# A New DPI Carrier – What About Dosing Performance?

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## Purpose

For dry powder inhaler (DPI) formulations so far the majority of powder blends are based on lactose monohydrate as an excipient. Despite the widespread utilization of this carrier, the micro-dosing of these blends into premetered DPIs is still a critcal step.

Recently, a new carrier based on a non-reductive mannitol (Parteck® M DPI excipient) has become available for the preparation of powder blends for inhalation. The aim of this study is to assess the dosing performance with some typical technologies used in DPI manufacturing and to examine the impact of the PSD of the carrier on this performance.

## Methods

### Material

Mannitol (Parteck® M DPI excipient, MilliporeSigma, USA) was used as carrier. Two different particle size ranges were used: abbreviated M 100 and M 200 having a d (50) of 100 µm and 200 µm respectively. Micronized lactose monohydrate (Lactohale LH300, DFE Pharma, Goch, Germany) was chosen as a model for the drug substance.

### Methods

Preparation of blends:
5 % model API (micronized lactose monohydrate) was added to the mannitol carrier and the mixture was forced through a 1 mm sieve to eliminate agglomerates. The mixture was homogenized for 20 minutes at 23 rpm using a Turbula® blender (Type T2A, Willy A. Bachhofen AG Maschinenfabrik, Basel, Switzerland).

Particle size distribution:
Laser light diffraction (Helos/BF, Sympatec, Clausthal-Zellerfeld, Germany); dry dispersion (Rodos/L): 0.5 bar.

Bulk and tapped density:
Ph. Eur. 8.0 (2.9.34, Method 1).

Powder flow properties:
An FT4 powder rheometer (Freeman Technology Ltd., Worcestershire, UK) with a 25 mm test cylinder has been used to characterize flow properties. Measuring the axial and rotational forces acting on a blade as it rotates down through the sample determines the Basic Flowability Energy (BFE). Applying a defined normal force (15.0 kPa) by a vented piston while measuring volume change will lead to Compressed Density or compressibility.

Powder dosing:
ModuC LS capsule filler with interchangeable dosing modules has been utilized with a dosator system. Dosator size 5, piston height 6.0 mm, powder bed height 13 mm, machine speed 50 cycles/min.

ModuC MS capsule filler with interchangeable dosing modules has been utilized with a vacuum drum system: Dosing chamber volume 22.5 $mm^3$, vacuum -400 mbar, machine speed 100 cycles/min.

(All dosing systems: Harro Höfliger, Allmersbach i.T., Germany).

## Results

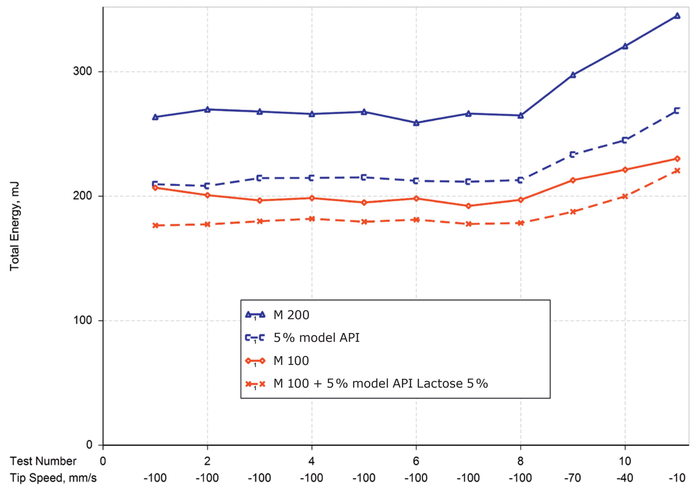


**Figure 1:** Measurement of total energy input by flow Rheometer FT4 shows significant lower energy input needed for a finer grade carrier. Also, the addition of the fine grade model API reduces the energy input. The lower the energy input, the better the expected dosage accuracy, we found in this case.

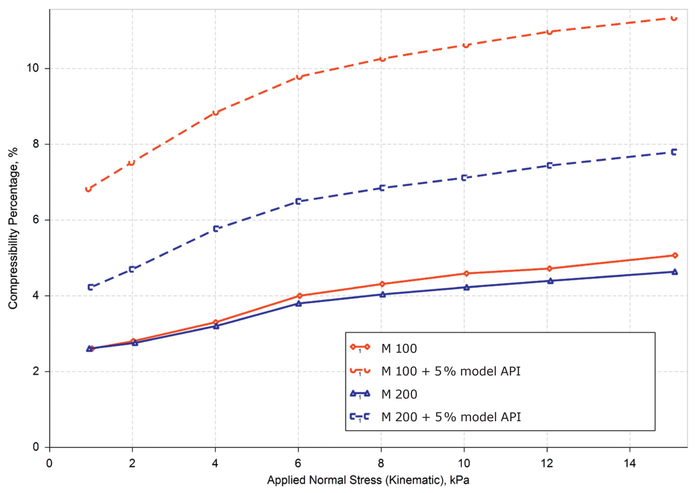


**Figure 2:** Measurement of the compactability of carriers with different particle sizes show a significant improvement in compactability if fine grade model API has been added to the carrier granulate. The finer grade carrier shows a better response to this addition of the model API than the coarser one, even though they performed similarly without the model API. A certain compactability is needed for dosage systems operating with compaction or vacuum to keep the dosage in a cavity for transfer.

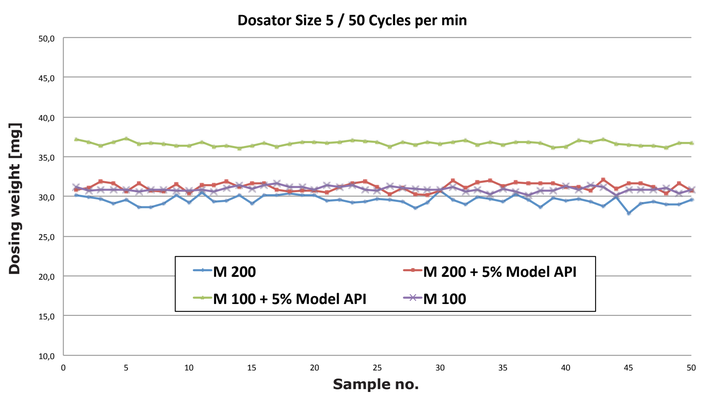


**Figure 3:** Practical trial with a dosator module using both carrier powders of different particle sizes and mixtures with model API. All powders and blends exhibited good reproducibility and a reasonable rsd of less than 2%. The finer grade carrier with an rsd of less than 1% showed even better results. The addition of a 5% model API in both cases displayed an improvement in accuracy. The higher weight of dosage in one case is related to its higher compactability.

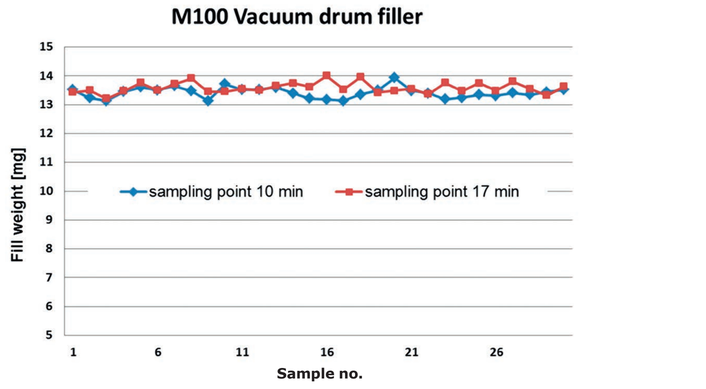


**Figure 4:** Practical trial with vacuum drum drum filler using the carrier M 100 with 5% model API.

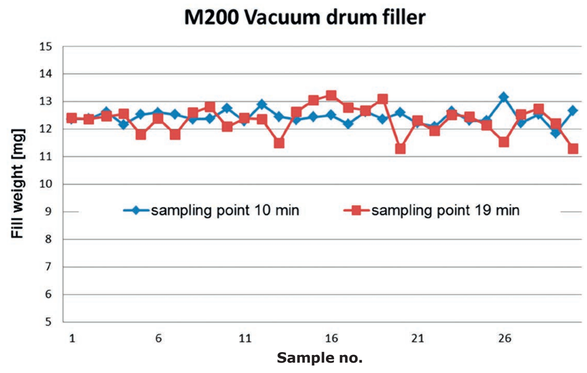


**Figure 5:** Practical trial with vacuum drum drum filler using the carrier M 200 with 5% model API.

- Measurements of Basic Flow Energy with the powder Rheometer FT 4 shows slightly higher cohesivity for finer grade carrier material and for carrier mixed with fine grade model API.
- Measurement of compactability using the flow rheometer predicts better dosing performance for the carrier mixed with fine grade model API.
- Dosing works well with a dosator device at commercial scale with all tested powders. Improvements can be achieved going from coarse to finer particle size range of carriers and by adding fine grade API particles.
- This result confirms the findings of measurement in the flow rheometer.
- Dosing on a rotating drum vacuum filler also shows satisfactory dosing results with all tested powder types.
- The better standard deviation in the vacuum drum filler can be found for the smaller particle size carrier which correlates to the better compactability found in the powder rheometer.

## Conclusions

**The study has confirmed the suitability of FT4 powder rheometer evaluation to predict the performance of powder blends in "real life" dosing technologies. The results also demonstrate the importance to evaluate the powder behavior of the final blends, as additional components can alter the powder properties significantly. Furthermore, it could be shown that the newly available carrier for DPI based on Mannitol (Parteck® M DPI excipient) is suitable for commercial dosing systems commonly used for inhalation powders. The PSD of such a carrier has some impact on dosing accuracy.**

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