Summary - Container Closure Integrity for Sterile Drug Products

Critical Factors That Affect Container Closure Integrity should be defined in written Standard Operating Procedures (SOP), controlled, and monitored and including, and not be limited to:

- Package component composition, dimensions, coatings, and critical defects;
- Sealing/packaging operation variables of time, temperature, pressure (seal force), gas flow rates, and torque;
- Processing variables of packaging components including washing, drying, siliconization, depyrogenation, and sterilization; and
- Final product processing, such as terminal sterilization or lyophilization.

Challenged Containers that Show Microbial Growth Upon Microbial Ingress Testing should be inspected to determine whether defects in the container closure seal permitted microbial ingress. All defects observed should be described and documented. An investigation should be conducted to determine the cause of the contamination, including a comparison of the contaminant organism(s) to the challenge organism.

Non-Microbial Methods for Container Closure Integrity Testing should be based on validated studies that correlate the test method to microbial ingress testing. Non-microbial integrity tests should be used during routine processing, at a minimum:

- During equipment set-up;
- As an In-Process Control (IPC) test;
- On representative samples of the finished batch/lot; and
- On stability samples during the shelf life and at lot expiration date.

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