

# SCHOTT forma vitrum NEWS FLASH

## PHARMACEUTICAL PACKAGING

ISSUE 8 June 2007

### NEWS

## Hungary increases capacity by 25 percent



New production building

A new building with 3,500 m<sup>2</sup> of floor space was constructed for vial production in Lukásháza, Hungary.

At the SCHOTT forma vitrum site in Lukásháza, Hungary, production capacities will be increased by 25 percent until 2009. A new building with 3,500 m<sup>2</sup> of floor space was constructed for vial production. Following almost 9 months of construction time, the first production machines will

be installed at the end of July. Production will start in September.

Further it is planned to double production capacity for cartridges and to increase ampoules production in existing production facilities.

In addition, Schott forma vitrum Hungary has invested in modern

production equipment and infrastructure. These measures will ensure to meet the high quality requirements of the customers also in the future.

The expansion in Hungary is mainly driven by a strong increase in demand, especially from Eastern Europe.

### EDITORIAL



Dear Readers,

Good News! We continue to expand our syringe operations. Having invested in the expansion of our syringe manufacturing facility in Switzerland last year, we are now prepared to move one step ahead. Next year, we will be setting up a second, state-of-the-art syringe manufacturing facility at our existing site in North America. This will enable us to offer a genuine second source and backup op-

tion for our syringes, as with all of our other products.

This decision underscores once again that reliability of delivery and quality are at the top of our priority list. At the same time, this investment will enable us to strengthen our position as a market-leading, global provider of parenteral packaging.

To find the best syringe solutions for you in the future, we can rely on a unique combination of strengths. Our strong expertise in glass manufacturing and glass forming, our proprietary camera inspection technology and, last but not least, our coating technology, make us an innovative and competent partner for the pharmaceutical industry. Let's look forward to the future.

For today, we hope you enjoy reading our latest edition.

Sincerely yours,

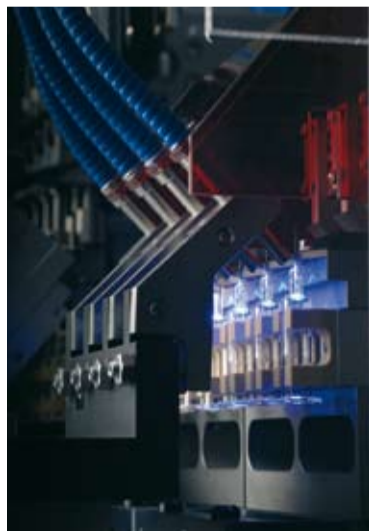
Christof Hanschke  
Vice President, Business Segment  
Pharmaceutical Packaging

### PRODUCTS

## Syringe needle glueing with fast speed and highest precision

A new high tech machine for glueing needles into the glass bodies of syringes was taken into operation at SCHOTT forma vitrum in Switzerland in May 2007. The development of the machine that was built especially for SCHOTT forma vitrum took two years. Following initial acceptance testing and trials on site, the qualification phase was successfully completed in April 2007.

The new machine is completely integrated into the manufacturing process, as in the past, between molding of the glass bodies and washing and silicization of the syringes. By multiplying the simultaneous processing per station from one to four syringes, reducing cycle times and improving efficiency the manufacturing capacity will be increased by a factor of five compared to the past. In addition, it even delivers a much higher level of manufacturing precision par-



Four syringes can be manufactured simultaneously.

ticularly with regard to free needle length and needle angle. In addition the assembly line is equipped with a new generation camera inspection system. Reducing tolerances from the norm by half will be



The new machine is completely integrated in the manufacturing process.

of special benefit for certain processing steps at the customer, for example for auto-injectors.

The new machine is located in a separate room with clean environment and controlled temperature

and humidity. The room even offers enough space to hold a second system that is identical in construction. During the transition period, the old machine will continue to be put to use, later on it will be used

for product development and process engineering.

The new machine relies on proven, validated and qualified techniques in accordance with GMP standards. "Both the system design and the entire procurement process were documented as carefully as if we were planning to use the new machine directly at a customer's site," explains Alphons Fakler, Manager Product and Process Development. The basic concept for the new machine was first introduced during SCHOTT forma vitrum Customer Day 2006 in Switzerland and has been the subject of continued customer audits. This invest is part of the overall syringe manufacturing project at the St. Gallen site.

**ON TOUR**

## World-class R&D from Pennsylvania



SCHOTT North America Regional Research and Development Duryea is the North American research group within the 18,000 employee global SCHOTT organization.

Situated in Pennsylvania, SCHOTT's Duryea facility has been a center of excellence for nearly 40 years. Chosen for its close proximity to major metropolitan areas such as New York, Philadelphia and Washington, D.C., it is within easy reach of key customers as well as many prestigious educational institutions.

Two buildings and a warehouse comprises the complex, which is located on 280,000 square meters of land. First established as primarily a manufacturing site, core competencies of the combined site include glass melting and hot glass forming, glass machining and fabrication, and, of course, research and development.

Initially a part of the manufacturing organization, R&D at Duryea served to support SCHOTT's historic quality in producing optical and technical quality glass and parts for defense, industrial, medical, aerospace and opto-electronic markets. However, as part of a global reorganization, it took on a new role in 2003, expanding in both equipment and expertise to serve as a corporate hub of innovation. "We needed a local presence in North America," says Sam Conzone, Director Research and Development SCHOTT North America. "We are driving a lot of advancement and have over 40 patents which showcase our technological expertise."

Housed in a 1858 square meters state-of-the-art facility, a 25-member, fulltime staff supports North American product development and fundamental research projects. "The staff is comprised of researchers with expertise in materials science, molecular biology, protein biochemistry, inorganic/organic chemistry, and coatings," says Conzone. "This multidisciplinary team is well equipped and trained to lead developments on topics ranging from optimized transparent armor materials/systems to advanced pharmaceutical packaging."

The facility is equipped with a variety of vapor and liquid phase coating machines, a world-class/small scale melting and materials development facility, molecular biology and proteomics laboratories,

and access to a class 100 clean room.

"We're very action/result oriented," says Conzone, "with 50-60% of our time focused on short term development and technical support and 40% on futuristic R&D. For example, our biotechnology group has recently developed advanced, high sensitivity microarraying platforms that are now being considered for use in bioterrorism agent



Engineers testing protein adsorption to pharma containers.

detection by the Department of Defense, while our materials team is focused on developing advanced glass ceramic materials intended to provide cost-effective, lightweight armor solutions."

R&D serves and shares the Duryea site with SCHOTT Advanced Optics (AO), a leading manufacturer of optical glass and glass ceramics with a comprehensive expertise in high precision processing of optical components. In addition, R&D

maintains strong business and technical interactions with the SCHOTT Pharmaceutical Systems division.

An extension of the SCHOTT research group in Marienborn, Germany, the Duryea group has two areas of uniqueness. One is proximity to North American customers and market needs. The other: "We have a fully staffed, fully equipped molecular biology/protein biochemistry group that is unique to our Duryea team and whose purpose is to delve into and understand drug container interactions when the drug itself is a biomolecule," says Conzone. Their focus: understanding how to quantify how drug potency is lost due to drug/container interactions and to come up with solutions to prevent it (for further information see page 4).

"Over the past several years SCHOTT has invested millions of dollars to build up R&D expertise

and manufacturing capabilities to support product developments in the area of biotechnology and advanced pharmaceutical packaging," says Conzone. "We're proud to be part of an R&D team that works around the world and around the clock to stretch the limits of materials and biotechnology in a manner that is driven by the markets of our leading SCHOTT business units."

### Site at a glance

SCHOTT North America, Inc. Regional Research and Development Duryea

<b>Location:</b>	Duryea, Pennsylvania
<b>Employees:</b>	25
<b>Quality certification:</b>	ISO 9001
<b>Capabilities:</b>	Full glass and glass ceramic development and analytical (wet chemical and optical property characterization) capabilities; analytical capabilities for characterizing drug container interactions; microarraying laboratories; coating facilities
<b>Production area:</b>	1858 square meters

**PEOPLE**

## Harmonizing interfaces



"Reliability is extremely important to me", says Christof Hanschke.

Christof Hanschke, Vice President of the Business Segment Pharmaceutical Packaging, is a fine mechanics engineer who previously worked in automotive engineering. "Precision mechanics used to be my specialty. As this suggests, my ability to pay close attention to details will be of great benefit to me in the pharmaceutical business," the 51 year-old explains. Without question, he is also capable of seeing the whole picture. Having worked in the automotive manufacturing industry, he developed this skill almost automatically. After all, hardly any other industry has internalized the issue of stable processes and reliable, continuous manufacturing to such an extent. While working for a subsidiary of BMW, he also gained many years of experience in areas like customer orientation, customer service, quality assurance and, most importantly, development of backup solutions.

This is certainly a topic that is currently taking up much of his attention at SCHOTT forma vitrum. "Even if cars and pharmaceutical packaging differ considerably from each other in terms of size, the challenges definitely remain the same." Further harmonizing interfaces and consequently delivering the same high quality from all of the plants have now become his

main objectives. Another priority in the best interest of customers is the set up of the plants in Europe in such a way that alternative manufacturing sites exist for all products.

Otherwise, Christof Hanschke considers himself to be a conservative person with a distinct sense of values. "Reliability is extremely important to me, as this means continuity, but also safety with respect to our products," he says. In his opinion, innovations and development projects form the basis for the company's ability to master the future, however, by no means may these be driven forward at the expense of quality. Here, too, he sees parallels to the automotive industry: "The lead time required to develop a new product is incredibly long. Nevertheless, speed is not measured in terms of product cycles, but rather by customer service and how efficiently claims are managed."

Perseverance is a virtue that Hanschke trains not only at work, but also during his spare time, by hiking, riding bicycle or swimming. Otherwise, he enjoys cooking, reads a lot and has an interest in culture and nature. Stress is not a problem for him. As he puts it: "I really enjoy my work and success is my motivation."

**Masthead**

SCHOTT forma vitrum  
NEWSFLASH  
Issue 8 / June 2007  
Copyright 2007:  
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SCHOTT Schweiz AG  
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## QUALITY

# Future US HSR test requirement already a SCHOTT forma vitrum standard

The U.S. Pharmacopoeia (USP) is planning to add the test for hydrolytic surface resistance (HSRT) for primary glass containers. SCHOTT forma vitrum customers, however, are well positioned for the change as this has been a standard at SCHOTT forma vitrum for well over a decade.

"SCHOTT forma vitrum finds itself in an excellent position to carry out the future USP requirements since the HSRT is already established as a standard for our products through all our plants," says Patrick Gruening, Business Development Manager North America. "Our employees are specifically trained, measurement equipment is in place, converting machines are optimized and influencing process parameters identified, understood and controlled. SCHOTT forma vitrum is prepared, and our customers are in a very comfortable place."

The new requirement is planned to be added by the USP under a new chapter (6.6.0.), the hydrolytic surface resistance test (HSRT) for the characterization of glass containers used for pharmaceutical applications. "In this, the USP follows the lead of the European Pharmacopoeia (EP) with the design and execution of the test, since the HSRT has been part of the EP for many years," says Gruening.

The HSRT establishes a limit for the quantity of glass components which tend to be extracted or leached out from the direct contact area (the inner surface). The test does not address each individual component extracted but the combined effect of those extractable in water, that is, hydroxide ions. The release of hydroxide ions may cause a pH shift to higher values in none or light buffered solutions.

"The HSRT provides a more practical value in understanding the reaction potential of the container as compared to the glass grain/powder test, which provides only a relative interaction potential of the entire glass and not specific for the surface." The grain/powder test is mainly used to classify the raw glass itself into different glass types according to their chemical resistance. "The HSRT, on the other hand, is directly influenced by the converting process, which at the end defines the container and its primary interaction potential."

Manufacturers of pharmaceutical packaging delivering to the US or under USP mandate will have to challenge their process and process control, according to Gruening. "Some might have to go through a certain learning curve in the beginning as we have seen in Western Europe, but



The test for hydrolytic surface resistance for primary glass containers has been a standard at SCHOTT forma vitrum for well over a decade.

at the end it will be just another step towards a better container. For pharmaceutical companies who currently specify existing USP requirements, the new chapter will provide customers a better container with a more consistent interaction potential. For pharmaceutical companies who already had defined USP and EP, we expect a very smooth transition since the HSRT-EP and HSRT-USP are equivalent."

SCHOTT forma vitrum customers are well positioned for the change, as many competitors of SCHOTT forma vitrum are currently not set up to offer HRS testing. "For us, it will be a very smooth transition," says Gruening, "mostly in the area of paperwork. Once the HSRT test is in effect, we will work in close cooperation with our customers to help them meet their documentation and procedures needs."

## EVENTS

# Workshops in US spotlight innovative solutions



Gary Waller, Regional Sales Director North America opened the workshop in Philadelphia.

Building on requests by pharmaceutical and biotech companies to increase their understanding of current and future innovative primary packaging concepts, SCHOTT forma vitrum has organized a series of technical workshops for customers across the U.S. Designed as intensive, one-day events convenient to key customer locations (Philadelphia, Chicago, and Los Angeles), the workshops are an active demonstration of SCHOTT forma vitrum's emphasis on providing innovative solutions to meet customer – and industry – demands, according to Gary Waller, Regional Sales Director North America of SCHOTT forma vitrum.

"New drug developments continue to challenge the current product offering by the primary packaging industry," says Waller. "As a leader, SCHOTT forma vitrum has not only responded but anticipated these with innovations in an array of solutions such as internal surface coatings and alternative packaging like cyclic olefin copolymers. In addition, SCHOTT forma vitrum continues to improve the understanding of drug to surface interaction at the R&D and formulation stages."

Such innovations were the focus of the roster of SCHOTT forma vitrum and industry experts who presented at the workshops.

These included Bernd Sparenberg, President, and Dr. Ron Lamonte, Technical Marketing Specialist, of Topas Advanced Polymers; Jeff Smythe, Technical Customer Support Manager, Brian Brucker and Adrienne Williams, Biotech Technical Account Managers, of West Pharmaceutical Services. Also, from SCHOTT, Dr. Robert Hormes, Director of Product Development; Rainer Schmitz, General Manager of Quality SCHOTT Rohrglas; Steve Russo, Director of Marketing and Sales NA SCHOTT Tubing; Patrick Gruening, Business Development Manager NA; Dr. Rajendra Redkar, Research Scientist; and Dr. Dan Haines, Coatings Development Scientist.

Their topics:

### \*Premium glass for pharmaceutical packaging

Material properties, manufacturing process & pharmaceutical requirements.

**\*Innovative packaging solutions**  
Market trends and product developments to meet the rigorous demands of the pharmaceutical industry and regulatory requirements.

### \*Elastomeric components

Extractables and leachables, regulations and quality.



Some 120 representatives from more than 50 companies joined the workshops.

### \*Protein interaction

Interaction of protein pharmaceuticals with primary packaging, and the methods to assess behavior patterns and predict interaction potential.

### \*Advanced Coating Technology

The current offerings and future development concepts of internal coatings for primary packaging based on existing and new drug formulations.

### \*TopPac, the polymer alternative container

A technical overview of Topas COC as an alternative to Type I glass and

the current market developments of Topas in various packaging industries.

The workshops were attended by more than 120 representatives from more than 50 companies. "This is the first time we have organized such a series of workshops and the response has been enthusiastic," says Waller. "SCHOTT forma vitrum is a provider of innovative solutions and we want to bring that innovation to our customers in pharmaceutical packaging. We are more than just vial and ampoule manufacturers and our focus is not only on today's business but tomorrow's."

## TECHNOLOGY

# Innovative coating solutions in the pipeline

Interview with Sam Conzone, Ph.D., Director Research and Development SCHOTT North America, Duryea and Robert Hormes, Ph.D., Director Product Development SCHOTT forma vitrum.

► for further information on R&D SCHOTT North America, Duryea see page 2

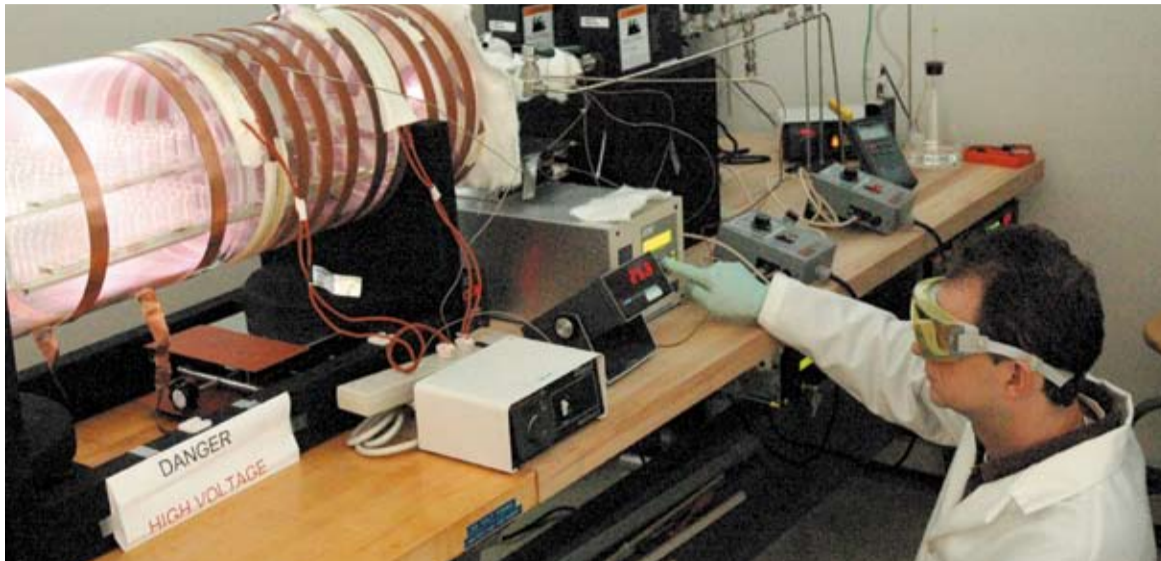
**The SCHOTT Research Center in Duryea provides support to SCHOTT forma vitrum pharmaceutical packaging operations. What type of support is offered?**

**Conzone:** In Duryea we have a scientific team with expertise in molecular biology, protein biochemistry, chemistry and coatings. We use this expertise to generate an understanding on how drugs interact with pharmaceutical containers (adsorption, aggregation, denaturation) and how to prevent deleterious interactions.

**Hormes:** The scientific know-how enables us to understand problems of biomolecule stability in pharmaceutical formulations. We use this scientific know-how to interact directly with formulation experts in the pharmaceutical industry to understand/overcome advanced packaging problems from a scientific perspective.

**What is the benefit of this co-operation for the customer?**

**Conzone:** The combination of advanced know-how in glass and glass forming, coating technology and biotechnology is unique and puts SCHOTT forma vitrum in the position to offer problem-oriented,



Engineer Joe Granko depositing protein detergent coating to 2 mL pharmaceutical vials on a laboratory scale radio-frequency plasma chemical vapor deposition system (RF-PCVD).

sophisticated solutions for complex packaging problems.

**Hormes:** Together with pilot customers we have been working on projects to understand the unmet needs in today's formulation work. For example, a customer had problems with adsorption loss with a low concentrated protein formulation. We have a fast method to quantify the protein adsorption to primary packaging container surfaces. So we were able to assist our customer with the quantification of protein adsorption and to suggest the ideal surface (glass, polymer, or coated surface) for their protein formulation.

**Coating of primary packaging containers has been a core competence of SCHOTT forma vitrum for more than 10 years. Would you say coating is a success story?**

**Hormes:** Yes, absolutely. The validated SCHOTT PICVD® coating process offers the possibility to improve the inertness and chemical stability of pharmaceutical Type I borosilicate glasses like Fiolax(R). With the silica coated glass SCHOTT Type I plus(R), which was introduced to the market in 1998. We have overcome problems related to the adsorption of radioactive diagnostics, eliminated the pH shift in water for injection and improved the stability of protein drugs in cases where the protein is sensitive to metal ions extracted from the glass.

**Conzone:** In addition, we are working on a number of promising, new coatings, such as a hydrophobic type of coating, which improves the emptying characteristics of vials, especially for solutions with higher viscosity, i.e. highly

concentrated recombinant antibody formulations. The hydrophobic coatings also improve the visual consistency and homogeneity of lyophilized cakes.

**SCHOTT Type I plus (R) containers offer maximum inertness for sensitive drugs. Why does SCHOTT forma vitrum work on the development of additional coating types?**

**Hormes:** More than 50% of the product developments in the pharmaceutical therapeutics pipeline contain biomolecules. Therefore it is not surprising to see a strongly increased interest in coated primary packaging. A pure silica layer (like in Schott Type I plus) on the inner surface of pharmaceutical packaging is an excellent solution for a number of specific requirements as described above. However, it cannot solve all stability issues with com-

plex, modern biomolecule drugs.

**Conzone:** Therefore we started to work on protein surface interaction about 2 years ago. We gained a lot of experience on protein/surface interactions and have identified several organic molecules which can be coated onto glass surfaces to prevent or deter protein interaction and binding to packaging surfaces.

**What are the next steps with respect to organic coatings?**

**Conzone:** Our initial results are very promising. Our organic coatings appear to deter drug adsorption sometimes by up to an order of magnitude. We are now attempting to refine our coatings to achieve a process that is suitable for mass production and robust enough to survive multiple methods of sterilization.

**Hormes:** We are performing in detail scientific tests including stability, leachables/extractables and toxicologic assessment. Further, we will be entering into beta tests together with pilot customers to determine the benefit of such organic coatings with real proteins of pharmaceutical interest.

Generally speaking, we will continue and evolve our development work in the field of coated packaging solutions. Coating is one of the core competences we rely on to solve packaging problems and to provide expertise and solutions for the pharmaceutical industry. We expect to pioneer the market with packaging solutions with new surface functions in the future.

**Thank you for the interview.**

## CUSTOMER FOCUS

# Consequent standardization, greater flexibility

Consequent standardization and harmonization of processes at the European SCHOTT forma vitrum manufacturing sites in France, Germany, Switzerland and Hungary are at the focus of an internal project called PEP (Power up European Plants). Optimized customer service and customer orientation are the objectives of the initiative that starts with uniform packaging and covers labeling, distribution, uniform documentations, quality systems, certifications and manuals. Also areas like manufacturing processes, quality inspections, warehousing, transportation, purchasing and sales are touched by the comprehensive alignment of the production and service network.

SCHOTT forma vitrum has been working on these topics for a number of years. Already today, many products can be offered in the same quality from more than one manufacturing site. However,



Production machines in Hungary are being overhauled and adjusted to ensure uniform manufacturing processes worldwide.

the company has recognized the need to drive standardization and harmonization even further. Also, preparations are taken to expand the back up concept to further products.

For example, in the future screw neck vials can be manufactured not only at the SCHOTT forma vitrum plant in Germany as in the past, but also in Hungary, as a second source. The same applies for

certain special ampoules that were produced only in France in the past, and can now be manufactured in Hungary, too.

Of course, at the end of the day it is the decision of the customer whether or not a specific product should be manufactured at a second or even a third manufacturing plant. To keep it simple for those customers who decide to validate more than one plant, SCHOTT forma vitrum has defined a systematic and controlled workflow which can be adapted to customer needs.

To ensure that manufacturing processes can be set up in a uniform manner for the above-mentioned products, comprehensive efforts to transfer know-how are now underway. Experts from Germany and France are training their colleagues in Hungary, machines are being relocated and new ones are being purchased. In any case,

technologies and equipment need to be closely coordinated. Machines are now being overhauled, adjusted and expanded.

"Once this project has been completed, we will have a backup system that enables us to offer our customers completely comparable quality for all products," says Tamas Feher, Technical Director for forma vitrum Kft. in Lukácsháza, Hungary. The changes will allow for processes to be coordinated in a more efficient manner. SCHOTT forma vitrum will become much more flexible. "We will be able to coordinate our manufacturing activities across Europe in a way that will allow us to incorporate more reliability and time buffers." Feher explains. "This translates into higher reliability of delivery and reduced delivery times for our customers."