EVERIC™ pure

Feature: Delamination under full control

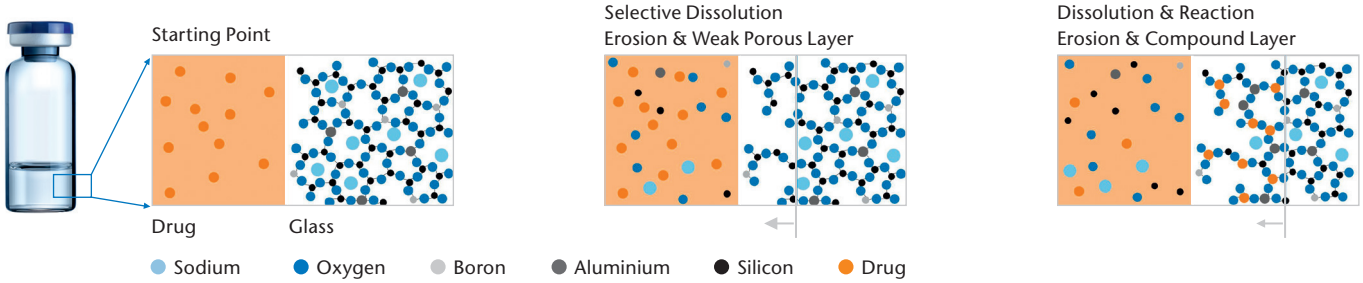
General Product Information

Recent achievements in the field of glass processing technology allowed for the development of EVERIC pure™ vials. The region near the bottom of these vials particularly show a unique surface homogeneity and chemical stability. As a result the tendency of delamination is reduced. EVERIC pure™ complies with all current standards, such as Ph.Eur., USP and JP.

Physical & Chemical Product Properties

Standard converting processes lead to inhomogeneities on the surface of the glass composition near the inner bottom region of the vial. This zone is highly sensitive to delamination. By using enhanced processing techniques SCHOTT is able to reduce the tendency of delamination.

Mechanisms of glass attack and delamination risk



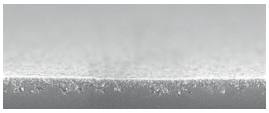
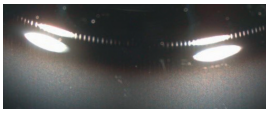
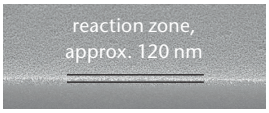
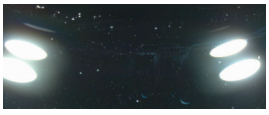
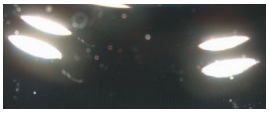
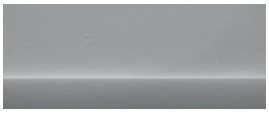
Verifications

The improved properties of EVERIC pure™ have been tested using the following methods:

- Corrosive stressing of the vial
- Analysis of the region near the bottom of the vial by Scanning Electron Microscopy (SEM) with the use of cross section polarized light microscopy
- Results of aging study with 2R vials after 12 weeks with 15 % KCl-solution, at **60°C**

Results:

- Stereo microscopy reveals colored diffusive areas in the region near the bottom of standard quality vials
- SEM and various additional studies proved that the extent of the colored diffusive areas correlate with an increased delamination risk under the same test conditions
- EVERIC pure™ does not show diffusive areas and have a high surface homogeneity (see SEM)

Time	T = 0		T = 12 weeks	
	Stereo microscopy	SEM	Stereo microscopy	SEM
standard quality vial				
	Quicktest results: **8.0 µg/ml Na_2O**		Reaction zone: **YES**	
EVERIC pure™I				
	Quicktest® results: **3.5 µg/ml Na_2O**		Reaction zone: **NO**	

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Testing Information

SCHOTT has developed the **"Dela Sample Kit"** to be tested at the customer which combines primary packaging containers of two different quality steps using FIOLAX® glass (Type I borosilicate glass).

	EVERIC™ vials	dela test vials
USP <660> & EP 3.2.1.	complies	complies
Quicktest limit value	complies	exceeds

EVERIC pure™ vials are produced with an improved production process to ensure that the glass surface in the delamination critical wall near the bottom area is homogeneous and therefore less susceptible to delamination. In addition, the Quicktest is applied to certify that the set sodium limit is not exceeded ensuring that the tendency of delamination is minimized.

The dela test vials are produced in accordance with regulatory requirements such as EP 3.2.1 and USP <660> surface glass test purposely exceeding the limits defined by the Quicktest, which is a measure for an increased vulnerability in the wall near the bottom area. This type of vial can be considered as vial with an increased risk of delamination and can therefore be used for positive testing.

Please note that SCHOTT does not recommend primary packaging containers with reduced surface alkalinity (low EP) value only to minimize the risk for delamination.

USP 1660 recommends predictive screening studies
Delamination of glass flakes in primary drug packaging has become a serious quality concern in recent years. Chapter <1660> of the United States Pharmacopeia (USP) therefore recommends performing predictive screening studies of the drug formulation with the glass container to evaluate the risk of delamination in an early stage of the drug development. The results of such predictive studies allow a graduated assessment of the delamination risk on the basis of early indicators of this phenomenon and help to select appropriate container/formulation systems to proactively prevent delamination.

Value-adding Product Benefits and Services

Optimized total cost of ownership
High quality vials with low delamination risk ensure a consistent, superior performance throughout the product life cycle.

High glass surface homogeneity and quality
The new processing technique achieves unique glass homogeneity and vial to vial reproducibility.

Applicable to registered products
Standard quality vials can be replaced by EVERIC pure™ without the need for a new registration of the pharmaceutical product.

Improved delamination stability
Due to the revised surface homogeneity, EVERIC pure™ shows greater delamination stability compared to standard quality vials.

Verified production quality
The stability of the production process is routinely inspected by the Quicktest.

Ready-To-Order

EVERIC pure™ is delivered in special trays with optional separators to avoid glass-to-glass contact.
A standard Euro Pallet (1200 x 800 mm) contains 15 – 27 layers of 9 trays.

Capacity	2 R	4 R	6 R	8 R	10 R	20 R	30 R
Pieces/tray	344	344	186	186	154	99	99

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SCHOTT AG
Hattenbergstrasse 10
55122 Mainz
Germany
Phone +49 (0)6131/66-1589
Fax +49 (0)3641/28888-9408
pharmaceutical_packaging@schott.com

www.schott.com/pharmaceutical_systems

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EVERIC™ pure

Feature: Unmatched drug stability for low-fill volumes

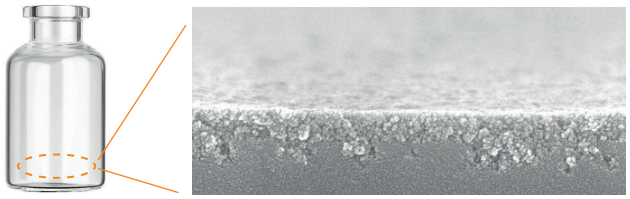
General Product Information

EVERIC™ pure gives evidence for the potential to reduce the vulnerability of tubular borosilicate vials by using an improved manufacturing process in combination with suitable monitoring tests.

The resulting EVERIC™ pure vials feature high resistance to dissolution and in consequence low concentration of lea- ched "glass" elements when using low filling volumes. In particular, the reduced sodium release could be very beneficial for unbuffered product solutions to prevent a shift in the pH-value and conductivity. The vials comply with all current standards, such as Ph.Eur., USP and JP.

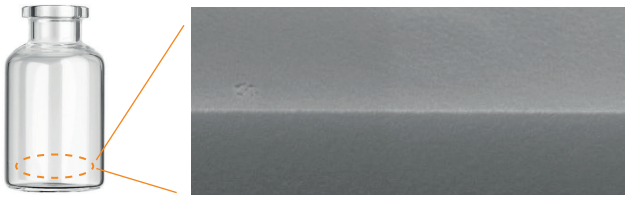
Chemical properties of EVERTIC™ pureresulting from an analysis of near-bottom region of vial after 4 h autoclaving

Standard vials



Inspection | Scanning Electron Microscopy

EVERIC™ pure vials



Inspection | Scanning Electron Microscopy

Verifications

Surface homogeneity and improvement for low filling volumes

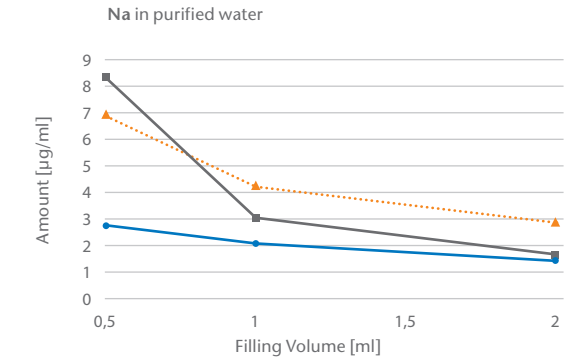
Method:

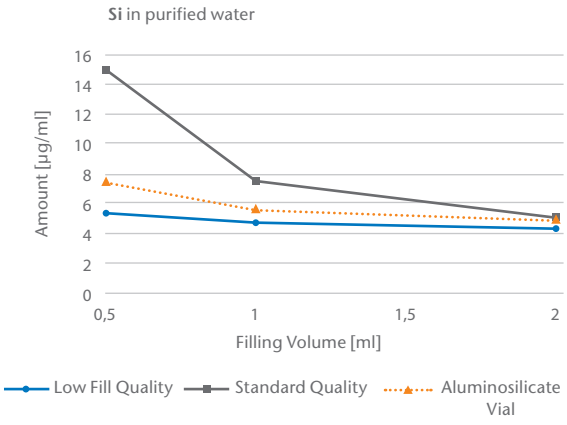
- Filling of 3 2R glass vials: standard quality (FIOLAX®), EVERIC™ pure (FIOLAX® CHR), aluminosilicate vials
- 3 filling volumes: 0.5 ml, 1 ml, 2 ml (by using a pipette)
- Solutions used: Na, Si in purified water
- Storage time and temperature: 24 weeks at 40 °C
- Measurement by ICP analysis for glass elements

Results:

- Guidance: limit of ISO 4802 is 2.4 Na µg/ml
- Amount of [µg/ml]

The two tested vial types from FIOLAX® demonstrate a significantly different impact of the filling volume on the leachable profile. EVERIC™ vials feature high resistance to dissolution and in consequence low concentration of leached glass elements when using low filling volumes. In particular, the reduced sodium release could be very beneficial for unbuffered product solutions to prevent shift of pH-value of conductivity. For the standard quality vials a strong increase of leached glass elements occurs in the heel region of the vials when using common converting procedures for low filling volumes.





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Testing Information

For production control, stereo microscopy is replaced by AAS, sodium content determination.

Quicktest testing procedure

Stage 1

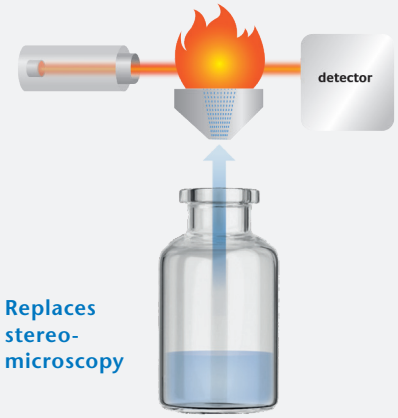
Autoclaving
Empty head first
t = 4 h
at 121°C

Stage 2

Autoclaving
Filled with H_2O
t = 2 h
at 121°C

Stage 3

AAS (Atomic Absorption Spectroscopy)



Replaces stereo-microscopy

Stage 1

Autoclaving induces glass stress in head first empty vials. Vials with poor surface homogeneity will be more affected than vials with high homogenous surfaces.

Stage 2

Autoclaving vials containing low water quantities will extract ions similar to ISO 4802.

Stage 3

The extraction solution of stage 2 is analysed by Atomic Absorption Spectroscopy (AAS) to determine the amount of sodium.

Specified Quicktest limits per format

Capacity	2/4 R	6/8 R	10/15 R	20-30 R
Filling Volume [ml]	1.0	3.5	4.0	7.5
Quicktest limits [µg/ml Na_2O]	4.5	2.7	2.5	1.5

Value-adding Product Benefits and Services

Optimized total cost of ownership

EVERIC™ pure ensures a consistent, superior performance throughout the product life cycle.

High glass surface homogeneity and quality

The new processing technique achieves unique glass homogeneity and vial to vial reproducibility.

Applicable to registered products

Standard vials can be replaced by EVERIC™ pure vials without the need for a new registration of the pharmaceutical product.

Verified production quality

The stability of the production process is routinely inspected by the above outlined Quicktest.

Ready-To-Order

EVERIC™ pure vials for an unmatched drug stability are delivered in special trays with optional separators to avoid glass-to-glass contact. A standard Euro Pallet (1200 x 800 mm) contains 15 – 27 layers of 9 trays.

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SCHOTT AG
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Phone +49 (0)6131/66-1589
Fax +49 (0)3641/28888-9408
pharmaceutical_packaging@schott.com

www.schott.com/pharmaceutical_systems

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