*

Greater quantities, shorter delivery times, and competitive product prices can only be ensured sustainably and economically by automation. With Totally Integrated Automation (TIA), a complete process chain from incoming logistics through the production process to the outgoing logistics can be achieved with a modularly structured system. However, great technical know-how is necessary to master, optimize, and maintain the full range of process automation. Sitrain therefore developed a sophisticated training concept to get people fit to handle the networked system components. The participants can try out the knowledge gained from the “Simatic PCS 7 System” course on a real, modularly installed system and train further to become service experts in the “Simatic PCS 7 – Practical” extension course.

System operators, service personnel, commissioning technicians, and maintenance specialists are the target groups for the TIA training. The courses are based on a confrontational teaching concept in which the focus is on learning on the specific problem or customer job. The participants learn to deal with varying problem situations and are not taught prefabricated solutions. The course participants’ positive response to the integrated course concept confirms the idea behind the TIA training: absolute practical orientation, learning under realistic conditions, well-documented training success, incorporation of all areas of process automation, and success that is proven by the solving of practical problems.

*www.siemens.com/sitrain*

---

**Sitrain in Bahrain**

*Tailor-Made Know-How Transfer*

Six employees of the Saudi Arabian company Industrial Instrumentation & Control Systems Ltd. were trained on the handling of the Simatic PCS 7 process control system in the Bahraini capital, Manama. In addition to teaching the basics, the emphasis was on practical exercises and the topic of process safety, which was treated in depth at the participants’ request.

The course participants were automation engineers and planners who, as Siemens Solution Providers, had the task of migrating an existing process control system and the associated safety switch-off logic to the Simatic PCS 7 process control system.

Thanks to the customer-specific training, the employees of Industrial Instrumentation & Control Systems Ltd. are now able to unite the process control and safety system on a common Simatic PCS 7 platform.

*www.siemens.com/sitrain*
RWE, Germany

Well Equipped for Gas Measurements

Marquis GmbH in Witten was contracted by the energy supply company RWE and Ermetek GmbH to equip two measuring vehicles for natural-gas filling stations with MicroSAM CV gas chromatographs. The new MicroSAM CV for biogas was also installed in the vehicles to monitor the hydrogen and oxygen concentration in addition to the 11 natural gas components.

Natural-gas engines require a high gas quality to avoid engine damage. Following a change in the law, compliance with the limit values must (as of 2009) be monitored at the interface to the vehicle being fuelled and no longer at the arrival at the gas station. The vehicles drive to a natural-gas station and are first fuelled to flush the pipes. Then the natural gas is drawn from the hose and the pump nozzle by a second tank nozzle and analyzed. At the end of the measurement, the chromatographs are transmitted from the vehicle via GSM and evaluated simultaneously in the vehicle and the laboratory. This dispenses with the need for expensive sampling with gas pressure tanks.

The equipping of other vehicles for measuring the gas properties in local network systems and biogas feed systems is planned.

www.siemens.com/microsam

Sitrans LR 250 for Vacuum Extruders

Consistent Control for Better Quality

Vacuum extruders are used for manufacturing profiles in the plastic and food industry as well as for producing brick veneers in the brick industry. Petersen Service GmbH in Netphen, Germany, is an experienced manufacturer and provider of tailor-made solutions.

For long time, the filling level in the vacuum chamber could only be measured by means of a few limit values. The main emphasis was on avoiding underfilling of the vacuum chamber and thus disturbances in production. A continuous filling-level measurement of the product in the vacuum chamber has a decisive advantage over this because a heavily fluctuating filling level causes less smooth operation of the conveyor screw and therefore has an influence on the quality of the end product. Controlling the product feed and the extruder screw at the product discharge leads to an even filling state and ultimately to better end-product quality.

Petersen found the solution in noncontact radar measurement with the Sitrans LR 250. Thanks to the microwave process, the robust sensors can also be used in difficult ambient conditions. The 25-gigahertz technology was chosen due to the small antenna design and the low dead zone. The integrated, easily programmable process intelligence ensures the right signal evaluation in the case of a restless surface and a stable measured value output.

www.siemens.com/sitrans
In Brief

Sitrans FUT 1010 Ultrasonic Flowmeter
Specialist for Oil and Gas

The new Sitrans FUT 1010 ultrasonic flowmeter was specially developed for the hydrocarbon industry. It features the nearly maintenance-free TransLoc mounting system that allows the transducers to be mounted on the outside of the pipe, preventing contact with the medium. This approach, which only Siemens offers, allows the externally mounted transducers to be calibrated for higher accuracy. It also has the additional benefit that it alleviates clogging of cavities by high-paraffin liquids, which is typically seen in conventional flowmeters used in hydrocarbon applications. TransLoc simply ensures less maintenance and downtime, leading to low cost of ownership and improved return on investment (ROI).

By combining the well-known WideBeam ultrasonic transit time flow technology with the delivery of the entire meter run, including the segments for upstream, downstream, and the flow conditioner, Siemens offers a unique flow solution that can be calibrated to American Petroleum Institute (API) and American Gas Association (AGA) specifications. It also ensures that the Sitrans FUT 1010 achieves highly accurate flow measurement.

www.siemens.com/sitrans

Simatic MV420 Stationary Code-Reading System
Compact and Powerful

The Simatic MV420 stationary 1D/2D code-reading system is characterized by high reading reliability and a wide range of communications and connection options. The compact device with a high IP67 degree of protection can read both standard high-contrast codes and DPM (direct parts marking) codes even under difficult ambient conditions. Typical uses include product tracking and process control applications in the automotive, packaging, pharmaceuticals, tobacco, cosmetics, electronics, and food and beverage industries. In addition, the MV420 is also suitable for shipment tracking in logistics and distribution.

The Simatic MV420 with 752 x 480 pixel resolution has integrated lighting, supports operating distances of 1.5 to 22 centimeters, and processes up to 70 codes per second. Using multicode reading, up to 50 codes and even different code types can be decoded from a single image. A special feature is the “auto trigger” image-recording mode. This enables the code reader to record images automatically without requiring external trigger signals.

The Simatic MV420 features integrated Profinet IO, Industrial Ethernet, and RS232 interfaces. A communications module is used to connect to Profibus, which also allows mixed operation with RFID (radio-frequency identification) systems. The Simatic MV420 code-reading system is parameterized and commissioned using a built-in Web server. The Web-based user interface provides extensive operator control and monitoring functions, even in evaluation mode.

www.siemens.com/simatic-sensors/mv
info

Do you want to know more about the systems and solutions for the process industry from Siemens Automation and Drives? Simply visit our information portal on the Internet at:

www.siemens.com/prozessautomation

Do you want to change your address? Subscribe to process news? Comment on articles in process news or request more information? Just send us an e-mail:

response.processnews@siemens.com

online

www.siemens.com/processnews

Here you can download the current issue and past issues of process news as PDF files, or search directly for articles about specific topics, technologies, and systems in the Reference Center.

knowledge

White paper on biometric authentication

Improved Security, Compliance, and Efficiency

Public institutions and companies must satisfy increasingly stringent requirements with regard to the correct use of data and the traceability of IT-based processes. The foundation for improving transparency and traceability is the implementation of reliable user authentication based on a biometric feature unique to each person.

However, user authentication is not a single function that is performed only by a specific application, but rather a common theme throughout all company functions.

In a white paper, Siemens IT Solutions and Services presents a concept for the introduction of an open, scalable framework for user authentication. The white paper shows new methods not only for increasing the security and reliability of authentication but also for gaining a considerable economic advantage with reduced administrative effort.

For more information about biometric authentication:

www.siemens.com/biometrics
it-solutions@siemens.com

process news 2-2010

Publisher
Siemens Aktiengesellschaft,
Gleiwitzer Str. 555, 90475 Nuremberg, Germany
www.siemens.com/automation

Drive Technologies Division
CEO Klaus Helmrich

Industry Automation Division
CEO Anton S. Huber

Responsible for Content
Arno Hoier

Responsible for Technical Content
Cornelia Dürrfeld

Concept
Christian Leifels

Editor
Cornelia Dürrfeld, Siemens AG, I IA AS SM MP 7
Siemensallee 84, 76187 Karlsruhe, Germany
Tel.: +49 (0) 7 21 5 95-25 91
Fax: +49 (0) 7 21 5 95-63 90
cornelia.duerrfeld@siemens.com

Editorial Committee
Sigrun Ebert-Heffels, Ute Forstner,
Petra Gers, Michael Gilluck, Walter Huber,
Rudiger Selig, Roland Wieser

Publishing House
Publicis Publishing,
Part of Publicis Pro
Postfach 32 40, 91050 Erlangen, Germany
Tel.: +49 (0) 91 31 91 92-5 01
Fax: +49 (0) 91 31 91 92-5 94
publishing-magazines@publicis.de

Editor in chief: Kerstin Purucker
Layout: Stefanie Eger, Jürgen Streitenberger
Copy editing: Imgard Wagner
DTP: Mario Willms

Printing: Wünsch, Neumarkt, Germany

Circulation: 32,000
Job number: 002800 26492
© 2010 by Siemens Aktiengesellschaft
Munich and Berlin

All rights reserved by the publisher. This edition was printed on environmentally friendly chlorine-free paper.

ISSN 1430-2284 (Print)
The following products are registered trademarks of Siemens AG:
ET 200M, ET 200S, MP 377, Serialization@Siemens, SIMATIC, SIMATIC PCS 7, SIMATIC IT, S7-300, SIPAT, SITRAIN, SITRANS, WinCC

If trademarks, trade names, technical solutions, or similar are not listed above, this does not imply that they are not registered.

The information provided in this magazine contains merely general descriptions or characteristics of performance, which in the case of actual use do not always apply as described or which may change as a result of further development of the products. An obligation to provide the respective characteristics shall exist only if expressly agreed in the terms of contract.

IFL: TPOG
Order number: E20001-M6210-B100-X-7600
Printed in Germany
What are the ingredients for your business success?

Perfect control of all quality aspects in the pharmaceutical and life science industries.

Siemens expertise and solutions for research and development, manufacturing, utilities and business processes, as well as a commitment to the environment help the industry to minimize risk, increase efficiency and improve patient safety. [www.siemens.com/pharma](http://www.siemens.com/pharma)

Answers for industry.