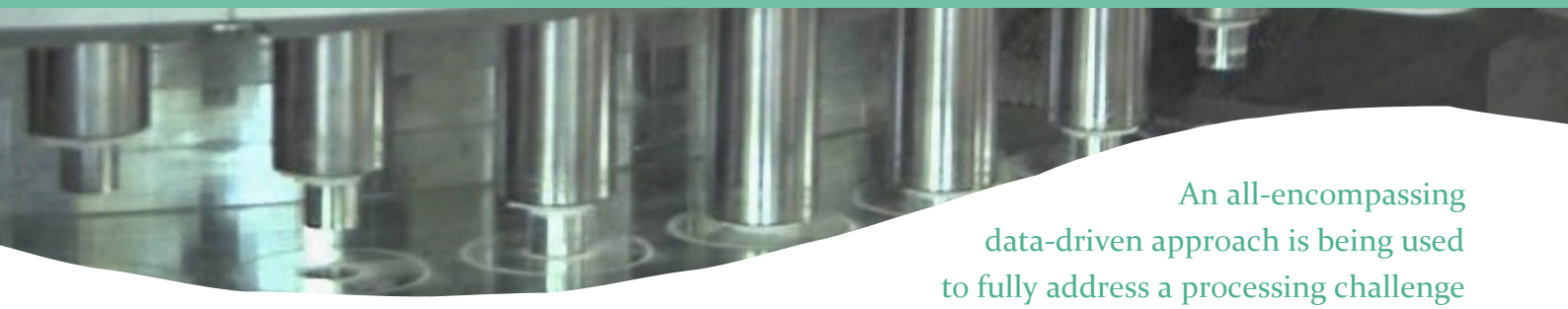
Using Big Data to Resolve Tablet Sticking Issues

Holistically mapping material attributes to a challenging manufacturing KPI



An all-encompassing data-driven approach is being used to fully address a processing challenge intractable to routine problem-solving methods

Drivers

Material sticking in the die head of a tablet press is a common issue in the manufacture of pharmaceutical tablets. This leads to significant downtime in manufacturing due to stoppages and the need to clean equipment. Better prevention and management of sticking issues would enhance both the commercial and development phases of the pharmaceutical lifecycle. The negative impact of sticking extends beyond the batches directly affected due to interruption of the manufacturing schedule. Estimated losses of around 700 hours a year on a fairly typical production line can be attributed to the implications of sticking.

Approach

What is needed is a framework and methodology that allows pharmaceutical scientists to examine large data sets and evaluate relationships between processing parameters, material attributes and key process performance characteristics.

Innovatively, this study combines Big Data sets from Drug Substance and Drug Product, material attributes and process parameters from multiple process steps, and is developing relationships from this data to manufacturing KPIs.

Key Features

- A structured and holistic framework approach to problem analysis and resolution
- Insight from statistical and mechanistic approaches providing links between processing parameters, material attributes and manufacturing performance KPIs
- Transferable learning on how to tackle other issues and opportunities

Tablet sticking is the first performance characteristic to be tackled in this way but other issues could be tackled similarly with a framework established.

This all-encompassing approach is necessary to fully address what is self-evidently not a “simple” cause and effect relationship between one material attribute and the phenomenon of sticking, since it has proven intractable to more routine problem-solving approaches.

An ADDoPT Case Study featuring collaboration between Pfizer and the University of Leeds

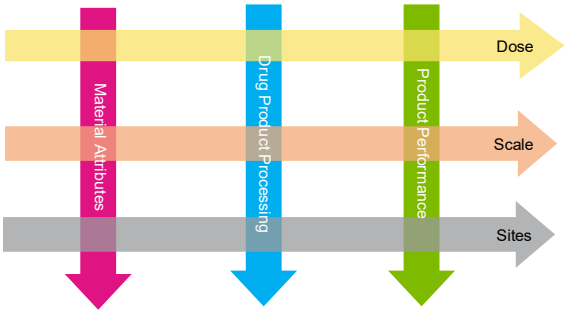
Mapping material attributes to manufacturing performance

When you're looking for direction, a map is helpful, but it needs to cover the right territory at the right level of detail. By compiling big data that captures characteristics from across the materials supply and manufacturing landscape, and "surveying" it in a thorough and structured way, Pfizer have opened up the possibility of mapping routes to more effective solutions to common manufacturing issues.

The characterisation of input materials goes far beyond CoA-defined attributes, and cuts across the multi-stage processes involved. It includes traditional and advanced analytical techniques (particle size distribution by multiple methods, particle shape, flow properties, compressibility and sticking measurements of isolated materials and intermediate mixtures), and product characterisation (*e.g.* chemical imaging of tablet composition). A quantitative analysis of manufacturing KPIs (number of stops for cleaning, process yield – number of bad tablets per batch) has been recorded at the manufacturing site.

This structured and holistic framework approach to problem analysis and resolution will also allow validation of development "Science of Scale" tools: for example by linking manufacturing data with small-scale tablet press models, the former can provide validation of the latter.

Characterisation Data Architecture



ADDoPT has acted as a catalyst, encouraging the resource commitment needed to secure a sufficiently holistic data set and structured approach

Results and Benefits

Data has been assembled for 144 measurements, made across 4 drug product process steps for 49 drug product batches made from 9 different Active Pharmaceutical Ingredients (APIs) and 7 excipients variants. Many of these measurements are multi-point, spectral, or image based. Taken together they constitute a meaningfully "big" data set, providing unprecedented coverage of a full and business-relevant materials and processing space.

Structured data analysis is underway. Although the primary goal is to draw out empirical, statistical correlations and relationships, linkages to understanding the role of surfaces in sticking provided by the mechanistic modelling software VisualHabit are also anticipated.

Ultimately this will provide a technique for better interpretation of manufacturing data relative to key outcomes in order to develop more effective solutions to common manufacturing issues. By better understanding the full range of causal relationships, it should be possible to prioritise which material attributes to monitor most closely for enhanced process control.

Further Steps

Beyond the current study, it is hoped to bring the insight gained to bear more generally upon the pharmaceutical sector's product development cycles. Similarly, beyond the immediate goal of resolving a specific sticking issue, the learnings made should be applicable elsewhere, for instance to elucidate other steps concurrently studied in the same process and further products.

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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