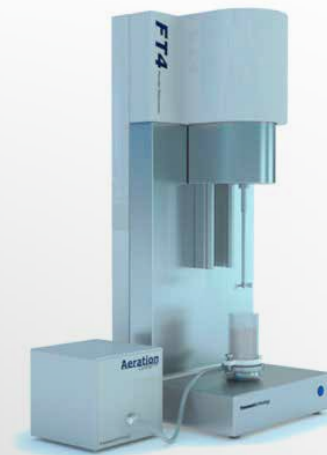


## MANUFACTURING SUPPORT USING THE FT4 POWDER RHEOMETER®



Powder rheology is used in a wide range of industries to support new product development and manufacturing. By investing in powder rheology, manufacturing sites can establish an understanding of their processes and unit operations based on a correlation between measurable powder properties and process performance. Changes in suppliers and/or equipment (for example, lower cost raw materials or process scale-up) can lead to variations in certain properties of the powder, even if other properties, such as particle size distribution remain unchanged. These changes can lead to process challenges, such as blockages, poor product uniformity and greater mass or volume variation in portioned batches.

By measuring and understanding powder behaviour, these challenges can be overcome, and effective decisions on changing raw materials or production methods can be made.



**FT4 POWDER  
RHEOMETER®**

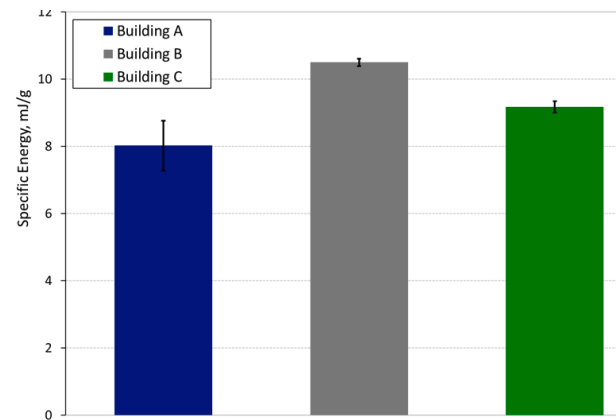
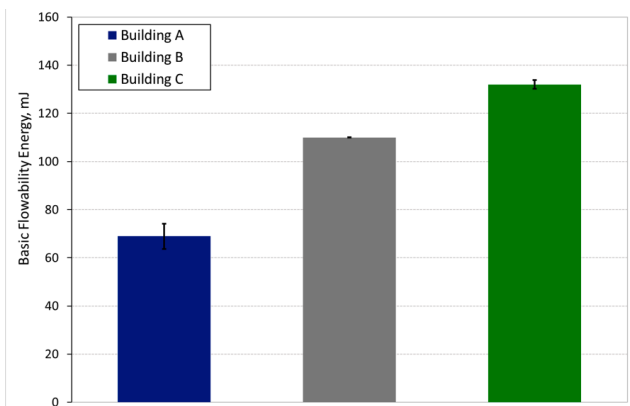
### FT4 Powder Rheometer

The FT4 is a universal powder tester that provides reliable, comprehensive and process relevant measurements of bulk material properties. This information can be correlated with process experience to improve processing efficiency and aid quality control. Specialising in the measurement of dynamic flow properties, the FT4 also incorporates automated shear cell tests, and the ability to measure bulk properties such as density, compressibility and permeability, enabling a comprehensive characterisation of powders in process relevant conditions.

### Case Study 1 - The Impact of Manufacturing Location

Samples of an Active Pharmaceutical Ingredient (API 1) were manufactured in three different locations, Building A, B and C. The API from Building B and C exhibited issues relating to inconsistent flow and blend uniformity, whereas the API from Building A consistently performed well. Samples from the three different locations were evaluated using the FT4 Dynamic Flow methodologies. Data from the tests show clear differentiation between the three samples. API 1 from Building A generated the lowest Basic Flowability Energy (BFE) and Specific Energy (SE) values, suggesting that this powder exhibited less resistance to dynamic flow. API 1 from Building B and C gave higher BFE and SE values suggesting a higher degree of resistance to forced flow and greater mechanical interlocking and inter-particle friction, both likely to contribute to the inconsistent flow and blend uniformity issues observed.

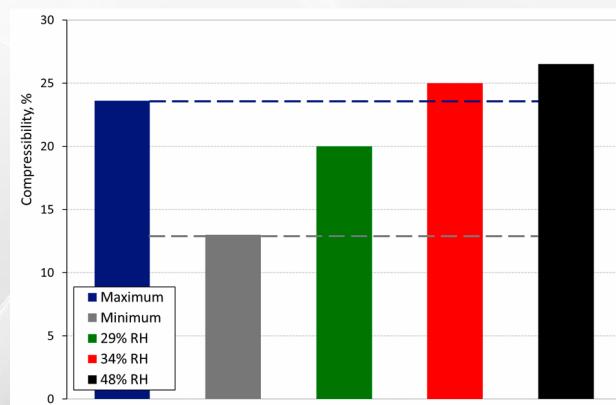
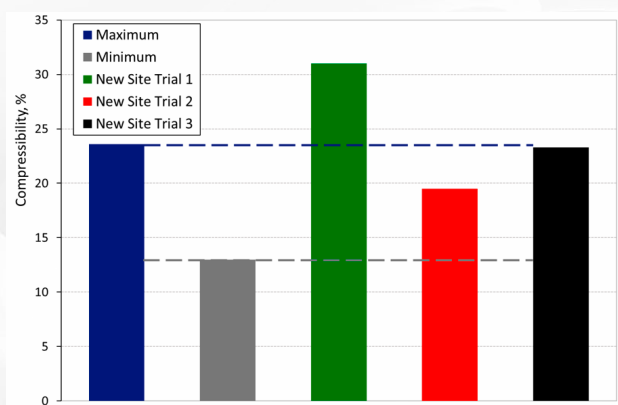
With this knowledge, processes employed in Building B and C can be modified and batches from those locations can be evaluated, prior to processing, to ensure that the properties are comparable with those from Building A and thereby compatible with the process.



### Case Study 2 - Blockages in a Filling Process

A second API (API 2) was used in a filling operation. Historical batches of the API had been characterised using a range of FT4 test methodologies, and Compressibility was found to be a key indicator of acceptable performance in the process. By assessing a range of samples, it was possible to determine acceptable limits for Compressibility. A new site began producing API 2 and handling issues were experienced during initial filling runs. A sample of the API was found to have a higher Compressibility, outside of the acceptable parameter space. Following this, the manufacturing process was modified, resulting in the next two batches having an acceptable Compressibility and, as expected, the powder subsequently performed well in the filling operation.

However, further issues were observed with changing weather conditions, specifically with respect to relative humidity. Powders processed at higher humidity levels (48% RH) exhibited poor performance. By evaluating the powder under the same environmental conditions, it was found that Compressibility increased with humidity and at a certain humidity, Compressibility exceeded previously defined limits. From this it was possible to determine an acceptable humidity range for the operation.

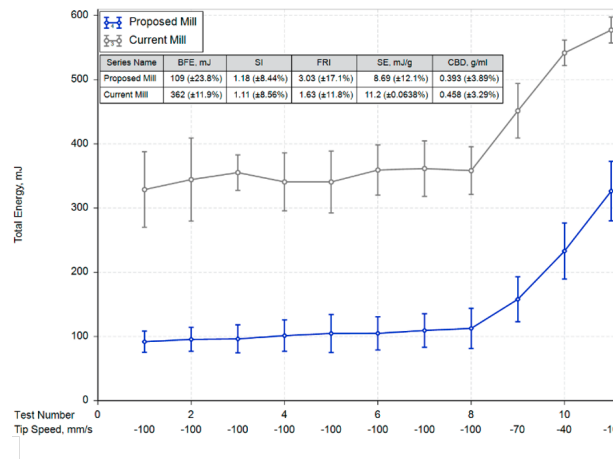


### Case Study 3 - API Milling Process

An API manufacturer was evaluating new milling equipment. The proposed new equipment produced material with a similar particle size distribution (PSD) to the existing mill.

Four batches were prepared on each mill and assessed using the FT4. Significant differences were observed in the Dynamic Flow tests with the proposed mill generating product with a higher Flow Rate Index (FRI), and lower BFE, SE and Conditioned Bulk Density (CBD) values. These are properties typically associated with more cohesive materials suggesting that the powder produced in the proposed mill is more likely to be problematic during process.

Powder rheology has enabled differences in the powders' flow properties to be detected that weren't identified by evaluating particle size alone. Introducing the new process equipment could have been detrimental to production. The application of powder rheology highlighted this risk suggesting further investigations are undertaken or preventive measures implemented.



## Conclusions

Successful troubleshooting and manufacturing support can be provided by the FT4 Powder Rheometer. Routine characterisation enables the user/operator to build up a knowledge database and can help determine the root cause of manufacturing issues. By understanding powder characteristics and their relationship with process outcomes, risks to changing raw material supplier or manufacturing method can be assessed.

The FT4's multivariate test methods are ideally suited to characterising the range of process-relevant powder properties that will influence flowability in different processes, specifically by testing the samples under low-stress, dynamic conditions that generate process-relevant properties that can be correlated with process performance. The correlations can be used to construct a design space of powder properties that pertain to good performance, against which both new formulations, or incoming or outgoing batches, can be assessed to predict downstream behaviour.