Mechanistic Modelling of Powder Feeding

Predicting flow performance and mitigating process impacts for new materials

A useful, user-friendly tool for predicting powder feeder performance has been developed with the potential for further development

Drivers

Powder feeders are an integral part of many pharmaceutical industry solid dosage form processing trains and are particularly critical in continuous processing equipment, where any fluctuation in the rate of delivery risks being propagated into downstream blending. Managing feeder performance is often less than straightforward when dealing with active pharmaceutical ingredients (APIs) in particular, due to their challenging flow properties.

An accessible predictive model of feeder performance would enhance both drug product development and manufacture, increasing the speed of development, reducing the associated costs, and improving process robustness.

Approach

A model based upon the best currently available in the public domain literature for powder flow[1] has been incorporated into a user-friendly interface suitable for use by "super-users" (scientists primarily focused on pharmaceutical materials but with some degree of comfort in the use of modelling tools), and by subject matter expert modelling specialists.

Key Features

- A state of the art mechanistic model implemented on an industry compatible, user-friendly, flowsheet based platform
- Material and time-consuming experimentation avoided by adopting a digital workflow for feeder optimisation
- Faster and less costly risk assessment and mitigation approaches for materials with marginal flow properties

The model as currently configured works well for powders with good flow properties, and there is potential for future development so that it can be used for the prediction of feeder performance for less free flowing materials.

[1] *Yu, Y. and Arnold, P.C. (1997) Theoretical modelling of torque requirements for single screw feeders, PowderTechnol. 93, 151-162.*

An ADDoPT Case Study featuring collaboration between PSE and Pfizer

Establishing a 'modelling-first' culture

Lead Users

There is a strong strategic move within Pfizer towards using computational tools for the sort of development task shown in this case study, and there is already a healthy subject matter expert community in place to develop the necessary models.

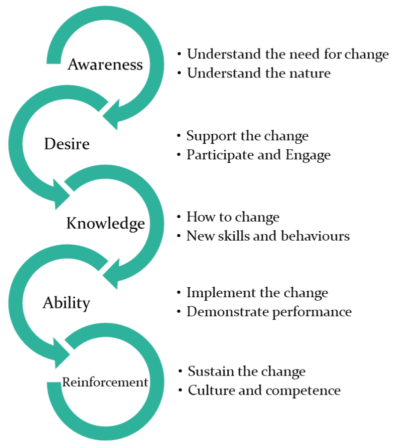
There is still a need to cultivate and grow the base of "super-users" - people with a practical/project-based background but with an early-adopter attitude towards using digital models. Ultimately this will aid the shift of the broader, perhaps somewhat more sceptical, general user base.

Trusted Models

A key success factor is the quality of the models: if a model "works" it will be trusted and used more widely and readily. Users have a learning, and confidence building, curve to travel on with any new model. Awareness raising actions, such as the development of bespoke digital workflows (piloted in ADDoPT via Britest technical facilitation), and helping potential users see the value of new models are helping to overcome the barriers to adoption, for example demonstrating that the amount of time that could be routinely saved employing a digital model more than outweighs the time taken to learn how to use it.

Leadership

Looking more broadly, the Medicines Manufacturing Industry Partnership's early instigation of digitalisation through ADDoPT resonates with companies who are now making prominent senior leadership appointments to roles entitled "Chief Digital Officer" or similar. This augurs well for positive leadership towards adoption of digital modelling approaches.



ADKAR Change Model, Hiatt, J. M., Prosci Learning Center (2006)

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Results and Benefits

The Yu and Arnold model has been implemented in the screw feeder module within PSE's gPROMS FormulatedProducts platform. This implementation makes the model available via a software platform upon which Pfizer are building end to end process flowsheet models.

The main advantage in using this model is in development. Current best practice is to optimise experimentally at small scale on a benchtop feeder. Typically, to test whether a material would flow at a given throughput would require around 1kg of API at a stage where not only is material extremely expensive but also scarce.

Use of the feeder model will deliver benefits of speed and cost in assessing and mitigating the risks associated with flow for materials which are intermediate between free flowing (no problem) and highly cohesive (no chance).

Further Steps

The focus to date has been to render the current state of the art in a user-friendly form. This is a precursor to further internal customisation of the tool within Pfizer for proprietary materials of direct interest.

Uptake by expert users for thorough model validation will be supported by a map indicating where the model performs and expected levels of confidence.

Further development in the underpinning science will be needed to generate models for less free flowing, cohesive powders. Here there is a potentially interesting correspondence with work elsewhere in ADDoPT exploring statistical relationships between particle properties and resultant flow.

Transforming pharmaceutical development and manufacture

Addressing the pharmaceutical industry's desire to deliver medicines more effectively to patients, the ADDoPT project has developed and implemented advanced digital design techniques that streamline design, development and manufacturing processes.

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