Applying Quality by Design Principles to the Migration of a Compendial Method between Multiple HPLC Systems

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PURPOSE
Within the pharmaceutical industry, compendial LC methods are used to assess whether the regulatory specifications for raw materials or finished products are met. Analytical laboratories are often required to migrate these methods to different laboratories or different models of LC instrumentation. The methods may be migrated without revalidation, however equivalent performance must be demonstrated.

Method migration can be challenging. Differences across HPLC systems can impact method performance. A plan designed to identify and control how method performance is affected by differences in instrumentation is a valuable tool in obtaining a successful outcome.

Quality by Design (QbD) Principles were incorporated in the development of a plan to migrate the USP Ibuprofen Tablets Organic Impurities method from a legacy HPLC system (originator system) to two modern HPLC systems (receiver systems) from different instrument vendors.

METHOD(S)

Migration Plan
Utilizing QbD principles, a migration plan was developed. This involved a three-step process:

1. System Comparison
2. Risk Assessment
3. Control Strategy

Migrated Method
The USP Ibuprofen Tablets Organic Impurities method was migrated from a legacy HPLC system to two receiver systems. The method parameters are in Table 1.

RESULT(S)

MIGRATION PLAN:

1. System Comparison: A review of each of the HPLC systems was conducted. Each of the receiver systems was compared against the legacy system to understand similarities and identify any differences that might impact method performance.

2. Risk Assessment: Identified system differences were examined to assess the risk posed to method migration. This assessment assigned a risk level to each identified parameter. Injector carryover, detector noise, and tubing dimensions were identified as the parameters presenting the highest risk to successful method migration.

3. Control Strategy: A control strategy was devised for the parameters having the highest risk. The control strategy included defining the needle wash composition and number of washes to control carryover, ensuring an adequate lamp warm up time, defining the sampling rate and degassing the mobile phase to reduce noise, and adhering to the vendor recommended tubing dimensions for each system.

METHOD MIGRATION:

With the control strategy in place, the method was run on both receiver systems. Each of the systems met the pre-defined acceptance criteria for successful method migration, specifically the USP system suitability requirements for relative standard deviation, resolution, and signal to noise ratio. In addition to meeting the acceptance criteria, the two receiver systems showed improved peak area percent (%URSD) and increased sensitivity (higher signal to noise value) compared with the legacy HPLC system.

CONCLUSION(S)

Quality by Design principles were utilized for the development and implementation of a plan for the migration of the USP Ibuprofen Tablets Organic Impurities method between a legacy HPLC system and two modern HPLC systems from different instrument vendors. The approach identified each system’s performance capabilities and provided an understanding of how different instrument parameters could affect method performance. Using this information, potential risks to a smooth method migration were identified, and a control strategy devised and implemented. The results obtained met acceptance criteria. Overall, the risk-based approach provided a proactive and successful strategy for method migration and the exercise demonstrated the performance benefits of keeping instrumentation assets up to date.

REFERENCES