MediZap

Advanced Sterilization

Testing Container Closure Integrity in Compounded Parenteral Drug Products

Container Closure Integrity (CCI) is a critical aspect that requires assessment during the drug product development phase. CCI refers to the package's capacity to prevent product loss, the entry of microorganisms, and the infiltration of harmful gases or substances throughout its shelf life, ensuring compliance with safety and quality standards. This term is interchangeable with package integrity. Failures in CCI for packaging and delivery systems include leakage, product loss, elevated product concentration, contamination, sterility failure, critical headspace loss, over-pressurization, or pressure loss. The United States Pharmacopeia (USP) also dedicates a chapter to address CCI. USP 〈1207〉 Package Integrity Evaluation – Sterile Products offers guidance on assessing the integrity of packaging designed for sterile products. It provides an overview, general introduction, and glossary and is divided into several sections. The chapter also emphasizes the importance of understanding package system integrity throughout the drug product's life cycle, encompassing package development, validation, product manufacturing, and commercial stability.

The initial section of the chapter focuses on test method selection and validation. It emphasizes the necessity of comprehending package design, construction materials, and mechanics to choose appropriate test methods. Furthermore, pharmaceutical manufacturers must define the Maximum Allowable Leakage Limit (MALL) for their products to evaluate package integrity effectively. MALL defines package integrity as the maximum permissible leakage rate or leak size for a specific product package that does not compromise product safety or quality. Integrity requirements should not solely concentrate on sterility risks posed by microbiological contamination but also consider product quality risks. Once MALL is defined, the subsequent step involves selecting the suitable technique for testing CCI.

The second section of the chapter covers leak test methods and their appropriate usage. The second section also highlights a shift in expectations, favoring the utilization of deterministic methods over probabilistic methods, which were previously prevalent in the industry. Deterministic methods, such as tracer gas and high voltage leak detection, are cited as examples.

The third and final section delves into package seal quality test methods, such as residual seal force. These tests evaluate and monitor parameters associated with the package seal's quality and consistency, offering assurance of the package's integrity. Seal quality tests and CCI tests complement each other in ensuring package integrity. When selecting techniques, it is crucial to recognize that no universally applicable test method exists for all product package systems. Method selection and validation should be based on the suitability of the given application, with a preference for quantitative results (deterministic methods) over qualitative results (probabilistic methods). Lastly, CCI should be considered during development and incorporated into stability evaluations throughout the product's shelf life and life cycle management.

MediZap has partnered with Eagle Analytical to offer USP 1207 testing services to validate CCI in all new drug development by compounders.