Sensitive Medical Packaging: Meeting the Needs of the Pharmaceutical Market

Today, biologics and biosimilars are in the focus of the pharmaceutical industry. Whether for inflammatory autoimmune diseases such as rheumatism, chronical metabolic diseases like diabetes or cancer suffering – biologics and biosimilars are one of the medical revolutions of the 21st century and have become indispensable. But this significance unfolds not only new potentials, but also many challenges that pharmaceutical companies and their suppliers have to overcome to guarantee a certain demand for quality and, from the patient's point of view, provide administration of the active ingredient as simple and suitable for everyday use.

The sensitivity of biologics and biosimilars regarding storage and packaging requirements, as well as their complexity during administration, led to the demand to meet the highest quality standards, including strict controls at all stages in the manufacturing process. For gentle storage, the right packaging plays a crucial role, especially when it comes to an appropriate protection of the drug. The efficacy and safety of the active ingredient can be negatively affected by even the smallest deviations and inconsistencies in production and material performance. That's why, in the field of sensitive biologics and biosimilars, the protection of the active ingredient is of key importance, and companies are constantly seeking for new packaging solutions in order to provide the best environment for packing and producing the drugs.

Requirements for Highly Sensitive Medical Packaging Solutions

The increasing demand for highly sensitive drugs such as biologics and biosimilars, which are often dispensed in liquid form, leads to constantly growing challenges for manufacturers of drug packaging and elastomer components. Elastomer components are frequently used, not only as closure solutions, but even in the area of prefilled syringes. Also in cartridges for pens, for example for self-administration of insulin, they are a central element. The rubber components are in long-term contact with the liquid pharmaceuticals.

It must be ensured that visible and subvisible particulates are reduced and that the compatibility of the rubber components with the drug formulation is guaranteed, which leads to a growing complexity of formulations and an increase in new types of components. It also means that the interaction of extractables and leachables from the rubber in the solution have to be limited to the absolute minimum. Therefore, innovative barrier technologies and manufacturing under cleanroom conditions are the key to fulfill these special requirements.

Figure 1: Biologics and biosimilars are often dispensed in liquid form. These liquid drugs require high quality closures.

Siliconisation: A Must for Good Processing and Functioning of Uncoated Closures

To achieve good processability and functionality, the sealing components usually have to be siliconised – which takes place at the end of the washing process and thus shortly before the products are packaged. The degree of siliconisation depends on the intended purpose of the product and is tailored to the type of seal. In general, a vial stopper gets a lower siliconisation degree than a plunger due to the specific use. The silicone oil prevents clumping in bags and makes sure the products are running perfectly on the filling lines of the pharma companies. The process also avoids the plunger sticking to the barrel during long storage and as such, contributes to achieving an acceptable break-loose force so that the syringe contents can be administered to the patient in a proper manner. It will also contribute to a good gliding of the plunger in the barrel, although gliding is more determined by the surface treatment of the barrel than by the plunger.

However, siliconisation entails challenges regarding biologics and biosimilars. Whenever the active ingredients get in contact with silicones, changes may occur: The proteins can aggregate, which potentially could result in ineffectiveness or immunogenicity of the protein. In the worst case, even the efficacy of the drug is no longer guaranteed. In order to counter the sensitivity of biologics and biosimilars to impurities, the production of all components must meet the highest quality standards. As a result, the siliconisation method for surface treatment is not recommended for all pharmaceutical components – especially not for the two mentioned above. The specific properties and characteristics of biologics and biosimilars require a barrier technology that ensures highest safety and effective drug supply.

Other barrier properties are the prevention of absorption and/or adsorption of the active ingredient or excipient to the packaging, which can lead to potency loss and stability issues. Due to the high number of challenges involved, the production of packaging specifically designed for these sensitive drugs and their properties can be seen as an extension of the manufacturing process of the drugs itself. As a result, packaging suppliers work closely with drug manufacturers to develop a solution that ensures drug effectiveness. An important step on the way to the best handling of biologics and biosimilars is fluoropolymer-coated closure solutions. The coating makes the use of silicone oils obsolete, which

is an advantage needed for silicone-sensitive proteins.

Fluoropolymer Coating: An Inert and Silicone-free Barrier

Taking the specific requirements into consideration, a fluoropolymer coating has many advantages in comparison to the siliconisation technique. Taking a look at its material composition, it is chemically inert and has a low permeability to organic molecules and aqueous ions. It can be applied by film laminate coating or spray coating. In the spray coating process, the fluoropolymer coating is applied in a two-step process. In the first step, the proprietary fluoropolymer film is applied by a tumble spray coating. The second step consists of a post-treatment process which provides sufficient thermal energy to bond the coating covalently to the butyl substrate and to form a smooth, continuous fluoropolymer film. Due to the line-of-sight nature of the spray coating, the entire closure surface is covered with a thin and flexible coating.

Thanks to spray coating technology, a big range of designs can be coated: from small components like 0.5 ml plungers to large closures like infusion stoppers. The total coverage by the coating stands in contrast with the partial coverage of most film coatings and therefore offers the benefit of providing a complete barrier. Due to the low coefficient of friction of the coating, there is no need for siliconisation of the closure in order to obtain a good processability and functionality. Fluoropolymer coated closures not only have barrier properties which enable superior chemical compatibility, but also the added benefit of eliminating the largest source of subvisible particles: silicone oil-based coating containing subvisible particles.

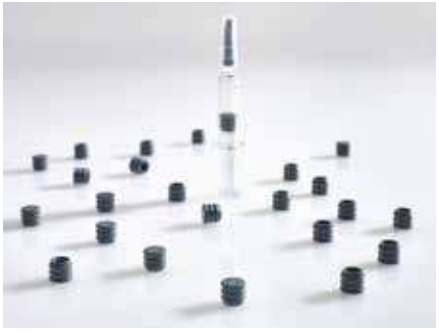

Figure 2: The plunger is a critical component of any prefilled syringe. Even after several years of storage, it must ensure that the medication is administered safely to the patient.

Figure 3: In state-of-the-art plants, products are manufactured under cleanroom conditions.

Cleanroom Manufacturing Environment and Strict Quality Standards for Maximised Safety

To ensure that the components for pharmaceutical packaging, especially for biologics and biosimilars, meet the highest demands, the production environment is a quality critical attribute. For this purpose, a cleanroom manufacturing environment is essential, including innovative automated processes and appropriate gowning, to conform to the highest industry standards. Each zone is designed and constructed to prevent bio-contamination and is equipped with easy to clean machines mainly made of stainless steel. Each zone is in overpressure versus the next zone. An example in this regard is the pass-through washing machines: automatic loading is done in one zone and its automatic unloading side is in a zone of even higher cleanliness. In addition, state-of-the-art camera inspection techniques are used to eliminate any remaining defect or contamination to ensure zero defects. The process flow, gowning protocols, personnel and material flow, and automation all result in the lowest endotoxin, bioburden, particulate, and defect levels available in the industry. Due to this high-level clean processing, absolute purity of pharmaceutical packaging components for drug administration can be guaranteed. Next to this, Good Manufacturing Practice principles are used in the production and control, which are of great importance for the safety of the patient. With regard to biologics and biosimilars, this is highly important because the purity of the sensitive drugs can be guaranteed not only by the coating, but also by the manufacturing itself.

Individual, Ideal Coating Solutions for Specific Drug Needs

Taken together, the proprietary, inert fluoropolymer spray coating is the most advanced coating technology on the market, providing unique barrier properties for biologics and biosimilars. Components treated with this material offer minimal interaction potential between packaging material and the filled drug, while the production environment and processes guarantee an uncompromising, consistent quality. Thus, the fluoropolymer coating can be considered as a response to the ever-increasing demands for better packaging solutions for sensitive drugs. The high-performance fluoropolymer coating technology meets all the compatibility and functional requirements of the biologics industry, and simultaneously improves the lives of patients who depend on treatments with these drugs.

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