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RESEARCH ARTICLE

DOE-Based CFD Optimization of Pharmaceutical Mixing Processes

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Abstract Fluid mixing and homogenization are key manufacturing processes in the pharmaceutical industry that in an industrial setting are typically optimized and adapted using empirical techniques rather than numerical methods. In the recent years, in silico techniques have increasingly attracted interest due to the many advantages and the increased information content. Computational fluid dynamics, for example, have often been applied to mixing problems. Although numerical flow simulations are nowadays common for simple applications, more complex cases (e.g., industrial mixing) still require much work to achieve reliable results with reasonable resources. In our work, we present an efficient procedure for optimizing the mixing performance of an unbaffled tank for pharmaceutical applications. The optimization objectives were the position of an impeller in the tank defined by the bottom clearance, the eccentricity of the impeller, the angle of the impeller shaft, and the impeller rotational speed. In order to generate a regression model for prediction of the optimal performance, design of experiments was used. Our optimization study showed that the impeller eccentricity had significantly more impact on mixing performance than the shaft angle, that the impeller speed was the main driver for the power input and the average shear forces, and that the bottom clearance may have strongly impacted the flow in the bottom tank area.

Keywords Mixing · CFD simulation · DOE · Optimization

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Notation

C	Bottom clearance, in meters
C_0	Bottom clearance in base position, in meters
D	Impeller diameter, in meters
E	Off-center distance, in meters
E_0	Off-center distance in base position, in meters
f	Elliptic relaxation function
g	Gravitational acceleration, in meters per square second
H	Filling level, in meters
I_T	Turnover rate, per second
k	Turbulence kinetic energy per unit mass, in square meters per square second
M	Torque, in newton meters
N	Impeller rotational speed, in revolutions per minute
P	Power input by an impeller, in watts
Q	Volumetric flow rate, in cubic meters per second
Q^2	Goodness of prediction
r	Distance between center points, in meters
R^2	Goodness of fit
Re	Reynolds number
T	Tank diameter, in meters
T_M	Mean tank diameter (cone-shaped tank), in meters
V_i	Cell volume of the computational cell i, in cubic meters
V_{tot}	Total volume of the domain, in cubic meters
x	x-coordinate, in meters
y	y-coordinate, in meters
α	Impeller shaft angle, in degrees
β	Cone angle, in degrees
γ_{av}	Volumetric mean shear rate, per second
γ_i	Shear rate of a mesh cell i, per second
ζ	Normalized velocity scale
ν	Kinematic viscosity, in square meters per second
ρ	Density of the liquid, in kilograms per cubic meter
φ	Rotating angle concerning the z-axis, in radians
ψ	Rotating angle concerning the y-axis, in radians
ω	Angular impeller velocity, per second