# Lyophilization: Small-Large Scale Comparability

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## PURPOSE

Lyophilization is used for drug products to provide for greater stability and increase the product's shelf life. The number of differences between commercial and laboratory scale processes dictates the development of some sort of strategy for transfer and scale up activities. The use of the same laboratory-scale recipe at larger scale lyophilizers may result in different product temperature profile primary drying time.

The most common and probably most important difference between commercial and laboratory dryers is the difference in pressure control. Usually, commercial dryers are programmed for larger pressure tolerances than laboratory dryers to accommodate possible deviations during manufacturing. Another common difference in process control is the condenser temperature, which is normally much lower in laboratory dryers, even at no load conditions.

## OBJECTIVE(S)

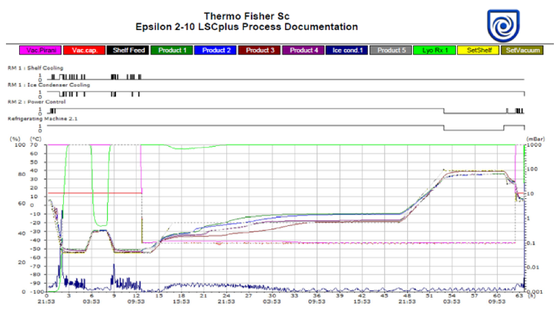
The study aimed to demonstrate comparability between the pilot lyophilization unit of the pharmaceutical development services department (Epsilon 2-10D) , and the Optima units located in large scale (Thermo Fisher Scientific's site in Ferentino, Italy).

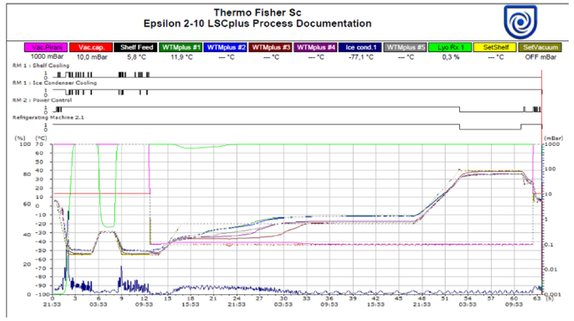
The investigation was carried out in a process development laboratory, with Epsilon 2-10D unit and Optima unit located in the site's good manufacturing practice. A model formulation 5% mannitol and a practical comparison study was performed.

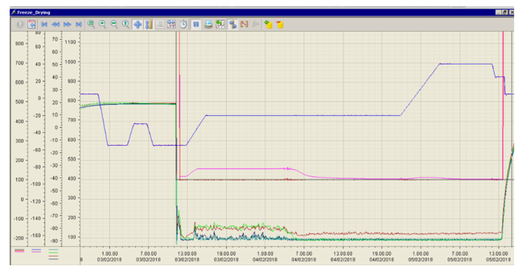
The key parameters for lyophilization comparability were: shelf temperature mapping with minimum lyophilization load, shelf temperature mapping with full lyophilization load, comparison of critical quality attributes related to lyophilization performance and formulation characterization (appearance of lyophilized product, reconstitution time and moisture content, specific surface, porosity and dimension of the pores).

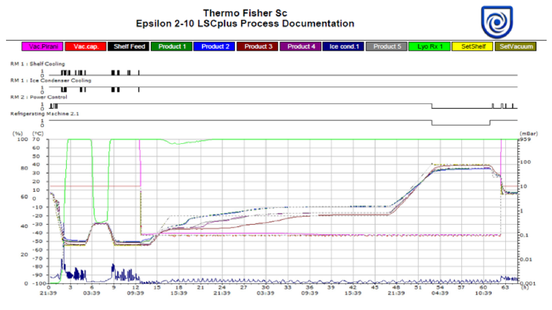
## RESULT(S)

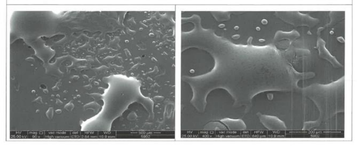
Appropriate bracketing strategy was applied: comparison of the technical specification of the freeze-dryers, comparison of the downloaded digital data of the lyophilization cycle performed at pilot scale and at production scale, Freeze-dryer plot from lyophilization cycles performed in the pilot and GMP units were compared.

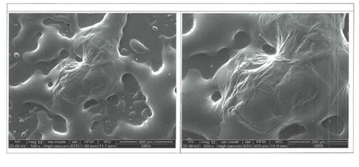


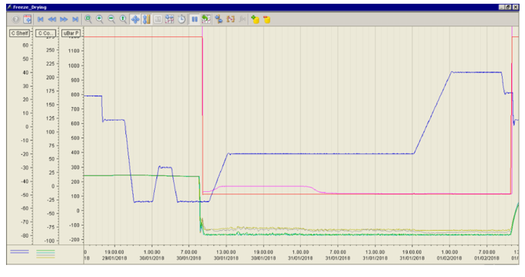









## CONCLUSION(S)

Some differences was observed due to product formulation, lyophilization recipe and loading conditions. As a risk mitigation it is suggested to introduce as a safety margin, 5 hours longer in the Primary drying length.

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