

newsflash

PHARMACEUTICAL PACKAGING



SCHOTT
glass made of ideas

ISSUE 17 | January 2012

PRODUCTS

SCHOTT TopYield™ Vials with Lotus Effect Help Lower Costs

Lotus flowers have the stunning ability to repel water liquid. The so-called "lotus effect" has enabled this famous water plant to become a symbol for purity in many regions of Asia for centuries. "SCHOTT TopYield", a new product application from SCHOTT, also makes use of the lotus effect.

A special hydrophobic surface on the inside of a vial is so water-repellent that practically nothing can cling to its walls. "With conventional pharmaceutical vials, about 10-20% of the medication usually remains inside the container due to the fact that it cannot be emptied completely because of

the medication interacts with the hydrophobic layer in any way. "In these tests, we detected four components as a result of the plasma reaction, none of them toxic," she adds. The good news for pharmaceutical companies is that "SCHOTT TopYield" remains completely stable with respect to its hydrophobic layer during all types of pharmaceutical procedures.

For pharmaceutical companies, this translates into significant cost savings. "We currently estimate the volume of savings, which depends of course on the individual case in which a medication is being put to use, to exceed the cost many times over," Dietrich says. These vials are currently available in the sizes 2, 6 and 10 ml. The manufacturing process has already been tested.

The coating is applied using the proprietary SCHOTT PICVD technique – "Plasma Impulse Chemical Vapor Deposition", as part of a validated and permanently inspected process. The entire layer is only 40 nanometers thick and, therefore, has no effect on the dimensions of the pharmaceutical container. Vials with these hydrophobic coatings have such homogeneous surfaces that liquids find it difficult to adhere to the inside walls of the vials. It remains stable during pharmaceutical procedures like washing, sterilization and depyrogenization (heat treatment of 300° C).

"SCHOTT TopYield" is based on the concept of "SCHOTT TopLyo", a product that is already well-



The "lotus effect".

established in the marketplace. Coated on the inside surface and improved in terms of its geometric design, "SCHOTT TopLyo" containers offer optimum efficiency for the lyophilization process. Vials with these hydrophobic coatings have such homogeneous surfaces that freeze-dried (lyophilized) substances find it difficult to adhere to the inside walls of the vials. The result gives the lyophilization cake a better appearance and enables less disruption of dry material, as well as reduced breakage during the lyophilization process.



"SCHOTT TopYield" coated vials minimize the residual volume of liquid drugs through a special coating.

its rougher surface," explains Dr. Claudia Dietrich, Global Product Manager for Vials & Coatings.

"SCHOTT TopYield" is a completely different story in this regard because it allows for almost all of the medication to be administered. "This effect really makes sense, particularly with expensive medications because, in the past, pharmaceutical companies have been forced to overfill these containers accordingly in order to ensure that the required dosage recommended by the doctor actually leaves the vial," she explains. In the meantime, SCHOTT has also completed comprehensive "leachables and extractables" tests performed in order to show whether

EDITORIAL



Dear Readers,

Our latest innovation, "SCHOTT TopYield", addresses the costly overfill practice of pharmaceutical companies. The "lotus effect" of this coated vial minimizes the residual volume of liquid drugs through a special coating. The product is not only proof of our power of innovation and high material expertise at SCHOTT, but also an example of our customer commitment. Our approach to providing quality solutions and services was also the key to success for one of our customers who contacted SCHOTT to help them meet their urgent demand for COC pre-fillable syringes for use in treating prostate cancer all over the world.

To serve the important market for pre-fillable syringes made of glass and polymer even better in the future, we set up a new unit within Pharmaceutical Packaging Business Segment: the Global Syringe Business based in St. Gallen. It is headed by Christophe Muguet, whom we would like to introduce to you in the form of a profile in this edition.

Last, but not least, I would like to draw your attention to another important topic that again illustrates the unique glass expertise we have at SCHOTT. In our article on glass delamination, we describe a two way strategy to minimize the risk of delamination. On the one hand, we recommend the implementation of container screening studies as offered by SCHOTT pharma services, on the other hand we describe a testing procedure to control the delamination tendency of tubular glass vials during production. By the way, delamination can be entirely avoided for the vast majority of applications with SiO₂ coated "SCHOTT Type I plus" vials.

Sincerely yours,
Andreas Reisse
Vice President,
Business Segment
Pharmaceutical Packaging

MATERIALS

Two Ways to Minimize the Delamination Risk of Glass Containers

The recent spike in market recalls for injectable drug products due to visible flaky particles associated with "glass delamination" demonstrates the need to solve these problems. It is important for both drug product and container manufacturers to understand the underlying mechanisms, to test for the potential risk, and to control drug container interactions to provide patients with safe medicines.



Risk: Flaky particles in glass containers.

The recalls span multiple types of drugs, buffers, containers, and age of product on the market, demonstrating that this is a multifactorial root cause problem. The good news is that there are multiple commercial packaging solutions available to solve this problem, along with the drug formulation changes that (theoretically) could be made. But due to the lack in

Continued on page 4

ON TOUR

Hungary – Important Pillar in the International Group

Lukácsháza is a small town in Hungary with a population of just under 1,000 that offers many advantages as a production site for a company like SCHOTT. Located directly on the Austrian-Hungarian border, Vienna and its international airport are only an hour's drive away. This small community is linked to the European traffic infrastructure just perfectly, has well-educated, German-speaking employees and yet historically grown ties to Eastern Europe. So the company decided to set up operations at this strategically interesting site back in 1995.

The development that Lukácsháza has experienced speaks for itself – with record figures in all fields. In 1995 the company started the production and achieved

already in 1998 an output of 380 million products in Hungary. Today, around 1.5 billion vials, ampoules and cartridges leave the factory each year. "In the early days, we had close to 40 employees. Today, we employ a staff of 520," explains Christoph Döpkes, Managing Director of SCHOTT forma vitrum Kft. in Lukácsháza, a site that also offers excellent expansion possibilities. "We currently manufacture on 22,000 m², but have another 95,000 m² space available for future expansion plans," he adds.

Hungary has also been taking on an important role in the SCHOTT group for quite some time now. When the SCHOTT pharmaceutical packaging manufacturing site in Russia was be-

ing constructed, the Hungarian employees assumed the role of mentors and not only installed the machines, but also trained its staff. Up to 40 Russian colleagues spent up to 6 months in Hungary to be trained on the defined standard procedures. In parallel some Hungarian employees travelled to Russia to support directly during the ramp up and ensure proper process transfer.

The plant is also home to centralized services for technical specifications for all of the SCHOTT pharmaceutical packaging production sites in Europe, for example, including technical drawings and tolerances as well as packaging specifications for currently more than 3,000 products. In the future, Hungary will take an additional important role. All of the production machines will be overhauled and maintained here at the Machine Overhauling Center, a project that was set up in 2011.

"Lukácsháza was once founded to supply mainly to the Eastern Eu-



The plant in Hungary relies on state-of-the-art production machines and sophisticated visual inspection systems, and it complies with cGMP.

ropean market. In the meantime, however, we are producing in both StandardLine and ClearLine quality and supplying to customers in Western and Eastern Europe and occasionally even Asia and USA," concludes Döpkes. "Our plant was built in accordance with the standard approach that

SCHOTT Pharmaceutical Packaging production sites follow on a global basis: state-of-the-art production equipment and visual inspection systems, a clean room environment and compliance with currently valid Good Manufacturing Practices (GMP)," says Döpkes.

Site at a glance

SCHOTT forma vitrum Kft.

Location:	Lukácsháza, Hungary
Employees:	520
Products:	ampoules, vials, cartridges
Production area:	22,000 m ²
Quality Certification:	ISO 9001, ISO 14001, ISO 15378

EXHIBITIONS & EVENTS

Come and see us in 2012 at

- Pre-Filled Syringes (smi), London (UK), January 18 - 19
- Pharmapack, Paris (F), February 15 - 16
- PDA Parenteral Packaging conference, Berlin (DE), March 13 - 14,
- CPhI/ICSE Japan, Tokyo (Jp), March 21 - 23
- PDA Annual Meeting, Phoenix AZ (USA), April 16 - 20
- Pharma-Kongress 2012, Düsseldorf (DE), April 24 - 25
- API China, Hefei (CN), April 25 - 27
- Interphex, New York (USA), May 1 - 3
- AAPS National Biotechnology Conference, San Diego CA (USA), May 21 - 23
- Pharmapack North America, Philadelphia PA, May 22 - 23
- Korea Pack, Gyeonggi-do (KR), May 22 - 25
- FCE Pharma, Sao Paulo (BR), May 29 - 31
- PDA FDA Glass Quality Conference, Bethesda (MD), June 4 - 5
- CPhI China, Shanghai (CN), June 26 - 28
- Interphex Japan, Tokyo (Jp), June 27 - 29

MASTHEAD

SCHOTT Pharmaceutical Packaging
NEWSFLASH
Issue 17 / January 2012
Copyright 2012:
SCHOTT Schweiz AG
Publisher:
SCHOTT Schweiz AG
Editors:
Christa Fritschi (Chief Editor), Michael Bonewitz,
Katherine Hause
Contact:
christa.fritschi@schott.com
www.schott.com/pharmaceutical_systems

Address:
SCHOTT Schweiz AG,
St. Josefenstrasse 20
CH-9001 St. Gallen
Layout: Agentur & Verlag Bonewitz,
www.bonewitz.de
Photos: SCHOTT AG, Fotolia, David Micolta
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EVENTS

Colombia Event Spotlights Innovations



The evening event was held in an impressive, inflatable tent...

They came from Colombia, Venezuela, Ecuador, Peru, Guatemala, Costa Rica and the Dominican Republic: 120 customers from 80 companies to learn about the latest innovations at the customer event hosted October 12-13 by SCHOTT Envases Farmaceuticos in Bogota, Colombia.

Held every three years, the purpose of the event was to show to customers the latest developments in facilities, products and processes, says Jhan Pierht Arevalo, SCHOTT Regional Sales Manager of the Andean Community, who coordinated the two-day event. At the top of the list: ampoule printing in two colors, and the new printing camera inspection system.

"SCHOTT Envases Farmaceuticos S.A. is the most important high-tech pharmaceutical packaging producer in the region," says Arevalo, "with products 100% controlled by camera systems in

the critical variables, printing and in the break systems, a controlled environment in production and packaging areas, and an excellent service ready to support our customers' needs."

Organized as a series of tours, expositions, presentations, and workshops, the event took place in – and around – the SCHOTT facility, where a vast inflatable "marketplace" served as a gathering point for attendees. Bathed in a soft blue light, it gave a high tech hint of things to come: the introduction by Plant Manager Mauricio Villegas, the tour of the plant itself, then back to the marketplace for

a look at the latest news from Arevalo, to be followed by cocktails and a cultural event of food, dance, and music of Colombian regions.

The next day, attendees delved deeper with presentations on such topics as "New Trends in Logistics," "Glass Delamination" (and how to prevent it), and "New SCHOTT Innovations against Drug Falsification." To encourage dialogue, the afternoon included three small forums: one on Logistics, one on Products and one on Innovation. Each highlighted activities and results, then opened the floor to questions, including: "How can SCHOTT contribute to your logistic process or product success?"

Located just outside Bogota, with 130 employees, SCHOTT Envases Farmaceuticos produces vials and ampoules for pharmaceutical and cosmetic customers in the region.



... where the participants could see and experience the complete product portfolio of SCHOTT technology group.

PROFILE

Trust in SCHOTT and its Products

A new unit was added to the Pharmaceutical Packaging Business Segment this July: the Global Syringe Business that is based in St. Gallen and regroups all global operational activities linked to glass and plastics pre-fillable syringes. According to its Vice President, Christophe Muguet, "Our main objective is to accelerate the presence of SCHOTT in the important growing market of pre-fillable syringes". He then adds, "We can achieve this by focusing on our key strengths: glass manufacturing and expertise, high quality, state-of-the-art technology, global reach, consequent research and development and innovative product solutions that meet the highest needs of the market, but also by offering prices that are competitive."

Nevertheless, the "soft" factors are also important to him. In fact, customer loyalty and confidence in SCHOTT and its products are just as important in Muguet's opinion. "Here, we have an excellent reputation among our customers and we need to develop it further for



Christophe Muguet, Vice President of the Global Syringe Business is a passionate mountain climber, skier and motorcyclist.

syringes by showing flexibility and responsiveness" he notes.

Around 250 people currently work for the Global Syringe Business with two manufacturing sites, one in St. Gallen, Switzerland, and the other in Lebanon in the U.S. Since it was set up six months

ago, Christophe Muguet has been concentrating on organizing his team and visiting customers in order to understand their needs and instill even greater confidence in SCHOTT. He spends about half of his time in Switzerland and the other half either meeting with custom-

ers in different parts of the world or at exhibitions like the PDA in Basel or PharmTech in Russia.

The 51-year-old Frenchman has learned to love St. Gallen, a city he clearly considers to be worth living in, open and quite beautiful. Both the location and the coun-

tryside are just perfect for him as a passionate mountain climber, skier and motorcyclist. Nevertheless, he still spends the weekends in Grenoble in France, where his wife still lives and works as a midwife. Their two sons have already moved out of the house. 21-year-old Antoine studies in Montréal, Canada, while 25-year-old Arthur works in Geneva. The only slight problem is really speaking the local language where he now lives and works. Here, however, the Frenchman who speaks English at work is also looking forward to learning German and some basis of "Schwyzerdütsch". Christophe Muguet has a Masters degree in engineering from Ecole Supérieure des Arts et Métiers. He gained initial work experience with Glaxo and Serono, mainly in areas of supply chain, procurement and manufacturing. Before joining SCHOTT in July, he worked for the Becton Dickinson Medical Group for over 15 years, most recently as Vice President of Worldwide Operations in the BD Pharmaceutical Systems Business Unit.

EVENTS

Brazil Hosts Pharma Symposium

For two days in October, some 100 representatives of 39 customers of SCHOTT Brasil Ltd. got an intensive course in pharmaceutical packaging that included a plant tour of the company's state-of-the-art facility near Sao Paulo, Brazil. Held every two years, the event was hosted by the company Sales Team, under the direction of Marcia Martins, South America Marketing Manager, Schott Brasil.

It was already the fourth event of this kind over the past decade. And, as customary, it was kicked off with a detailed tour of the state-of-the-art manufacturing facility in groups. In the evening, the guests enjoyed dinner and dancing to a Bee Gees cover band in Sao Paulo.

The symposium on the second day was opened by Jurgen Buhr, General Manager of SCHOTT in Brazil. Topics of the symposium included glass quality, coated vials for biotech drugs, and anti-counterfeiting features, as well as the recent GMP legislation. A special focus was on SCHOTT Brazil's processes and services, such as the Technical Assistance Project, with customized trainings for pharmaceutical industry professionals on different levels.

"Our goal was to show our customers how we can address their specific packaging needs now and in the future and how we can add value for them." says Martins.



The detailed plant tour was one of the highlights of the event.

"From the comments we received, a lot of customers were especially impressed by our technical expertise and our innovative packaging solutions." With some 450 employees, SCHOTT Brasil produces ampoules, vials, cartridges and tubes for test and culture, for

customers mainly in Brazil and other South American countries. Quality certifications include ISO 9001:2008, OHSAS 18001:2007, ISO 14001:2004 (with SCHOTT Integrated Management System for Safety and Environment-IMSU), and ISO 15378:2006.



Some 100 customers participated in the symposium on the second day.

EVENTS

On the Road in Central America

Three days, three countries: May 16-18. For the first time in four years, SCHOTT representatives packed up their experts and took their show on the road to host a series of one-day events for customers and potential customers in Costa Rica, El Salvador, and Guatemala.

From the beginning, it was planned to be a two-way street, according to Carlos Ortega, Regional Sales Manager for Mexico and Central America, SCHOTT in Mexico, who organized the series. "Our objective from the outset was to exchange information with our target customers, to focus on technical aspects, to get their feedback, to offer our support and answer any questions about packaging, about our solutions and about SCHOTT."

Attending the one-day sessions were representatives of a total of 12 pharmaceutical or cosmetic companies – 73 in all – including technical functions such as manufacturing, quality, and packaging design, as well as commercial functions such as purchasing and supply chain.

Their focus was vials and ampoules, with the emphasis on ampoules, and SCHOTT sought to comply with a roster of expositions by knowledgeable speakers. Or-

tega led the way with a commercial presentation on SCHOTT, the facilities in Veracruz, Mexico, its production capacity and product portfolio (vials, ampoules and cartridges). Next was Ricardo Aburto, Manufacturing Manager, SCHOTT facility in Mexico, who spoke on the complexities of ampoule production. He was followed by Eusebio Rodriguez, Quality Control Manager from the SCHOTT facility in Colombia, who presented both the process and the technology behind the consistent high quality for which SCHOTT is renowned.

As an added bonus, each event included technical information from two external speakers, Luis Valencia and Damien Saleur, from Stelmi, the global company already known to many of the attendees as specializing in the development and production of elastomer components for parenteral pharmaceutical packaging.

The feedback of the participants was very positive, says Ortega. "Our customers are first and foremost committed to quality, as are we. And because of that, a lot of our relationships go back as many as 30 years. Events like these are one way for us to strengthen these relationships, which is why we plan to continue with them in the coming years."

SOLUTIONS

Tolmar Transitions to SCHOTT TopPac® Syringes

Confronted with a critical change of packaging material, Tolmar Inc. called on SCHOTT to meet their urgent demands for specialized pre-fillable syringes used in treating prostate cancer around the world. "They came to SCHOTT looking for proven expertise in COC polymer prefillable syringe materials and manufacturing and a global presence," says Michael Regn, Area Sales Manager, SCHOTT North America. What they brought with them was a unique set of challenges and an intractable deadline.

A fully integrated pharmaceutical company, Tolmar was in need of an additional supplier for part of a two-syringe drug delivery system for Eligard leuprolide acetate, a prescription medication for the palliative treatment of prostate cancer. Eligard is administered subcutaneously and provides continuous release of leuprolide acetate over a one, three, four or six month treatment period. The injection delivers the dose of leuprolide acetate incorporated in a polymer diluent just prior to injection. "Ours is a fairly complex syringe system," says Kevin McCann, Packaging Engineer, Tolmar. "It consists of two syringes, packaged in either trays or pouches. Syringe 'A' is prefilled with a



The Eligard two-syringe drug delivery system for treating prostate cancer contains "SCHOTT TopPac" syringes.

biodegradable polymer diluent. Syringe 'B' is prefilled with leuprolide acetate powder. The two are combined just before administration by screwing the syringes together and injecting the polymer of 'A' into the powder of 'B', then pushing the mixture back and forth between the two for some 45 seconds to obtain a uniform suspension. The contents are then drawn into Syringe 'B', which is uncoupled from 'A' and attached to a sterile needle cartridge for injection." In Fall 2009, Tolmar contacted SCHOTT regarding a time sensitive supply of Syringe "B."

"We had only a finite supply available," says Michelle Mantas, Vice President Logistics, Tolmar. "We bought all the bridging material we could but time was going to be a challenge. We needed to transition to a new supplier and fast." With that in mind, Tolmar turned to SCHOTT and "SCHOTT TopPac" to meet the urgent timeline of Eligard Syringe 'B' in 1ml and 3ml sizes. Says Regn, "SCHOTT TopPac' has all the advantages they were looking for: glass-like transparency, tight dimensional tolerance, chemical resistance, good barrier proper-

ties, plus design flexibility like integrated luer-lock, compatibility between male-female luer system, and lyophilization capability." Also critical to success was SCHOTT's commercial presence – including prior DMF at US FDA and other products already in the market in "SCHOTT TopPac" syringes, assurance of supply, scientific and technical expertise, and document and regulatory support. "We respect and support SCHOTT's commitment to quality," says McCann. "Even before we audited their production facility in St. Gallen, Switzerland, we knew SCHOTT's reputation." Not surprisingly, the TopPac syringes exceeded expectations, with greater clarity and better "tack" for labeling, making them more "pharmaceutically elegant" in appearance. Supported throughout by Michael Regn, Anil Busimi, Global Product Manager "SCHOTT TopPac" Syringes, and the team in St. Gallen, the site of manufacture, both Mantas and McCann have been pleased with the results. "Our syringes are subjected to a pretty demanding process," says McCann. "One of the biggest challenges is understanding the 'syringability' of our product, the dynamics, the force required to

reconstitute the solution. We had a fairly aggressive timeline, but SCHOTT was always upfront and responsive to any questions or requests." SCHOTT continues to be responsive, according to Mantas. "Eligard is now approved and marketed in 56 countries, and we're pursuing 25 more over the next three years. Just since SCHOTT came on board, we've experienced a substantial increase in demand and SCHOTT has been able to meet all our needs. It's been a good collaboration. Eligard is extremely important for us; it's our major product in uro/oncology. As it turned out, the project exceeded our expectations and we were very happy with the performance of the SCHOTT team." Tolmar is a Colorado-based pharmaceutical research, development, manufacturing and commercial operations company with specific focus in therapeutic areas of dental, dermatology and oncology. Production facilities include chemistry and microbiology laboratories, multi-shift production operation, cGMP and EU cGMP compliant manufacturing, liquid, semi-solid, lyophilization, and injectable filling lines, as well as warehouse and cold-chain distribution capability.

MATERIALS

Two Ways to Minimize the Delamination Risk of Glass Containers

Continued from page 1
response time of the "delamination" appearance it is urgent to have tools on hand which give fast evidence about potential risks of the chosen drug-container combination.

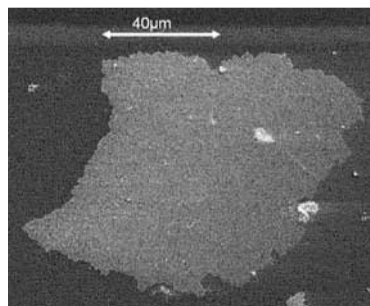


Image of an isolated flake.

To minimize the risk of delamination we strongly recommend a two way strategy:

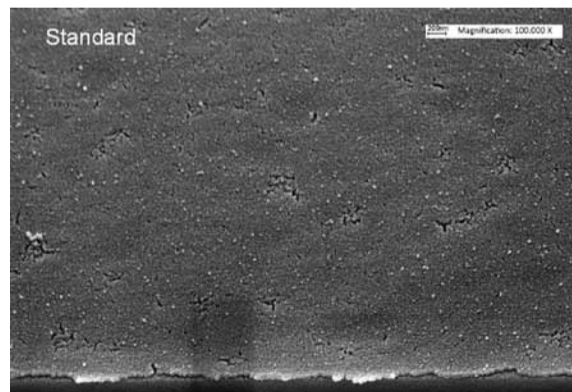
1. Implementation of container screening studies evaluating the glass surface morphology, glass surface composition, and solution composition of leached glass elements should be included as part of normal stability studies to determine if glass delamination occurs and what the root cause is (drug formulation/container process or drug formulation/container composition).

2. To optimize the process window of the container production the implementation of an offline "fast" testing method for the use in daily operation can also help to run the production lines in a "low delamination risk" mode.

Test methods

Because delamination requires drug product exposure to occur, no conclusive incoming inspection method currently exists to determine upon receipt of a container from the glass manufacturer if a vial will or will not delaminate. Regarding the variety of chemicals used for drugs and formulations and the variety of filling, sterilization, and autoclaving procedures, it seems reasonable that no one general test will be able to assess the specific delamination risk. Knowing the big variety of influencing manufacturing parameters, the state-of-the-art technology of type I glass containers does not force an implementation of validated processes guaranteeing "minimal delamination risk" for all container types. Therefore, the first way to minimize delamination should be the implementation of a standard test method like ISO 4802 / Ph.Eur. 7.0 for the chemical

durability of container glass which defines maximal tolerances for a kind of delamination affinity. Within SCHOTT, such a testing procedure to give a "go" / "no go" hint to the specific production process for a quick routine control



Very good delamination resistance of "SCHOTT Type I plus" coated vials (right) compared to uncoated vials (left) has been confirmed by 6 months accelerated aging study.

of the delamination tendency of tubular glass vials has been developed. The new test method has been filed for patent and is now in the validation phase for routine application. The second way to minimize delamination is strongly addressed to the drug product manufacturers to implement accelerated aging tests for container screening methods dur-

ing stability testing. If the current drug/container product generates glass flakes, from the container perspective one can quickly test other type I glass(es) or containers by the same manufacturer, or switch to a different manufacturer.

SCHOTT has completed a recent internal study with focus on the attack of various buffer formulations on standard 2 ml vials and "SCHOTT Type I plus" vials (SiO₂ coated) under accelerated conditions, both made of "SCHOTT FIOLEX" type I tubing glass. Good delamination resistance compared to uncoated vials was demonstrated. Delamination can be en-

tirely avoided for the vast majority of applications with SiO₂ coated "SCHOTT Type I plus" vials. For specific drug/buffer container combinations "SCHOTT Type I plus" can be the solution of choice, showing no tendency for delami-

nation within a three years period. By the way, because of the quartz-like surface, customers do not even have to change the registration when they switch from an uncoated vial to "SCHOTT Type I plus" for a specific product. Overall it is important to note that the vast majority of injectable drug products on the market today are safely packaged in type I glass.