

- Appropriate gauge size of needle for product and its indication within the syringe. Syringe needle gauges range from 21 to 32 gauge (G). It is important to note that some suspensions may not syringe properly if the needle gauge is not carefully considered.

One of the most challenging aspects of syringe quality control is the assurance of container/closure integrity during and after filling and terminal sterilization (chap. 30).

Siliconization Issues with Syringes

Like rubber closures, syringes require a “slippery surface.” Rubber requires such a surface for facile movement of closures along the stainless steel tracks of a rubber closure hopper or feeding machine to deposit the rubber on top of a container at a rate of hundreds per minute. Without the slippery surface, rubber closures would move haltingly, if at all, and filling at any speed could not be accomplished. For syringes, the rubber plunger must move easily within the syringe barrel with the “glide force” being the same throughout the barrel (from distal to proximal end).

There are several concerns related to siliconization of syringes—functionality, potential for protein aggregation, and increased potential for particulate matter. Syringe functionality involves forces both to initiate movement of the plunger rod within the syringe barrel and to maintain movement of the plunger rod throughout the barrel to the end of the syringe. Siliconization significantly facilitates both forces. However, excess silicone is a problem from a physical stability standpoint both with respect to visible appearance of silicone droplets in the product and greater potential for protein interaction with these hydrophobic droplets. Therefore, great effort is made by syringe manufacturers to minimize the amount of silicone applied within the inner surface area of the syringe. However, sometimes not all the inner surface of the barrel is coated with silicone. This will potentially lead to an effect called “chattering” where the syringe barrel will “stick” and require greater force to make it move again. This may not be a problem with manual injections where the health care professional or the patient giving self-injections will simply apply more pressure with the fingers to overcome the lack of siliconization. However, if autoinjectors are used, sometimes the spring or compressed gas force will be insufficient and incomplete delivery of medication will occur.

The FDA added a requirement for functionality testing as part of long-term stability testing of drug products contained in syringes and cartridges because of the possibility of inadequate/incomplete siliconization of syringes resulting in potential inadequate/incomplete drug delivery (8). Articles are being published about technologies that apply optical techniques such as confocal Raman spectroscopy, Schlieren optics, and thin film interference reflectometry to visualize and characterize (in situ morphology, thickness, and distribution) of silicone oil in prefilled syringes (9). The articles demonstrate that these techniques show that uneven distribution of silicone oil within syringe glass barrels as potential sources of chattering and stalling of the syringe plunger during injection using autoinjectors.

Syringe siliconization raises the potential for protein aggregation. This is a primary driver for plastic syringes perhaps becoming more popular for use with biopharmaceutical products because the plastic surface does not require silicone for facile movement of the rubber plunger and plunger rod through the plastic barrel. Manufacturers of plastic syringes have developed alternatives to silicone to provide lubricity within the plastic composition of the syringe to achieve acceptable functional performance. Studies have been published that implicate silicone as the cause of turbidity and particle formation in insulin products (10) and other protein products (11). Until plastic syringes without the presence of silicone become more common, continuous improvements in the consistent application and distribution of silicone in syringe barrels must be pursued.

Siliconization also increases the potential for increased particulate matter, either real or the fact that electronic particle counters detect a silicone droplet as a particle. Thus, products in syringes could experience higher levels of particles as measured by light obscuration compared with the same product in a vial. Typically, the levels of particulate matter for syringes still fall way below the required limits for subvisible particles as defined by the United States Pharmacopoeia (USP) General Chapter <788>. However, if the USP ever decides to require