

# Case Study

Pharma Automated Powder Dosing Solutions



## Micro-dosing system eases clinical manufacturing at Catalent – a solution for inhalation drug delivery

**Catalent Pharma Solutions, Sommerset, NJ, operates a facility in Research Triangle Park, NC, that offers expertise and a full range of services for pulmonary and nasal drug delivery.**

In 2008, the company was conducting development work on behalf of a client who sought help with a new chemical entity to be delivered via a dry powder inhaler (DPI). Part of development included characterizing the aerosols and the performance of the DPI. "We were working on inhalation drug delivery, and one issue with dry powder inhalers is filling the powder into the dose unit assembly," said Lei Mao, the senior scientist at Catalent who led the formulation development team working on the project.



### **Catalent Pharma Solutions**

New inhalation drug development

Weighing micronized API

Traceable data management



ErgoDisc for 15 capsules

**METTLER TOLEDO**

"We needed to fill powder into size 3 HPMC capsules. Then those capsules would be placed in the device, pierced, and inhaled by the patient." The goal was to fill the capsules with 25 milligrams of a dry powder mixture of the carrier - lactose - and a micronized API. "The micronized drug was attached to the lactose surface to form what we call the interactive powder," Mao said. "That way the mixture acts as a uniform powder."

Nonetheless, filling such a small amount into the capsules raised concerns about variability. There was also concern about segregation, in which the fine API particles detach from the surface of the large-particle lactose. "If that happens, we would lose the dose uniformity, as well as the aerosolization performance," Mao said.

#### **Capsule filling options**

■ During laboratory tests, Mao's team filled the capsules manually using spatulas, which required weighing the empty capsule before filling, during filling, and afterward. "For a small number of capsules, just for device testing, etc., we can do that. However, when we need to fill many of them, say for feasibility and stability [testing], that's several hundred capsules. And when we move on to Phase I or Phase II clinical manufacturing, that would involve several thousand capsules. In those cases, obviously, manual filling is not an option."

Mao said he knew of several capsule filling machines, but "they were very expensive, both in terms of investment and the maintenance. So I tried to identify another way to replace the manual filling, because we were about to manufacture a clinical batch, which would be about 10,000 capsules."

Soon thereafter, Mao attended a demonstration of a powder dosing system, called Quantos, that METTLER TOLEDO was introducing. The demonstration focused on filling vials for HPLC standards and other powder dosing applications, but Mao recognized the promise of the device for filling capsules, and he discussed his ideas with the supplier's representative. "So she talked to her colleagues in Switzerland and they came up with quite a good solution. They made a capsule holder that fits into a slot on the Quantos system. Then we started dosing."

#### **Accelerated filling**

■ "The dosing is quite accurate and we started testing with their prototype model for our feasibility [study], where we filled about 700 capsules. The fill weight was very tight and using chemical assay, we saw no segregation of the blend being filled and we saw no significant change in the aerosolization performance of the filled capsules. So that was good news." METTLER TOLEDO also offers software for the system that can electronically capture all sample weights and other information as-

sociated with the compound.

Based on that success, Catalent purchased two Quantos systems and used them for clinical manufacturing. "Once again, the fill weights were very precise and accurate. The other good thing was that we could print the fill weight of individual capsules. So we had a very good monitoring of how much fill is in each capsule, which was more good news."

The Quantos system is designed to handle a variety of dosing applications, including bottling, making reference standards, screening, and conducting formulation work in small- to medium-scale lab and production applications. "This is in no way a commercial manufacturing tool," Mao said. "But so long as you're not talking about filling 100,000 capsules, it's very good." On the other hand, the micro-dosing system may help with technical transfer. "If you have this set up in the R&D laboratory and in clinical manufacturing, then you don't have to do any technical transfer. But on the larger scale, if you were moving from manual filling to machine filling, you'd need some data to support that this transfer is not going to affect the performance. So the Quantos system can provide a kind of stability, number one, and also direct transfer from R&D to manufacturing."

► [www.mt.com/quantos](http://www.mt.com/quantos)

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