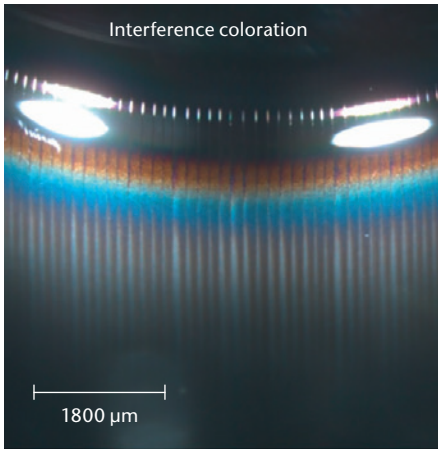
Does your vial fit to your drug product?

SCHOTT pharma services offers studies focused on glass delamination testing USP <1660>, particle ID and leaching behavior

SCHOTT pharma services provides compatibility testing for drug products in glass vials including a delamination screening package aligned with USP <1660> guidance «Evaluation of the Inner Surface Durability of Glass Containers» and EP 3.2.1. recommendations. The containers to be tested can be drawn from real time stability samples or stored under accelerated aging conditions. The extent of glass corrosion and chemical attack is assessed by analyses of the inner glass surface morphology, the concentrations of extracted elements in solution, and by identification of particles and flakes.

SCHOTT pharma services uses a combination of the recommended analytical techniques:

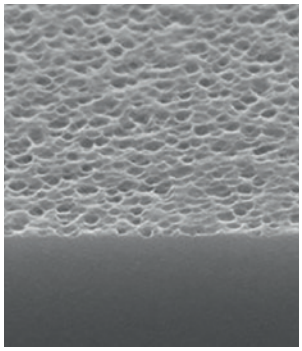
Flake-like particles by visual inspection



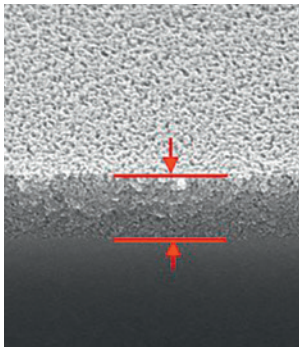
Coloration ring by stereo-microscopy

Visual and Optical Inspection

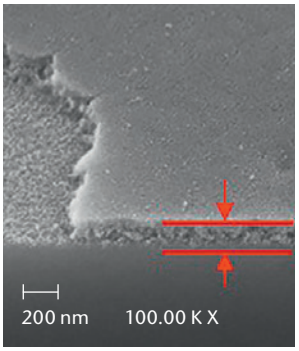
- Used to detect particles via visual inspection by eye and camera (filled vials) and to visualize coloration and scattering (empty and emptied vials)
- Allows for the identification of containers with high particle load and with changed regions to determine the worst samples of a set by stereo-microscopy



Roughening



Reaction Zone



Delaminated Area

SEM cross section analysis

- Used to determine the extent of chemical attack of inner glass surface
- Allows for classification between different levels of glass corrosion. Typical features are roughening, formation of reaction zones and/or delaminated areas at the interior surface in contact with the drug product

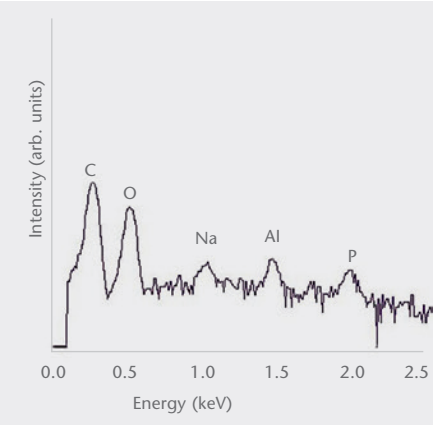
Element (mg/L)	Citrate buffer (pH 6.0)	Sodium bicarbonate (pH 8.0)	Phosphate buffer (pH 7.0)
B	2.1	2.0	1.1
Al	3.0	0.05	0.06
Si	20.1	8.2	9.2

Concentrations of selected leachables found after storage for different filling solutions

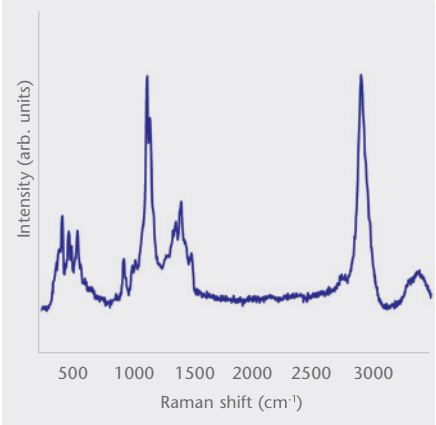
ICP analysis

- Used to quantify the amounts of leached glass elements
- Allows for the confirmation of the chemical mechanism of drug container interaction

SCHOTT
glass made of ideas



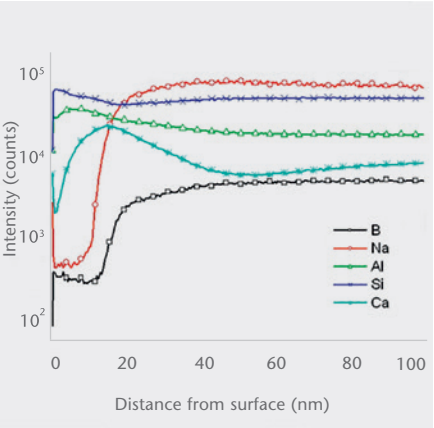
Exemplary EDS spectrum of a particle



Exemplary Raman spectrum of an organic particle

SEM/EDS and Raman microscopy

- Used to analyze the composition of particles after filtration
- Allows to identify morphology (SEM), elemental components (SEM/EDS), and molecular structure (Raman) of isolated particles



Altered elemental composition of surface near layer with B and Na depletion

TOF-SIMS

- Used to characterize the elemental composition of the near surface region of container interior
- Allows a better understanding of the mechanism of drug container interaction and induced glass corrosion

Study protocol example:

1. Visual inspection by eye and magnifying video camera with respect to the presence of particles or flakes (10 filled vials per time point according to Tables 1+2).
2. Optical inspection of emptied containers per time point: Stereo-microscopy with extended depth of focus to qualitatively determine if there are any indications for reaction zones present on the interior surface (10 vials per time point according to Tables 1+2). Selection of 2 'worst' samples on the basis of stereo-microscopic inspection for subsequent SEM cross-section analyses.
3. SEM (Scanning Electron Microscopy) cross-section analyses on the interior surface of 2 vials for selected test conditions and selected time points as described in Tables 1+2; analyses of three areas: wall near bottom,middle of the vial body, and wall near shoulder. These investigations reveal the presence of a potential reaction zone.
4. ICP (Inductively Coupled Plasma) analyses of 10 mL drug solution pooled from the vials of each batch for selected test conditions and selected time points according to Tables 1+2 to quantitatively determine the amount of "glass" elements leached into solution for 4 selected "glass" elements (Si, B, Ca, Al) to ascertain if the amounts and ratios found are normal or if there is a pronounced chemical attack.
5. Filtration of the solution of one selected vial according to Tables 1+2 through a silver membrane (pore size approx. 0.2 µm) using a vacuum filtration unit. Subsequent SEM/EDS and Raman analyses of found particulate matter to determine the elemental composition and morphology of the particles by SEM/EDS and the molecular structure by match of Raman signals to library.

Optional: (If the mechanism of glass corrosion is unclear or reaction zones are observed)

6. SIMS (Secondary Ion Mass Spectrometry) depth profiling of the interior surface to get information about the composition of the surface near layer.

The techniques described above are applied at different time points under accelerated storage conditions. These conditions are defined on the basis of the drug product application and customer requirements. Exemplary study designs for drug products with a shelf life of 3 years at 5 °C (Table 1) and 25 °C (Table 2) are shown below.

The tables illustrate the test methods applied for one set of vials filled with drug product and stored until different time points and include the number of characterized samples.

Method	Empty Vial	Storage conditions / time points			
		After filling	Storage at 40 °C		
	Control	0 weeks	4 weeks	8 weeks	12 weeks
Visual inspection	–	10	10	10	10
Optical inspection	5	10	10	10	10
SEM cross section	2	2	2	2	2
ICP analyses	–	x	x	x	x
Particle analyses by SEM/EDS and Raman	–	–	1	1	1
SIMS (optional)	–	1	–	–	1

X: Drug solution pooled from multiple vials

Table 1: Exemplary study design for a drug product with a shelf life of 3 years at 5 °C tested by using accelerated storage at 40 °C

Method	Empty Vial	Storage conditions / time points			
		After filling	Storage at 60 °C		
	Control	0 weeks	6 weeks	11 weeks	16 weeks
Visual inspection	–	10	10	10	10
Optical inspection	5	10	10	10	10
SEM cross section	2	2	2	2	2
ICP analyses	–	x	x	x	x
Particle analyses by SEM/EDS and Raman	–	–	1	1	1
SIMS (optional)	–	1	–	–	1

X: Drug solution pooled from multiple vials

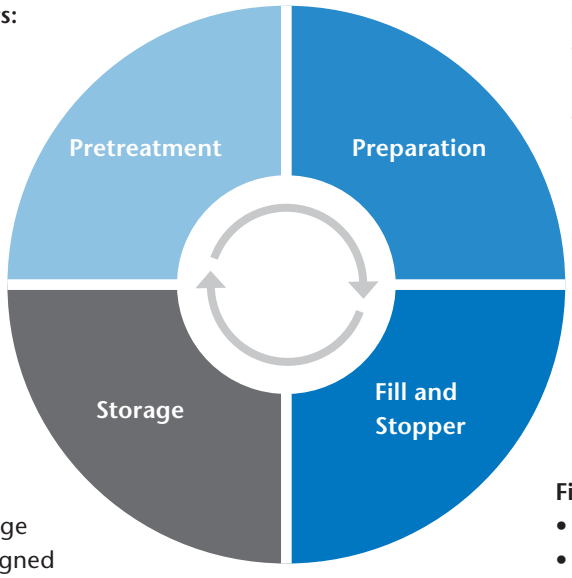
Table 2: Exemplary study design for a drug product with a shelf life of 3 years at 25 °C tested by using accelerated storage at 60 °C

Manufacturing services for analytical samples:

Container compatibility testing requires a small number of filled containers, often in a pre-production phase of drug development. Thus, SCHOTT pharma services offers an individualized manufacturing service for a manual, non-sterile preparation of the samples needed to conduct the analytical studies.

These services are including the pretreatment of the containers like washing and depyrogenation, filling with the provided drug solution, and the sealing and storage of the filled samples under accelerated test conditions.

Pretreatment of glass containers:
- Washing, drying
- Depyrogenation



Preparation:
- Handling of drug solution according to customer requirements
- Support for preparation of model buffer formulation from excipients according to customer procedure

Storage:
- Accelerated and real-time storage according to test conditions aligned with customer requirements

Fill and Stopper:
- Filling under laminar flow (non-sterile)
- Closure with stopper and sealing

Sample requirements:

At least 10 vials per each time point and per each sample set and 5 additional empty vials per each vial container type as reference samples. In addition, 20 mL of drug product solution for verification of ICP method and the material safety datasheet (MSDS) of the drug product.

Deliverables:

The drug container compatibility study will be conducted in alignment with EP and USP requirements and according to the requirements of DIN EN ISO/IEC 17025 accreditation standard. At the end of the study, an analysis report including a summary report of the results and interpretation for a risk assessment concerning delamination propensity, particles and leaching behavior will be delivered.

Locations:

SCHOTT pharma services provides the full compatibility testing from 2 sites working with harmonized analytical techniques and identical quality policies. One laboratory is located in North America (PA) and the other one is situated in Germany (Mainz). The shipment addresses are given below:

Laboratory address in Germany:

SCHOTT AG
SCHOTT pharma services
Hattenbergstraße 10
55122 Mainz
Germany

pharma.services@schott.com

Laboratory address in USA:

SCHOTT North America, Inc.
Attn. Dr. Dan Haines
201 South Blakely Street, #121
Dunmore, PA 18512
USA

Phone: +1 570 457-7485 x 653
daniel.haines@us.schott.com

Quality:

Laboratories of SCHOTT pharma services are DIN EN ISO/IEC 17025 accredited (DAkkS) and FDA registered.

SCHOTT pharma services can access more than 40 years experience in analytical testing of pharmaceutical packaging containers. All quality relevant documents are electronically available ensuring a hassle-free audit process.

Deutsche
Akkreditierungsstelle
D-PL-14645-01-00

For a quotation, a request or further information, please contact us:

SCHOTT AG
Hattenbergstraße 10
55122 Mainz
Germany

Phone: +49 (0)6131/66-7339
pharma.services@schott.com

Or please click here:

Quotation **Request**

Brochures, Sample Submission Form, Publications

SCHOTT AG
Hattenbergstraße 10
55122 Mainz
Germany
Phone: +49 (0)6131/66-7339
Fax: +49 (0)3641/2888-9125
pharma.services@schott.com

www.schott.com/pharmaceutical_systems

SCHOTT
glass made of ideas