CCIT—Practical Aspects and Approaches in the Pharmaceutical Industry

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Abstract: The assurance of sterility of a parenteral drug product, prior to any human use, is a regulatory requirement. Hence, all strategies related to CCI must demonstrate absence of microbial contamination through leaks as part of the container closure system (CCS) qualification, during manufacturing, for quality control purposes and to ensure microbiological integrity (sterility) during storage and shipment up to the end of product shelf life. Current regulatory guidances, which differ between countries and regions, provide limited detail on how to assess CCI. The new revision of USP <1207> aims to provide extensive and detailed guidance for CCI assessments for sterile products. However, practical questions and considerations are yet to be addressed by the pharmaceutical industry. These may include:

1. choice of method, for example whether a deterministic CCI method (e.g., helium leak) is preferable over the probabilistic CCI method (e.g., microbial ingress)
2. the type of primary packaging (e.g., vial, syringe, device)
3. dosage form (e.g., liquid versus lyophilisate)
4. suitable acceptance criteria
5. appropriate sample size
6. the most appropriate way to introduce artificial leaks into the CCS
7. ensuring suitable assurance of CCI during drug product manufacturing, and
8. evaluating CCI under intended shipment and storage conditions (e.g., in the frozen state)

A group of European industry peers have met to discuss these and other related questions in order to provide their viewpoint and best practice on practical approaches to CCI. Their perspective is provided in this white paper. Through these discussions, it became clear that there is currently no gold standard for CCI test methods or for the generation of artificial leaks; therefore flexibility toward CCI approaches is required. Although there should be flexibility, any CCI approach must consider the intended use (e.g., CCS qualification, routine manufacturing, or quality control) and product design (e.g., primary packaging, liquid versus dried product).

Reference: Container Closure Integrity Testing—Practical Aspects and Approaches in the Pharmaceutical Industry | PDA Journal of Pharmaceutical Science and Technology