ABSTRACT

Kodam, Madhusudhan. Ph.D., Purdue University, December, 2010. Attrition of Pharmaceutical Tablets. Major Professor: Dr. Carl R. Wassgren, School of Mechanical Engineering.

This dissertation work focuses on attrition of pharmaceutical tablets, which is one of the problems faced by the pharmaceutical industry during tablet coating operations. The present method used to estimate tablet attrition is the standard USP (United States Pharmacopeia) friability tester. This is merely a "Go or No-Go" test before the coating operation and does not quantify the amount of attrition in a coating process. Modeling tools for predicting the degree of attrition by considering the material properties and process conditions would be helpful to assess attrition during coating processes. The goal of this study is to develop discrete element method (DEM) based models for predicting tablet attrition and to validate them experimentally.

Edge chipping and abrasion are identified as the important attrition mechanisms for pharmaceutical tablets. Models have been developed by conducting experiments to measure tablet mass loss due to these attrition mechanisms in terms of measured material properties and loading conditions. Loading conditions were predicted using DEM simulation of tablets in a standard pharmaceutical friability tester and in a simple rotating drum. Since most pharmaceutical tablets are non-spherical, a new class of contact detection algorithms was developed for cylindrical shapes. The contact detection algorithms were verified and validated by analytical and experimental comparisons. By using the combination of DEM simulations, material property measurements and the attrition sub-models, predictions of tablet attrition are made for friability tests and simple rotating drum tests, and validated with mass loss experiments. Experiments, simulations,

and analysis indicate that edge chipping is a much more significant attrition mechanism than surface abrasion for coating operations and friability tests. Mass loss due to edge chipping depends on material parameters such as critical stress intensity factor, hardness and particle size, and, process conditions such as impact velocity.

Based on the parametric studies in rotating drum simulations, it was found that the attrition of tablets increases with increasing drum speed but is nearly independent of fill level within the rolling regime. Hence, it is advisable to perform tablet coating at lower speeds with fill levels that maintain the rolling regime to reduce attrition while maintaining acceptable mixing performance.

System level models like DEM (to predict process conditions), along with material characterization tests (to measure mechanical properties) can be used to evaluate tablet attrition in a more meaningful way than the current standard friability test. The attrition models can provide information about the effects of various material and process parameters on the attrition of pharmaceutical tablets and can suggest methods for reducing attrition.