

Designing Transfer Carts for Class 100 Conditions

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FDA has found several pharmaceutical companies not maintaining Class 100 conditions within transfer carts. Implementing a solution is not a simple task. The author discusses an approach for designing a transfer cart that will satisfy Class 100 requirements.

A seemingly simple question raised during an FDA inspection is bringing about a major modification of the way many parenteral manufacturing operations transport vials.

The question is: Are Class 100 conditions being maintained during the transfer of vials from the filling line to the freeze dryer? The industry norm and practice for many years of placing vials in carts without air handling systems, closing the door, and wheeling them through lower classification areas was suddenly being challenged by FDA and most companies did not have the data to answer the offhand question. A number of companies quickly conducted testing to prove that such a question had no merit. Surprising to many

industry experts, the results showed that Class 100 conditions were not being maintained in the environment where partially stoppered vials were transported. Panic arose on two fronts. The first concern was product integrity and the second was finding a solution to the problem. The level of concern was somewhat mitigated by the fact that manufacturers felt that the problem would be relatively simple to correct.

However, the design of a new cart has turned out to be a complex task. Many design attempts have failed as a result of the many constraints and variables. A successful design requires unique engineering skills and an understanding of the facility and process.

Requirements of a transfer cart

Design. The design of a new cart requires an air handling system with unidirectional airflow that can remove particulates that are generated when thousands of vials are jarred against one another during movement of the cart and can maintain these conditions while the cart is being moved from the filling line to the freeze dryer. The new cart must be large enough to accommodate an on-board air handling system, and fitting the larger cart into the existing space may prove to be a formidable task.

Space. Most parenteral manufacturing facilities are built with a minimal amount of space in the sterile block. Designs are driven by the expense of construction and the cost of maintaining high-quality spaces. A majority of parenteral manufacturing facilities have filling lines located separately from the freeze dryers within the sterile block. Products that are to be freeze-dried are transported from the filling line to the freeze dryers through zones of lower air quality within the sterile block. At the filling line, products are put into vials that are then partially stoppered and placed onto trays. The trays are then loaded into the transfer carts and transported to the freeze dryer.

Current transfer carts have two major design flaws that have surfaced as a result of the FDA question. The first flaw is a

lack of an air handling system that can maintain unidirectional airflow during transport, and the second is a lack of integrity in the construction of the carts, which are not gas tight.

Finding a solution

Building a cleanroom on wheels and incorporating the advantages of an isolator by making the environment gas tight seems to be the solution. This requires complex engineering plus an understanding of the human interaction of handling trays of vials while not violating the clean loading zone. The technical details that must be considered include proper airflow velocities, pressurization and patterns to deliver product protection within the carts, and the physical limitations of the facilities. Because most facilities are designed to be as small as possible, space is very limited in the Class 100 zones of the filling line, loading areas, and the freeze dryer. These space constraints play a major role in the functional requirements of a cart design. Time constraints also play a large role because of regulatory demands to get the problem fixed.

The functional requirements must be built around the space available in the sterile block to load, unload, and manipulate the carts. The space constraints include not only the loading and unloading zones, but also the route the carts travel from the filling lines to the freeze dryers, and careful attention must be paid to turns and door openings. Once the facility constraints are defined, then the size of the transfer cart can be determined. The cart, which consists of the product chamber and support systems, is designed, in most cases, to maximize the number of trays in the product chamber. A larger product chamber, however, requires larger support systems. Thus, the optimum solution requires a balance of the two variables to maximize the vial load of the cart. Additional considerations include ensuring proper aseptic techniques during the loading and unloading operations and analyzing the ergonomics of loading the trays, which weigh more than 10 kg, and moving trays loaded with vials.

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The tray-loading area at the end of the filling line typically has Class 100 laminar flow coverage provided by hanging or ceiling HEPA-filtered units. The coverage patterns within these zones change as different objects are placed in this area. A larger cart may change the loading position for the operator, which can change the airflow dynamics. Testing for any potential change is critical and should include mapping the area for airflow using a videotaped smoke test to identify positioning problems. Smoke testing can be conducted only when the sterile block is not in operation, which limits the amount of time for testing. To compensate for this short window, well-designed tests and schedules are required.

The workstation at the freeze-dryer also must be reviewed. Videotaping of smoke patterns during the unloading of vials at the freeze dryer and reloading after the freeze-drying is complete provides the best documentation that neither the cart nor freeze dryer are compromised during these operations. The videotape also provides a useful tool for operator training.

The carts operate in the sterile block and must have surfaces that can be cleaned and sanitized, which presents another design challenge. The surfaces must be of high quality and designed to eliminate any potential contamination points. From the wheels to the interior chamber, consideration of good aseptic design for all components is needed. Testing of materials of construction is important to ensure that they are compatible with the products used for cleaning and sanitizing the cart. The quality in the finish of the surfaces to be cleaned must be considered from two points. The first is having a surface finish that can be cleaned to the proper level, and the second is having a surface finish that can withstand normal activities. The adhesives and gaskets must withstand the harsh chemicals to which they are exposed. The method of application of the cleaning and sanitizing materials should be considered when testing for compatibility. A majority of operations still use manual cleaning and sanitizing of the exterior and interior of the carts. Also, if the racks are to be autoclaved, they must be removable and must fit into the existing autoclave.

The gray side mechanical components required for the air handling system, which includes blowers, HEPA filters, and a uniform airflow membrane, also present a challenge. The system has exacting performance criteria required to fit into limited space. Design restrictions such as the inability to exhaust the cart airflow into the surrounding space require special engi-

Characteristics of a Class 100 transfer cart

- Gas tight environment
- Proper space availability to load, unload, and manipulate
- Well-designed smoke test
- High quality, cleanable surfaces
- Good aseptic design
- Removable racks
- Controlled temperature range
- Monitored battery usage

neering expertise. Recirculating the air within the cart can create a temperature build up. The system must be tested to ensure that the product is maintained within the defined temperature range. Verification of the temperature profile of the cart and the product also should include complete testing of conditions while on battery power. The test protocol should include a profile of both performance and heat load.

While in motion, the carts use a battery-powered system to support the unidirectional airflow systems and controls. Ensuring adequate power to run the air handling system requires a control system that monitors battery usage and will sound an alarm in time to place the system on normal AC power before the product is compromised. The value of the products being transported can range into the millions of dollars and any out-of-specification event would result in loss of load.

When stationary, the carts use normal AC power, accomplished by simply plugging the cart into a power source. Planning for adequate staging may require facility modifications because of the number and increased size of the carts. The power sources and energy loads must be considered. The batteries must be charged, either by an onboard system or at a charging station. Because of the critical area in which the carts operate, the onboard system located in the gray zone of the cart is preferable.

A successful design

The many constraints and variables described above are just a few examples of why the design of a transfer cart for freeze-dried products is anything but simple and why many design attempts fail.

A successful design that meets regulatory expectations will require unique engineering skills and an understanding of both the facility and the process. To achieve this, the pharmaceutical manufacturer must partner with the cart manufacturer to evaluate the unique nature of the facility and develop the proper solution. **PT**