SPECIFICATIONS FOR DUAL CHAMBER LYOPHILIZED PRODUCT PACKAGE SYSTEMS

The product specifications describe tests that are utilized to demonstrate that each batch of product has met appropriate quality criteria. However, it should be noted that these may differ depending on which countries the product has been registered for sale. Dual chamber packages typically have specifications for the active-containing chamber, the diluent-containing chamber, and the reconstituted product. Example specification assays for the lyophilized powder containing chamber might include identification, appearance, moisture, pH, potency assay, dose uniformity, and purity. Note that additional potency and purity assays will be required for biological type products. Example specification assays for the diluent chamber might include identification, appearance (including color, clarity, and particulates), preservative potency, pH, etc. Example assays for the reconstituted solution might include appearance (including color, clarity, and particulates), pH, reconstitution time, subvisible particulate matter dose uniformity, deliverable volume, purity, endotoxins, and sterility.

Additionally, functional testing according to ICH Q6A (30) may be included in specifications for dual chamber products. Potential functional testing may include pressure and seal integrity, resealability, tip-cap removal force, piston release force (break-loose force), piston travel force (glide force), and power injection function force. Note that data generated during product development may justify elimination of functional testing as part of the specifications.

STABILITY EVALUATION OF DUAL CHAMBER LYOPHILIZED PRODUCT PACKAGE SYSTEMS

A unique aspect for designing stability studies for dual chamber package systems is that stability of the active-containing chamber, diluent-containing chamber, and reconstituted solution must be monitored. This is similar to the three sets of specifications that must be set for a dual chamber lyophilized product. Specific guidances for stability testing of dual chamber package systems, in-use reconstituted solution stability testing, and sterility/container closure integrity are discussed below.

Active-Containing Chamber

At a minimum, potency assay, impurities, and water content are the chemical tests that should be performed on stability for the lyophile powder. Hydrolysis resulting from moisture content is a common cause of chemical instability and one that is potentially important in a lyophilized formulation. Temperature and pH can affect the rate of hydrolysis. Another potential cause of chemical instability, but not common for lyophilized products, is oxidation. If the formulation is susceptible to oxidation, typically a nitrogen overlay is used. Typical chemical tests for evaluating stability for small molecules are assay, degradation products, moisture content, and pH. Typical chemical tests for evaluating stability of biologicals include identity, protein concentration, purity (e.g., aggregates, etc.), biological potency, product-related substances (e.g., charge variants), oxidation for some cases, moisture content, and pH. If a functional excipient is part of the formulation, for example an antioxidant or preservative, then a test