



Integration of a Vial Filler and Lyophilizer within the same Isolator

In a typical filling line involving freeze-drying, the lyophilizer is located away from the filling machine, in a separate room or even another part of the facility. As a result, it requires special transfer and isolation considerations. A recent project was completed by Walker Barrier Systems for an H1N1 vaccine filling line running at 80 – 100 vials/min. In this project, the filling machine and lyophilizer were integrated into the same isolator, which is unique in the industry.

The requirement for this project was to provide an aseptic environment for vaccine filling using isolators for vial depyrogenation, vial filling and lyophilization in an existing small room measuring 22' long x 13' wide x 10' high. A positive pressure, non uni-directional airflow isolator was interfaced to a Gruenberg Oven. A positive pressure, non uni-directional airflow transfer isolator was to be used to transfer vials from the oven to the fill machine isolator. Due to the room constraints, a uniquely shaped isolator was designed to interface with both the M&O Perry liquid fill machine and the SP Systems Lyophilizer.

The Filler/Lyophilizer isolator was L shaped with two 45° angles in which 350mm RTP flanges were placed. This allowed docking of the transfer isolator and provided space for operators to walk around the equipment. This isolator also operated under positive pressure but included uni-directional airflow at 45fpm.

The process flow for filling included:

- Decontaminate all isolators using vapour hydrogen peroxide.
- Unload vials from oven into interface isolator.
- Transfer vials from interface isolator into transfer isolator via RTP door.
- Move transfer isolator from oven interface isolator to Filler/Lyophilizer Isolator.
- Transfer vials from transfer isolator into Filler/Lyophilizer isolator via RTP door.
- Vials are placed on accumulator table. Stoppers and caps enter isolator via a 270mm RTP system located near the feed bowls.
- Finished vials exit the isolator via the transfer isolator connected to the second 350mm RTP and are taken to a packaging area.

The filling machine is set up to fully stopper and cap non lyophilized vials.

All isolators in this system are constructed of 316L stainless steel with laminated safety glass windows, silicone gaskets and hypalon gloves. Allen Bradley PLC is used to communicate with the VHP generators and control isolator pressure and uni-directional airflow speed. To assure successful distribution of vapour during decontamination of the filling equipment and isolator, vapour is introduced into the uni-directional airflow plenum. Mix fans were added to direct vapour under blind spots such as turn tables.

This approach results in a more compact design and eliminates the need for a lyophilizer interface isolator which in turn saves costs and reduces validation time. All while providing an aseptic, clean environment with an excellent sterility assurance level for vaccine production.