

Predictive delamination screening – offer by SCHOTT pharma services

Predictive delamination screening aligned with USP <1660>

Over the past several years we have developed a delamination screening package aligned with the new USP <1660> guidance «Evaluation of the Inner Surface Durability of Glass Containers». The containers to be tested can be drawn from real time stability samples or generated under accelerated aging conditions to determine the amount of chemical attack from drug products on containers and assess the risk of glass delamination occurrence through the shelf-life of the drug product. SCHOTT pharma services uses a combination of the following methods:

Study protocol:

The design of the study protocol depends strongly on customer requirements. An exemplary study design for the predictive delamination screening at 60°C of a product with a shelf life of 2-3 years at 25°C is depicted in Table 1.

1. Visual inspection by eye and magnifying video camera with respect to the presence of particles or flakes (10 filled vials per pull point according to Table 1).
2. Optical inspection of emptied containers per set and pull 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 pull point according to Table 1). Ranking of samples on the basis of optical inspection and selection of 2 'worst' samples for subsequent SEM surface analyses.
3. SEM (scanning electron microscopy) cross-section analyses on the interior surface of 2 containers per set and for selected test conditions and selected pull points as described in Table 1; analyses of two areas: wall near bottom and middle of the vial body. 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 pull points according to Table 1 to quantitatively determine the amount of "glass" elements leached into solution for 4 elements (Si, B, Ca, Al) to ascertain if the amount found is normal or if there is a pronounced chemical attack.

Option 1:

If flakes are observed: Filtration through a filter with a pore size in the sub-micrometer region of 1 container with flakes and SEM/EDS analyses of the filtrate residues.

Option 2:

If the corrosion mechanism is unclear or reaction zones are observed, we conduct SIMS depth profiling (secondary ion mass spectrometry) of the interior surface to get information about the composition of the surface near layer

Method	Storage conditions / pull points						
	After filling	Storage at 60°C					
		0w	1w	2w	4w	6w	8w
Visual inspection	X	X	X	X	X	X	X
Optical inspection	X	X	X	X	X	X	X
SEM cross section anal.	X				X		X
ICP analyses	X				X		X
X: Method applied							

Table 1: Test methods applied for one glass container set and selected pull points for SEM surface and ICP analyses (exemplary study design)

Samples:

At least 10 vials per pull point, we recommend including 5 additional empty vials as reference samples. In addition 20 mL of the placebo or drug solution is needed to adjust the matrix of the ICP measurements and the MSDS sheets and/or product data sheets are mandatory.

Deliverables:

The study will be conducted aligned with USP <1660> and according to the requirements given by DIN EN ISO 17025 standard. At the end a summary report with the respective results and an assessment of the delamination risk will be created.

Estimated price: (for exemplary study design without options)

EUR 9,736.0

For detailed quotation or further information please contact:

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