Achieving the Basics in Viscosity Measurement to Comply with 21CFR Part 11

By Len Thibodeau

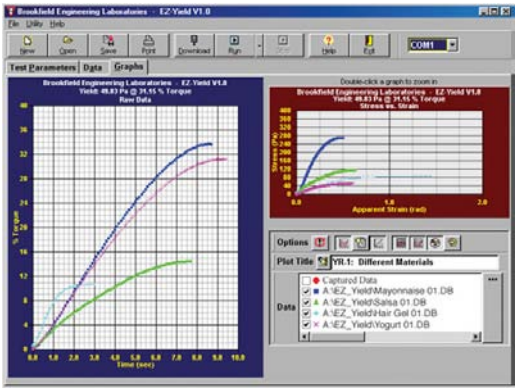

Figure 1: Yield Stress Curve Quantities Amount of Force Required to Squeeze Material out of Tube

The pharmaceutical industry relies on viscosity measurement to qualify the flow behavior of materials for a variety of applications. For example, the way in which a topical ointment squeezes out of the tube depends on the yield stress in the material. **See Figure 1**. Too thin a formulation results in runny material flowing too easily from the orifice, too thick and the material is overly difficult to extract.

Customers pay dearly for ointments and they expect ease of use when applying them to the skin. A properly formulated material flows in such a way that the "right amount" can easily come out and rub into place with minimal effort by the customer. The force required for the rubbing action is easily determined by running a viscosity flow curve. **See Figure 2**. Note that the viscosity or "resistance to flow" is much higher when rubbing slowly (low shear rate) compared to a vigorous rubbing action (high shear rate).

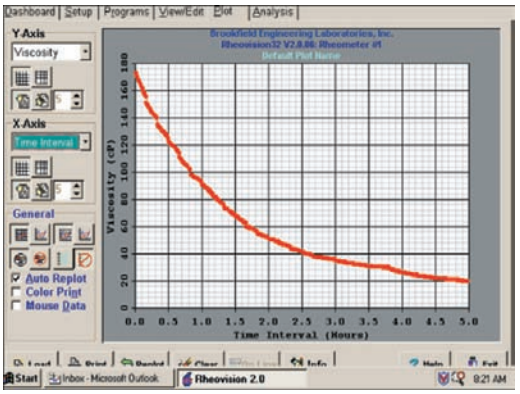

Figure 2: Viscosity Flow Curve Tells How Easily the Rubbing Action is Accomplished

The preferred instrument used by the pharmaceutical industry for these types of measurements is the DV-III Ultra Rheometer with appropriate choice of spindle system. **See Figure 3**. For expensive formulations with precious ingredients, the Small Sample Adapter or Cone/Plate type instrument are selected because they require small sample sizes, 16mL or less for the former and 2mL or less for the latter. **See Figure 4A** and **Figure 4B**. For materials that are plentiful and can be tested in a beaker,

Figure 3: Brookfield DV-III Ultra Rheometer

Figure 4A: Brookfield Small Sample Adapter

Figure 4B: Brookfield Cone/Plate Spindle Systems

Figure 5: Brookfield Standard Disc-Type Spindle, T-bar Spindle, and Vane Spindle

the choice of standard spindles, T-bars or Vanes is considered. **See Figure 5**. Vane Spindles are increasing in popularity because they readily give more accurate information on both yield stress and viscosity flow curve behavior, especially when measuring samples with suspensions.

The pharmaceutical industry devises test methods which accomplish the types of yield stress and viscosity measurements shown in Figures 1 and 2. These are multiple step tests, which control the speed and time of rotation for the spindle immersed in the material, as well as the temperature of the material during test. These methods are either programmed directly into the instrument or they are constructed on a PC using software such as Brookfield's Rheocalc. **See Figure 6**. The advantage of the DV-III Ultra Rheometer is that it can work in stand-alone mode running a programmed test entered on the instrument keypad or it can operate under PC control. In both cases the security of the test method is a key requirement so that the same procedure to measure the material is guaranteed, time after time.

Figure 6 Top: Brookfield Rheocalc Software

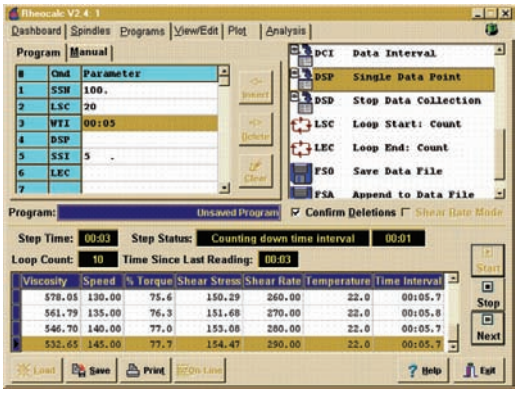

Figure 6 Bottom: Viscosity Data Table From A Flow Curve Test

Both the DV-III Ultra Rheometer and the latest version of Rheocalc software (V3.1) have a built in security feature which locks the test method and prevents alteration by any operator. This is essential to guarantee that the test is run without interference from any outside influence.

The data gathered from the yield stress and viscosity tests also requires a similar level of security. Figure 6 shows a data table from a flow curve test run under Rheocalc control. The information cannot be modified when the secure mode is in effect. Again, this is a necessity in the pharmaceutical industry where data integrity without the possibility of outside tampering is critical. An additional advantage of software control is that the data table can easily be converted into a graphical flow curve, similar to Figures 1 and 2, for rapid pass/fail analysis.

The Federal regulations in the United States defined in 21 CFR Part 11 have received significant discussion regarding the generation, handling and storage of electronic data files. Viscosity and yield stress measurements made on pharmaceutical materials clearly come under this heading. While there is mixed opinion on how far to go as regards controlled procedures for test method and data security, there is no debate that inexpensive approaches are welcome. This is the value that Brookfield has brought to the QC and R&D labs of the pharmaceutical industry.

By Robert G. McGregor, Sales & Marketing Manager Brookfield Engineering Laboratories, Inc., Middleboro, MA 02346
Reprint Permission from Pharmaceutical Online (VertMarkets, Inc.) - February 1, 2007