for the excipient is needed. Other tests that measure product quality may be included as warranted. Physical stability is also important for establishing product quality. The lyophile should preferably retain the original cake appearance, color, and morphology over its shelf life.

Diluent-Containing Chamber

The diluent-containing chamber should be tested for identification, appearance (including color, clarity, and particulates), preservative potency, pH, etc.

In-Use Reconstituted Solution Stability Studies

Reconstituted stability studies should be performed with product in full contact with the closure system (e.g., side-stored or inverted) to confirm compatibility. In-use test patterns applied to reconstituted small-molecule lyophiles typically include assay, degradation products, clarity of solution (USP and EP), pH, and visible and subvisible particulates. In-use test patterns applied to reconstituted biological lyophiles typically include identity, protein concentration, purity (e.g., monomer purity, IgG, etc.), biological potency, product-related substances (e.g., charge variants), oxidation for some cases, clarity of solution (USP and EP), pH, and visible and subvisible particulates. Functional excipient in-use testing of preservatives, antioxidants, etc. should be included when present in formulations. Other tests may also be added if critical to product quality.

Functional attributes of the syringe or cartridge should be monitored on stability because silicone disposition over the barrel may shift with time and could adversely impact compatibility with the device. Functional tests include pressure and seal integrity, tip-cap removal force, piston release force (break-loose force), piston travel force (glide force), and power injection function force.

Sterility/Container Closure Integrity

The requirement for sterility in parenteral products is absolute throughout the product shelf life at the intended storage condition. The sterility and container closure integrity should be monitored during the registration stability program. If the reconstituted liquid is to be multiused, or used over an extended period of time, an antimicrobial preservative may be part of the formulation. If a preservative is present, an antimicrobial effectiveness test should be part of testing. Preservative concentration that provides adequate antimicrobial protection should be determined in early development. The preservative stability in the reconstituted liquid needs to be assessed on stability; however, this is usually evaluated via a chemical test. During registration stability, AET is performed on the reconstituted product at initial and end of shelf life time points for the product. Unlike chemical and physical stability tests, microbiological tests are not normally performed at each time point, but instead are run on an annual basis. Usually only one lot per formulation is subjected to microbiological testing when multiple lots are placed on stability. CCIT is performed to evaluate the ability of the container closure system to provide protection and maintain integrity during the shelf life of the sterile drug product. According to a recent FDA guidance to industry, container closure system integrity testing can be used in lieu of sterility testing as a component of the stability protocol for sterile