The design of experiments for qualifying CCS for lyophilized pharmaceutical products is centered on extractable studies, incorporating factors associated to the manufacturing process and variables indicating worst-case exposure conditions. Recommendations for a practical leachable assessment model are given based on

1. Qualitative and quantitative extraction studies
2. Assessment of CCS analytical profile
3. Evaluation of lyophilized pharmaceutical products for leachables
4. Correlation of leachables to extractables and lifecycle management

CRITICAL QUALITY ATTRIBUTES FOR CCS

Pharmaceutical product CQAs are managed through the critical process parameters (CPP) established during the validation of the manufacturing process. A subprocess to the pharmaceutical product manufacture is that of the CCS in which CQAs are established to ensure suitability for use, along with employing good manufacturing practices (GMP).

> Device containers should not be reactive, additive or absorptive as to alter the safety, identity, strength, quality or purity of the drug beyond the official or established requirements for the drug product. Standards or specifications, methods of testing, and where indicated methods of cleaning, sterilizing and processing to remove pyrogenic properties shall be written and followed for drug product container and closures (1).

CCS for lyophilized products and their associated components have a direct impact on the pharmaceutical product CQA. Suitability of CCS is based on the four major building blocks shown in Figure 1 (2). The sum of these characteristics define the target CCS and establish CQAs.

Safety is paramount to package suitability and the factors that define patient safety are linked to the chemistries of the materials of construction and the potential to contaminate the pharmaceutical product. A CQA of a CCS is the absence or control of substances that may leach into the pharmaceutical product from the CCS in conjunction with aspects of performance, protection, and compatibility. Building quality into the manufacturing process requires an enhanced understanding of the component manufacture, properties, and chemistries to identify CPP. Chemical entities that are needed to enhance the properties of the materials for superior performance can influence the overall compatibility as well as the functionality and container closer integrity. There are unique approaches for evaluating the key aspects indicating that the CCS is suitable for the intended purpose; however, there is a universal approach to address the safety aspect. A chemical evaluation of the critical materials of construction for extractables, followed by a leachable study, will indicate the risk for pharmaceutical product contamination and patient safety contributing to a scientifically informed decision for material selection and qualification of the system components.