SCHOTT pharma services
Specialized analytics for pharmaceutical packaging

SCHOTT pharma services specializes in the following areas:

**Chemical Durability**
- Predictive and real-time delamination studies
- Particle analysis
- Glass surface testing (wetting and adsorption issues)

**Mechanical Stability**
- Fractography and breakage analysis
- Container strength testing
- Training course for fractography and strength

**E&L + System Performance**
- Extractables & leachables
- Elemental impurities
- Packaging components compliances
- Pharmacopeia testing

More than 40 Years Experience in Testing of Pharmaceutical Packaging

- Testing according to current EP, USP, and JP regulatory guidelines and ICH recommendations.
- Laboratories are DIN EN ISO/IEC 17025 accredited (DAkkS and ILAC) and FDA registered.
- High level of quality management confirmed by regular customer quality audits.

[Logos and accreditations]
SCHOTT is a leading international technology group in the areas of specialty glass and glass-ceramics. With more than 130 years of outstanding development, materials and technology expertise we offer a broad portfolio of high-quality products and intelligent solutions that contribute to our customers’ success.

SCHOTT pharma services provides analytical laboratory services for pharmaceutical packaging. Our unique combination of specialized analytics and expertise in materials, products, and processes enables us to support pharmaceutical companies in finding solutions for the most challenging packaging requirements.
Mechanical Stability Tests
Basis for weak point analyses of production lines or container design

Breakage Analysis – Fractography
- Broken samples and cracks tell stories and leave behind clues. By applying optical and scanning electron microscopy, the fracture origin and propagation of glass breakage can be determined.
- Clear evidence for the root cause can be drawn and the applied force leading to failure can be determined.
- The glass container integrity can be additionally assessed by dye penetration testing.

Strength Testing
- Strength testing allows the prediction of fracture probabilities of glass containers.
- Samples from different process steps (purpose: process mapping), different lots or different manufacturers can be compared and evaluated.
- Burst pressure testing reveals the weakest spot of a container, while specific tests target critical areas like the flange or cone.

Training Course for Fractography and Strength
- Two day on-site course focusing on glass production, testing, glass properties, fracture mechanics and statistics, strength testing and Weibull distributions, fracture patterns, fracture surface markings, sample preparation, imaging techniques, and detailed hands-on learning.

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Extractables and Leachables
E&L data for material characterization and for registration purposes

<table>
<thead>
<tr>
<th>Elements Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
</tr>
<tr>
<td>Class 2 A</td>
</tr>
<tr>
<td>Class 2 B</td>
</tr>
<tr>
<td>Class 3</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Additional</td>
</tr>
</tbody>
</table>

Elements to be tested on the basis of ICH / USP route-of-administration risk assessment using High Resolution ICP-MS

- Customer oriented extractables studies for determination of organic and inorganic substances extracted out of primary packaging materials that can potentially migrate into the drug product.
- Study protocols are based on most recent guideline recommendations: USP <1663>, USP <1664>, EP, ISO 10993 and PQRI.

- Determination of leachables and cross reaction products with validated methods after storage of drug product within a closed container under accelerated and real time test conditions.
- All analyses are performed with current state-of-the-art equipment.
- Guideline expertise (e.g. ICH M7) for assessment of results. Support for toxicological assessment possible by collaboration partner.

- Determination of elemental impurities (USP <232>, ICH Q3D) using validated methods by High Resolution ICP-MS.
- Determination of extractable and leachable silicone by GF-AAS.

Chromatogram of leachables testing with an antioxidant in different oxidation states

Taking secondary packaging materials into account concerning potential leachables

E&L data for all drug contact materials such as polymer barrel and rubber components

Carbon neutral print production
System Performance Tests
Based on long term expertise in glass, coatings, polymer and elastomer components

Glass Composition
- Identification of chemical glass composition of primary packaging containers and manufacturer based on comprehensive database of published glass compositions.

Siliconization/Coating/Treatment
- Determination of applied coatings/treatments such as silicone oil, barrier coating, hydrophobic coating, chemical strengthening.

Compliance tests for packaging components and rubber characterization
- Compliance test methods available for glass containers e.g. USP <660>, EP 3.2.1. (alkalinity, hydrolytic resistance, arsenic, needle) and rubber components (physico-chemical tests and particles).
- Identification of rubber material and coating by combination of different analytical methods.

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Chemical Durability Tests
Glass delamination in accordance with USP <1660>

**Container Inspection and Screening**
- Glass delamination screening starts with visual inspection by eye and camera methods to detect flake-like particles.
- After emptying the container, stereomicroscopy is used to look for changed regions of a container for further surface analysis to determine the worst samples out of a sample set.

**Glass Delamination Confirmation**
- SEM cross section analysis, in combination with ICP-OES/MS solution analysis, is used to determine the extent of attack of glass surface and confirm the mechanism of drug container interaction.

**Drug Container Interaction**
- SIMS depth profiling, SEM cross section analysis, and ICP-OES/MS solution analysis is used to determine the mechanism:
  1. Dissolution
  2. Selective dissolution
  3. Dissolution and reaction

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**Table:**

<table>
<thead>
<tr>
<th>Element</th>
<th>Citrate buffer (pH 6.0)</th>
<th>Sodium bicarbonate (pH 8.0)</th>
<th>Phosphate buffer (pH 7.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B (mg/L)</td>
<td>2.1</td>
<td>2.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Al (mg/L)</td>
<td>3.0</td>
<td>0.045</td>
<td>0.058</td>
</tr>
<tr>
<td>Si (mg/L)</td>
<td>20.1</td>
<td>8.2</td>
<td>9.2</td>
</tr>
</tbody>
</table>

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**Diagram:**

- 1. Dissolution
  - Erosion
- 2. Selective Dissolution
  - Erosion and weak porous layer
- 3. Dissolution and Reaction
  - Erosion and compound layer

**Notice:**
- No risk for flakes (maybe precipitations)
- Risk for silicate flakes
- Risk for compound flakes

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Chemical Durability Tests
Screening packages to assess potential risks and future avoidance

Predictive Delamination Screening
• Specially developed delamination screening package in accordance with USP <1660> to assess the likelihood for delamination occurring during the shelf life of the product.
• A combination of tests investigating the container surface, the surface near region and the solution, allowing a determination for the risk of glass delamination to occur.

Particulate Analysis (Inorganics)
• Inorganic particles, particularly flake-like particles, need to be isolated via filtration and analyzed for chemical composition by SEM-EDS, Raman/FTIR and morphology by SEM-EDS to identify and determine root cause.
• Common sources of inorganic particles are e.g. manufacturing by-products, deposits from processing, particle from breakage.

Particulate Analysis (Organics)
• Organic particles need to be assessed in the same manner.
• Common sources of organic particles that are of human nature (skin, hair), fibers (clean room cloth, filters), formulation precipitates or secondary packaging material (polymer boxes, shrink wrap).

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State-of-the-Art Analyses
Unique set of highly sophisticated and precise analyses methods performed by SCHOTT pharma services experts on packaging analytics

Below you will find a selection of our analytical testing methods:

**Chemical Durability Tests**
- ToF-SIMS Secondary Ion Mass Spectrometry and Depth Profiling
- SEM Scanning Electron Microscopy
- LiMi Stereo Microscopy
- EDS Energy-dispersive X-Ray Spectroscopy
- F-AAS, GF-AAS, HG-AAS Atomic Absorption Spectrometry
- HR ICP-MS High Resolution Inductive Coupled Plasma-Mass Spectrometry
- ICP-OES, Spark-OES Atomic Emission Spectrometry
- ICP-MS, Laser Ablation ICP-MS
- FTIR- and Raman-Microscopy
- Wet Chemistry, Gravimetry, Titration
- Hydrolytic Resistance Tests
- Sample Preparation for Tests including Washing, Depyrogenation, Filling, and Sealing

**Mechanical Stability Tests**
- Fractography, Crack Origin, Microscopic Fracture Patterns
- Stress-optical Measurements
- Statistical Analysis of Strength Data
- Fracture Toughness
- Crack Initiation Load, Elastic and Plastic Indentation
- Static Strength, Tension-compression (uniaxial)
- Bending, Bursting (hydrostatic)
- Dynamic Strength, Notch Test, DCDC (crack growth)
- Climate Testing
- FEA Finite Element Analysis

**E&L and System Performance Tests**
- GC-MS Gas Chromatography – Mass Spectrometry
- GC-FID Gas Chromatography – Flame Ionisation Detection
- HS-GC Headspace – Gas Chromatography
- TD-GC Thermal desorption – Gas Chromatography
- LC-Q-Tof and LC-MS-IT-TOF Liquid Chromatography high resolution Mass Spectrometry
- LC-DAD Liquid chromatography with UV/VIS detection
- IC Ion Chromatography
- ICP-OES Inductive Coupled Plasma – Optical Emission Spectrometry
- ICP-MS Inductive Coupled Plasma – Mass Spectrometry
- HR ICP-MS High Resolution Inductive Coupled Plasma – Mass Spectrometry
- F-AAS, GF-AAS, HG-AAS Atomic Absorption Spectrometry
- Hot Gas Extraction Methods for C, O, S, N Determination
- Transmission, Reflection, Remission, Absorption in UV-VIS-IR Range
- FTIR- and Raman-Microscopy
- X-ray fluorescence spectrometry

**Accredited according to DIN EN ISO/IEC 17025:**

Recent Publications & Whitepapers


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