

Optimizing the Throughput of Freeze-Dryers Within a Constrained Design Space

Jim A. Searles

Aktiv-Dry LLC, Boulder, Colorado, U.S.A.

INTRODUCTION

The objective of freeze-drying process development is to deliver to manufacturing a cycle that achieves all of the following:

1. Acceptable product quality, consistent within a batch and from batch to batch
2. Operation within the capabilities of the equipment, with appropriate safety margins to ensure robustness
3. Efficient plant utilization via the shortest possible cycle time and full loading of the lyophilizer

This chapter highlights key aspects of how to achieve all three at the same time with a methodology for optimizing the throughput of a group of freeze-dryers. It includes an actual case study in which most of the dryer time was spent on a single product, and the vast majority of processing time was taken up with primary drying. The case study therefore focused on maximizing primary drying rate while avoiding product failure. The reader will also find sections further exploring heat transfer phenomena within the freeze-dryer's shelves, and advice for specifying, procuring, testing, qualifying, and validating freeze-dryers.

This chapter is aimed at those supporting freeze-dryers in manufacturing, as well as scientists and engineers in manufacturing technology, technical services, and process development groups. The latter will find this information very useful for ensuring that the freeze-drying cycles that they develop on laboratory-scale freeze-dryers will be transferrable to production-scale units.

This chapter employs symbols and nomenclature that engineers are taught in heat transfer, fluid mechanics, and transport phenomena classes. For the reader's convenience, the symbols are consistent with those defined and used in Ref. 1, which is an excellent, well-respected heat transfer textbook that can be downloaded free on the Internet (1). The terms "drying" and "sublimation" are used interchangeably.

ANALYZING FREEZE-DRYER TIME

The overall productivity of a freeze-dryer can be defined in terms of annual throughput, or number of vials of product produced per year. Manufacturing organizations should always have an eye toward maximizing throughput of quality products because it increases the return on investment for the facilities, equipment, personnel, and supporting infrastructure. Freeze-dryer time should

This chapter was completed while the author was affiliated with Eli Lilly & Company, Inc., Manufacturing Science, and Technology, Indianapolis, Indiana, U.S.A.