WHITE PAPER

Secure sterile transfer in pharmaceutical production

Proving leaktightness of the DPTE® system

Transfer with minimal contamination

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Sterile transfer of components and other materials between sterile and non-sterile areas has always been a major concern in the pharmaceutical production industry. Previously, injectables and other medicinal products were produced in conventional clean rooms with insufficient protective barrier systems and several manual interventions by operators. The risk of contamination was high.

Since its introduction to the biopharma industry in the 1970s, the DPTE® system for sterile transfer has revolutionized pharmaceutical production lines. Minimized manual intervention and the ability to transfer components such as stoppers, caps, bottles, plungers via a DPTE-BetaBag® into an isolator via a secure lock with a DPTE® Alpha port have increased productivity and reduced the risk of microbial or particulate contamination.

Background

The DPTE® system was designed in the 1960s to solve the problem of safe and secure transfer of nuclear waste in nuclear research. Ten years later, the pharmaceutical industry became interested in its capabilities for the safe, sterile transfer of material. Today the DPTE® system is a global standard with more than 40,000 units installed worldwide.

How it works

The DPTE® patent consists of an Alpha port, fixed to a filling line or isolator for fast transfer, and the DPTE® Beta part which docks onto the port. This Beta part can be a rigid container, a DPTE-BetaBag®, either empty or containing sterile items, tubing for liquid transfer, or a waste collection device.

The Alpha and Beta parts are fitted together by an ingenious patented locking method which is leaktight, meaning the integrity of the transfer operation cannot be broken. At the same time both the doors are detached from their respective flanges and fixed together, while the flanges and seals continue to maintain the leaktightness of this new joined assembly (see figure 1). The Beta part can then be used to transfer material into, or collect components from, the isolator. By reducing the number of operator contacts with the sterile products during the manufacturing process, the risk of microbial contamination is minimized.

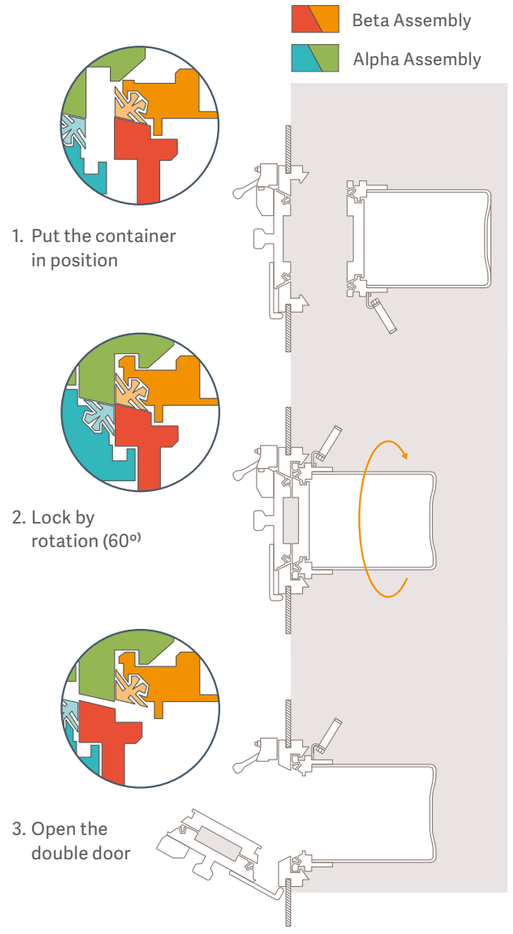

Figure 1 - DPTE® transfer system

Leaktightness

Leaktightness is the basis of the DPTE® system for safe transfer avoiding the spread of contamination from microorganisms and/or particulate matter.

Primarily a system with high performance in airtight status, DPTE® has a very low leak rate. Prior to installation, each DPTE® system is tested for leaktightness. Differential pressure testing performed using 4000 Pa, a robust test pressure which is around 100 times greater than the working pressure in isolators, showed that the DPTE® system itself is more airtight than the isolators on which the DPTE® system is installed.

Microbiological validation

The DPTE® system was rigorously tested in a study at the French Agricultural Institute (INRA) in France. The methodology consisted of contaminating an airtight enclosure equipped with a sterile DPTE® Beta container with a large population of bacteria, and then checking for the presence or absence of contamination following repeated transfers in a second sterile enclosure, attached to the first via a DPTE® Alpha port.

The first step of the microbiological validation was to contaminate and maintain the level of contamination in the airtight enclosure. The second step was to qualify the bio-decontamination and maintain the sterility of the sterile enclosure. Then the third step was to control the presence/absence of contamination when connecting and disconnecting the sterile DPTE® container. The differential pressure between the two enclosures was + 120 pa, which is three times the usual differential pressure, from the contaminated enclosure to the sterile one (see figure 2).

The results showed that the performance of the DPTE® containers maintained the environments without any contamination. Even in a hostile environment, despite numerous constraints and from a clean point of view, all transfers were performed with safe results. Few bacteria were detected on the seals of the gaskets. Known as the "ring of concern", this surface contamination is localized on the gaskets and is not found either in the air or on the surfaces of the enclosures. The "ring of concern" can easily be disinfected by hand with decontamination agent – i.e. by wiping it clean.

Particulate validation

An official study on particulate contamination was conducted at the French Nuclear Safety Institute (LECEV of IPSEN) to quantify the efficiency of the DPTE® system. The rigorous test conditions were identical to the ones used during the microbiological validation to be able to correlate study and methodology. The results showed that the efficiency ratio for DPTE® was at a level higher than the efficiency of an HEPA filter, demonstrating its capacity to effectively isolate particulate contamination.

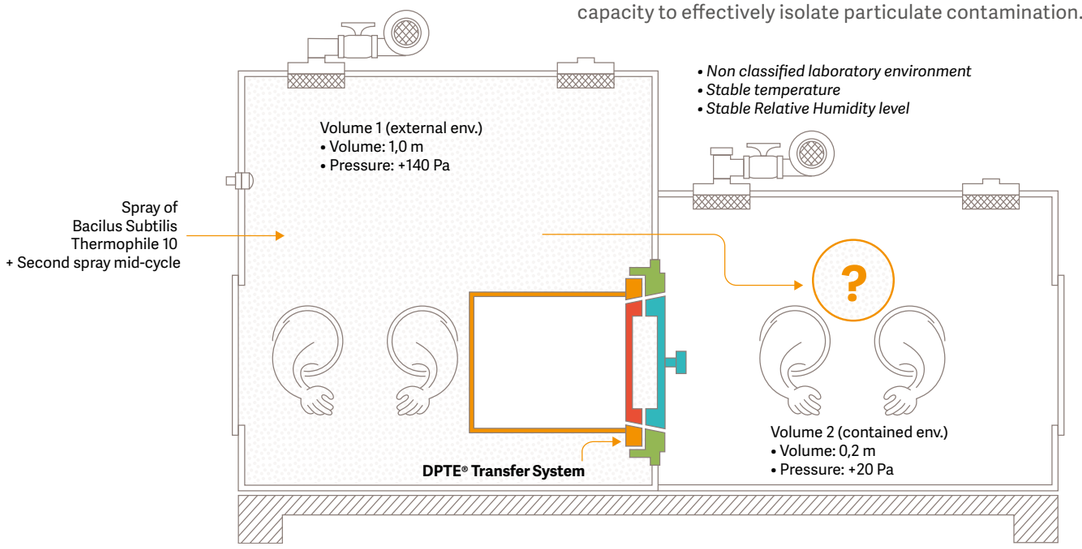

Figure 2 - Diagram of the test equipment for microbial validations

Conclusion

The DPTE® System is the industry benchmark for secure sterile transfer in pharmaceutical production. It has become a worldwide reference through the development of its performance in developing markets markets like biopharma. Validatable and reproducible performance in safety, airtightness and protection against particulate and microbial contamination puts it on the top in market terms, regardless of the multiplication of copies and parallel double-door technologies.

This unique system allows multiple purpose secured connections on different barrier systems (RABS, cleanroom, isolator, etc.). Any DPTE® Beta part can be connected to any DPTE® Alpha part with an identical diameter, whatever material they are made of – stainless steel, plastics, machine tooled, injected, etc.

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