GLASS TO PLASTIC
An innovative prefilled syringe (PFS) for biopharmaceutical products

**New directions in the parenteral industry issues**

Historically, glass has been the preferred primary container material for parenteral medicines mainly due to the material technical attributes of permeability. However, bio pharma drugs, new technologies and manufacturing processes are changing the glass dominated industry, and are opening the doors for an alternate material: Cyclo Olefins Polymers (COP) plastic.

Drugs used to be contained in glass vials and administered in healthcare facilities by professionals but with an increasing trend towards self-administration and at-home administration, prefilled syringes (PFS) has emerged in the early 2000’s. The growing popularity of PFS is due to the ease of facilitating the injection process, the reduction in the total injection steps, the improved user safety and the reduction dosage errors.

Even though glass syringes are capturing most of the market share today, plastic has successfully replaced it in numerous applications thanks to key advantages. When developing a drug for PFS, the Pharmaceuticals companies consider the following four aspects: the drug/ primary container interaction; the user interaction; the machinability; quality and regulatory compliance. Plastic offers advantages over glass in each of these categories.

**Advantages of plastic over glass**

Drug formulations are highly sensitive to any contact materials. Even though glass itself offers high barrier properties to gas and oxygen, the usage of silicone oil, tungsten and adhesive are mandatory in the manufacturing process of glass PFS. The glass PFS use silicone oil to lubricate the syringe to lower the gliding force. Tungsten pins are required in the manufacturing process to keep the bore of the syringe open while the cone is being shaped. Heavy metal is inherent to the primary container and its manufacturing process.

Those materials being absent in plastic PFS, and the no PH variation, makes plastic a challenging material to consider. The absence of silicone oil replaced by other processes allows for a constant gliding and prevents improper lubricated areas, resulting in increased force required to inject with glass PFS. Moreover, studies have highlighted the impact of silicone oil and tungsten residues in protein aggregation. Their absence in plastic prevents this phenomenon.
From a machinability point of view, glass breakage and cosmetics defects are a common problematic with glass PFS. Glass is highly sensitive to shocks, either during transport, storage, assembly or handling. However, COP plastics are known for their robustness and resistance to shocks, preventing potential drug loss prior injection. Indeed, COP materials are a relatively new class of amorphous thermoplastic polymers. Key characteristics are their glass-like transparency, good mechanical properties and good permeation properties.

With the increase in biologics drugs, new problematics arise. Drugs are often highly viscous, making them hard to self-administer, with syringes equipped of thin needles (e.g. 27G). This phenomenon has led to the development of combination drug delivery system as autoinjectors, pens and safety devices to overcome those issues. This new trend has made glass breakage an even more critical consideration as, a pressure is exercised on the syringe’ flange, during either the insertion into the device or the release of the spring to deliver the drug. The flange being the weakest part of the syringe, delivery systems and pharmaceuticals are limited by the pressure that can be exerted the syringe flange.

Thanks to plastic’ robustness, risk of breakage are prevented and high forces can be applied on the syringe. It gives pharmaceutical also the opportunity to use very thin needles (e.g. 29G) even with viscous drugs, but also to improve patient comfort. Plastic PFS provide also tighter dimensional tolerances compared to glass, thanks to the precision of the process.

Indeed, glass process induced a conical shape whereas plastic provides a perfectly straight one (see picture following picture). As a result, dosage accuracy, injection systems dimensional and gliding force can be optimized.

Remaining plastic challenges

Standard plastic syringes (COP/ PP) offer lower barrier properties to oxygen and gas than glass, making its adoption for certain type of drugs (sensitive to those parameters) not compatible. Improving those barriers while lowering drug-container interaction would be a game changer.

The solution: Nemera Glass to Plastic innovation process

Nemera, with this innovation process, leverages its know-how of plastics, designing, developing and manufacturing complex injection devices over decades. The innovative manufacturing process was patented. This process limits gas permeation, combining premium COP material with a label through in-mold labelling. This expertise has allowed Nemera to overcome current plastic PFS challenges.
Nemera Glass to plastic innovation process also differentiates itself from co-injection on many aspects. Whereas co-injection is a complex manufacturing process associated with high investments, in-mold labelling (IML) is a well known process, steady and implemented into the manufacturing environment. Co-injection requires the injection of two materials in a highly complex manner. First the outer material is injected, followed by the inner one and finally the outer material is injected again to encapsulate the core. As a result, co-injection requires long adjustment process to obtain reproductive layers in which consistency of thickness can vary.

In comparison to co-injection, IML is relatively simple and known process which has made its proofs over the years, providing flexibility and ease of implementation. Differentiating to other processes where a label is added once the part has been injected, with In-mold labeling the label is inserted into the mold during the manufacturing process, the inner layer of the label being welded with the primary container (see picture above).

By selecting a label with high gas properties, Nemera has developed an innovative primary container offering pharmaceuticals increased gas barrier properties compared to standard COP materials. In order to obtain such permeability results, Nemera investigated multiple combinations and patented its own technology.

In this technology the external layer of the label is composed of PET and SiOx to improve the gas properties. The label's inner layer is composed of cyclo olefin to perfectly melt with the COP ZEONEX® 5000 of the cartridge. The ZEONEX® 5000 has been selected due to its natural gas barrier properties compared to other COPs. In order to improve gliding properties and prevent performance issues and aggregation due to silicone oil, the inner layer of the container is treated with a silicone free technology (e.g. Triboglide).

**Investigation results**

In order to validate the technology, permeability tests on molded parts have been conducted at an external laboratory facility. The objective of the tests were to determine the oxygen transmission coefficient at a room temperature of 23°C and relative humidity (HR) of 21%. Measures were performed according to the Norm ASTM D3985 with a OXTRAN 2/20ml machine.

For the purpose of the testing, glass cartridges and plastic ZEONEX® 5000 ones (with and without label) have been provided to the laboratory to test their permeability to O2. Each sample was obstructed at each extremity with a stopper.
Specific gigs were developed to install the parts on the machine. The inner of the parts were continuously sweep by a flow of dry nitrogen before being measured once the process was stabilized. See below a picture of the machine and process.

On the other hand, the ZEONEX® 5000 combined with the specific label presented OTR results as low as $16.10^{-4}$ml per cartridge per day.

Those results are confirming the validity and efficiency of the technology, increasing significantly the gas barrier properties compared to commercialized Cyclo olefins polymers.

**Conclusion**

Glass is no longer the only primary container offering high permeability properties. Combining high quality plastic and specific label with high gas properties, IML provides to pharmaceuticals an alternative to glass with multiple advantages:

- Improved permeability, adjustable according to customer’ needs
- Resistance to shocks
- Flexible design/ and tighter dimension
- No tungsten, no Silicone oil and no adhesive

Results are expressed as Oxygen Transmission Rate (OTR) in milliliter per day per product. Glass presented an OTR of $4.10^{-4}$ml per cartridge per day. ZEONEX® 5000 without label had OTR results of $63.10^{-4}$ml thus fifteen time worse than glass.

Please consult us for more information