Sample Delivery Systems for High Performance Liquid Chromatography and Mass Spectrometry

Programmable syringe pumps in applications ranging from method development to instrument calibration

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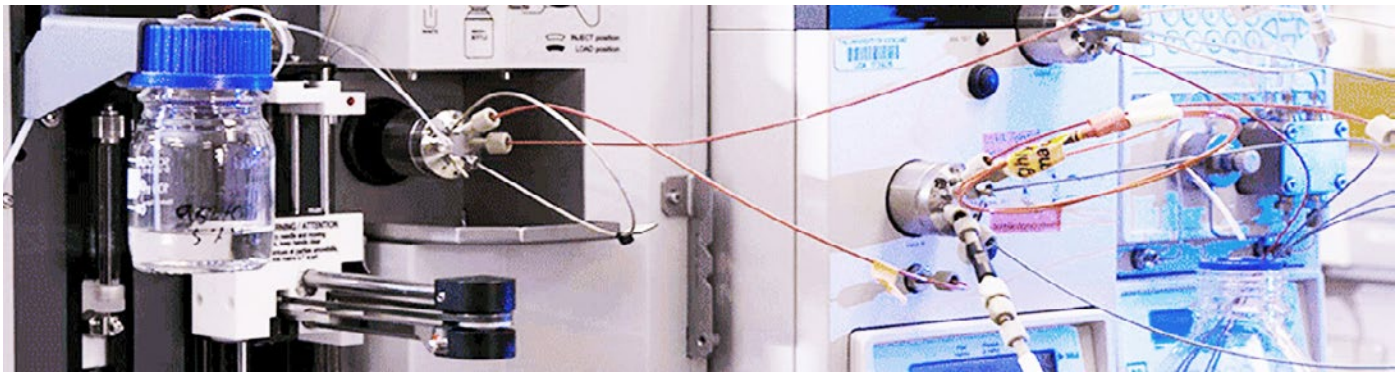

Overview

High precision analytical techniques, including mass spectrometry (MS) and liquid chromatography (LC), require high performance sample delivery systems to ensure the best possible results. The sensitivity and accuracy of the data is not only dependent on the analytical instrument, but also on the upstream components that supply the material to be analyzed. The variability and precision of the data is dependent on the robustness of these components as well and whether performance can be maintained over repeat analyses. High performance programmable syringe pumps are tasked with supplying the accuracy and precision required for the most demanding fluid delivery applications.

LC samples are delivered typically to a sample loop or directly injected onto the LC column for separation. MS samples can be introduced directly into the LC flow or to the ionization source where the analyte undergoes a process of charged vaporization, as an example electrospray ionization (ESI), prior to entry into the mass analyzer.

LC most often involves separation based on partitioning from a mobile (liquid) phase to a stationary phase. Volume differences can translate to changes in both molecular interactions on the column and detection sensitivity. Variability in sample volume can affect the efficiency of ionization as well as MS detector sensitivity as well. Regardless of the platform, it is clear that the analysis is not only highly dependent on the analyte concentration, but on the sample delivery volume as well.

Sample delivery systems for research applications

Research applications involving proteomics or replicate measurements using LC, MS, or the combined (LC-MS) techniques often involve large numbers of samples. In method development, variations in sample delivery to these instruments must be kept to a minimum. Any changes can be amplified by downstream analysis such that observed differences are actually due to analyte delivery fluctuations.

This can be particularly serious when considering the context. LC-MS based proteomic experiments often require detection of minute differences in protein profiles, sometimes involving very small sample volumes. Large arrays of proteomic samples are typically handled by dedicated autosamplers upstream of LC-MS analysis. Regardless, variations in sample delivery can dramatically affect interpretations. Time course or tissue dependent experiments require a high level of consistency as well, and fluctuations in sample volumes can have serious impact on these resource demanding applications.

Clinical applications

The need for high quality sample delivery systems also translates to the clinical laboratory. LC-MS based assay development for clinical samples requires strict control of conditions in order to detect changes in blood, urine, and other biofluids. Clinical LC-MS analysis of large numbers of patient samples typically involves dedicated liquid handling devices and autosamplers upstream of the analysis. When analyzing material from patients burdened with severe illness,

such as infectious disease or cancer, chemical changes in the biofluids can be complex. Detecting physiological changes can lead directly to diagnostic decision thresholds – all dependent on the analytical test quality and the sample delivery system.

Laboratory Developed Tests (LDTs) for clinical diagnostic applications depend heavily on the integrity of the equipment and methods. These tests are essentially "mature" assays which have evolved from the method development stage to clinically validated diagnostic status suited for patient use. Validation is in fact an essential process that can encompass a broad range of bioanalytical methods across both the clinical and research spaces. As such, governing bodies including the Federal Drug Administration (FDA) have published bioanalytical method validation criteria as guidance for industry (and academic) labs. Sample delivery systems serve an essential role in satisfying these performance metrics.

Method validation and test calibration

Validation of LC-MS analytical methods and assays involves testing to ensure the quantitative measurement procedures are reliable and reproducible for the intended use. The fundamental parameters for validation include: accuracy, precision, selectivity, sensitivity, reproducibility, and stability. In addition to these measures, all methods and results need to be documented, and all changes to published methods require subsequent (re)evaluation of performance metrics. The extent of the validation process is tied to certain distinctions – full validation for a new method or clinical approval versus informal validation for method modifications and instrument or detection system changes.

A validated method may become a routine assay such as a LTD in the clinical lab. Therefore, beyond validation the test instrument will to be calibrated on a regular basis to stay in compliance with internal guidelines. Should the LTD move on to FDA approval as an In Vitro Diagnostic, strict federal regulations will need to be followed. Calibration stringency applies to those tests that will be implemented under Good Laboratory Practice (GLP) or Good Manufacturing Practice (GMP) standards as well.

Regardless of the methods of validation and calibration, bioanalytical assays must perform at the highest levels of accuracy, precision, reproducibility. This can only be accomplished with the highest quality instruments which deliver reliable results under demanding conditions. The volume and integrity of each sample must be carefully measured to ensure the fidelity of the test is intact. Clinical tests that are capable of discerning critical results may in turn affect diagnostic decision making.

The role of precision syringe pumps in analytical testing

The importance of sample delivery systems for use in bioanalytical applications is clear. Applications including proteomic discovery and large-scale clinical testing typically enlist dedicated autosamplers upstream of LC separation. High performance syringe pumps can make a significant impact on the method development, validation, and calibration stages of assay development by ensuring accuracy and precision in sample delivery.

Programable pumps can increase the throughput of method validation and instrument calibration, therefore enhancing productivity. Syringe pumps that are built to handle diverse solutions, such as organic or caustic liquids, can expand the scope of test applications. Furthermore, robust pump design has direct influence on the reliability of the test, the integrity of the calibrations, as well as the general productivity of lab operations.

In summary, precision programmable syringe pumps have a range of applications in bioanalytical methods such as LC, MS, LC-MS, and others. These methods require accurate, precise, reliable, and robust performance, particularly for the validation and routine calibration of diagnostic tests. A syringe pump system that can function across the entire spectrum, from the research lab to the clinical diagnostic lab, exemplifies the qualities of robust design built for superior versatility and performance.

This article was written by LabX in conjunction with Chemyx.

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Chemyx syringe pumps are designed with advanced, highly durable materials that provide extreme laboratory precision at the best value to our customers. For more specific application requirements, Chemyx scientists also build custom units and can provide additional OEM manufacturing services that expand our customers' offerings in the market.

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