

Standard Operating Procedure

Title: Aseptic Media Fill/'Soup' Test Guidelines

Procedure

Aseptic Media Filling for all Sterile filling areas

Media Fills are designed to verify the entire process, equipment and staff (see MICLAB 035). This process simulation should be performed as initial validation with three (3) consecutive satisfactory simulation tests per shift and repeated at defined 6 monthly intervals (twice per year per process per shift) and after any significant modification to the HVAC-system, equipment, process and number of shifts" for aseptically filled process.

For terminally sterilised lines and non-sterile process once per year per shift.

Validation and re-validation media fills are to assure the sterility of the entire process. This process simulation test should imitate as closely as possible the routine aseptic manufacturing process and include all the critical subsequent manufacturing steps.

The Media Fill should challenge the "worst case" situation and should include all the possible interventions of a normal production run. The duration of the media run should be at least 4 hours or half a production shift to allow for all routine interventions.

An example of valid media fill is 10,000 units per shift for a high speed filling machines.

1.1. Routine revalidation

Two (2) per year, per shift, for each machine at defined 6 monthly intervals. One media run at start-up of a year and another in the mid year. If however no work is conducted at shutdown and major maintenance is scheduled for a later date, then conduct the media run after the maintenance. These media runs are to simulate the complete process with both the bioburden reducing filter and the sterilising filter in place.

However, due to the physical properties of the media, it will be necessary to use a pre-filter before the bioburden reducing filter.

Revalidation studies are to be conducted in the time frame of plus or minus one month of the most recent past revalidation. If revalidation does not take place as per the schedule and the process has moved out of compliance raise a DR to document the non compliance to revalidation procedures.

High Speed Filling Machines are to fill equal to 10,000 units.

Low speed Filling Machines are to fill equal to 5000 units.

1.1.1. Chaser Media Fill may be used at the discretion of the Microbiology Manager or the Validation Manager under certain circumstances to protect a particular batch or due to an investigation. In this case the media is filled immediately after the batch with no steaming in between the batch and the media. The sterilising (secondary/product) filter is left in place so the sterility of the line is not broken. The filter integrity test must be performed in line for the batch in question prior to filling the media and will serve at the pre-filling test for the media. A post-filling filter integrity test must be performed after the media fill.

1.2. Validation

Initial Validation – i.e. A new process line, requires 3 consecutive satisfactory simulation tests per shift. Batches will not be released for sale until the validation file has been signed.

High Speed Filling Lines must simulate extended filling. 5000 units are to be collected at the start, middle and end of a typical process run to produce >10,000 units required for a valid run. The process can be stopped in the sterile state for the period between the start and middle collection and again between the middle and end collection. The run must be completed within the holding time of the solution.

1.3. Revalidation

Revalidation includes changes to validated equipment. A DR must be raised to ensure all product manufactured after the change is on hold until the completion of the media run and/or "Soup" Integrity test. Once the results and report have been written and assessed and all criteria have been met, the DR can be completed and the batches released for sale.