Prefilled Syringes for Deep Cold Storage

New Primary Packaging Solution for Biologics based Drugs Requiring Storage at -80°C

Autor:

Philip Bortner
Global Product Manager Syringes

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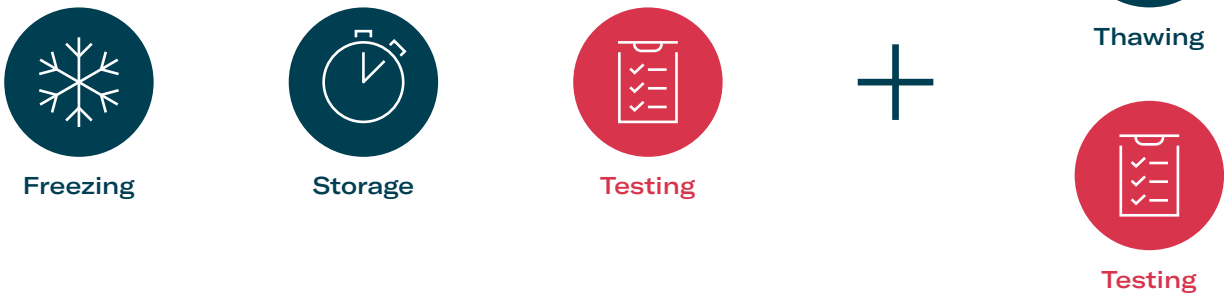
Background

- Pharmaceutical market is developing rapidly into the direction of highly sensitive biologics based drugs
- COVID-pandemic specifically accelerated the development of mRNA vaccines which are extremely sensitive
- mRNA vaccines typically require storage at -80°C due to their high sensitivity
- State-of-the-art packaging is a miultidose vial a shift towards PFS is longed for due to higher dose accuracy, more exact filling volumes and easier handling
- Maintaining functionality and container closure integrity throughout the storage process is essential for prefillable syringes and must be proven

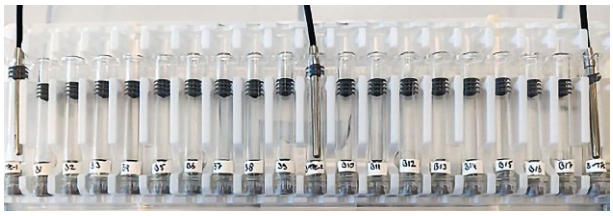
Principle of Testing Functionality

Principle of Testing Container Closure Integrity



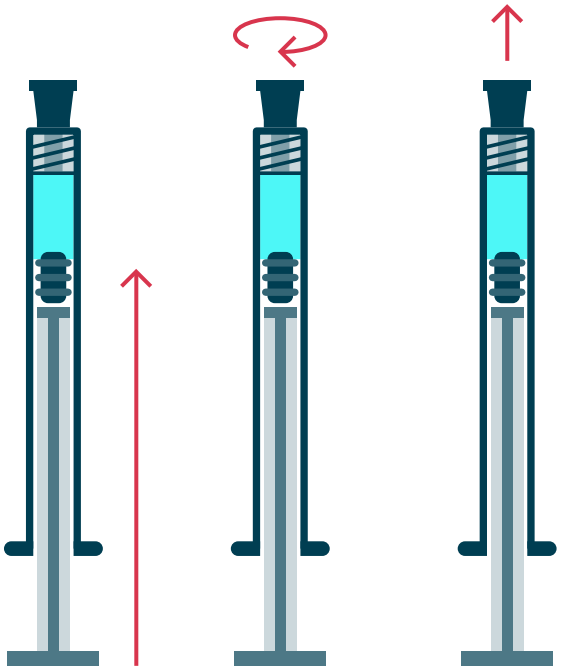
Container Closure Integrity

- Container Closure Integrity is the most challenging requirement for -80°C storage since it must be maintained during the entire storage process
- For testing the CO_2 ingress method followed by laser headspace analysis with a light-house instruments FMS analyzer was used
- COP syringes with uncoated plunger stopper were tested
- Test samples were stored for 24h at -80°C
- Positive and negative controls, as well as temperature probes were included in the test setup
- To create a CO_2 atmosphere during storage and thawing, syringes (put in trays) were placed inside a Zip Lock Bag filled with CO_2



Functionality

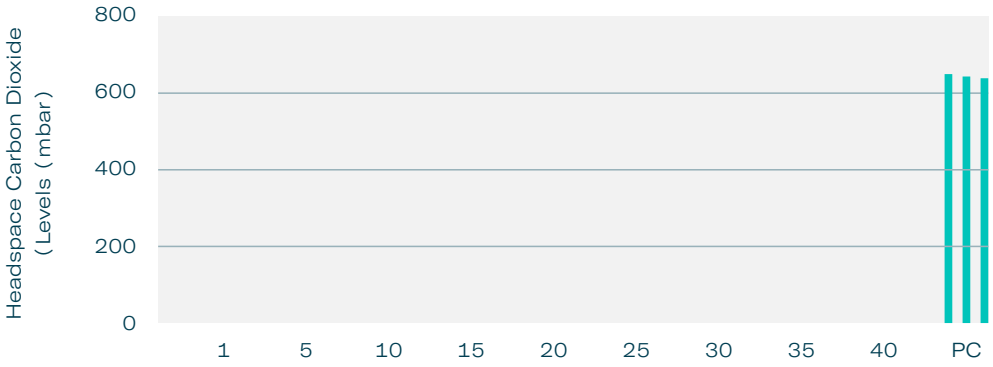
- Functionality includes tests for Break-loose- & gliding-force, mechanical stability, tip side opening torque and Tip side pull-off-forces
- All tests (except mechanical stability) were performed after 6 months storage at -80°C with filled syringes and after thawing
- To display mechanical stability, breakage force was measured for frozen syringes as well as for thawed syringes
- All tests were performed with a ZWICK tensile strength testing machine



Container Closure Integrity – Results

40 samples have been tested, with positive controls (=„PC“) and temperature controls placed on the edge and the middle of the tray. Temperature was tracked throughout the thawing process to determine the maximum thawing rate. No test sample showed CO_2 ingress above the threshold of 10 mbar.

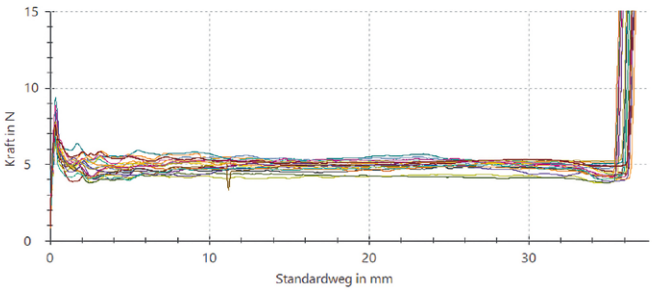
CO_2 ingress after 24h storage and thawing



Max. thawing rates (°C/min)	
Outside	18,3
Center	15,5

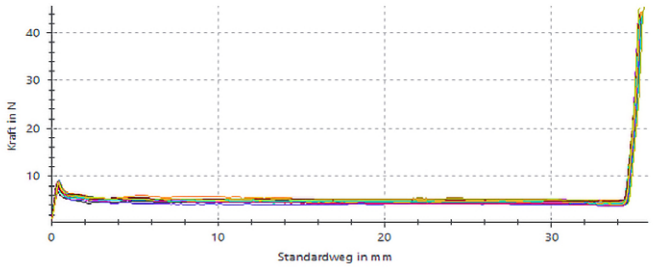
Break-lose & Gliding Force – Results

6 months storage at -80°C



X	7,41N
S	0,84N

6 months storage at room temperature



X	8,34N
S	0,47N

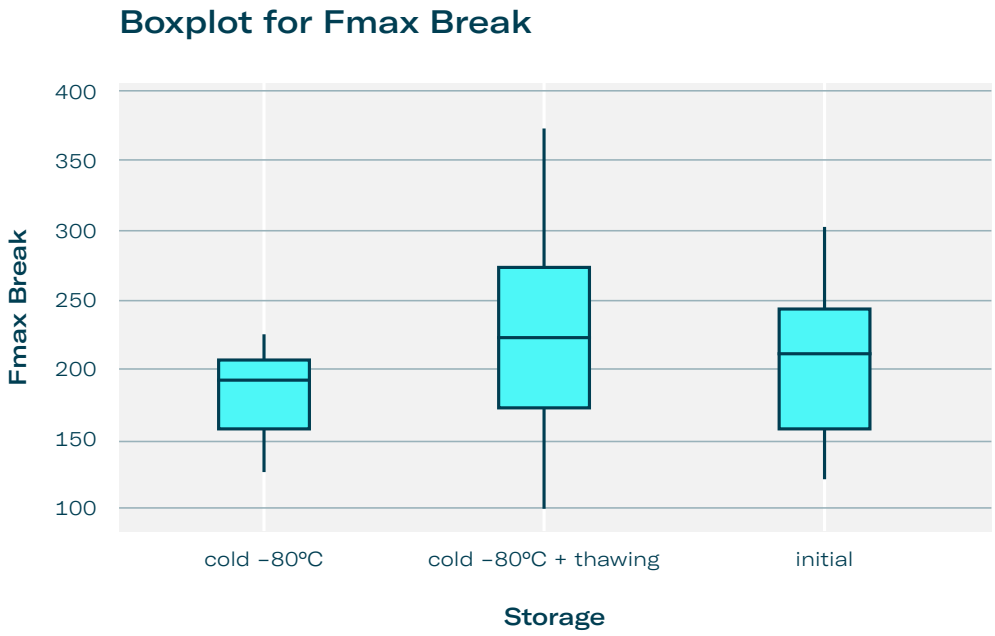
For Break-loose- and Gliding-Force no negative impact caused by -80°C storage can be noticed

– Functionality for BLGF is maintained

Breakage Resistance – Results

Breakage resistance is not impacted during storage at deep cold temperatures. Thawing causes wider spread minimum and maximum values.

- mechanical stability is still maintained at deep cold temperatures
- further investigations need to be done for behavior after thawing



Conclusion

Functionality is not impacted negatively by storage at deep cold temperature

CCI is maintained for the combination of COP and uncoated rubber formulations at thawing rates of up to ~18 °C/min

Outlook

To further investigate suitability for deep cold storage test with higher thawing rates need to be performed

To create a deep cold suitable portfolio and to target biologics with silicone sensitive LNP's, different plunger stopper and siliconizations need to be tested.

Contact

Philip Bortner
Global Product Manager Syringes

T +49 9431 639 6515
M +49 170 1981105
F +49 9431 639 89 6921
philip.bortner@gerresheimer.com

Medical Systems
Gerresheimer Regensburg GmbH
Oskar-von-Miller-Straße 6
92442 Wackersdorf

www.gerresheimer.com

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