newsflash

PHARMACEUTICAL SYSTEMS

SCHOTT
glass made of ideas

ISSUE 25 | February 2017

NEWS

SCHOTT Expands Portfolio of Ready-to-use Pharma Vials as Adoption Increases

SCHOTT has expanded its portfolio of ready-to-use pharma containers to meet growing market demand from drug manufacturers. The latest nest format will be able to hold 2R–15R, 20R, 25R, or 30R ISO vials when it's released in 2017, and will add to the existing 2R to 15R formats. The adaptiQ® concept permits pharma firms to fill different container formats on one production line while minimizing burdensome changeover times in between. SCHOTT developed adaptiQ® to be compatible with the industry's filling and finishing equipment, and collectively, industry leaders such as Bausch + Ströbel, Bosch Packaging Technology, groninger, OPTIMA, and Vanrx have tested and verified adaptiQ® on a large number of machine types.

This ready-to-use packaging solution enables pharma companies to react quicker to new industry trends without building specific manufacturing capabilities. The vials are nested securely, protecting them from scratches caused by vial-to-vial and vial-to-machine contact, and reducing breakage and contamination. As they are already sterilized, pharma companies can load them directly onto filling lines without expensive and time-consuming washing, sterilizing, and depyrogenation.

"Razor-thin margins and regulatory pressure have forced pharmaceutical manufacturers to make smarter packaging choices," said Christopher Cassidy, VP Sales and Marketing for SCHOTT's Pharmaceutical Systems Business in North America. "When the 20–30R ISO format comes online, SCHOTT will give pharma companies even more flexibility. The entire portfolio of ready-to-use vials allows pharma companies to trim costs while boosting efficiency, leading to higher profits."

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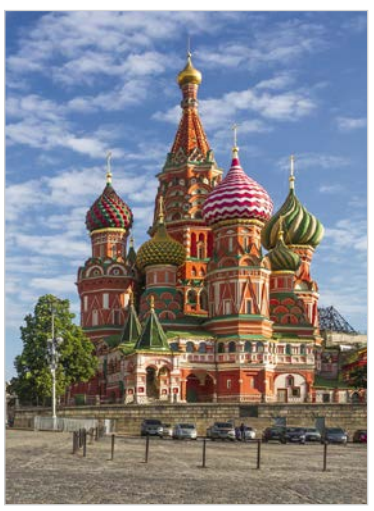


MARKETS – SCHOTT Underscores Commitment to Russian Pharma Market. Read more on page 4.

EDITORIAL

Dear Reader,

There is a lot of movement in the pharma industry at present. Just look at the many M&A activities and the thriving startup scene. In times as lively like these, it is good to have a reliable partner, also from a packaging perspective. Someone who understands the market and its demands, identifies trends, develops corresponding products and adapts processes. A partner who serves the entire spectrum, from the perfect glass at the beginning of the value chain to completely flexible filling concepts.

This is precisely our approach, and we underline it with a range of innovations: SCHOTT Vials Delamination Controlled, our adaptiQ® concept for sterile filling, or SCHOTT's innovative Big Data approach for pharmaceutical tubing are just a few examples. All with the aim of allowing you more freedom to focus on your core business.

I hope you enjoy reading this new issue of newsflash.

Andreas Reisse
Executive Vice President
Pharmaceutical Systems

NEWS

Why do Pharmaceutical Glass Containers Break: The Underestimated Power of Strength Testing & Fractography

In the pharmaceutical industry glass is by far the dominant material used for the packaging of liquid and lyophilized drugs due to its impermeability and chemical inertness for drug product stability, transparency for ease of inspection, thermal stability for flexible use and processing, low extractables and leachables, and cost. Although glass breakage events occur at every pharmaceutical company, the methods of strength or reliability testing and fracture analysis (fractography) remain relatively unknown and severely underutilized to determine the root cause of failure and make the necessary changes to reduce future occurrences. Fractography is the science of analyzing the macroscopic and microscopic fracture patterns of cracked or broken objects to qualitatively and semi-quantitatively determine the root cause of failure.

Importance of appropriate strength testing strategies

Due to the high complexities and the low overall incident rate of glass breakage the strategy of the pharmaceutical industry today is to forgo strength testing and to assess the criticality of surface flaws/non-conformities by using optical/visual inspection with defect manuals. The danger in this approach is that defect manuals are designed for cosmetic assessment of containers and the categorization of non-conformities (disturbances) just by their lateral dimensions. They cannot provide an assessment to the criticality with respect to container strength, because optical inspection cannot provide the full information required to assess the criticality of a disturbance in terms of strength. So judging the criticality of disturbances in terms of strength solely from their optical appearance can lead to misinterpretation. Appropriate strength testing strategies routinely implemented into production processes can help to lower the risk.

Fractographic investigations – three examples

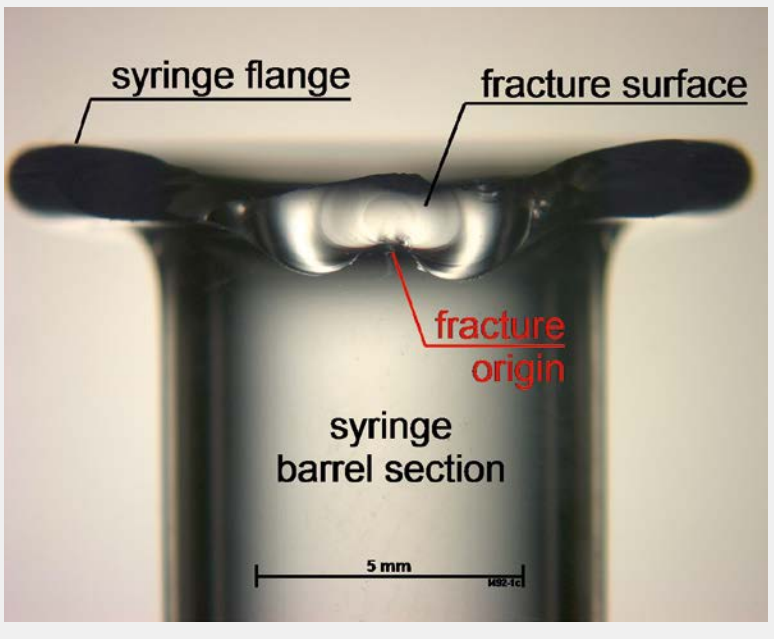
SCHOTT pharma services was contracted by a client who was filling a product for clinical trial into vials and during post-fill inspection found approximately 20 % of the lot had chatter marks / "scuffs" of varying size which were detected by visual inspection after processing. The pharmaceutical company was concerned about risk of breakage at the clinic and contracted strength testing to be done to assess the strength criticality of the scuffs and whether or not the scuffed containers could be safely used. Burst pressure testing was done on 100 samples featuring scuffs, 92 samples without scuffs, and 43 control samples (vials processed but taken out after depyrogenization). Data evaluation revealed quite similar distributions, with even a little higher strength for the vials featuring scuffs compared to vials without scuffs. This difference in strength was mathematically determined to be statistically significant. Additionally, a fractographic examination on every broken sample from the rejected lot showed that not a single fracture origin coincided with a scuff. This means that while scuffs indeed represent a cosmetic defect, in this particular case they were proven not to decrease the container strength compared to containers without scuffs.

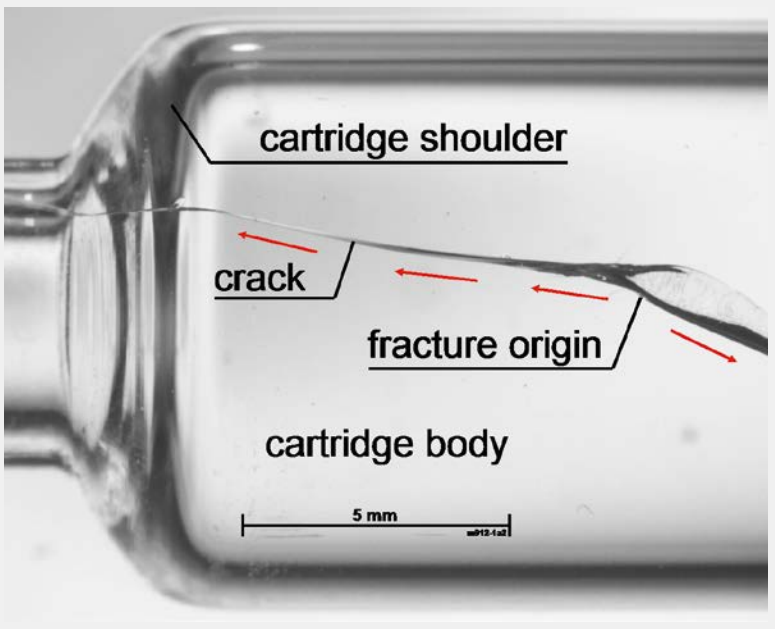
Strength testing is also invaluable for determining or selecting appropriate containers and/or drive springs for auto-injection devices. SCHOTT pharma services was contracted to perform flange strength testing on glass syringes by a client who wanted to determine and compare the device failure probability when using two different drive springs on three different lots of glass syringes. While performing flange strength experiments with a slow, constant load rate as a destructive lifetime test, all syringes exhibited breakage in a range of forces far above the range of the application forces. To get an impression about the failure probability under real conditions, a suitable continuous statistical distribution function was fitted to the strength data as a first step. In a second step, the mechanical loads of the true force-time profiles of the two drive springs were transformed to single "equivalent" force values which can be compared to the data of the strength experiments. An estimation of the failure-probability of the syringes under the load of the two different drive springs then is achieved by an extrapolation of the fitted continuous statistical distribution function to the two equivalent force values of the drive springs.

A last example demonstrates the effectiveness of root cause analysis and corrective action when combining strength testing with systematic fractographic analysis. SCHOTT pharma services was contracted to perform syringe strength testing on samples before and after a particular processing step that was introducing sporadically-observed surface flaws. The client wanted to know the extent of strength decrease and whether or not the observed defects were responsible for the strength decrease. Burst-pressure testing of the syringe was conducted on samples drawn before and after the suspicious process step showing a statistically significant decrease in strength in the samples after the processing step as well as a narrowing of the strength distribution. Assessment of each syringe after breakage for the location of the fracture origin found an enlarged population of fracture origins in the flange region after the processing step, as well as a second large population in the shoulder region in the lower strength regime as was found in the samples before the step. So the combination of systematic strength testing with fractographic examination was able to reveal damage mechanisms on the outer surface in the flange and the shoulder section of the syringes. With this type of insight into processes, appropriate corrective and preventive actions were suggested to be applied to eliminate severe damage mechanisms and thus successively improve the strength of the product.

Conclusion

Strength testing methods in combination with fractographic investigations and appropriate evaluation procedures are available to provide the pharmaceutical industry the methodology for determining the root cause and help in identifying effective corrective actions for glass breakage events during processing, filling, shipping, or during administration.





INNOVATION

SCHOTT's New Rigid Caps Add a New Twist to Prefilled Syringes

Advanced closure systems for glass and polymer syringes improve patient safety while securing packaging supply chain.

SCHOTT has added new closure systems to its already extensive portfolio of prefillable syringes (PFS), offering more flexibility for pharma companies while keeping patients safe. syriQ® Rigid Cap (SRC) and SCHOTT TopPac® Rigid Cap (TRC) feature an intuitive twist-off mechanism. The caps ensure the integrity of the container, yet they can easily be opened by healthcare professionals or patients. The new closure systems offer a seamless fit for SCHOTT's prefilled glass syringes known under the brand name syriQ®, and SCHOTT TopPac®, its polymer equivalent.

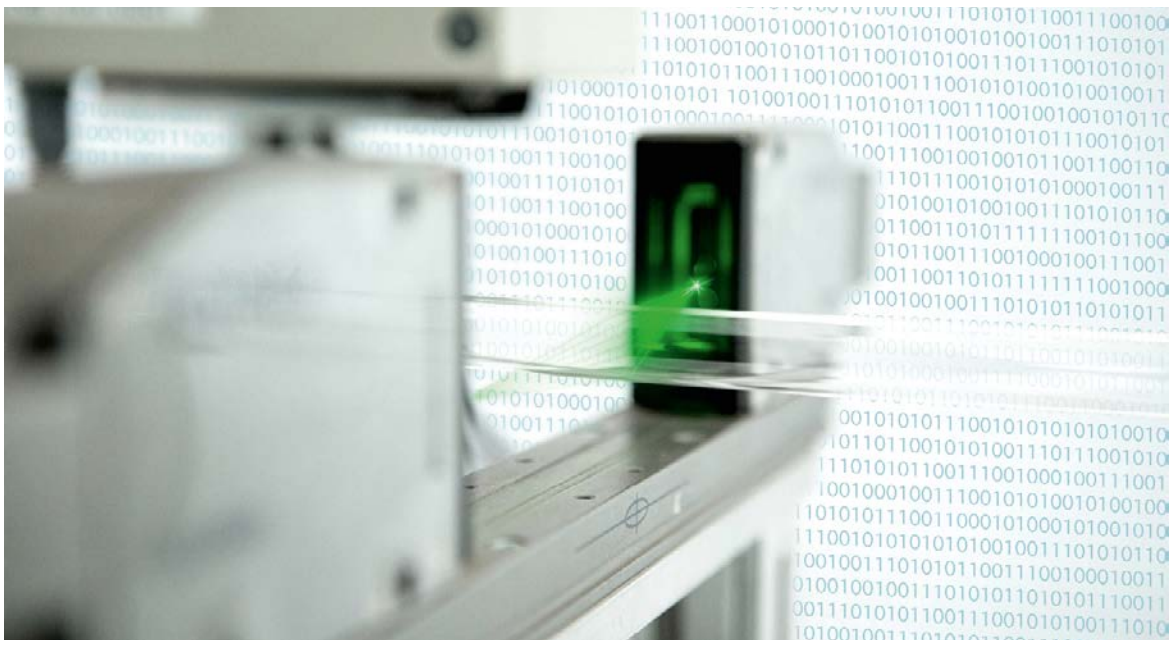
"Container closure integrity (CCI) is one major concern in the pharma industry. Another one is usability. Our new closure systems deliver in both areas", said Nicolas Eon, Global Product Manager syriQ® at SCHOTT Pharmaceutical Systems. "The design of SRC, our solution for syriQ® glass PFS, matches a closure system the industry is already familiar with. This adds a great deal of flexibility to our customer's supply chain, and it speeds up time to market for new or already existing drug products."

SRC combines a rubber tip cap with a rigid cap screwed in a Luer Lock adapter. The closure system comes pre-assembled with SCHOTT's high-quality syriQ® glass syringe barrels, all pre-sterilized and in a standard nest and tub configuration. Thanks to standardization and since the materials are similar to SCHOTT's existing product line, drug manufacturers can quickly integrate SRC into existing production set-ups. SCHOTT is also ready to support drug developers in product documentation and the regulatory approvals process. This will help drug manufacturers get their product to market faster.

Simultaneously, the rigid cap TRC, fitted with a rubber tip cap and twist-off mechanism, offers superior CCI during filling, processing, transportation, and shelf life. Like its equivalent, TRC is easy to open and easy to connect with hypodermic needles, IV connectors, or vial adapters, and reduces the risk of contamination while opening the closure system.

TUBING

New Quality Approach perfeXion™ – From Statistical Quality Control to 100 % Inspection of Each Individual FIOLAX® Tube



In quality control, details matter. When it comes to pharmaceutical primary packaging such as vials, cartridges or syringes, fluctuations in tubing dimensions such as the inner diameter or wall thickness can have a significant impact on the container performance – for instance, the filling or dosing accuracy for high potential drugs. Up until now, manufacturers of glass tubing have usually been monitoring quality parameters on a random sample base. SCHOTT, however, has developed a new production quality process called perfeXion™. It controls and monitors every FIOLAX® pharmaceutical glass tube and enables an improved glass tubing product that supports container production and container processing efficiency. With this, SCHOTT aims to contributing to patients' safety from the very beginning of the value chain and pushes towards a zero defect philosophy in pharmaceutical glass tubing production.

Towards zero defect

SCHOTT Tubing recognizes that glass tubing manufacturers need to advance and continuously improve uncompromised quality standards as certain critical container parameters are directly determined by the quality of the tube. The challenge lies in monitoring and measuring the curved tubing surface with 100 % accuracy, in a high speed production process. This is achieved by using a combination of line scan and area cameras, laser and IR inspection systems that literally investigate the entire glass tube on-line. The measurement data is then collected and evaluated by a holistic inter-connected IT solution. This system recognizes even the smallest defective spots in the 'endless' glass tube that comes from the melt. It is then able to attribute these spots to a certain position at a single tube once the cooled down glass string is being cut. This sophisticated system enables SCHOTT to customize the quality level to the specific needs of the industry.

Worldwide implementation in progress

SCHOTT has already equipped and validated all FIOLAX® lines in Europe according to the perfeXion™ process. The roll-out to other facilities in South-America and Asia has started. By doing so, SCHOTT is not only passing another milestone of its future oriented quality roadmap. More importantly, the company's pharma glass will enable even more sophisticated primary packaging solutions for advanced medical treatment than it already does today.

INNOVATION

SCHOTT Vials DC Demonstrate Resistance Against Delamination in New Screening Study

A new series of studies has once again demonstrated the effectiveness of SCHOTT Vials Delamination Controlled (DC). These pharmaceutical vials have a particularly high chemical durability and are therefore less susceptible to delamination. SCHOTT has had this property confirmed in various storage studies. First, substances were used that have already caused product recalls due to delamination. In a second series of studies, the question of how effectively buffer systems can be stored in the new bottle was examined more closely. The result: if the respective substances were stored in SCHOTT Vials DC, the vials remained stable and no glass delamination was observed. A detailed presentation of results was published in the November / December issue of the PDA Journal.

The delamination studies were conducted in accordance with USP1660 using two different types of formulations: a 15-percent potassium chloride solution and a 10-percent sodium thiosulfate solution for which recalls due to delamination had been announced. Nevertheless, established buffer or formulations that are often used to develop drugs were also tested, for instance ultrapure water, citrate buffer, phosphate buffer, sodium bicarbonate buffer and EDTA (ethylendiamintetraacetic acid).

"Both series of studies clearly show that switching to SCHOTT Vials DC as primary packaging materials significantly reduces the risk for pharmaceutical manufacturers to experience delamination recalls", says Florence Buscke, Product Manager Vials.

Available in many different sizes

Thanks to SCHOTT Vials DC, pharmaceutical companies now have an interesting alternative course of action against the "phenomenon of delamination" i.e. the detachment of flakes from the inner glass surface due to interaction of the formulation with the pharmaceutical vials. SCHOTT Vials DC are based on established hot forming principles without any additional post process steps and can therefore replace the packaging that is already being used with approved drugs without causing expensive re-registration. The vials are available in the ISO sizes 2R to 10R. SCHOTT has also already produced larger sizes to meet individual customer needs, for example, a large-scale 50 ml vial for a biotech company based in the United States.

PROFILE

Innovative Solution Provider Keeping Pace with the Times

Everything for the sake of the patient. "That is the philosophy driving SCHOTT's employees' actions, and what our products stand for," explains Michael Vollgold, Vice President, Global Sales & Marketing, Pharmaceutical Systems at SCHOTT. The better a drug's packaging is adapted to its use, the more it contributes to the safety of the patient. Yet this is challenged by constant change in the pharma industry, which has to respond to ever-increasing regulatory requirements, rising cost pressures and the increasing digitalization of industry. "To a large extent, we see the challenges of pharmaceutical companies as ours, too. Since our packaging materials always make us part of the drug, we also have to provide our customers with the packaging solution that meets their demands. We cater to our customers' needs by providing tailor-made solutions," Vollgold says.

The economics graduate knows what he is talking about. With over 20 years of professional experience in the pharmaceutical industry, he has a pretty good handle on its requirements. Yet, it hasn't gotten boring for Vollgold: "In my job there is little routine. I am facing new challenges every day. This is one reason why global cooperation in my organization makes the job incredibly exciting."

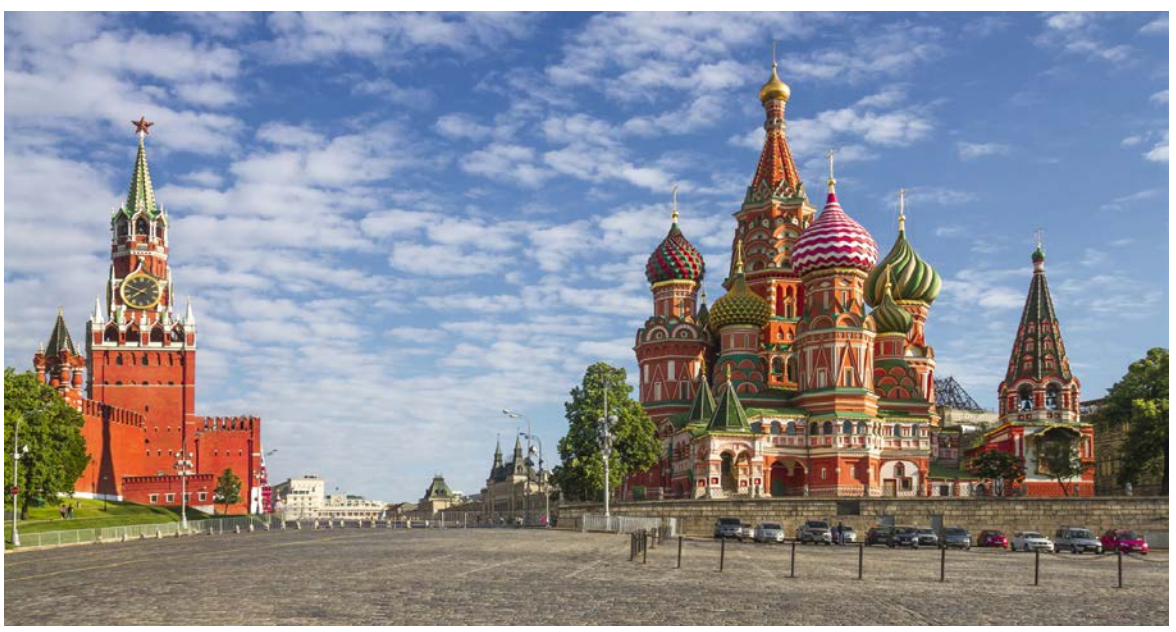
Industry knowledge and proximity to the customer are of great importance in Vollgold's field "since an important task for our sales and marketing organization is to survey the market and to recognize the challenges faced by the pharmaceutical industry. From this, we derive trends, play them out at company-level, and develop corresponding solutions to introduce into the market." With its technical expertise, its quality leadership in glass and its global presence with 16 production sites, SCHOTT does this very well. For example, the company has developed a ready-to-use packaging solution with adaptiQ® that allows pharmaceutical companies to react more quickly to new branch centers without having to set up specific manufacturing capacities. Vollgold adds, "with innovative product features and solutions to come we are very well prepared and will further improve the support of our clients in the future."

MARKETS

SCHOTT Underscores Commitment to Russian Pharma Market

Against the backdrop of the 5th anniversary of its manufacturing site in Zavolzhe, SCHOTT has renewed its commitment to the Russian pharma market. For the international technology group, Eastern Europe represents one of the most exciting regions within the global pharma market, showing significant growth opportunities. During a symposium that accompanies the five year anniversary celebration industry experts discussed innovations and trends within the pharma industry. "Our intention is to keep working closely with the Russian pharma industry and to support their growth plans by offering just the right packaging solutions," said Andreas Reisse, Executive Vice President for SCHOTT Pharmaceutical Systems.

Innovation and local production are two key features of "Pharma 2020", an initiative of the Russian government. Launched in 2009, this programme is dedicated to developing the domestic pharmaceutical and medical industry – and it also increases the need for high-quality packaging solutions. SCHOTT was the first international player to open a packaging production in Russia and invested roughly 12 million euros in this field. Every year, the site in Zavolzhe manufactures up to 500 million vials and ampoules.



EXHIBITIONS & EVENTS

Meet SCHOTT in 2017

Pharmapack, Paris (FRA)
February, 1–2

CPhI Istanbul, Istanbul (TUR)
March, 8–10

PDA Parenteral Packaging,
Barcelona (ESP)
March, 14–15

Interphex, New York (US)
March, 21–23

Exhibition CPhI SEA,
Jakarta (IND)
March, 22–24

Pharmakongress Produktion & Technik, Düsseldorf (GER)
March, 28–29

MASTHEAD

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TUBING

25 Years of Pharmaceutical Packaging Production in Mexico

The story of high quality packaging in Cordoba, Mexico, began a quarter of a century ago. Today, SCHOTT Mexico forms the hub for the company's activities in Central America and supplies one of the broadest portfolios of ampoules, vials and cartridges to the market.

During the company's 25 years anniversary celebration in October SCHOTT announced to increase the investment in its pharmaceutical packaging production in Cordoba to further support the pharmaceutical industry in North and Central America with high-class packaging products. Over the last few years, the company has already invested a high seven-digit number in Mexico, with this figure set to increase. In 2016 alone SCHOTT spent over 4 million euros in Cordoba for the benefit of the customers, emphasizing the commitment to establish SCHOTT as a long term partner for customer business, with the objective to offer highest quality, delivery and reliability concepts to their customers.

During the celebratory event, SCHOTT representatives gave a comprehensive tour of the production site and showcased different packaging solutions to an interested customer audience.

Every year, the site in Cordoba manufactures up to one billion vials, ampoules, and cartridges. All products manufactured in Cordoba work in line with GMP (Good Manufacturing Practice) principles and relevant ISO standards.