# Functionality of Glass Pre-fillable Syringes After -40°C Storage: Data on the Glass Barrel and Sealing Interfaces **NIPRO** Live Longer. Live Better.

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# Introduction

mRNA technology represents a significant break through in drug development. Several mRNA- based vaccines candidates are in the pipeline for the prevention of influenza, respiratory syncytial virus, cancer, and other diseases.

When glass pre-fillable syringes have been developed, typically tests have not been carried out at temperature below 0°C.

Low temperatures can affect the flexibility and visco-elasticity of rubber components, potentially causing functionality concerns and impact the container closure integrity (CCI)

With this poster, we provide new data on low temperature storage with a focus on the behavior of the glass barrel and the sealing interfaces.

#### Materials and Methods

Nipro D2F1 mllong glass pre-fillable syringes with Luerlock Integrated Cap(LInC), FM30 Tip cap, spray-on silicone (Nipro low silicone amount), plunger stopper FM457.

32 samples per each test and time point, for plunger position test 16 samples per time point. Filled with 1ml WFI, plunger placement with vent tube.

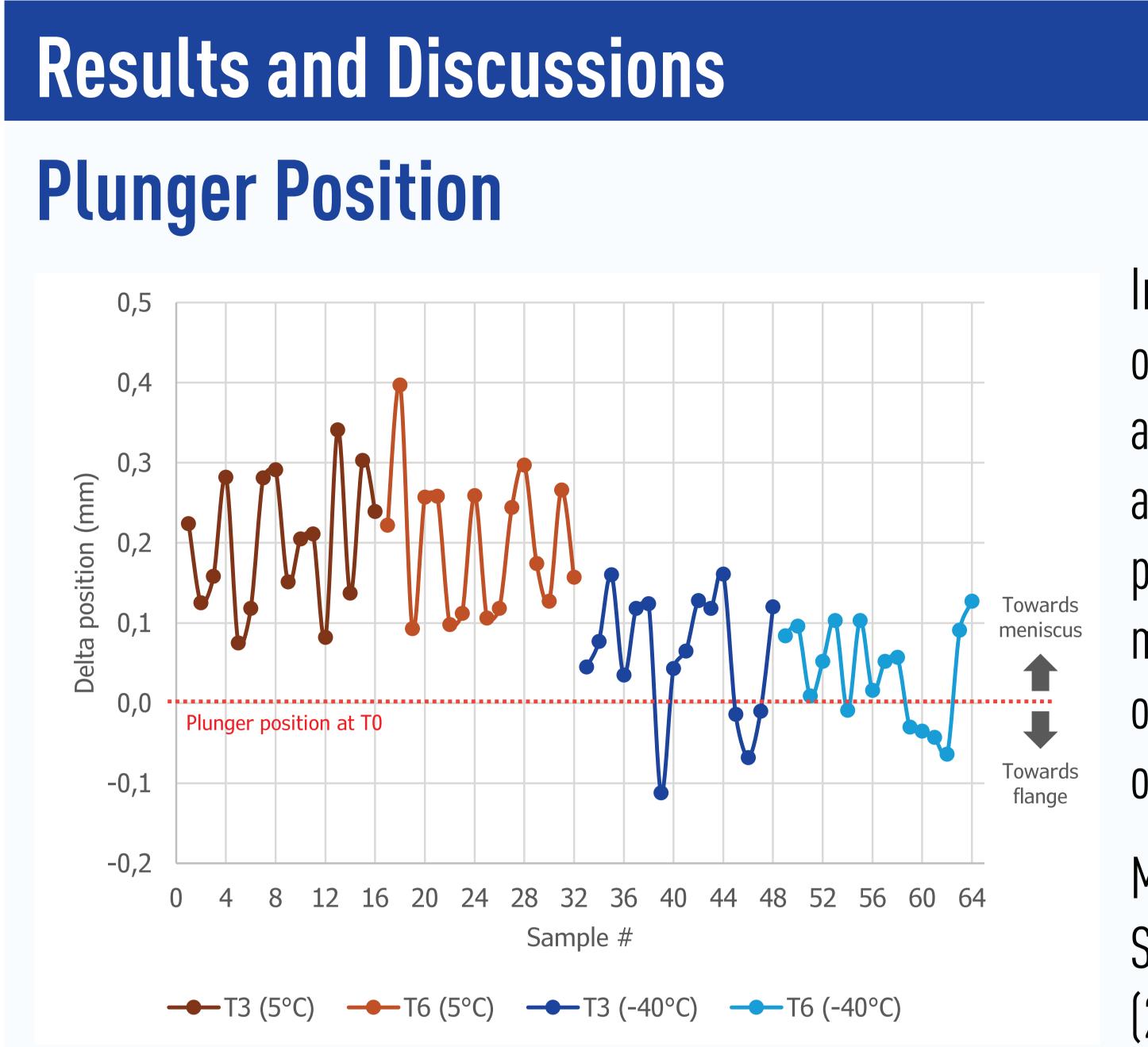
Storage in freezer at constant T°C of -40°C up to 3 months (T3) and 6 months (T6). For plunger position, also control samples stored at 5°C have been evaluated. Samples have been thawed at room temperature and tested after 30 minutes of resting time.

Key Attributes	Test
CCI related	<b>Dye solution tightness</b> (acc. ISO 11040-4 an
	<b>Plunger position</b> (profile projector)
Functionality	<b>Break-loose &amp; Gliding force</b> (speed: 100mm / min)
	<b>LLA pull-off force</b> (bench top lloyd measuring device)
	LLA torque & RC unscrew torque (zwick measuring device)

[PFS: Pre-fillable syringe | LLA = Luer-lock adapter | RC = Rigid cap | PoF = Pull-off force | Tg = Glass transition temperature | CTE = Coefficient of thermal expansion]



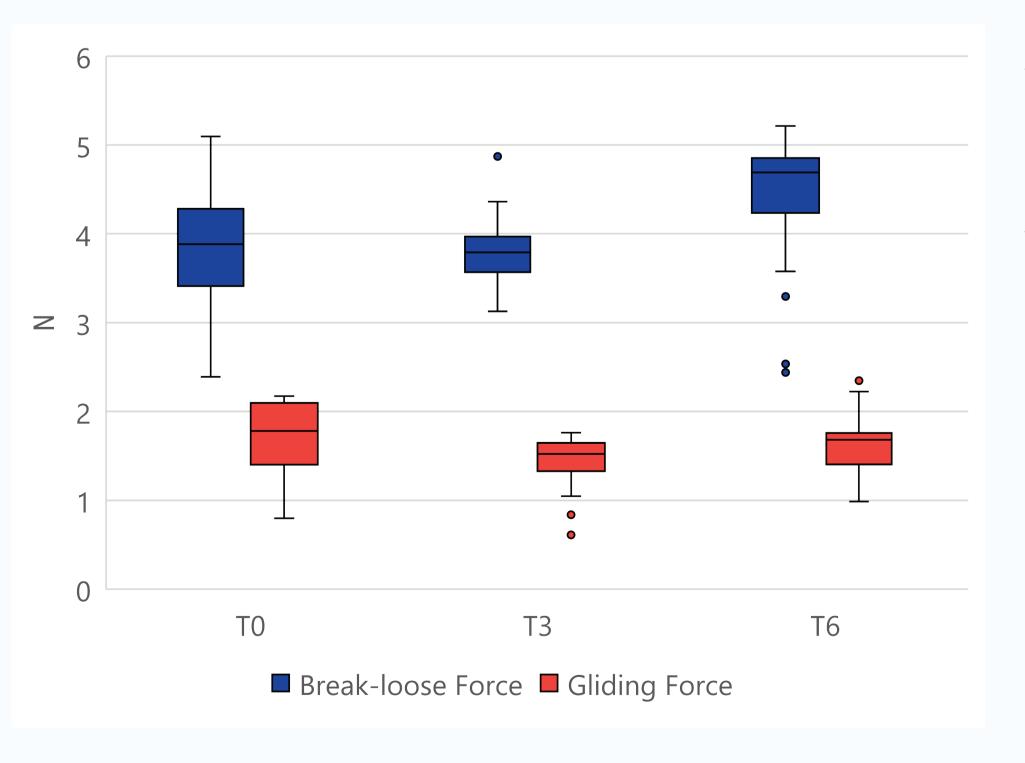
nnex H)



Minimum rubber stopper diameter is 6.8mm. Seen the CTE of the rubber stopper formulation  $(221\mu m/m °C)$ , it will shrink until the diameter of 6.77mm and 6.70mm if they are undergone to a cooling from RT to 5°C ( $\Delta 20$ °C ) and from RT to -40°C ( $\Delta 65$ °C) respectively. CTE of the glass is 5.1µm/m °C between one and two orders of magnitude lower with respect to the CTE of the rubber, so it has been considered neglectable.

In addition, low temperatures decrease the pressure of the gas in the headspace dragging the stopper towards the meniscus. Behavior of the plunger at  $-40^{\circ}$ C is more difficult to predict, due to the increase of the volume of the frozen water that is affecting the headspace and the plunger position potentially. Further study is planned by adding measurements points right after removal of PFS from cold storage, it might provide a more accurate and continuous behaviour of the rubber stopper overtime.

# **Break-loose and Gliding Force**



After thawing, 25G  $\frac{1}{2}$  disposable needle was connected to the PFS (T3 and T6). Limits are not set-up because syringes are filled.

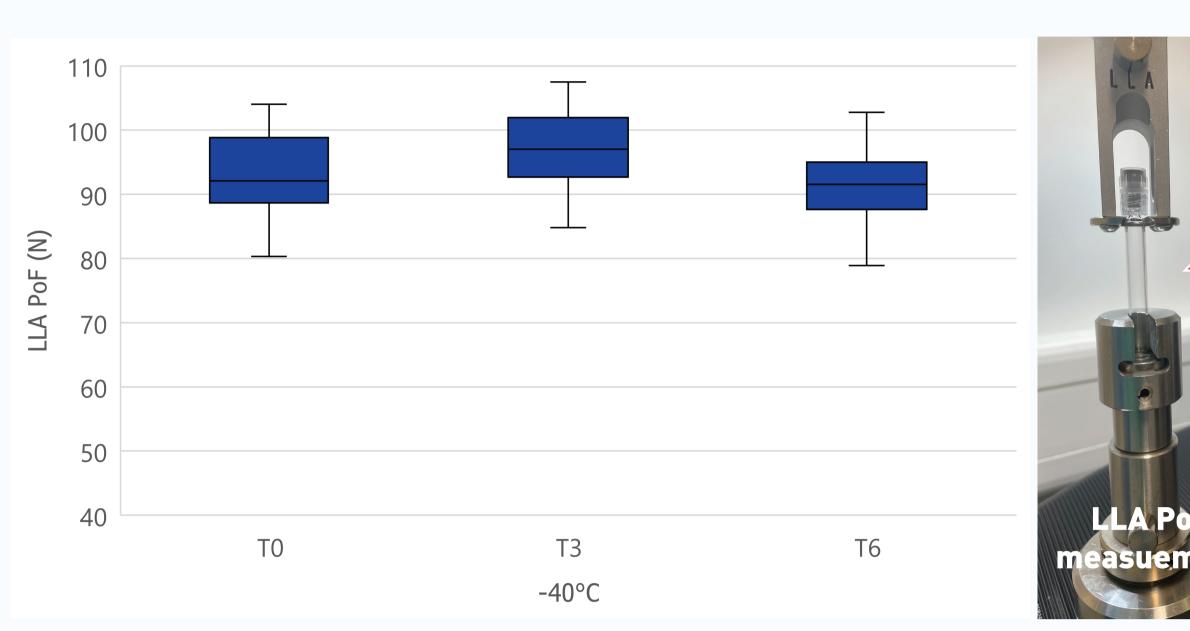
We can observe a narrow distribution of value for break-loose and gliding force after 3 and 6 months of storage, indicating comparable performance than at TO. Silicone oil functionality is not impaired.

#### **Results & Discussions**

This study demonstrates suitability of glass pre-fillable syringes down to -40°C storage. All key attributes for container closure integrity and functionality of glass pre-fillable syringes have been met. Break-loose & Gliding force, LLA Pull-off force, LLA torque & RC Unscrew torque data are within the industry-acceptable limits. The plunger position measurement confirms that consideration must be taken by using rubber materials designed to maintain physical and mechanical properties at low temperatures.

In order to guarantee the CCI (so the sterility) of the PFS system the movement of the plunger after storage should be evaluated. Since we are above the Tg temperature of rubber, the parameters playing a pivotal role in plunger movement after cold storage are: the behavior of the gas in the headspace and the shrinkage of the rubber stopper.

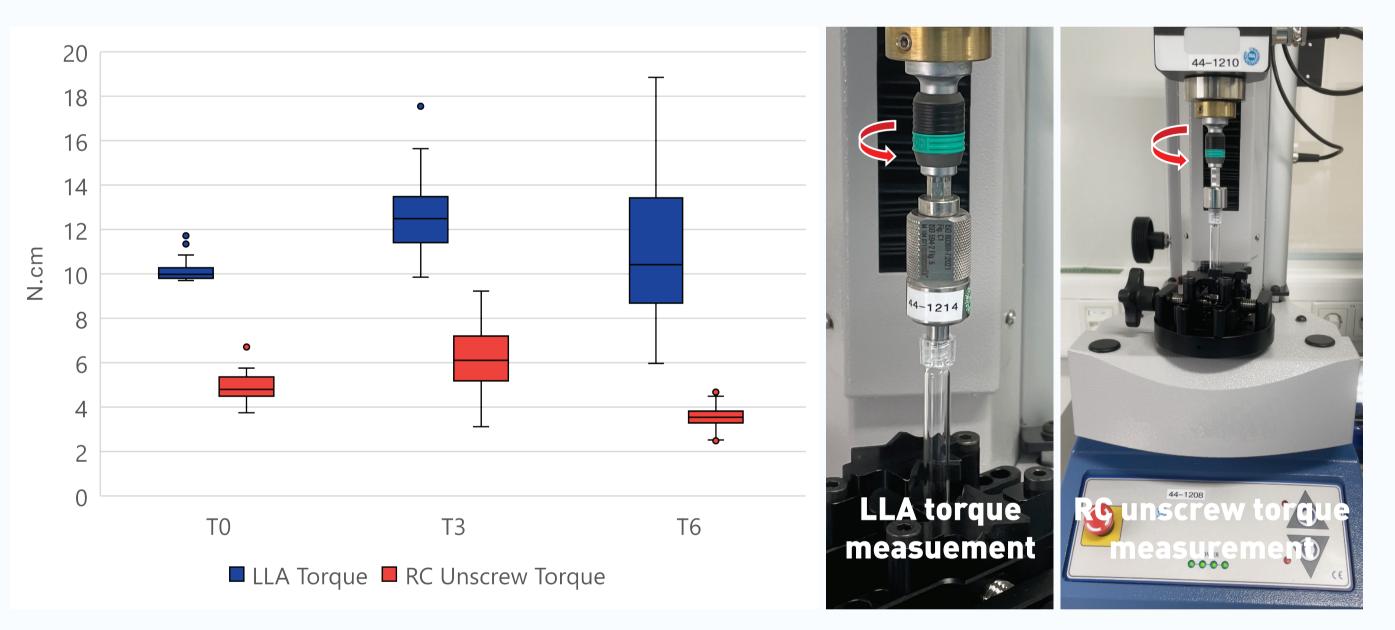
## **LLA Pull-off Force**



All single data remains above the industry- acceptable lower limit.

Cold storage does not impact significantly the connection tightness between the LLA (Polycarbonate PC material) and the glass conus. Since the Tg of the PC is very high (> 100°C), the LLA has a brittlelike behavior at both room  $T^{\circ}C$  and  $-40^{\circ}C$ . This could explain the comparable values at TO, T3 and T6.

### **LLA Torque and RC Unscrew Torque**



storage and a narrow distribution of value for RC unscrew torque. This can be seen as neglectable as all single data are within the industry-acceptable limits.

The screw coupling between LLA and RC is a pivotal factor to guarantee an unscrew force above a threshold value. The thermal shrinkage of the two components and the switch from a plastic-like behavior to a brittle-like behavior of the PP-made RC (Tg  $\simeq$  -10°C) might affect this parameter.

# **Dye Solution Tightness Test**

All passed at -40°C.



Pull-off force is an indicator of proper functionality and CCI over fill-finish processing steps and end-user final usaqe

We can observe similar distribution of value after 3- and 6-months storage, indicating comparable performance to TO.

> LLA torque & RC unscrew torque are indicators to proper functionality and CCI over fill-finish processing steps and end-user final usage.

> We can observe an increase in the distribution of value for LLA torque after 3 and 6 months of