

NEWS

50 ml vials available in TopLine quality

SCHOTT forma vitrum has increased the production capacities for "TopLine" vials. On two new production lines in Muellheim, Germany, SCHOTT forma vitrum can produce vials which hold more than 50 milliliters and have a diameter of over 40 millimeters. This means an extension of the "TopLine" vial product portfolio by bigger dimensions.

"We experience a rising interest in our TopLine containers, and this also for bigger volumes," says Dr. Norbert Reiser, General Manager of SCHOTT forma vitrum, Germany. "The first order was placed by a US customer who ordered some million 50 ml vials for delivery this year. They will be used for highly sensitive oncological drugs."

TopLine customized packaging solutions are tailored to the product requirements and the product environment of the customer. They are defined and designed in close cooperation with the pharmaceutical company. The benefits for the customer are a reduction or elimination of the incoming inspection, a higher yield and productivity on the filling line, a low reject rate and an assured product safety - providing for lower overall cost.



Visual inspection of TopLine vials

TopLine vials rely on premium quality glass tubing and advanced forming technology, excellent process capability and validated processes, 100% inspection of cosmetic aspects with inhouse

developed vision systems, full compliance with GMP requirements for primary packaging and an efficient quality organization and continuous improvement culture (six sigma).

Pharma Symposium 2006

What are the latest developments in syringes? What are the needs of the patients today? What global challenges is the pharmaceutical industry facing? How can quality and safety be achieved with both medications and their packaging?

At the beginning of May, more than 100 experts from the pharmaceutical industry met for three days to attend the "2. SCHOTT Pharmaceutical Symposium" in Bamberg. "Tailor-made Solutions for Challenges and Trends in the Pharmaceutical Industry" was the theme of the event and representatives from well-known international pharmaceutical companies took part in guest lectures, podium discussions



Attentive international audience

[Continue Appendix](#)

EDITORIAL

Dear Readers,

The many photographs in this edition should at least give you some feeling for how comprehensive, diversified and informative our second European Pharmaceutical Symposium truly was.

At least in my opinion, the message that left the symposium was unmistakable. The increasing regulatory requirements, more challenging demands of the pharmaceutical industry, but also new drug applications definitely require closer cooperation between all of the companies involved in the manufacturing process. Thanks to the presentations, but even more importantly, the interesting workshops that were held, our Symposium certainly made a valuable contribution towards this. For many of the participants, the plant tour at SCHOTT-Rohr glas, Germany, was a special highlight of the event. Just in time for the Pharmaceutical Symposium, we were able to announce that SCHOTT-Rohr glas had become the world's first manufacturer of glass tubing to be certified



according to ISO 15378. Congratulations on this success! Cooperating so closely with SCHOTT-Rohr glas provides us with a sound foundation as a supplier. After all, the pharmaceutical industry, in particular, views reliability of delivery and back-up capacities to be extremely important. With such a strong partner within the company group, SCHOTT forma vitrum can certainly offer the best service to the industry.

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

Sincerely yours,
Dr. Peter Knaus
Vice President, Business Segment
Pharmaceutical Packaging



Sam Conzone moderated the Pharma Symposium 2006

PRODUCTS

SCHOTT Type I plus – for ultimate inertness

For approximately ten years, SCHOTT has been producing pharmaceutical glass containers with high-tech barrier layers that substantially improve the chemical stability of the glass surface. This SCHOTT forma vitrum specialty is produced in Müllheim, Germany and marketed globally under the brand name SCHOTT Type I plus®. The product is currently meeting with a sharp increase in demand due to the advances taking place in the field of biopharmaceutical technology.

Using the Plasma Impulse Technique ("PICVD") developed by SCHOTT, the vials are coated on the inside with extremely thin layers of silicon dioxide. Product advantages include a more homogeneous surface, improved barrier characteristics and therefore increased stability and shelf life of the active ingredient of a medication. Through the silicon dioxide layer, almost no more metal ions are able to leach out. This is of immense importance, particu-

larly to biomolecules. At the same time, the surface is more homogeneous and shows low granularity, an aspect which is of benefit during the freeze-drying process. The plasma layer also prevents the adsorption of some proteins and thus even makes liquid formulations possible. "SCHOTT Type I plus" is also suited for use with unbuffered diluents, such as water for injection, because

it keeps the pH value stable for a longer time. Even solutions with high pH values that normally have corrosive effects on glass can be stored longer in "SCHOTT Type I plus" vials.

"SCHOTT Type I plus" is a unique high tech product and combines the advantages of the premium quality "SCHOTT Fiolax" tubing glass and the



SCHOTT Type I plus containers

"SCHOTT PICVD" coating technology. Strictly controlled and validated production processes at SCHOTT forma vitrum in Müllheim, Germany ensure that the final products constantly meet the high requirements they have to fulfill.

"SCHOTT Type I plus" was the first coated pharmaceutical container marketed by SCHOTT forma vitrum. "In the meantime, we are testing new coating types to be

combined with different pharmaceutical containers, for various product and application needs", says Dr. Robert Hormes, Manager Competence Center Coating of SCHOTT forma vitrum. "Facing the development in the field of biotechnology on the one hand and our possibilities to improve pharmaceutical containers on the other hand, we see big opportunities for additional coated packaging solutions in the market."

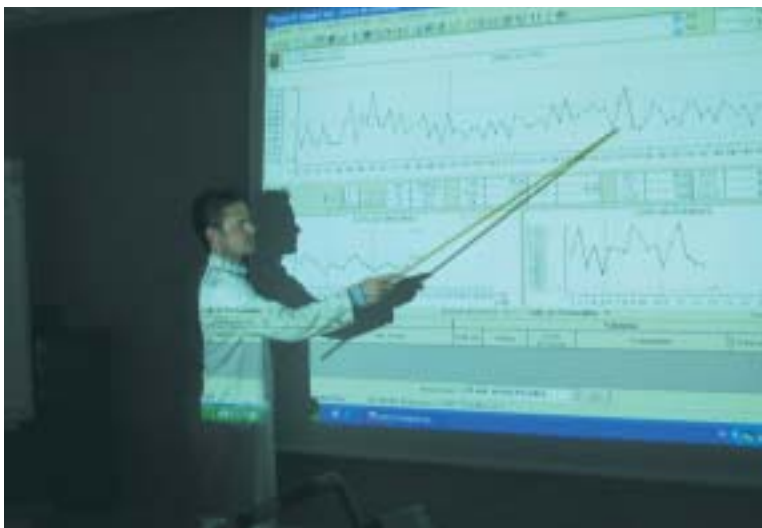
QUALITY

Advanced Statistical Process Control

Customer audit at SCHOTT forma vitrum in France: A pharmaceutical company visits its supplier to check the performance of a pharmaceutical container, eg a TopLine ampoule, in the running production. Product specifications are checked and compared one-by-one against real performance, and any special issue or problem is discussed and agreed upon.

At SCHOTT France SAS, the performance of a specific product in the manufacturing process can be demonstrated "live" in the conference room. By a few mouse clicks, the participants of the meeting get the most up-to-date online-information directly from the running production before moving out to the shopfloor. Computerized quality control combined with advanced statistical tools make this possible. There is no longer a need to gather information via a specialist, eg from the Quality Department, but the information is directly available. This level of service is only one aspect of the innovative technology.

Whereas zero defect manufacturing would have been completely unthinkable only a few years ago, it has become a reality today, thanks to new developments in computer-aided quality control that can be tailored to specific customers and products. SCHOTT



"Live" quality monitoring in the meeting room of SCHOTT forma vitrum, France

forma vitrum in Pont-sur-Yonne, France, has decided to implement this advanced development. "We completely modernized our quality control only three years ago. Our experience clearly shows that we are able today to guarantee a low defect rate (even zero defect on some characteristics) for highest product safety and better machinability at customers' facilities. We are thus able to increase the satisfaction of our customers and their confidence in us," summarizes Etienne Vallery-Radot, President of SCHOTT France.

The process has been optimized as follows: during manufacturing, the batch inspection takes place

according to DIN/ISO 2859.1 standard. For 1 ml printed ampoules, whereas before 200 samples per batch (400,000 pieces) were collected, the quality inspectors now monitor 500 samples (measurement film available for all dimensional characteristics). During the production, the quality inspectors control the samples, release the sub batches and then consolidate the pallets for pre release. The release authority performs double checking when consolidating the results per batch, validates the batch conformity and issues the batch documentation. As Etienne Vallery-Radot expresses: "Reinforced inspections lead to more reliable testing results."

Traceability and documentation

Sophisticated product documentations can be produced on all the important parameters and can be adjusted to meet the demands of individual customers. Customers receive detailed additional information: certificates of analysis, histograms of critical dimensions, detailed break force results, etc. Inspection systems and release procedures ensure that each product can be traced back to its origin and documented.

"The internal advantage lies in the fact that we are able to use the Cpk index to assess the ability of the process to perform its function with a reduced standard deviation as well as offering the lowest number of defective products in ppm (parts per million).

The Cpk value for dimensional characteristics can be taken to illustrate this. With a Cpk of 1.5, we have 3.4 ampoules per 1 million

with defects. A Cpk of 1.9 means there are zero defects," explains Etienne Vallery-Radot.

Shared information via SCHOTT France intranet

An added advantage: Quality control can be monitored using basically any computer. "During a meeting, the managers can directly analyze the results of a running production in the conference room," as Etienne Vallery-Radot explains.

Two main advantages of this new quality control organization:

A better product quality through a quicker reactivity and process adjustment in case of deviation

Improvement of the process through the analysis of the statistics mirroring the machine capability

Masthead

SCHOTT forma vitrum
NEWSFLASH

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The following product names (set off in this publication in quotation marks) are registered brands or product names of SCHOTT: TopPac, Fiolax, Iilax, AR-Glas, Densopack, Denso-can, Type I plus, Duran, PI, PICVD

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ON TOUR

Creating quality in Colombia



SCHOTT forma vitrum in Colombia

SCHOTT Envases Farmaceuticos S.A., the SCHOTT forma vitrum plant in Colombia, originated from a merger between SCHOTT and a local family business in September 1999. The product line is vials and ampoules, manufactured from SCHOTT glass tubes to exacting SCHOTT quality standards.

"From the beginning, our goal was clear," says Mauricio Villegas, General Manager, SCHOTT Envases Farmaceuticos S.A., who went through the merger: "To achieve and maintain the technical, process and quality levels exhibited by SCHOTT forma vitrum plants around the world. We have an extremely committed workforce and work very hard with our customers in order to deliver the quality products they need."

One of the smallest SCHOTT forma vitrum companies, the Colombia site is located in Cota, some 25 km from Bogota. There,

130 employees produce ampoules and vials for markets in Colombia, Peru, Venezuela, Ecuador and the Dominican Republic. The customer base is primarily pharmaceutical, with a balance of cosmetic. The market is a growing one, particularly with the increased government emphasis on healthcare.

To meet the customer requirements, significant investments in machines and process upgrades were made over the past six years, most with an eye toward quality. For example, all production lines are equipped with 100% on line camera inspection and the plant maintains class 100,000 clean room facilities that meet Good Manufacturing Practices (GMP). "We also reviewed our ISO 9000 certification in order to have a stronger quality system and are now working toward certification in both ISO 14000 and OSHAS 18000," says Villegas.

Customer relations are a high priority. With the aid of Abelardo Riveron, Technical Manager, the company has embarked upon a number of technology transfers within SCHOTT forma vitrum group as well as a program of technical visits to customers – many of which involve a highly motivated team including production, quality and logistic managers. In addition, four years ago, the unit also began a series of customer days. The first, in 2002, was

customers along with a mix of sales and technical people from SCHOTT forma vitrum worldwide. Topics range from the latest products and improvements to important upcoming items on the political scene.

"The political and economic situation in Colombia has improved over the past three years and external investors have invested an important amount of money," says Villegas. "To do business in Latin America, you must be open,

quick and responsive. Our biggest challenge will be to meet these needs while continually improving our already high levels of quality."

Meet Esmeralda

One way Colombian employees are meeting customer needs are through Project Esmeralda. Spanish for the word "emerald", Esmeralda is a project that is proving a real gem for the site, employees and customers as well. Launched last year, the project seeks employee ideas for production improvements and cost reduction. Currently there are around 90 ongoing Esmeralda projects, some small, some large. "In the beginning, we thought we might achieve some cost savings," says Mauricio Villegas. "But after one year, we found that we had not only identified opportunities for cost savings but employee motivation was much higher and our quality level had improved due to optimized production processes. That makes it good for everyone."



Insight in the production facilities

in Bogota; inspired by its success and customer feedback, it has been repeated in Caracas, Venezuela and Lima, Peru. Typically the numbers include around 70 representatives from some 35

Site at a glance

SCHOTT Envases Farmaceuticos S.A.

Location:	Cota, 25 km west of Bogota, Colombia
Employees:	130
Products:	vials and ampoules
Capacity:	140 million units per year
Production area:	3.200 square meters
Quality certification:	ISO 9000/2000

PEOPLE

Knowledge is no end in itself



Dr. Klaus Holtzhauer,
Product Manager Syringes
SCHOTT forma vitrum

Anyone who looks at Dr. Klaus Holtzhauer's working career may be surprised by his professional versatility and will, at first glance, probably not recognize the unbroken thread within his résumé. The chemist started in the cement industry with material analysis, changed to an engineering company in the field of environmental

technology, then he accepted a technical sales position for a Japanese manufacturer of analytical instruments, and finally, he has been employed at SCHOTT forma vitrum as product manager dedicated to develop and expand the syringe business.

"In all these different jobs, material technology and applications were always my main focus," Holtzhauer says. As a salesman with specific know-how in total organic carbon analysis (TOC) of waste water, he made his first contacts with the pharmaceutical world. Some of his business partners from the pharmaceutical industry made use of that technique to analyze ultra pure water (wfi, cleaning validation). Holtzhauer learned very quickly that for pharmaceutical customers it was not sufficient to show that an analytical instrument works properly and delivers accurate results. "This was self-evident," he adds. At least as important, however, was the software support for

GMP/GLP compliant documentation for the validated processes.

"The main objective was not to convince the customer to buy a product but rather to provide him with a solution," he explains. His current role with SCHOTT forma vitrum emphasizes precisely this approach. "When I started here four and a half years ago, the syringe business at SCHOTT forma vitrum was still at the beginning. In fact, the company had essentially one single customer," he adds. In the meantime, SCHOTT forma vitrum has become internationally well known for offering a comprehensive product portfolio consisting of sterile, pre-fillable glass and polymer syringes and, with respect to glass syringes, its production capacity is currently being increased substantially.

Today, Holtzhauer is a true expert in the field of syringes. Together with his colleague, Walter Schiess, he is currently responsible for providing technical support to the

worldwide sales team. "We accompany customer projects, sometimes during several years, until the product has been exactly specified according to the customer's needs and mass production can begin," Holtzhauer explains.

For him, success is always the result of a successful cooperation between all parties involved, including development, manufacturing and quality assurance. The main questions are "what is the customer looking for, what is most important and how can we meet these requirements?" A good solution always starts with attentive listening, a clear understanding of a problem and the optimum use of the available possibilities and resources. This implies intensive scrutiny, internal feasibility studies as well as technical know-how of complex syringe systems. The objective is to come up with a customized product that meets a high quality standard and is even

appropriate for use with sensitive drugs.

During his daily work, the graduate chemist truly benefits from his educational background: knowledge of materials, analytic thinking as well as careful, precise, highly systematic and goal-oriented working. Two main principles have accompanied him throughout his life: "whenever you do something, do it right", and "knowledge is no end in itself and must always be useful".

These principles help him even in private life. For example, together with his 7 year-old son, he is currently constructing a complex railway system in his back yard which gives him great pleasure in mastering the material-related challenges. If he has enough time, he plays in an amateur acting group at a local theater club and claims that there is an analogy to his professional career, too. "Both on stage and at work, one realizes very quickly that a well-balanced team is the basis of each success," he concludes.

MATERIALS

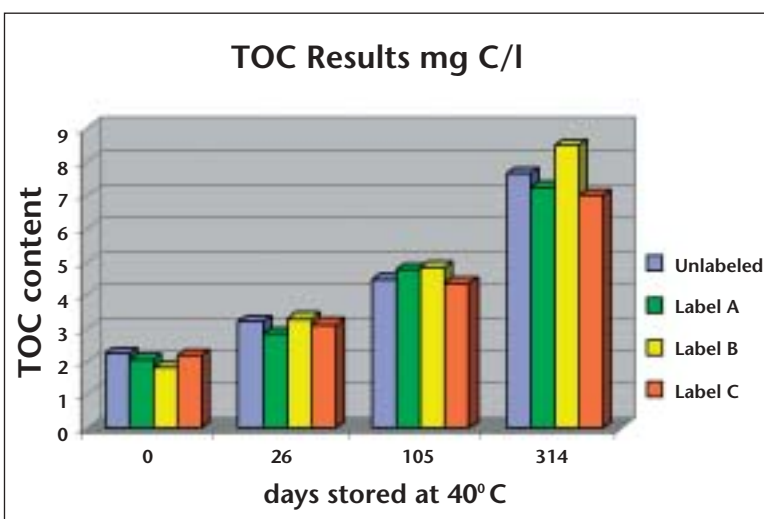
Customer support for the registration of SCHOTT TopPac containers



When a pharmaceutical company decides to introduce a new medication to the market it must first arrange for its primary packaging system to be approved by the respective regulatory authorities. For SCHOTT TopPac® containers made of the cyclic olefin copolymer (COC) Topas®, which is not specifically listed in the European Pharmacopoeas, pharmaceutical companies must present conclusive evidence that the packaging system is compatible with the

formed with the raw material, and that the FDA is already familiar with this material and regards it to be suitable for use in pharmaceuticals. FDA approval is an important decision criterion for pharmaceutical companies when it comes to the choice of a material. Schott has also filed a Drug Master File with the FDA for the "SCHOTT TopPac" syringes.

Horst Koller, Head of Scientific & Regulatory Advisory of SCHOTT forma vitrum, offers spe-



Label test of "Schott TopPac" containers: No active migration of label adhesive substances

medication. For Europe, the regulations that apply to the approval of medications are set by the "European Medicine Agency Inspection" (EMA). Their guidelines determine how plastic materials that come into direct contact with medications should be tested and documented.

Topas® COC was developed by Topas Advanced Polymers GmbH (former Ticona GmbH) which owns a drug master file on Topas® with the FDA. This means the FDA is aware of all of the relevant data and testing that has been per-

cial support to customers who decide to use "SCHOTT TopPac" containers for a new medication. By collecting and evaluating scientific data on COC polymer on a regular basis, he knows about all of the most important research that has been performed on COC. He also gives pharmaceutical companies insight into this information. This can include basic information on the structure of the polymer and its composition, information about extraction, leaching as well as results from interaction studies.

All about SCHOTT TopPac containers

The guideline "Plastic Immediate Packaging Materials" of the EMEA (effective December 2005) asks for information on ingredients that can be extracted from the container. Under a worst case scenario involving the most difficult of conditions, a respective extraction study was conducted by a specialized external laboratory. "The excellent results of the study show that "SCHOTT TopPac" containers can be classified as extremely clean," concludes Koller.

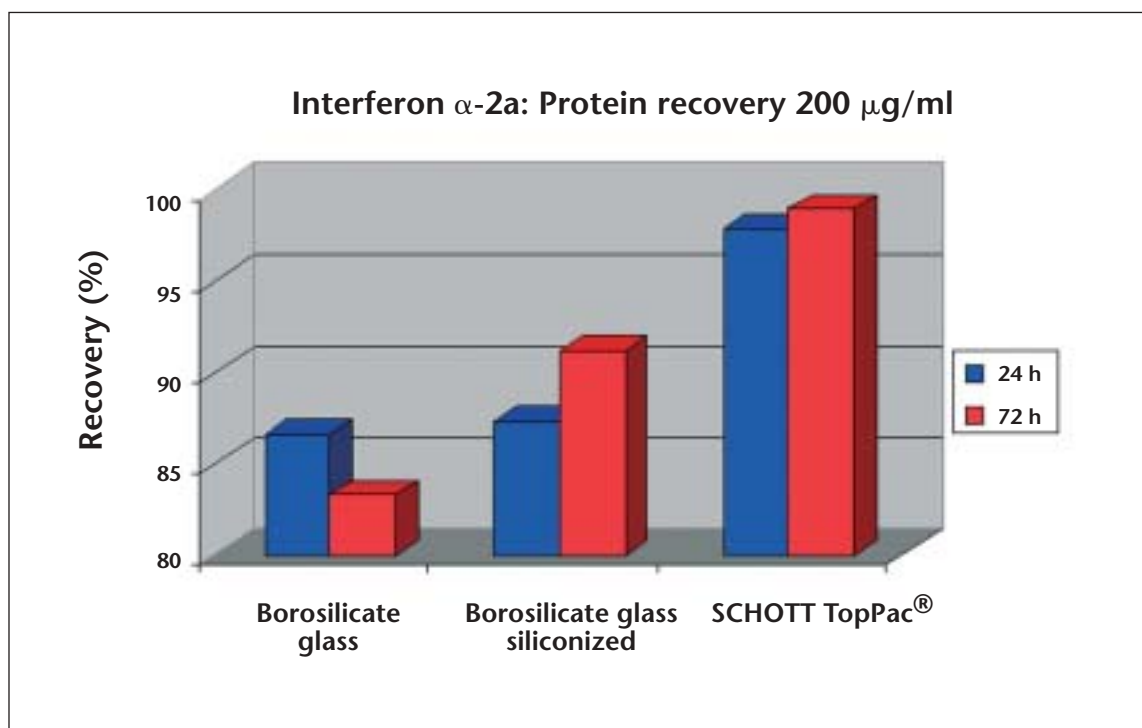
In addition to the observations gained during the extraction study under extreme conditions, another test was performed to document which substances leach out from the container under normal conditions. These are commonly referred to as leachables. COC polymer performed extremely well in this test, as well.

Theoretically, it is conceivable that substances from outside could migrate through the wall of the container into the drug. For example, substances contained in a pharmaceutical adhesive (eg for the use of labels or stickers) could penetrate through the wall of the container. A specific test with SCHOTT TopPac containers revealed no significant differences with regard to the containers with and without labels.

So-called interaction studies also provide pharmacists with important insights. They answer the question to what extent extremely sensitive active ingredients, generally proteins, interact with the wall of the container. Topas® was compared with standard Type I "Fiolax" glass packaging. For example, the tests with COC and Interferon α -2a exhibited an approximately 10 percent higher recovery rate than the glass container, meaning less interaction and therefore loss of product. This is a dimension that appeals to pharmaceutical audiences, especially when it comes to costly and highly sensitive active ingredients.

"It is no doubt, a "SCHOTT TopPac" syringe is definitely a highly complex system", says Koller. "SCHOTT forma vitrum has access to the necessary knowledge, many years of experience and the appropriate skills that are needed not only to manufacture a perfect pharmaceutical container but to provide the pharmaceutical industry also with the much-needed support in choosing the appropriate type of packaging."

Interaction Study with Interferon α -2a: Significantly higher recovery rate of "SCHOTT TopPac" compared to glass



EVENTS

Exhibitions & Events

Come and see us at

- A3P, Biarritz (France), October 17 – 19, 2006
- PDA PFS 2006, Bethesda/MD (USA), October 23 – 25, 2006
- AAPS, San Antonio/TX (USA), October 29 – November 2, 2006
- PDA, Tokyo (Japan), November 13 – 15, 2006
- Pharmtech, Moscow (Russia), November 20 – 23, 2006

Pharma Symposium 2006



Pleasant atmosphere at the Altenburg, Bamberg



Dr. Karl-Peter Merz, member of the Management Board SCHOTT AG



Time for discussions between the presentations

Pharmaceutical world guest at SCHOTT 2nd Pharma Symposium in Bamberg / tailor-made solutions in the focus

and interactive workshops on the latest trends, research findings and regulatory requirements that apply to primary pharmaceutical packaging made of glass and polymers.

SCHOTT Board Member Dr. Karl-Peter Merz emphasized that manufacturing pharmaceutical primary packaging ranks as a strategic core competence at SCHOTT. "This clearly distinguishes us from our competitors," he says. Furthermore, he referred to the company's international presence as an extremely important success factor. "We are able to provide our customers worldwide with the same consistent level of top quality from various production sites. This means we are also able to offer an unparalleled level of delivery reliability," Merz concludes. He then referred to several major investment projects that the com-



From left to right: Dr. Peter Knaus, SCHOTT Pharmaceutical Packaging, Andreas Reisse, SCHOTT Tubing, Dr. Karl-Peter Merz, SCHOTT AG.



pany has been pursuing only recently, including construction of a "Fiolax" melting tank in Baroda, India, as well as the establishment of a production facility for vials and ampoules in Suzhou, China. "The objective of our pharmaceutical symposium was to reflect already today on the requirements of tomorrow's medications," explains Dr. Peter Knaus, Vice President of the Business Segment Pharmaceutical Packaging at SCHOTT. The goal is to provide the pharmaceutical industry with customized solutions, based on specific medications and areas of application. SCHOTT manufactures the preliminary product, narrow tolerance tubing made of spe-



Prof. Dr. Thomas Beck, Drug Commission of German Pharmacists



Dr. Manfred Kern, Bayer CropScience AG



Some 100 people attended the Pharma Symposium 2006



"Dr. Fritsch" and Dr. Klaus Holtzhauer, SCHOTT forma vitrum



Plant tour at SCHOTT-Rohrglas, Mitterteich, Germany



Dr. Armin Raible, University Hospital Tübingen



Saxophone players

cialty glasses, but also the final containers, e.g. syringes, cartridges, vials and ampoules, and is also a pioneer in the field of pharmaceutical coating. As part of the Pharmaceutical Symposium, the industry experts also paid a visit to the manufacturing site, SCHOTT-Rohrglas in Mitterteich, Germany.



A highlight of the event: impressive glass tubing production



Socializing at the evening event



The moderators of the workshops, from left to right: Dr. Berthold DÜthorn, Robert Bosch GmbH, Prof. Dr. Wolfgang Friess, University Munich, Dr. Robert Hormes, SCHOTT forma vitrum, Dr. Volker Lang, A.T. Kearney GmbH, Dr. Joachim Pfeifer, SCHOTT-Rohrglas GmbH.