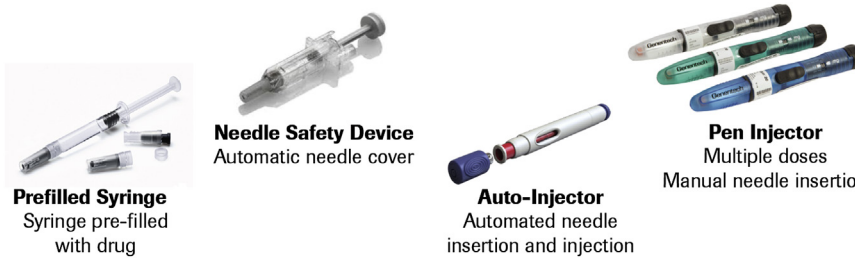

Figure 8.1 Injectors used for subcutaneous (SC) delivery.
From French (2013).

a product. Current regulations require the use of a needle safety device for prefilled syringes to prevent accidental needle sticks for the end user, and there are several commercial systems available (Hyman, 2002; Trim, 2004).

Silicone oil interactions with proteins and mAbs in prefilled syringes

Prefilled syringes have been traditionally manufactured from glass, which require silicone oil coating to avoid high glide forces. Silicone oil has been implicated in the generation of aggregates and particulates of mAbs (Britt et al., 2012; Thirumangalathu et al., 2009). Both of these studies investigated the impact of formulation excipients on the interaction of mAbs with silicone oil emulsions. The key findings were that formulations buffered with 10 mM L-histidine at pH 6 with addition of 140 mM NaCl resulted in increased absorption of the mAb to the silicone oil. The addition of surfactants such as polysorbate 20 resulted in a decrease in the absorption. Although intrinsic tryptophan fluorescence quenching using acrylamide suggested that the tertiary structure of the mAbs was significantly changed, there was not any observed precipitation of the mAbs. However, in a separate study, the tertiary structure of a mAb was perturbed at lower ionic strength, but not at higher ionic strength after absorption to silicone oil droplets (Gerhardt, Bonam, Bee, Carpenter, & Randolph, 2013). It was also shown that the secondary structure of the mAb was unaltered after adsorption to the silicone oil–water interface suggesting that the adsorbed mAb has a molten globule-like conformation. This partially unfolded mAb was prone to aggregation, especially during agitation. In another study, mAb formulated without surfactant was filled into prefilled syringes where the mAb was exposed directly to silicone oil/glass surfaces, air–water interfaces, and agitation (Gerhardt et al., 2014). Flow microscopy was used to detect the presence of particles $\geq 2\,\mu m$ in diameter. The greatest particle concentrations were found in agitated syringes containing an air bubble, which contributed to the generation of air–water interfacial surfaces. A mechanism was proposed that involved the overall impact of silicone oil–water interfaces, air–water interfaces, and agitation on the generation of particulates. Essentially, protein/mAbs without surfactant are adsorbed to the silicone oil–water interface that can result in formation of a