Pharmaceutical Powder Flow Characterization:

Small Volume Testing Needed

There is a saying: Go big or go home. But not when dealing with sample testing of pharmaceutical powders. Then the saying is: Waste not, want not. In the cutthroat world of Big Pharma, staying one step ahead of the competition is imperative. Research to create the next new drug is a costly endeavor. Once a new product is developed, speed to market is the next challenge. This is where the complexity of the production phase comes into play and the necessity for accurate sample testing arises.
Profit in pharma is made by producing tablets or capsules quickly and accurately; production speeds of 50mS a tablet is not unheard of. To ensure there is minimal downtime during production, the product needs to be characterized for flow properties. Properties such as flow function, arching dimension and bulk density ensure proper flow to the tablet die or capsule, no jams in the process occur and proper compaction force to produce the tablet is defined. These properties need to be accurately measured for the production run to maximum production with minimal downtime. But there is a cost, and not just in producing product.

An API (Active Pharmaceutical Ingredient) can cost millions of dollars a kilo. Due to this expensive nature of some pharmaceutical API's, it is an obvious requirement to use a minimal amount of product for test characterization. The test is destructive and the powder cannot be reused. And therein lies the problem. Simplistic, subjective tests such as angle of repose and tapped bulk density use minimal amounts of product, but give no information on the flow characteristics of the material. Instrumentation can yield the necessary flow data, but use somewhat larger volumes for sample tests. If a single instrument test requires 300cc of powder and three tests are needed for proper characterization, this can quickly become a costly endeavor.

So what to do? Rely on subjective tests with a minimal amount of test sample and risk a costly, faulty production run? Or use more volume of expensive test sample and get accurate data for the production cycle? Of course, the ideal scenario is the best of both worlds: Test using small amounts of sample and achieve accurate, comprehensive flow data ensuring a smooth production run.

Shear Cell Testing: Small Volumes, Large Returns

The more common historical test methods for defining pharmaceutical powders (and others) involves using an angle of repose test and/or a tapped bulk density. An angle of repose test measures the angle of a powder when poured on a flat surface. Angles of less than 30° are considered more free flowing; angles greater than 30° are considered more cohesive. A tapped bulk density test consists of using a graduated cylinder or small beaker. This is filled with sample and the fill volume recorded. The container is then tapped a certain number of times (100 and 150 are common) and the change in volume recorded. The larger the change in volume, the greater the bulk density and the harder it is for the material to flow.
The issue with these tests is they can be subjective and, thus, inaccurate. Plus, they give no comprehensive flow data. These are simply go/no go tests, but they address the need for utilizing small volumes of sample, hence their historical popularity.

The solution for gathering accurate, comprehensive flow data is through the use of an annular shear cell; this is the accepted test method in the bulk solids industry. By shearing a sample of powder at defined consolidations and determining the inter-particle friction, flow data can be quickly gathered to represent the flow characteristics of a sample of powder (see figure 1).

Figure 1: Brookfield Powder Flow Tester with Shear Cell

Figure 2: Brookfield Shear Cells

Brookfield Powder Flow Tester is one such instrument that utilizes shear cell technology. Data is provided for flow function, fill and final bulk density, rat-hole diameter, arching dimension, internal friction angle. This data is usually parsed to 3-4 pieces of pertinent information, then used to create an SOP on the material. This SOP is implemented as a guide for creating future batches of material and for in-process QA/QC testing (see figure 2).

To address the need for small volume sample testing, the PFT supports interchangeable shear cells for standard volume (263cc) and small volume (43cc) sample testing. The small volume shear cell is ideal for the pharmaceutical industry. Using only 43cc of sample, the user gets the same accurate results as the standard volume shear cell in the same amount of time (see figure 3).

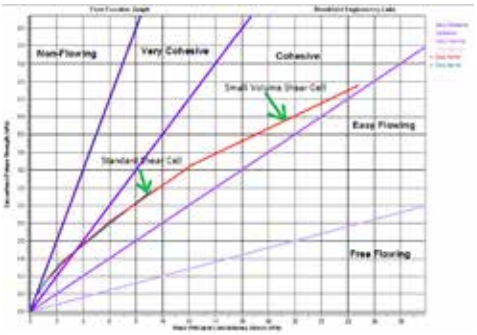

Figure 3: Flow Function Graph with Small Shear Cell

Final Considerations

While methods for testing small amounts of sample exist, the most important consideration is the accuracy of the test itself. Shear cells have been around for decades and are known to be accurate, repeatable and reliable. The smaller version of the shear cell addresses the need for using small volumes of expensive powder for accurate test characterization. This is ideal for pharma and other industries where limited volume of sample is available.

Small volume testing is a reality with annular shear cells. The results are tried and true and have been used in the pharmaceutical industry for precise characterization of new formulations and production run batches. Cost savings can add up quickly due to the small amount of product required to perform the test requirements.

Author: Vinnie Hebert Sales Manager - Powder Flow Tester
AMETEK Brookfield, Instrumentation & Specialty Controls Division
11 Commerce Boulevard | Middleboro, MA 02346 USA | Tel: 800.628.8139 or 508.946.6200 | Fax: 508.946.6262
E: vinnie.hebert@ametek.com www.brookfieldengineering.com