What is the Risk of Losing CCI of Syringes at Cryogenic Temperatures?

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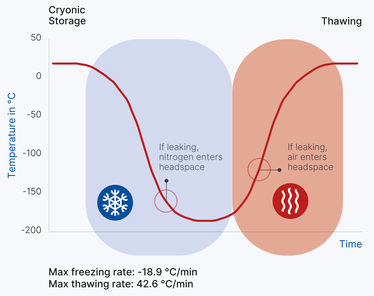
Introduction

Maintaining container closure integrity (CCI) during cryogenic storage is a challenge for syringes. To address this, LIGHTHOUSE developed two USP <1207> compliant methods that either measures CCI loss during storage or CCI loss during thawing. These methods use non-destructive headspace oxygen gas analysis to detect CCI failures. [1] [2] This poster elaborates on the method's application by testing a range of real-world defects in SCHOTT TOPPAC® polymer syringes and assessing their impact on CCI, ensuring robust detection of potential risks.

Method

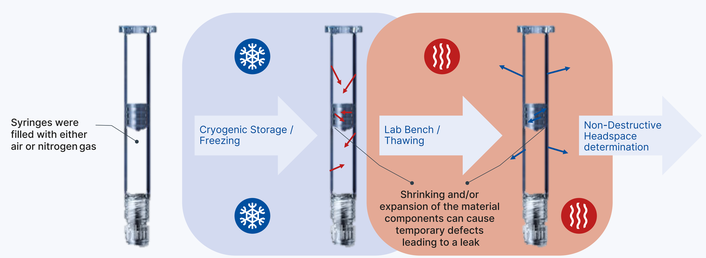
Two sets of empty samples were tested: one with an air headspace to assess CCI during cryogenic storage, and another with a nitrogen headspace (nitrogen >99.5%) to evaluate integrity during the thawing process. These samples were stored in a cryogenic freezer at approximately -170°C for either 24 hours (air headspace) or 2 hours (nitrogen headspace). Headspace oxygen levels were measured non-destructively both before and after storage. Any CCI failure would be indicated by a corresponding increase or decrease in oxygen levels, depending on the initial headspace composition.

Representation of the temperature of the TOPPAC syringe over time into, during and after cryogenic storage



Max freezing rate: -18.9 °C/min
Max thawing rate: 42.6 °C/min

Schematic overview of the TOPPAC syringe CCI testing methods

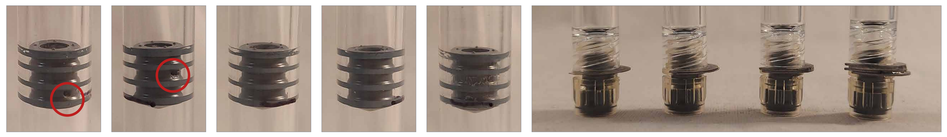


Results

The results show that the methods successfully detected a large variety of real-world defects. The intact test samples, the silicon free barrel and the worst dimensional fit samples showed no loss of CCI during cryogenic storage and thawing, indicating a robust container closure system. The other chosen defects showed loss of CCI during the cryogenic storage, while only the 2.0 mm rigid cap gap and the 1.0 mm hole between the trim and 1st rib showed loss of CCI during thawing.

	Test Samples	Syringe Needle 25G x 25 mm	10 µm Laser Drilled Hole	200 µm Drilled Hole on a Frozen Sample	Short opening of Rigid Cap	Minor Scratches	Severe Scratches	Micro-Wire 41 µm	Micro-Wire 64 µm
# of samples per set	40	3	10	10	10	10	10	10	10
CCI failure # during cryogenic storage (rejected: ≤15.0% atm headspace oxygen)	0	3	10	NA*	NA*	0	2	1	5
CCI failure # during thawing (rejected: ≥5.0% atm headspace oxygen)	0	3	NA*	10	10	0	0	0	0

* This permanent defect is not representative of a failure during this CCI method



	1.0 mm Hole between 1st and 2nd Rib	1.0 mm Hole between 2nd and 3rd Rib	Worst Dimensional Fit Low	Worst Dimensional Fit High	Silicon Free Barrel	0.2 mm Rigid Cap Gap	0.4 mm Rigid Cap Gap	1.0 mm Rigid Cap Gap	2.0 mm Rigid Cap Gap
# of samples per set	10	10	10	10	10	10	10	10	10
CCI failure # during cryogenic storage (rejected: ≤15.0% atm headspace oxygen)	6	0	0	0	0	2	4	7	8
CCI failure # during thawing (rejected: ≥5.0% atm headspace oxygen)	1	0	0	0	0	0	0	0	0

Conclusion & References

- The SCHOTT TOPPAC® polymer syringes maintain CCI during cryo storage and after thawing, when no defect is manually introduced.
- The rapid, non-destructive method can detect in a wide range of real world defects during cryogenic storage.
- The headspace oxygen analysis differentiates between different CCI failure modes, offering data-driven insights into potential risks to package integrity during cryogenic storage and subsequent thawing.
- The impact of different freezing and thawing rates on the CCI of polymer syringes should be further investigated.

[1] P. Bracco, and T. van Ginneken, Challenges and Solutions of CCI Syringe Testing at -180°C. Presented at the PDA Parental Packaging Conference in Copenhagen, Denmark on 23-24 April 2024.
[2] USP, "Package Integrity Evaluation – Sterile Products," in United States Pharmacopeia, U. S. P. Convention, Ed., 2017, p. 1707.

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