A turning point

Where does manual sample preparation stand?

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The pressure is on to do more with less. Whether this applies to increased workload with lower headcount or more analytical tests with less milligrams of sample, how can today's pharmaceutical and biopharmaceutical companies make ends meet?

The answer is by automating the tedious, repetitive laboratory processes to free up chemists and analysts precious time to concentrate on higher value tasks.

Weighing out powders to prepare samples and standards for analytical methods such as HPLC can be a time-consuming task with high error risk. The trend of recent years has shown that automated analysis systems are getting faster, safer, and more precise. With the advent of faster analytical methods, such as UHPLC, and rapid advances in software developments providing faster data processing, attention is once again focussing on sample preparation as the bottleneck in the process. Manual sample and standard preparations are still heavily influencing the daily routine in the laboratories.

In a recent survey, groups from method development, stability testing, formulation, and quality control all identified the manual preparation of samples and standards as the most time consuming and error prone part of their process.

The preparation of a solution is very time consuming and challenging. Imprecise sample preparations lead to Out-of-Specification (OoS) results and can cause time and cost intensive analyses of the variation. Challenges or errors can stem from inaccurate weighing, loss of substance in transfer from weighing paper to flask and documentation, tracking and labelling of samples. Due to the minimum weight range of balances typically not allowing the required concentration to be made up directly, serial dilutions with volumetric flasks potentially compound any errors. Variability and OoS results in analytical testing of active pharmaceutical ingredients is still at the top of the list of critical issues registered by the regulatory inspectorates.

Implementing automated powder and liquid dosing into the sample preparation workflow can bring massive gains in speed, safety and savings. The amount of time and money spent on Out-of-Specification investigations and inconclusive results can be reduced, by eliminating errors in weighing and sample preparation.

Preparation of multi-component standards

A good example is the preparation of multi-component standards. Using manual weighing, the risk of overshoot of each individual component weighing and potential loss of valuable material if a mistake is made on the final component is too high. So typically substances tend to be weighed into a weighing paper and transferred into the volumetric flask one at a time rather than all weighed directly into the target vessel. Obviously this gives an additional area of doubt: Is the amount of the weighed substance correct or did we lose some material whilst transferring to the volumetric flask?

A simple example of the preparation of a multi-component standard demonstrates the advantages of using the Quantos automated powder dosing system equipped with a liquid dosing head. A 5-component mixture was prepared in a single vial per concentration level. The 5-compounds were all weighed into the same vial at different target weights. Linearity tests were performed

by UHPLC measurement at 5 different concentrations. The correlation coefficient is greater than 0.999 for all analytes and the intercept is close to zero. A five-component standard plus the diluent can be prepared by this automated method in 10 minutes.

An analyst at Dionex Corporation compared the time taken for the manual preparation of these 5 multi-component standards of 3-4 hours and the automated preparation of these samples, which was less than one hour including filling the five dosing heads used.

This simple example nicely illustrates the time savings that can be made by automation: multi-component standards prepared in 25% of the time, whilst delivering high quality data, but perhaps more importantly reducing the error risk involved in the sample preparation process.

The future

Improved performance in analytical processes is only possible by improvements in the critical steps – sampling – sample preparation – weighing – sample clean-up and dilution! Repetitive tasks such as weighing and preparing samples for method development and method validation can be performed typically four times faster with automation than traditional manual techniques. Automating the sample preparation steps significantly improves the precision of the process!

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