Application of Computational Fluid Dynamics in Facility Fit for Manufacturing Cell Culture

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Abstract

Among many operating parameters that control cell culture environment, appropriate mixing and aeration are crucial for cells to meet oxygen demand in aerobic microbial and mammalian production processes. A model-based manufacturing facility fit approach was applied to define agitation and air flow rates during cell culture process scale-up from laboratory to manufacturing, of which computational fluid dynamics (CFD) was the core modeling tool. The realizable k-ε turbulent dispersed Eulerian two-fluid model was used to simulate gas-liquid flow in the bioreactor and predict volumetric oxygen transfer coefficients (k_La), where the simulation was performed in the basal medium and the resulting k_La was adjusted using modification factors for surfactants such as Pluronic F68 and Antifoam C. The CFD prediction of k_La resulted in adequate agreement with the empirical values in 15,000-L and 25,000-L bioreactors. The model was then applied to define a range of agitation and bottom air flow rates for meeting cellular oxygen demand and mitigating risks of cell damage and safety hazards. The recommended operating conditions led to the completion of five manufacturing runs with a 100% success rate. The model-based approach reduced the required number of at scale development batches and hence enabled seamless scale-up, shortened timelines, and cost savings in cell culture process technology transfer.

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