THE NEXT GENERATION OF COATED PLUNGERS

In this article, Carina Van Eester, Global Platform Leader, Prefilled Syringes and Cartridges at Datwyler Pharma Packaging, explores the benefits of fully coated plungers for prefilled syringes and cartridges.

These days, it is difficult to avoid the topic of COVID-19. In the healthcare industry, we are seeing the implications of the disease play out not only from a world health perspective but also in the work we do on a daily basis. When our new coated plungers, NeoFlex™, were launched back in February at Pharmapack, we were aware of the crisis our Chinese colleagues were facing but did not expect the global scale that this pandemic would reach only two months later.

With the knowledge that many pharmaceutical companies are developing medication to either treat the effects of or vaccinate people against COVID-19, we are aware that the packaging components accompanying these drugs will be an important factor in delivering these life-saving medications in a safe and reliable way to patients in need.

The common delivery applications for these medications will be sure to involve prefilled syringes and cartridges, which means it is essential to have a robust plunger solution offering exceptional reliability and functionality. Datwyler's solution for this drug delivery challenge is its NeoFlex coated plunger (Figure 1).

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ADVANTAGES OF FULLY COATED PLUNGERS

With the rise of therapeutic biologics, as well as autoinjectors and wearables that facilitate self-administration, there are more drug delivery challenges than ever before. In these prefilled syringe and cartridge applications, plungers must meet strict requirements for drug compatibility, functionality and machineability. The best way to achieve these standards is through a complete fluoropolymer coated plunger.

Figure 1: NeoFlex coated plungers are the ideal solution for sensitive drugs in prefilled syringe or cartridge applications.

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While many coated plungers on the market are only partially laminated, the NeoFlex plunger is fully spray coated, offering several advantages:

1. The fluoropolymer coating is naturally lubricious, so no silicone is required to avoid stickiness of the plunger to the barrel or to other plungers. The absence of added silicone oil also reduces particulate levels
2. There is no ring of uncertainty where the partial fluoropolymer laminate ends and the siliconisation begins. The ring of uncertainty poses a risk that the drug will come into contact with the non-coated part of the product, negating its effectiveness. NeoFlex plungers are fully coated so the drug runs no risk of touching uncoated rubber
3. Processing of the plungers in vibratory bowls is easier due to the uniformly reduced surface friction and the smoothness of the plunger surface
4. The trim edge is at the bottom, undercut and coated. There is no shedding of particulates from the trim edge and no influence on the break-loose and gliding forces.

SPRAY COATING VERSUS FILM COATING TECHNOLOGY

NeoFlex plungers are made with Datwyler's proprietary fluoropolymer spray coating technology. Laminates that are used on some plungers on the market are typically made with polytetrafluoroethylene (PTFE) or ethylene tetrafluoroethylene (ETFE) film. Both the spray coating and laminate technologies have barrier properties. However, many other characteristics are quite different:

1. **Flexibility of the coating**: Datwyler's NeoFlex plunger coating is very flexible and is, in fact, a fluoro-elastomer. As a result, the coated component is able to seal against inherent glass surface imperfections. Under compression, no wrinkles occur which could potentially lead to leakage
2. **Compatibility with gamma irradiation**: while some fluoropolymer films cannot be gamma irradiated, the NeoFlex coating can be, and is not negatively impacted
3. **Uniformity of the coating**: Datwyler's fluoropolymer spray coating is applied in conjunction with a tumbling technology that guarantees uniform coating. In the case of film coating, the film is stretched onto the moulded product, which means there is a higher risk of small holes in the coating and variation in the film thickness across the moulded component.

"Analysing extractable and leachable substances is a significant step in guaranteeing the safety of the drug to the patient."

EXTRACTABLES AND LEACHABLES EVALUATION

Extractables and leachables analysis is a significant step in guaranteeing the safety of a drug to the patient. The rubber compound needs to be assessed in the fully assembled prefilled syringe, including the barrel siliconisation, the needle and the needle adhesive. Extractable studies evaluate compounds which have been forced out from the rubber components into the drug product under laboratory conditions. Similarly, leachables studies test for the migration of rubber into the drug product which has been forced out under laboratory conditions. These tests help to determine drug and rubber compatibility – and serve as an initial determinant for whether the rubber should be coated or uncoated.

It is known that fluoropolymer coatings act as a barrier between the rubber and the drug product. Depending on the rubber formulation, the type of coating and test conditions (e.g. extraction solvent, extraction temperature and sterilisation conditions), the list of potential extractables will vary. The extractables are generally grouped into different categories: metal ions, volatile organic compounds, non-volatile organic compounds and semi-volatile organic compounds. All the various coatings on the market – film and spray coating – considerably reduce extractables.

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FUNCTIONAL PERFORMANCE

The main characteristics to be taken into account to assess the acceptable functionality of a plunger include: break-loose and gliding forces, seal integrity and plunger movement under pressure fluctuations.

While designing the NeoFlex plunger, Datwyler developed a standard between the various performance criteria in order to make sure that the plunger can be used in a wide range of applications. The compression of the plunger and the design of the sealing ribs is optimised to ensure that the break-loose force remains low enough for manual injection while maintaining complete seal integrity and limited plunger movement in the presence of air space. In order to make sure that the plunger is suitable for secondary devices, the consistency of the break-loose and gliding force over the product shelf life is essential.

To preserve sterility, the plunger and the barrel must have an appropriate interference fit. The NeoFlex plungers are designed with a minimum compression of the first sealing rib of 3% during worst-case conditions (e.g. large barrel, small plunger). Due to the flexibility of the coating, there is no negative effect on the performance of the plunger: the coating does not wrinkle, which guarantees seal integrity and no substantial increase of break-loose and gliding forces.

All sealing rib dimensions are controlled by the mould, which guarantees that they are produced with narrow tolerances, with a minimum process capability of 1.33. The trim edge is undercut which prevents contact of the trim edge with the wall of the barrel, giving a better consistency in gliding forces over multiple batches.

BREAK-LOOSE AN GLIDING FORCES

The break-loose and gliding forces of a plunger depend on many factors: barrel siliconisation, needle size, viscosity of the drug, drug formulation, sterilisation conditions, etc.

The plunger force is measured on empty syringes to characterise the interaction between the barrel and the plunger – and to avoid interference from the fluid or the needle size. The gliding force in empty syringes can be substantially different from the gliding force in filled syringes. However, the break-loose force will remain relatively the same.

In order to have data available with regard to interference from the sterilisation on the final break-loose and gliding forces, a test was done with both gamma and steam sterilised plungers. The break-loose and gliding forces were tested in multiple syringes – both glass and plastic/cyclo-olefin polymer – with standard siliconisation, low siliconisation, and cross-linked siliconisation.

Most biological drugs are stored in refrigerated conditions, although in some cases room temperature may be acceptable. While not necessarily representative, accelerated studies at 40°C have been completed to assess the functional performance.

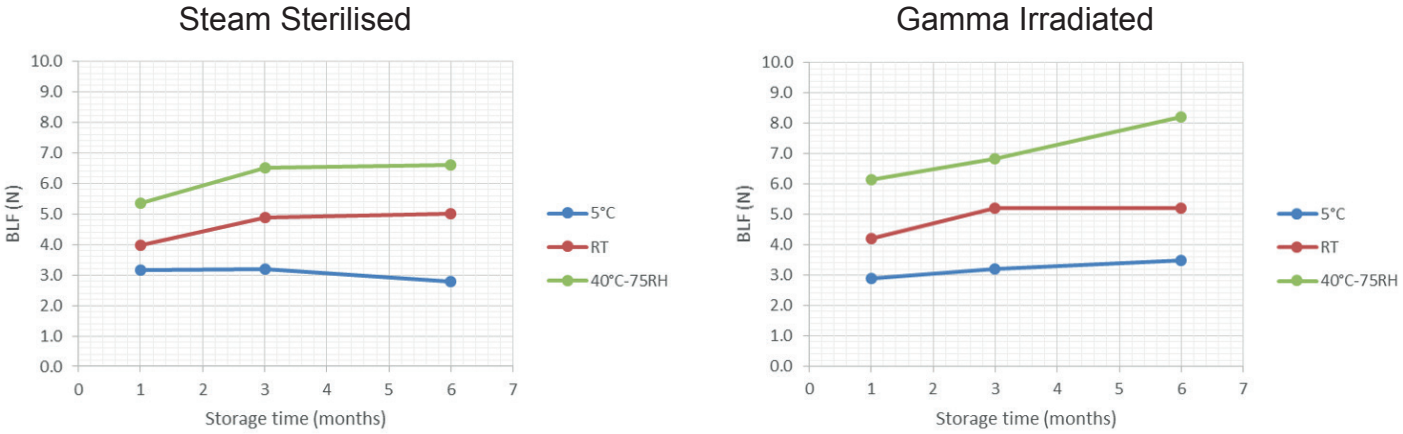

Figure 2: Break-loose force (BLF) at one, three and six months for steam sterilised (left) and gamma irradiated (right) NeoFlex 1.0 mL long plungers in a low siliconised barrel stored at different temperatures.

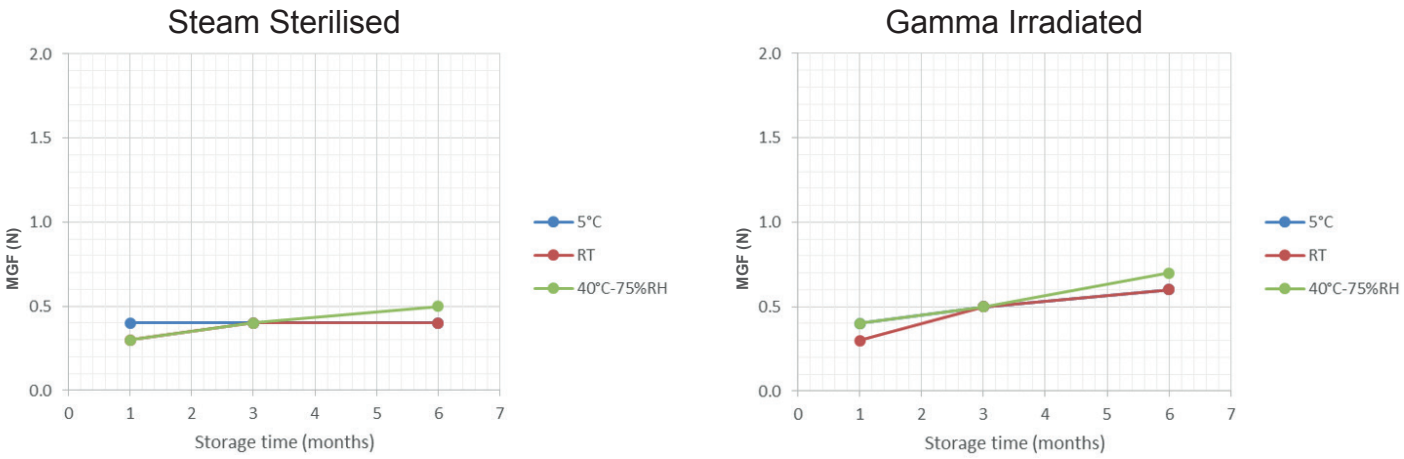

Figure 3: Maximum gliding force (MGF) measured at one, three and six months for steam sterilised (left) and gamma irradiated (right) NeoFlex 1-3 mL plungers in a standard siliconised barrel stored at different temperatures.

The data show that, within a specific temperature range, the break-loose and gliding forces remain low and consistent during storage, even in worst-case conditions – e.g. small barrel, big plunger (Figure 2 and Figure 3).

SEAL INTEGRITY

The sealing ribs of a plunger have two functions:

1. **Guarantee the sterility of the drug:** it is important that no microbes pass the rib farthest from the drug
2. **Prevent loss of content through leakage:** the drug must not pass the first sealing rib and enter the space between the first and second rib. Although all designs have three ribs, Datwyler considers leakage as occurring as soon as the drug passes the first rib.

> "Seal integrity has to be maintained during storage, transport and use."

The rib in contact with the drug is the most important one and, therefore, was tested by means of Helium leak testing, as well as blue dye testing, in both nominal and worst-case conditions – e.g. large barrel, small plunger (Figure 4).

To assess the performance of the seal during use, syringes are filled with blue dye and tested with a pressure of 6 N on the plunger. When no liquid passes the first rib, the plunger seal is guaranteed in dynamic conditions. All NeoFlex designs meet this requirement.

PLUNGER MOVEMENT

Seal integrity has to be maintained during storage, transport and use. In certain instances, the plunger can move under the influence of a change in pressure during air transport. The plunger movement will be limited or zero when there is no air bubble between the plunger and the drug. When there is headspace, the plunger will move if the headspace expands (Figure 5).

Two limits were specified:

- **Warning limit:** the distance between the second and third ribs. If the plunger travels less than this warning limit, it means the third rib is moving into the non-sterile area but the first and second ribs stay in the sterile area and will assure the integrity of the drug
- **Outer limit:** the distance between the first and third ribs. If the plunger travels more than this outer limit, it means all ribs go into the non-sterile area and there is a high risk of contamination of the drug.

In the case of the 3 mL cartridge, it can be concluded that it is safe to have an air bubble of up to 7 mm.

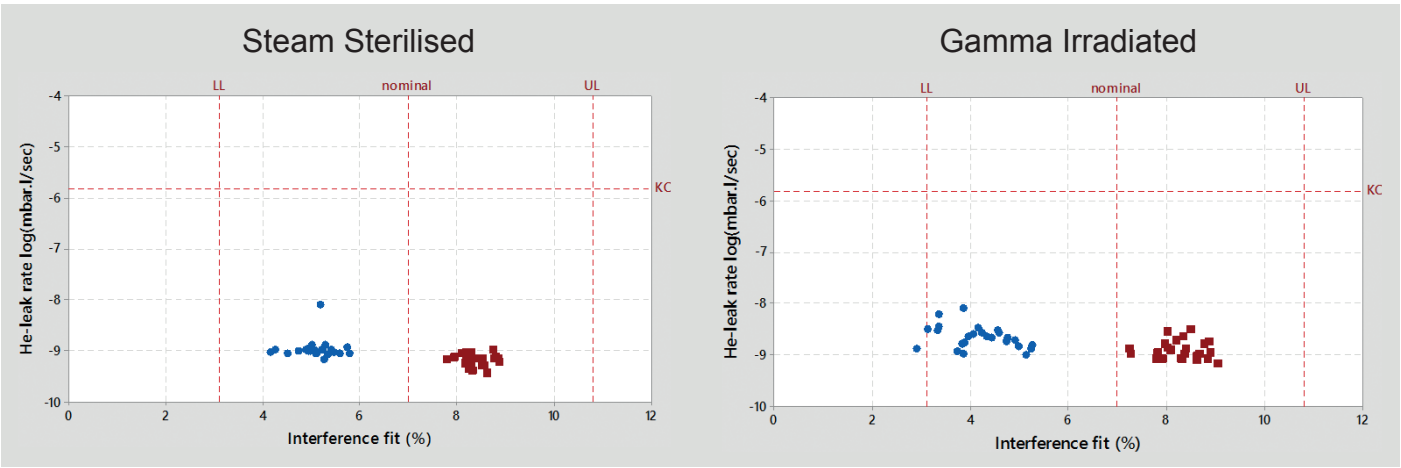

Figure 4: Helium leak rate against interference fit for steam sterilised (left) and gamma irradiated (right) 0.5 mL Neoflex plungers. All cases easily meet the Kirsch Criterion (1.6 x 10^{-6} mbar.L/sec).

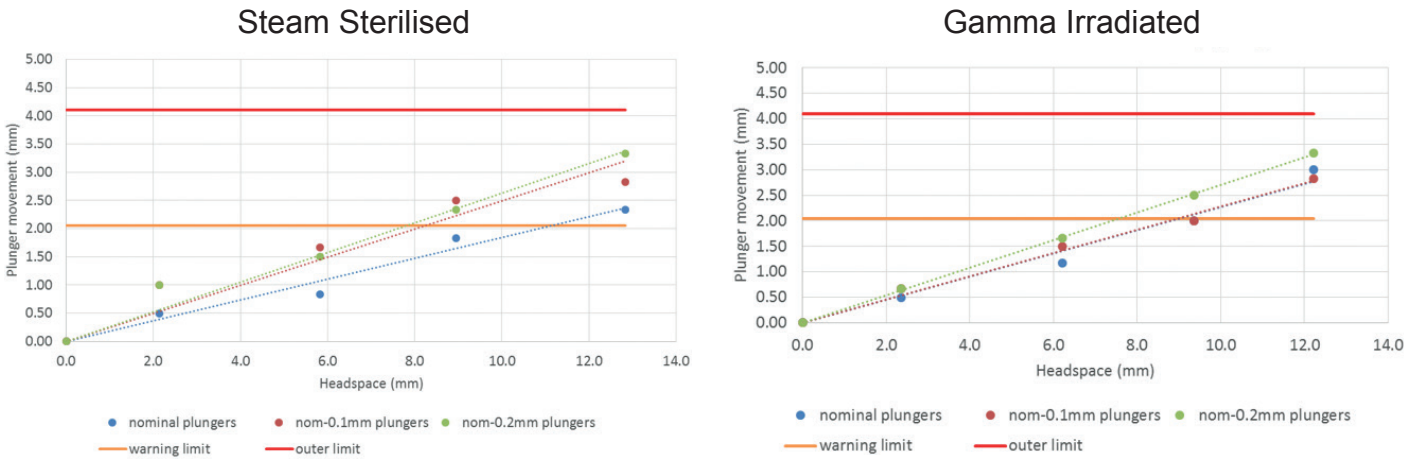

Figure 5: Plunger movement of steam sterilised (left) and gamma irradiated (right) NeoFlex plungers in 3 mL cartridges with different headspaces. Plunger movement is tested in a vacuum chamber at 752 mbara (=8000 ft) at room temperature. This condition is typical of the pressure decay in a pressurised cargo jet.

A ROBUST COATED PLUNGER FOR SENSITIVE DRUGS

Datwyler's NeoFlex plungers are proven to provide reliable drug compatibility, superior functionality and excellent machineability. The fluoropolymer spray coating provides a barrier to extractables and leachables, while ensuring smooth delivery in the field. NeoFlex plungers meet the demand for quality and performance for highly sensitive, large-molecule drugs.

ABOUT THE COMPANY

Datwyler is focusing on high-quality, system-critical elastomer components and has leading positions in attractive global markets such as healthcare, mobility, oil and gas, and food and beverage. With its recognised core competencies and technological leadership, the company delivers added value to customers in the markets served. It has more than 20 operating companies, sales in over 100 countries and more than 7,000 employees. Within the healthcare solutions business area, Datwyler develops, designs and manufactures solutions for injectable packaging and drug delivery systems.

ABOUT THE AUTHOR

Carina Van Eester graduated as an industrial engineer in chemistry and started her career in pharma, where she gained 15 years of experience as a packaging development engineer and project manager. She has been with Datwyler for 12 years, spending seven years as a Technical Key Account Manager, providing technical support to customers, and four years as a Global Qualification and Validation Manager. She moved into the role of Global Platform Leader for Prefilled Syringes and Cartridges in 2018, making sure that the standard portfolio of rubber components used for these applications secures Datwyler's position as a market leader.

INTRODUCING DATWYLER'S NEXT-GENERATION COATED PLUNGER: **NEOFLEX™**

Datwyler's range of NeoFlex™ plungers offers a robust packaging solution for the prefilled syringe and cartridge markets, taking into account the need for superior functionality and exceptional compatibility. Coated with Datwyler's proprietary spray coating technology, NeoFlex™ plungers are the ideal solution for your drug product needs.

At Datwyler, we help to improve patients' lives – because we care.

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