

SYRINGE COATING TECHNOLOGIES: OLD, NEW, AND DEVELOPING



This review details the latest lubrication options and their impact on particle formation.

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Intravitreal injections have become a mainstay of treatment regimens for many ophthalmic conditions, such as AMD, diabetic macular edema, and retinal vein occlusions.¹ As such, the syringe is a crucial tool for retina specialists, and the technology is constantly improving to optimize the safety, efficacy, and functionality of intraocular administration.² Here, we review the current options and discuss the latest innovations in syringe technology.

TRANSFER VERSUS PREFILLED

The two major types of medical syringe systems are transfer syringes and prefilled syringes (PFS). Transfer syringes are traditional syringes that require the transfer of medication from a vial to the syringe barrel before administration. The overall drug time in the syringe is minimal, with the average storage time being only minutes up to a few hours.¹

PFS were designed to decrease medication dose errors and microbial exposure; reduce drug waste and costs; and increase ease of administration.¹⁻⁴ They are becoming more common in clinical practices and are typically filled with the drug at the manufacturing facility. The overall drug storage time is much longer than that of traditional syringes, with a maximum of 2 years, raising concerns about the increased probability of protein-surface interactions.¹ PFS may decrease drug waste and increase efficacy; however, many physicians may hesitate to use them due to the increased upfront cost.

MECHANISTICS

Studies of syringe functionality and safety most often measure glide force, break-loose force, container closure integrity, lubricant displacement, and protein aggregation.⁵⁻⁹ Container closure integrity refers to the seal of the barrel created by the plunger on one side and the needle on the other. A proper

seal ensures product quality and sterility, particularly in PFS.^{5,6} Break-loose force refers to the force needed to initiate movement of the plunger, and glide force refers to the continuous amount of force necessary to maintain the plunger movement down the barrel. Increased break-loose and glide forces can cause difficulty in drug administration, including increased injection time and incomplete injections.⁷⁻⁹

Lubrication within the barrel of the syringe decreases these forces and enhances gliding mechanics. However, certain lubricants can increase the chance of lubricant displacement and formation of protein aggregate, which can taint ophthalmic solutions with unwanted particles.^{1-4,7,9,10} The current United States Pharmacopeia (USP) guideline states that there should not be any visible particles in ophthalmic solutions; particles with a diameter $\geq 10 \mu\text{m}$ or $\geq 25 \mu\text{m}$ are limited to 50/mL and 5/mL, respectively.¹¹

COATING TECHNOLOGY

The original coating of a syringe barrel is sprayed-on silicone. However, studies show that extended drug exposure to silicone can cause formation of silicone oil droplets—part of the particle formation count of a syringe—that may interact with proteins and cause aggregation.^{9,10} An increased particle count can reduce drug efficacy and cause complications, such as inflammation and IOP increases.¹²

With the expanding use of PFS, different techniques have been developed to minimize silicone droplet leakage during long storage times. Glass syringes with baked-on silicone have been shown to have a much lower particle formation than their sprayed-on silicone counterparts. The process of baking heats the siliconized glass barrel, vaporizing the low-molecular-weight silicone molecules and further immobilizing the coating.^{7,13} The Gx Baked-on RTF Syringe (Gerresheimer) with the OmniflexCP Plunger (Datwyler) is one example of

a syringe system that uses the baked-on silicone technology with a non-siliconized plunger to limit particle formation. The plunger uses a patented flexible fluoropolymer spray-coating and has been shown to decrease total particle formation in syringes stored for 3 months compared with plungers coated with either high or low viscosity silicone.¹⁴

A newer process of crosslinking also shows promising results. Crosslinking allows for a stronger chemical bond between the silicone layer and the barrel, which reduces the silicone migration into the solution. Alba (AlbaChem) and TriboLink-Si (TriboFilm Research) are two silicone-based lubricants currently on the market that use crosslinking technology. Both manufacturers advertise decreased silicone layer mobility and low silicone oil concentration, while maintaining low break-loose and glide forces in both short- and extended-storage time studies.^{7,15}

ALTERNATIVE TECHNOLOGIES

Silicone-based syringes still dominate the market, but several silicone-free syringes are also available. Two options are the Norm-Ject (Henke-Sass Wolf) and the Injekt-F (B Braun), which are transfer syringes coated with oleamide. A study found that this type of syringe produced fewer particles than a traditional sprayed-on silicone syringe, but it also had the greatest time-dependent increase in particle formation (including visible particles) after 15, 30, 45, and 90 days.¹ In addition, oleamide-coated syringes had a significantly greater number of particles larger than 10 µm compared with baked-on silicone PFS syringes. However, when particles between 1 µm and 10 µm were considered (not included under the USP guideline¹¹), particle formation in baked-on silicone syringes was no longer significantly lower than oleamide-coated syringes.¹

StaClear (TriboFilm Research) uses TriboGlide-DS (TriboFilm Research) as a coating. TriboGlide-DS uses a similar crosslinking technology as TriboLink-Si, but is based on perfluoropolyether, not silicone. It creates significantly less particle formation and a lower break-loose force but has a slightly increased glide force compared with TriboLink-Si.⁷

The NovaPure plunger (West Pharmaceutical Services) with the Crystal Zenith syringe (Daikyo Seiko) and the Improject plunger (Gore) with the syriQ BioPure syringe (Schott) are also silicone-free PFS systems on the market. Although they don't require a liquid lubricant, they both use a polytetrafluoroethylene laminated coating on the piston.

CLINICAL RELEVANCE

Chronic retinal conditions may require repeated intravitreal injections, and it is imperative that retina specialists use technologies that administer proper and efficacious doses. Since PFS are becoming more prominent, it is important to monitor the quality of the solution contained within them. Extended storage of the drug in the syringe can potentially

increase the chance of particle formation, especially in silicone-based systems. Unwanted particles in the solution can cause irritation in the eye and potentially react with the active drug to lower efficacy. Technologies such as baked-on lubricants and crosslinking have been developed to decrease silicone mobility and particle formation, with crosslinking technology providing better results.

Decreased lubrication mobility also helps to ensure proper coverage and maintenance of low break-loose and glide forces for a smooth and safe administration. Silicone-free syringes are additional resources that can dramatically decrease particle formation; however, more research is needed to determine whether the lack of silicone causes decreased lubrication and increased break-loose and glide forces that may hinder drug administration. ■

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