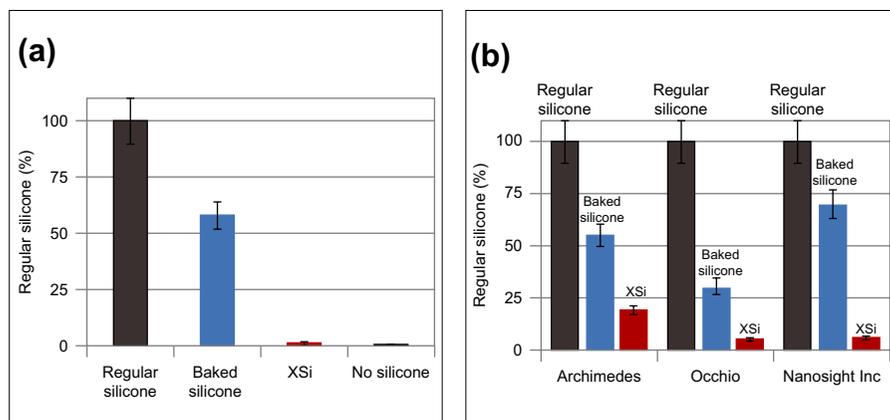


gel. The air bubble during agitation creates sufficient shear to dislodge this surface gel into the bulk of the solution. Although silicone oil droplets confound the determination of subvisible particulates, flow microscopy can discriminate between the irregular shaped protein particulates and round silicone oil droplets. In this study, both types of images were detected, as well as agglomerates of aggregated proteins and silicone oil droplets. It was suggested that additional refinements of the flow microscopy technology are needed in order to fully characterize the observed particulates. Recent studies have shown that it is possible to distinguish silicone oil droplets from protein particles and dust particles using enhanced flow microscopy technology (Sharma, King, Oma, & Merchant, 2010; Vandesteeg & Kilbert, 2013).

To avoid the issue of silicone oil, companies have developed plastic syringes that are now available and used commercially (Kiang, 2011; Markarian, 2013). Another approach has been to use baked-on silicone oil on glass syringes, but this has been difficult to do with glued-in staked needle syringes because of the high temperatures required for the process. It was shown that a baked-on silicone oil surface resulted in less particulate formation for an IgG<sub>2</sub> mAb compared to a standard siliconized glass syringe (see Figure 5 in Badkar, Wolf, Bohack, & Kolhe, 2011). Alternative technologies using cross-linked silicone oil to minimize sloughing from the surface have also been developed (Depaz, Chevolleau, Jouffray, Narwal, & Dimitrova, 2014). A comparison of submicron particulate counts in polysorbate 80 solutions in phosphate-buffered saline shows a reduction in counts for a baked-on silicone oil layer and a chemically cross-linked silicone oil surface compared to a standard sprayed-on process for prefilled syringes (Figure 8.2(a)) using different instruments (Figure 8.2(b)). The cross-linked silicone oil surfaces in the prefilled syringe resulted in the lowest amount of particulate counts and enhanced durability of the silicone layer in the presence of two mAbs.



**Figure 8.2** Particle released for polysorbate 80 solutions in phosphate-buffered saline for (a) sprayed-on silicone (regular), baked silicone, and cross-linked silicone on glass (XSi) and (b) submicron counts measured by Archimedes, Occhio, and Nanosight instruments.

From Depaz et al. (2014).