369b Population Balance Equation Modeling of Drop Size Distributions in Turbulently Prepared Emulsions

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Emulsions play an important role in the delivery of many therapeutics. Pharmaceutical applications of emulsions include injectable vaccines and anticancer formulations, fluorocarbon-in-water emulsions for blood oxygenation, oral administration of immunosuppressive agents, and dermal delivery agents (creams and ointments). Emulsions also serve as precursors for other delivery vehicles, such as solid lipid nanoparticles. Emulsions for pharmaceutical applications, as well as for food and personal care products, are usually generated in high-pressure homogenization chambers. The flow fields in the chambers units are typically highly turbulent and mechanisms for drop formation under these conditions are not well understood.

The preparation of pharmaceutical emulsions that target specific organs requires that the drop size distribution is very narrow, nearly monodispersed, with a well-defined and controlled mean size. The drop size affects both biodistribution and uptake rates into different organs. The turbulent processing conditions present in high pressure homogenizers have a substantial impact on drop breakup and coalescence that ultimately determined the drop size distribution. Several investigators have developed population balance equation (PBE) models of turbulently agitated vessels for emulsion preparation. A major focus of these studies is the determination of the breakup and coalescence kernels, but there is no general agreement about the appropriate functional forms of these kernels. The modeling literature on high pressure homogenizers is rather sparse and although computational fluid dynamics has been applied, we are not aware of any PBE modeling efforts for pharmaceutical emulsions.

This paper describes a PBE model for predicting drop size distributions in high pressure homogenizers. We consider a typical oil-in-water emulsion that can solubilize hydrophobic drugs and has a negligible rate of drop coalescence. Our focus is sensitivity analysis of model predictions to the mathematical forms and parameter values of the PBE kernels for drop breakage and daughter drop density under the simplifying assumption of binary breakup. The computational results are used to determine functional forms consistent with available experimental data and to identify parameters that are readily estimated from transient drop size distributions measurements available in our laboratory.