Summary - Defining Worst Case Conditions for Aseptic Process Simulations

What are the "worst case" attributes to be considered in an aseptic process simulation (*i.e.* media fill program) for aseptic filling of sterile drug products within conventional cleanrooms?

Aseptic process simulation tests (*e.g.* media fills) "are used extensively and are recognized as an effective way to validate aseptic filling" processes for the purpose of complying with regulatory GMP expectations. A media fill begins at the point where the final sterilization of the product takes place (*i.e.* where aseptic operations are performed) through the completion of filling operations with the sealing of the filled containers.

Media fill operations involve aseptic filling using microbiological growth medium in place of the product. This document presents the common "worst case" attributes to be considered within a media fill program for aseptic manufacturing processes. Also, "worst-case" conditions should be considered and defined within the media fill simulation program for product holding times, process filling times, filling line speed, container sizes, interventions and personnel.

Media fill process design should also consider not only specific product filling line equipment and components, but also local facility (*e.g.* HVAC) and environmental characteristics (*e.g.* personnel traffic patterns, process flow, etc.) where the aseptic filling operations take place.

Other media fill design options can be used and may include performing the media fill immediately following the completion of routine production operations, which is also known as "piggybacking", or alternating the filling of media fill vials with just operating the filling equipment (without vial filling) to allow for continuous processing time while minimizing the total number of media filled vials.

The media fill program design should consider and is expected to "emulate the regular product fill situation in terms of equipment, processes, personnel involved and time taken for filling as well as for holding". As part of media fill design, there is an expectation to consider "worst case" conditions. A number of these have been presented including: holding times, aseptic process times, number of units, line speed, container size, process matrix, personnel, process setup, and interventions. Within each of these highlighted categories an attempt has been made to provide guidance on what to consider a "worst-case" condition within the media fill program.

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