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Homogenizing biologic drug substance bulk using single use mixing systems

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Mixing of biologic Drug Substance (DS) is a critical process step during manufacturing of biologic Drug Product (DP). Generally, mixers used are equipped with either bottom-mounted or top-mounted agitators. Bottom-mounted mixers (BMMs), particularly those that are magnetically driven, are preferred because of their associated low risk of contamination, ease of use, and ability to accommodate low minimum mixing volumes. Despite these benefits the mechanical coupling of the rotating impeller and the male bearing on the tank may lead to shearing of monoclonal antibody (mAb) formulations generating elevated amount of particles in the DS or DP solution. This may lead to filter fouling during microbial reduction filtration or sterile filtration. Newer and advanced technologies incorporated in single-use mixing systems may help overcome this challenge. The objective of this study was to understand the impact of various bottom-mounted single-use mixer designs on product quality attributes and process performance. Four single-use mixing systems equipped with bottom-mounted impeller were evaluated using an IgG1 mAb at two tip speeds under worse mixing conditions. The homogenized samples were analyzed for any increase in particles or any changes in size variants or turbidity. Filtration study was also performed to determine whether mixed material would clog the filter. The results suggested that mixers that are designed to function with no contact between the impeller and the drive unit are the most favorable and gentle to mAb molecules. Designs with contact or a narrow clearance tended to shear and grind the protein and resulted in high particle count in the

HOMOGENIZING BIOLOGIC DRUG SUBSTANCE BULK USING-SINGLE USE MIXING SYSTEMS

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References: Gikanga B.; Chen Y.; Stauch O.; Maa Y. *Mixing monoclonal antibody formulations using bottom-mounted mixers: impact of mechanism and design on drug product quality*. PDA J Pharm Sci Technol. 2015 Mar-Apr; 69(2):284-96.