34g Challenges of Scaling up a Highly Hydrophobic Corticosteroid

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Abstract

The scale-up manufacturing process for a highly hydrophobic corticosteroid formulation posed a number of challenges ranging from formulation to equipment design that have been successfully overcome. The major challenge is to control the foam. It has been determined that the nonionic and cationic surfactants in the formulation create two types of foam - unstable foam created during wetting and homogenization of drug substance in nonionic surfactant solution and a stable foam produced when the cationic surfactant is added. Moreover, adding stabilizing aqueous dispersion to the API dispersion acts to stabilize the foams from both nonionic and cationic surfactants. Thus the manufacturing challenges become not only of minimizing creation of stable foam during processing, but also of finding a way of avoiding the stabilization of the foams. Several processing techniques to reduce or eliminate foam were tried and have been discussed. Control of the foams is important because the potency of the suspension was found to be low, as more stable foam was formed. This is partially due to the hydrophobicity of the API. The authors summarize their findings and propose techniques to achieve a better API wettability along with foam management.