chamber is a single stream containing dried particles suspended in the gas. In the ideal case, each droplet of the solution has been dried to form a single particle, as it has been carried downward through the chamber by the surrounding gas and the force of gravity. The particles are removed from the gas stream with a cyclone or a filter.

There is a common belief that the high temperatures usually used for the inlet drying gas would lead directly to product degradation. However, the drying droplet's temperature is much closer to the wet-bulb temperature of water due to evaporative cooling, and the residence time of a given droplet from the time it is sprayed to the time that it has completed drying and is in a cooler collection vessel is on the order of seconds. In addition, it is possible to use very low drying gas temperatures if one is willing to accept lower throughput. As discussed in the recent reviews cited above, many have found that spray-drying can be used for thermolabile products, including vaccines [5, 15, 18].

Development of a sterile spray-dryer requires addition of full sterilization-in-place (SIP) capability, sterilizing vent filters on the inlet gas line, and fully aseptic powder harvesting. In addition, one must have the ability to perform sterile powder filling into vials or other suitable containers. Fortunately, sterile powder-filling technology has been in use for many years. One challenge associated with filter sterilization of the inlet gas is that relatively large filter banks are required, and these must be tested for integrity. Integrity testing of very large filter banks can be a challenge.

While formulation and process development for lyophilization can be reliably carried out on a small scale, spray-drying presents special challenges in this regard. Benchtop spray-dryers are known to lead investigators to "false negative" conclusions of the feasibility of using spray-drying. The principal challenges with benchtop spray-drying are that it is very easy to "overheat" the sample during drying, and the percent recovery of powder can easily be $<50\%$ due to deposition on the walls of the drying chamber and powder collection cyclone. Both of these problems are known to diminish with increasing spray-dryer size.

A recent paper addresses these challenges, showing that for multiple recombinant monoclonal antibodies, a "laboratory scale" dryer (chamber diameter 30 cm) significantly outperformed three benchtop scale units (chamber diameters 11–17 cm) with respect to product recovery, which was $>90\%$ [3]. They also observed that higher ratios of antibody to trehalose resulted in higher recoveries, because the trehalose imparts additional tackyness or stickyness to the formulation, increasing the deposition of partially dried droplets on the walls. Reconstitution times were <3 min. After 3 months of stability testing at 40 °C, the decrease of monomer content was greater (worse) for formulations with less trehalose. This observation brings about the need to optimize the formulation composition in concert with process development and scale-up, for while higher trehalose concentrations improved stability, they negatively impacted product recovery. This suggests the need for an additional excipient such as maltodextrin to be used as a "drying aid" to reduce tackyness and improve product recovery [21].