17 Extractables and Leachables as Container Closure Considerations in Lyophilization

Diane Paskiet and Fran L. DeGrazio
West Pharmaceutical Services, Inc., Lionville, Pennsylvania, U.S.A.

INTRODUCTION

The suitability of the container closure systems (CCS) for lyophilized pharmaceutical and biological products can be enhanced using the principles of quality by design (QbD) and employing risk management tools. Leachables, chemical constituents that migrate from packaging materials into the pharmaceutical product under normal conditions, can be minimized or eliminated when components are considered early in the pharmaceutical development process. A set of experiments can be designed to facilitate material selection by profiling materials for extractables using exaggerated conditions and assessing the impact to the pharmaceutical product and ultimately patient safety.

The classification of a CCS is not limited to the final package with respect to extractables and leachables in lyophilized pharmaceutical products. Materials that directly or indirectly come into contact with the pharmaceutical product at any time during the manufacturing, cleaning process, storage, or administration are candidates to be considered for extractables/leachables evaluation. In addition, secondary and ancillary or associated components may have an impact on patient safety and should be considered in the overall design space.

Sources of potential hazards can be traced back to the chemistries of the CCS materials of construction. Functional parameters for CCS materials used with a lyophilized pharmaceutical can be identified from a set of experiments designed to lead to an in-depth understanding of the chemistries of the critical components. Knowledge gained from these studies will enable science-based decisions for identifying critical quality attributes (CQAs) and provide a proactive approach to achieving quality. This chapter illustrates the selection and qualification of critical CCS components intended to be in contact with a lyophilized pharmaceutical or biological product and strategies for acquiring the appropriate data to contribute to the overall drug product quality.

OVERVIEW

The principles of QbD can be qualitatively applied to selection and control of materials used in the manufacture, storage, and administration of lyophilized pharmaceuticals. The following concepts are considered with respect to CCS:

1. CQAs for a CCS
2. Identification of critical CCS components for extractable/leachable—assessment using risk management tools
3. Strategies for CCS qualification and control