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SCHOTT pharma services

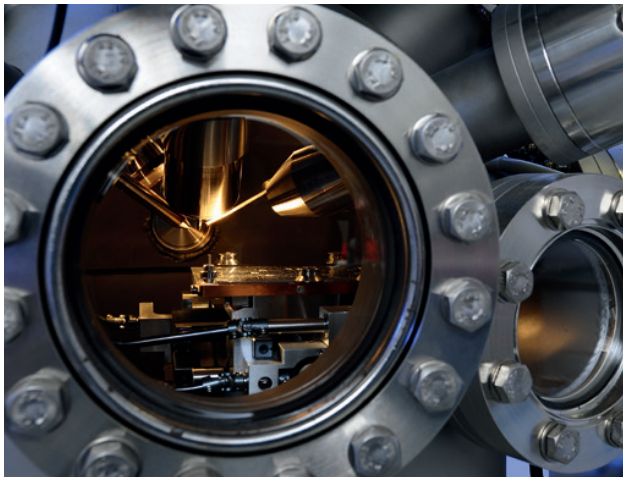
SCHOTT pharma services
Specialized analytics for pharmaceutical packaging

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.

ilac-MRA

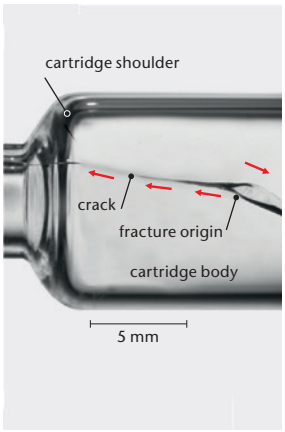
DAkkS
Deutsche
Akkreditierungsstelle
D-PL-14645-01-00

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.

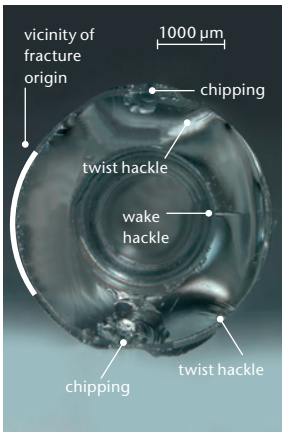
SCHOTT pharma services provides analytical laboratory services for pharmaceutical packaging. Our unique combination of specialized analytics and expertise in materials, products, and processes enables us to support pharmaceutical companies in finding solutions for the most challenging packaging requirements.

Mechanical Stability Tests

Basis for weak point analyses of production lines or container design



Fracture surface of a cracked cartridge revealing macroscopic fracture patterns

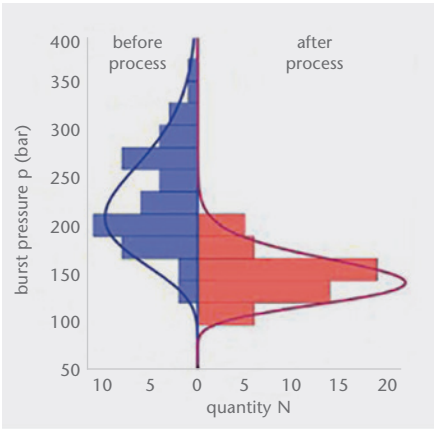


Fracture surface of a broken syringe revealing microscopic fracture markings

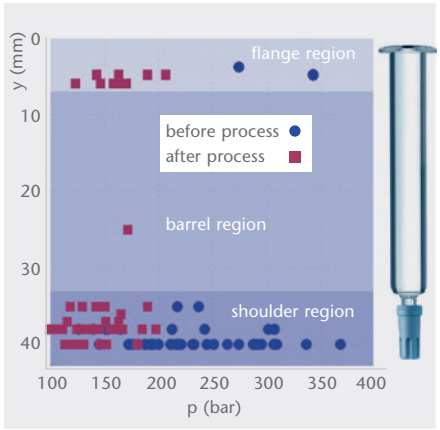
Dye penetration testing concerning glass container integrity

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.



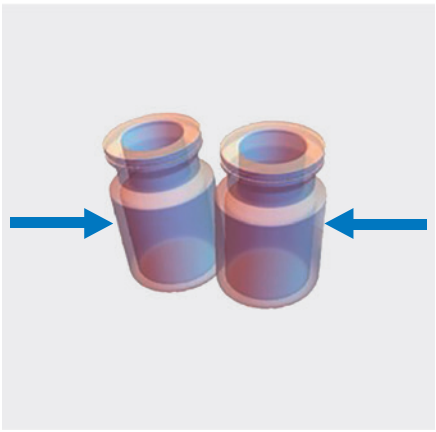
Burst strength distribution, statistical evaluation by hypothesis testing



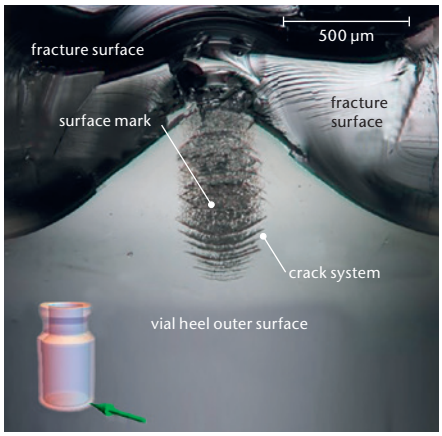
Determination of fracture origin confirms additional damage occurred near flange

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.



Visualizing the mechanisms associated with glass to glass contact events



Photograph of a typical fracture origin caused by a contact with a blunt object

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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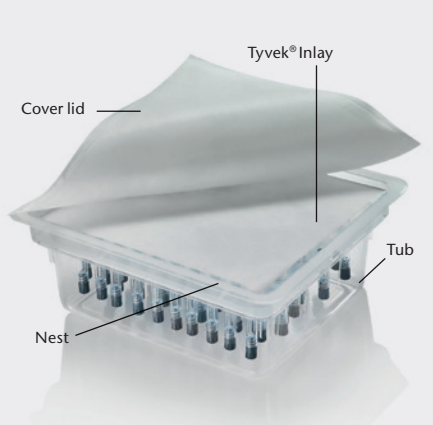
Extractables and Leachables

E&L data for material characterization and for registration purposes

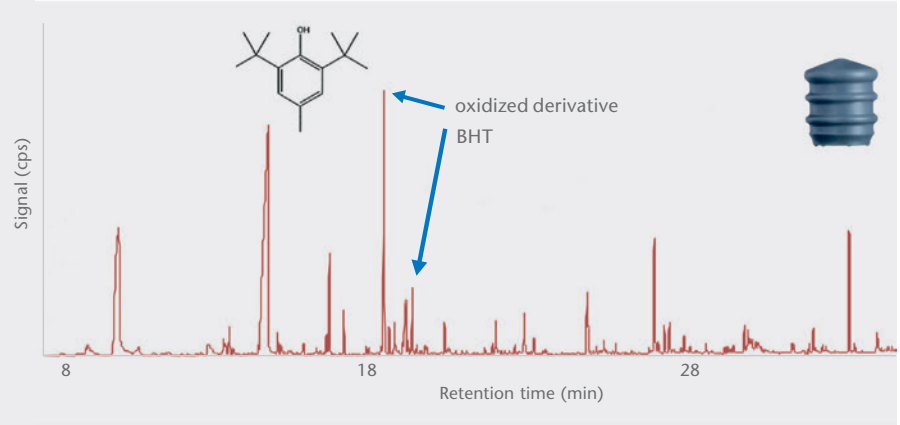
E&L data for all drug contact materials such as polymer barrel and rubber components



Taking secondary packaging materials into account concerning potential leachables

Extractables Studies

- 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.



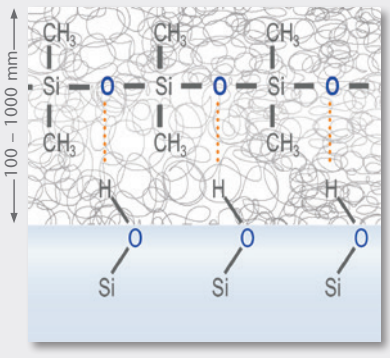
Chromatogram of leachables testing with an antioxidant in different oxidation states

Accelerated and Real Time Leachables Studies

- 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.

	Elements Tested
Class 1	Cd, Pb, As, Hg
Class 2A	Co, V, Ni
Class 2B	Tl, Au, Pd, Ir, Os, Rh, Ru, Se, Ag, Pt
Class 3	Li, Sb, Ba, Mo, Cu, Sn, Cr
Other	Al, B, Ca, Fe, K, Mg, Mn, Na, W, Zn
Additional	Si

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



Determination of total and free silicone by Graphite Furnace Atomic Absorption Spectrometry (GF-AAS)

Elemental Impurities, total silicone, and free silicone

- 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.

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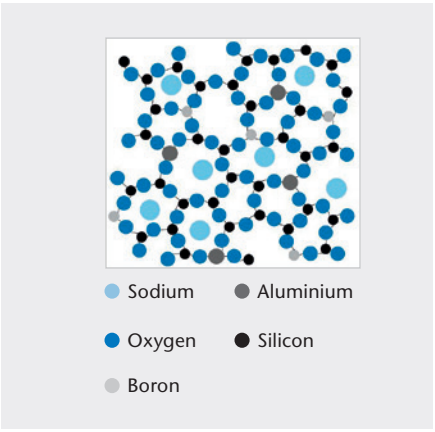
System Performance Tests

Based on long term expertise in glass, coatings, polymer and elastomer components

Glass composition

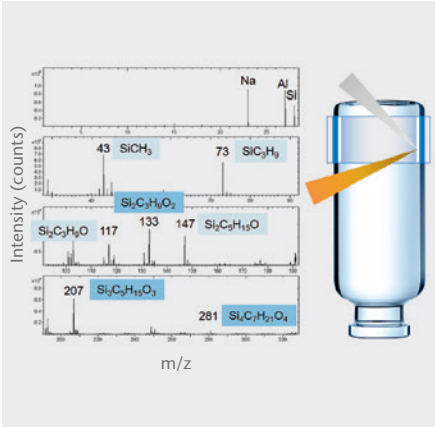


Chemical structure of borosilicate glass

Glass Composition

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

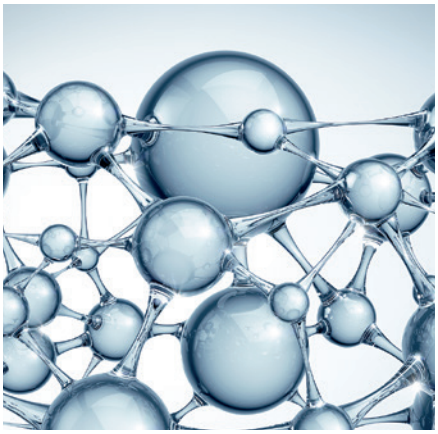
Siliconization presence/absence and uniformity using colored water droplet test



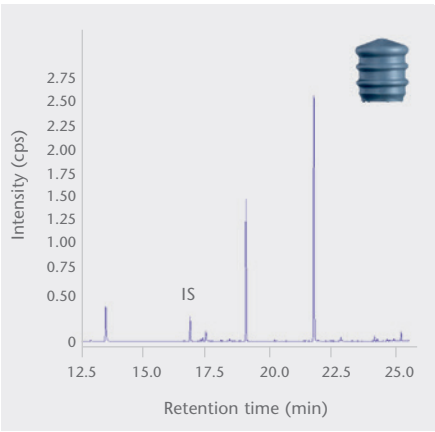
Characterization of inner container surface by Time of Flight – Secondary Ion Mass Spectro-me-try (ToF-SIMS)

Siliconization/Coating/Treatment

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



Standardized compliance testing (EP, USP, JP, ISO and other industry standards)



Fingerprint of rubber extract by GC-MS

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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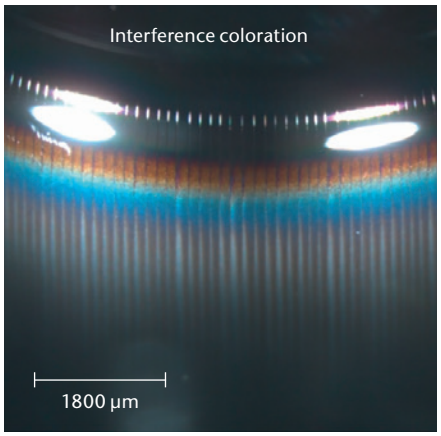
Chemical Durability Tests

Glass delamination in accordance with USP <1660>

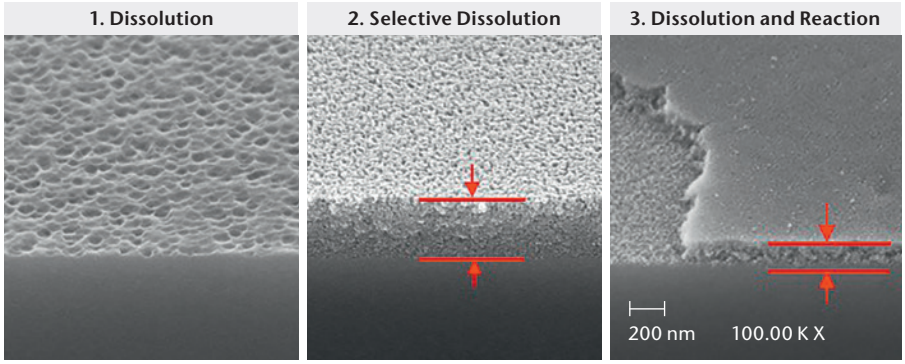
Flake-like particles by visual inspection



Coloration ring by stereo-microscopy

Container Inspection and Screening

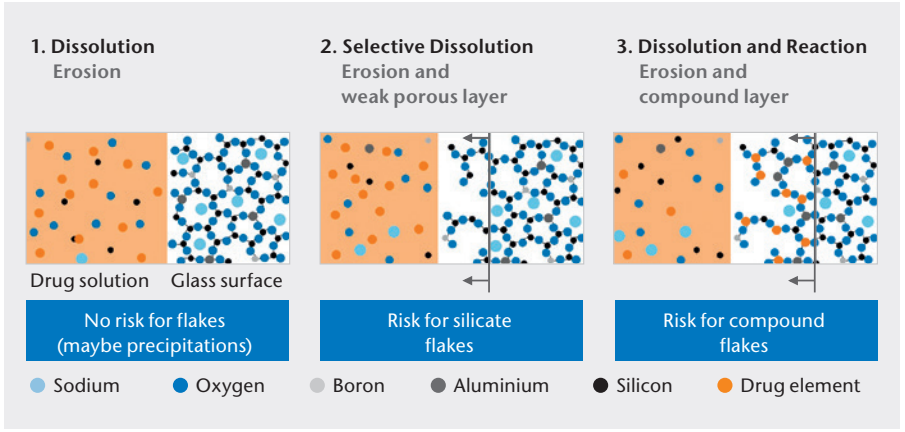
- Glass delamination screening starts with visual inspection by eye and camera methods to detect flake-like particles.
- After emptying the container, stereomicroscopy is used to look for changed regions of a container for further surface analysis to determine the worst samples out of a sample set.



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.

Element	Citrate buffer (pH 6.0)	Sodium bicarbonate (pH 8.0)	Phosphate buffer (pH 7.0)
B (mg/L)	2.1	2.0	1.1
Al(mg/L)	3.0	0.045	0.058
Si (mg/L)	20.1	8.2	9.2



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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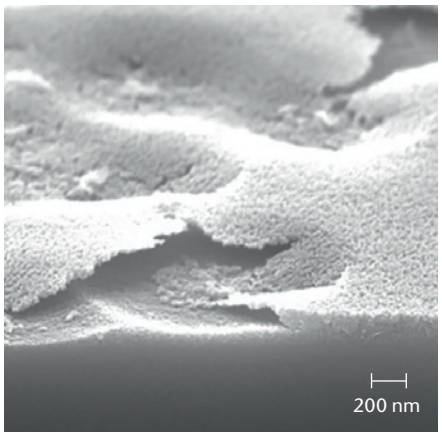
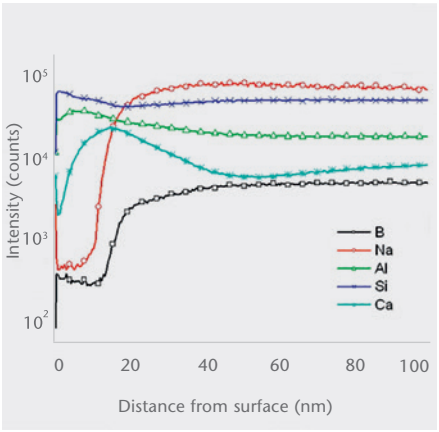
Chemical Durability Tests

Screening packages to assess potential risks and future avoidance



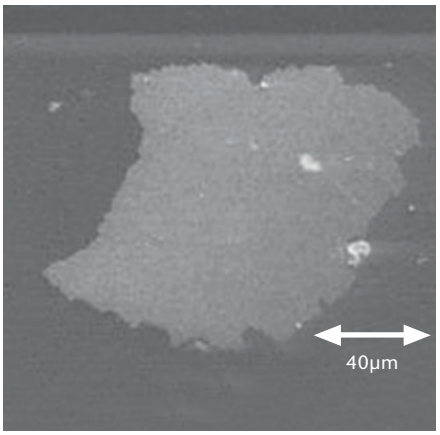
Delamination of the container wall by Scanning Electron Microscopy

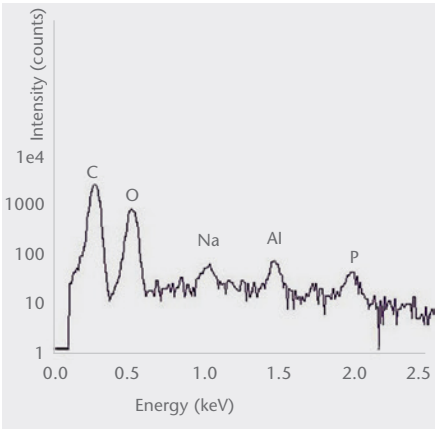


Altered elemental composition of surface near layer with B and Na depletion

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.

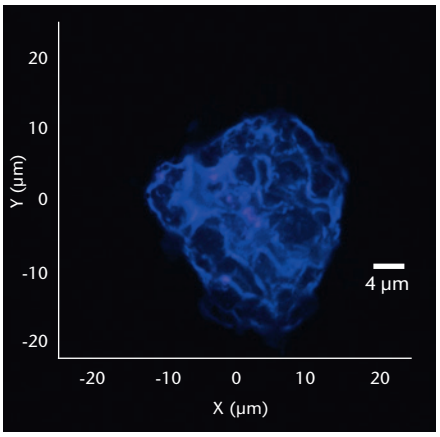




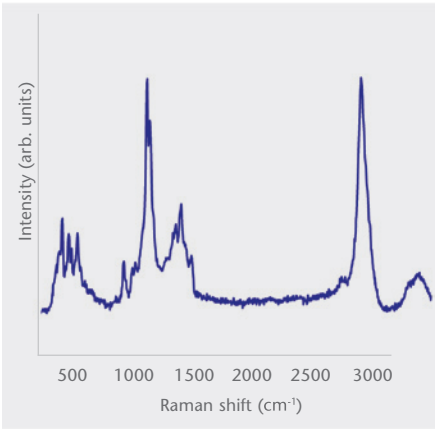
Flake-like particle (left) which is an Al-Phosphate rich material (right)

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.



Micrograph of cellulose particle for morphology and size



Corresponding Raman spectrum of cellulose with 532 nm laser excitation

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

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

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

Accredited according to DIN EN ISO/IEC 17025:

ilac-MRA DAkkS Deutsche Akkreditierungsstelle D-PL-14645-01-00

Recent Publications & Whitepapers

1. | Hladik, B., Buscke, F., Frost, R., Rothhaar, U. Comparative Leachable Study for Glass Vials to Demonstrate the Impact of Low Fill Volume, J. Pharm. Sci. Technol. 2019, 73.
2. | Rothhaar, U., Klause, M., Hladik, B. Comparative Delamination Study to Demonstrate the Impact of Container Quality and Nature of Buffer System, J. Pharm. Sci. Technol. 2016, 70, pgs 560 – 567.
3. | Haines, D., Maurer, F., Rothhaar, U. Why do Pharmaceutical Glass Containers Break: The Underestimated Power of Strength Testing and Fractography, International Pharmaceutical Industry, 2016, Vol 8, Issue 1, pgs 88 – 92.
4. | Soegding, T., Canton, D.; Haines, D., Rothhaar, U. How Sterilization of Primary Packaging Influences the Results of E&L Studies, Contract Pharma, 2015, June, pgs 88 – 94.
5. | Haines, D.; Scheumann, V., Rothhaar, U. Glass Flakes: Pre-Testing Stops a Big Problem before it Even Starts, Contract Pharma 2013, June, pgs 92 – 98.

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