

Abstract Submitted  
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**The Structural Properties and Stability of Monoclonal Antibodies at Freezing Conditions** TATIANA PEREVOZCHIKOVA, University of Delaware/NIST, ISIDRO ZARRAGA, THOMAS SCHERER, Genentech, Inc, NORMAN WAGNER, University of Delaware, YUN LIU, University of Delaware/NIST — Monoclonal Antibodies (MAb) have become a crucial therapeutic agent in a number of anti-cancer treatments. Due to the inherent unstable nature of proteins in an aqueous formulation, a freeze-drying method has been developed to maintain long-term stability of biotherapeutics. The microstructural changes in Mabs during freezing, however, remain not fully described, and it was proposed that the formed morphology of freeze drying samples could affect the final product quality after reconstitution. Furthermore, it is well known that proteins tend to aggregate during the freezing process if a careful processing procedure is not formulated. Small Angle Neutron Scattering (SANS) is a powerful tool to investigate the structural properties and interactions of Mabs during various stages of lyophilization in situ. Here we present the SANS results of freeze-thaw studies on two MABs at several different freezing temperatures. While the chosen proteins share a significant sequence homology, their freezing properties are found to be strikingly distinctive. We also show the effect of excipients, concentration and quenching speed on the final morphology of the frozen samples. These findings provide critical information for more effective lyophilization schemes for therapeutic proteins, as well as increase our understanding on structural properties of proteins under cryogenic conditions.

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