SP Industries

935 Mearns Road Warminster, PA 18974 800.523.2327 Phone: 215.672.7800 Fax: 215.672.7807 www.SPindustries.com

TECH BRIEF: HUMIDITY CONSIDERATIONS FOR COLD SHELF LOADING

by Charles D. Dern, P.E.

It is common practice during the production of a freeze-dried parenteral drug for the solution first to be formulated and the vials then filled at room temperature. Afterwards the vials are placed onto the shelves of the lyophilizer, which are usually at or near room temperature (5°C is a common temperature). However, recent changes in Parenteral development processes, such as quick freezing, have lead to the need for loading pre-frozen product onto shelves that are much colder (-50°C or more) than the room's ambient temperature. With this development has come the problem of condensation and even frost buildup on the lyophilizer cabinet and shelves. Such frost build-up has multiple consequences.

First, frost buildup on the lyophilizer shelves can have three effects: 1) It can insulate product from direct contact with the heat transfer shelf. 2) It will cause an extra, albeit slight, initial load on the system. 3) It can impede loading tray positioning on the shelf. One also should consider that frost will collect on product previously loaded into the chamber. This can cause potential differences in drying between product that is loaded first and the product that is loaded last.

Second, frost can buildup on the door flange, particularly near the bottom due to cold air dropping out of the chamber and flowing over the flange. This causes two concerns: 1) The gasket material becomes less pliable 2) The ice itself can inhibit the door from making full contact. Both make the door to chamber interface less conducive to forming the tight vacuum seal necessary to commence the freeze-drying cycle.

The ideal solution would be to remove virtually all of the humidity from the room, which would almost completely eliminate the above problems. But such an approach is, of course, highly impracticable for many reasons. Extremely low humidity is very uncomfortable for human occupancy. This condition also increases problems with static electricity. Last but not least, there is the need for potentially expensive and esoteric dehumidification technology.

On the other hand, the experience of several producers of pharmaceuticals who load lyophilizers with the shelves at very cold temperatures has shown that humidity in the standard 50% to 60% Rh range usually causes the above problems to occur to the point where safe, sterile and proper operation of the clean room and lyophilizer are hampered.

Given the above, an Rh in the 20% to 30% range would seem to be the ideal compromise. A desiccant wheel dehumidifier is one device that can provide these humidity levels and is readily available. This technology has been used at several major pharmaceutical firms with reasonable success in limiting the above problems. Of course, one must still take into consideration personnel comfort and static electricity concerns particularly where cleaning solutions are involved.

An alternate solution is to fit the freeze-dryer with a subdoor (a smaller door within the main door.) For cold loading conditions, the subdoor is fitted with heating elements about the door and its flange. These elements warm the subdoor and contact surfaces to slightly above the icing temperature. SP has produced several systems with this feature and has successfully precluded ice buildup on the systems on which it was installed.

In concert with the reduced opening of the subdoor, one also can maintain a minimal positive pressure of nitrogen (N2) in the chamber. This too will reduce if not eliminate ingress of load room air into the chamber.

Finally, in addition to the above solutions, an automatic load/unload system (ALUS) can help reduce the need for human presence in the loading area thus not only minimizing personnel problems with low humidity but also reducing potential bioburden in the clean room.

For more information on our products, please contact our corporate office at 800-523-2327 or visit our website (www.SPindustries.com).

Charles D. Dern is a Project Engineer for SP Industries.