Spray Freezing and Dynamic Bulk Freeze Drying for the Manufacture of Sterile Lyophilized Microspheres

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Dynamic Spray Freeze Drying combines spray freezing and rotary freeze drying. For parenteral products, a fully contained process line is utilized. The innovation of the technology is related to formulation and product areas like processing highly concentrated protein formulations or reduction of reconstitution time. By generating highly homogeneous bulkware, it also opens new options related to manufacturing logistics like avoidance of cold chain requirements, time-to-market reduction and allows for a highly flexible Supply Chain.

Technology

The substrate liquid is dispersed into similar size droplets using a controlled laminar jet break up process. The droplets travel through a gaseous cooling zone by gravity, congealing into frozen spheres. The frozen bulk is then lyophilized homogeneously in a rotary freeze dryer under constant rotation, with IR radiation and the wall temperature of the drum as heat sources.

The combination of the freezing and the lyophilization step in one process line with vertical product flow by gravity allows for a fully contained process set up with minimized product handling requirements.

Concept of Bulkware Use

By Spray freezing and dynamic rotary freeze drying, sterile lyophilized microspheres as bulk can be generated. The final bulk product is homogeneous, free flowing and dust free. It therefore allows for an intermediate storage of the (also sterile) bulk product, with a subsequent filling of microspheres - the filling step and the lyophilization step are separated. As a

consequence, filling on demand with flexibility regarding dosing, unit quantities or primary packaging devices is possible. Since lyophilization is already accomplished, there is no need that the primary packaging is suited for lyophilization. Also combinatory products can be formulated by filling various components with even different dosing into one vial.

The technology is specifically designed for parenteral pharmaceuticals, but also used outside pharma applications for specialty chemicals. The talk will highlight technical features and selected process characteristics and comment on scale-up data from lab and pilot scale, as well as on production scale data of a fully contained production scale process line for the manufacture of sterile lyophilized microspheres.