An area in which the sterilized dosage form, containers, and closures are exposed to the environment (FDA definition).

3.6 Grade A

Zone of local protection for high risk operations such as the filling of open containers, operations involving exposed primary packaging materials and the making of aseptic connections. Normally provided by laminar air flow work station. Generally corresponds to US/FDA Class 100 at rest and in operation.
Note: "At rest" conditions are with HVAC in operation, equipment off manufacturing personnel not working. "In operation" conditions are with equipment on and personnel at work.

3.7 Grade B

Background environment for a grade A zone used for aseptic preparation and filling operations. Generally corresponds to US/FDA Class 100 at rest and Class 10,000 in operation.

3.8 Grade C

Classification used for carrying out the less critical stages of sterile product manufacture. Also used as the background area for the preparation of solutions and components and as the background for filling of terminally sterilized products. Generally corresponds to US/FDA Class 10,000 at rest and Class 100,000 in operation.

3.9 Grade D

A classification used for carrying out the least critical stages of sterile product manufacture. A minimum standard, for example, for areas used for the manufacture of sterile products where solutions and packaging or other components are prepared, stored or handled or otherwise processed after the commencement of manufacture. Generally corresponds to US/FDA Class 100,000 at rest.

4 Responsibilities

4.1 R&D Line Management

The management of R&D at the site are responsible for ensuring that appropriate procedures for sterile manufacturing and testing are in place at sites where sterile manufacturing will occur, and that sufficient training is conducted.

4.2 R&D Quality Management

R&D QA management is responsible for ensuring that the quality systems described in this guideline are established and monitored.

terminated (i.e. PST cancellation policy) must be in place.

- Circumstances under which a satisfactorily filled unit can or cannot be discarded (i.e. container discard policy) must be described in procedures. Normally only containers identified as broken must be excluded from incubation after filling. All units which have been satisfactorily filled and closed must be incubated.
- 'In-process' checks must be simulated where appropriate, but filled containers must generally not be discarded unless they were not satisfactorily filled and closed.
- It may be beneficial to have trained observers who are independent from the production team monitor the PST, or portion of it. Written observations may be helpful in routinely providing feedback to operators in terms of good or poor aseptic techniques, or otherwise may provide valuable in the event of a PST failure.
- Consideration should be given to overlaying filled containers with compressed air rather than Nitrogen to avoid the production of anaerobic conditions preventing microbiological growth in a contaminated container.
- Any contaminated unit must be investigated.

5.5 Sterility Testing

Specific guidance for microbiological laboratories is given in the FDA 'Guideline on Sterile Drug Products Produced by Aseptic Processing'.

- Collection of batch samples for sterility testing must follow established sampling plans to ensure that the containers chosen are representative of the critical parts of the process or sterilizer load.

- The microbiological testing laboratory environment for sterility testing of aseptically manufactured products must employ facilities, controls and monitoring comparable to those used for filling/closing operations.

