

# Lyophilization Strategies for Development of a High-Concentration Monoclonal Antibody Formulation: Benefits and Pitfalls

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## Abstract

Development of a successful subcutaneous antibody therapy requiring chronic administration at high dosing (several mg/kg), particularly when coupled with prefilled syringe and autoinjector device for at-home administration, is dependent on the development of a stable formulation at high concentration. This is very challenging due to a few key factors. First is the current limitation on subcutaneous injection volume ( $\leq 1.5$  ml), and more importantly due to limited intrinsic stability in a highly concentrated aqueous solution. To overcome the instability barrier of the aqueous antibody solution, products are typically stored in a lyophilized (freeze-dried) state. Besides stability, the development of room temperature products, improved patient compliance and easier worldwide distribution are additional advantages of lyophilization. Unfortunately, the lyophilization process also generates a variety of freezing and drying stresses. Additionally, other factors such as a sub-optimal drying process, limited long-term storage stability and slow reconstitution time could influence the choice between a liquid and a lyophilized formulation. The purpose of this review is to discuss the scientific foundation and the critical issues related to the lyophilization process for development of stable antibody-based formulations. Additionally, some guidelines for successful development of lyophilized high concentration antibody formulations are presented.

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