Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion
This procedure provides guidance for validating sterilization and depyrogenation of equipment, and containers and closures with direct or potential contact with sterile medical devices, sterile drug products, or sterile **a**ctive pharmaceutical ingredients (API).

1. Preventive Maintenance (PM) Measures should include, and not be limited to, the following:
   For Steam
   - Calibrate instruments and elements (I/Es);
   - Check operation of vacuum pumps;
   - Clean chamber, steam traps and drains;
   - Perform leak test of the chamber;
   - Replace and integrity test vent filter;
   - **Verify*** the operation of safety devices; and
   - Check door seals and gaskets for deterioration.

   For Dry Heat Ovens and Tunnels
   - Calibrate I/Es;
   - Check operation of electric heating elements;
   - Operation of pressure differential monitoring equipment and alarms;
   - Clean chamber, belts, baffles, and dampers;
   - Verify fan and belt speed;
   - Replace belt when required;
   - Integrity test HEPA Filters; and
   - Check door seals for deterioration.

   For EtO
   - Calibrate I/Es;
   - Check operation of vacuum pumps; □ Replace vent filter;
   - Verify integrity of heat exchangers;
   - Clean chamber;
   - Perform leak test of the chamber;
   - Check operation of exhaust gas scrubbers; and
   - Check door seals and gaskets for deterioration.

2. Critical Process Parameters (e.g., temperature, exposure time) for each type of sterilization or depyrogenation method should be automatically recorded during each phase of the sterilization/depyrogenation cycle (e.g., continuous chart recorder or print out at least once a minute).

3. Sterilizer Monitoring and Control I/Es should be calibrated before the operational qualification (OQ) study and routinely according to a defined calibration schedule

- Incubation of BIs at 30ºC-35ºC withno growthafter seven(7) days or at the temperature and time interval recommended by the BI supplier.

16. DH Sterilization (e.g., 140ºC -180ºC) OQ/PQ Studies should be performed and include, and not be limited to, the following:
    - A minimum of three (3) temperature distribution runs on an empty chamber to confirm heating uniformity and identify the slowest-to-heat zone;
    - Heat penetration runs on each different load configuration, including minimum and maximum loads, to identify cold spots and the worst case load configuration; and
    - A minimum of three (3) consecutive, successful runs using the worst case load configuration using minimum cycle parameters and BIs and meeting all validation acceptance criteria.

17. DH Depyrogenation (e.g., > 180ºC) OQ/PQ Studies for DH ovens should be performed and include, and not be limited to, the following:
    - A minimum of three (3) temperature distribution runs on an empty chamber to confirm heating uniformity and identify the slowest-to-heat zone;
        - Heat penetration runs on different load configuration using a matrixing approach (e.g., smallest and largest glass vials) including minimum and maximum loads, to identify cold spots and the worst case load configuration; and
        – A minimum of three (3) consecutive, successful runs using the worst case load configuration using minimum cycle parameters and EIs and meeting all validation acceptance criteria.

18. DH Depyrogenation OQ/PQ Studies for continuous belt tunnels should consist of a minimum of three (3) consecutive, successful runs based on a matrix approach for varying vial sizes, using minimum cycle parameters, and EIs and meeting all validation acceptance criteria, to confirm heating uniformity in each tunnel zone and across the belt, and to identify tunnel cold spots.

19. DH Tunnel Temperature Distribution Runs should evaluate and determine the following:
    – Effects that tunnel load (e.g., empty, partially full, and full) has on temperature distribution;
    – Positioning of baffle plates or gates in each tunnel zone for each container size; and
    - Belt speed for each container size.

20. Each Lot of EtO Gas supplied by a vendor should be approved by the Site Quality Team and have a COA that certifies the gas concentration.

21. For EtO Sterilization Processes, BIs are available in two (2) forms:
    – Spores added to a carrier (e.g., paper strips); and
    – Self-contained packaged indicator that includes the culture medium separated from the BI (e.g., Attest, test pack).

