Advances in Process Analytical Technology in Freeze-Drying

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Introduction

Rational design and utilization of freeze-drying processes are essential to minimize their impact on drug product quality and assure consistent clinical performance. Development of the formulation and lyophilization process should focus on the product quality attributes. The International Conference on Harmonization (ICH) guidance Q8 (R2) suggests that the product quality cannot be tested in a product by using limited off-line measurements, instead it should be built in by design of the formulation and manufacturing process. This guidance lays the foundation for a quality-by-design (QbD) paradigm, which stresses the scientific understanding of formulation and processing factors on product quality and also the ability to assure product consistency [25, 26]. Process analytical technology (PAT) is a vital part of the implementation of QbD. Based on the in-line real-time measurement of critical process parameters (CPPs), the manufacturing process can be monitored and further controlled with appropriate feedback mechanisms. PAT can also facilitate the trending of the process operations to support continuous improvement efforts. Even though multiple off-line analytical techniques, such as chromatography and

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