Automated and Validated Bioanalytical LC-MS/MS Data Analysis

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Overview

- Bioanalytical projects require numerous types of calculations to be performed on LC-MS/MS data.
- Manually transferring MS/MS data into an external spreadsheet program to perform calculations requires in-depth secondary review.
- A more efficient workflow is presented here in which LC-MS/MS data is acquired directly into a LIMS system and automatically accessed by an electronic laboratory notebook for performing calculations.
- This validated workflow does not require, nor allow, manual data manipulation, simplifying quality review.

Introduction

Typical bioanalytical projects require that numerous types of calculations be performed with LC-MS/MS data. Examples include stock solution comparisons, system suitability analysis, scientific review of a run in Watson, working solution comparisons, and even tabulation of data for selectivity, matrix factor, and whole blood stability experiments. Most often, performing such calculations requires importing or copying and pasting LC-MS/MS data into a spreadsheet program. Any procedure dependent upon and/or allowing manual data manipulation is susceptible to at least the possibility of human error, and thus requires in-depth secondary review, especially for regulated work. Presented here is an automated and validated workflow in which LC-MS/MS data acquired by a LIMS system is directly accessed by an electronic laboratory notebook (ELN) for performing numerous types of calculations, all without requiring, or allowing, manual data manipulation. This approach is instantaneous, accurate every time, and eliminates the need for in-depth secondary review, reducing turnaround times for bioanalytical validations and other projects.

As an example, the workflow for performing a **stock solution stability evaluation** is presented here.

Methods

Bioanalytical LC-MS/MS data is acquired directly into the Watson LIMS database via the TSQ Module interface using a Thermo TSQ Vantage mass spectrometer. A customized, validated ELN (IDBS E-WorkBook Suite) template used for comparing stocks or assessing stock stability pulls the required information from Watson into the template using database links. Using pre-defined sample nomenclature in Watson, the data is sorted for each analyte and internal standard (IS) with the appropriate SOP acceptance criteria applied. The template automatically verifies sponsor and compound for each experiment and ensures that comparison solutions originate from intended stocks. It also confirms that the stock and comparison dilutions were prepared on the same date. Embedded logic calculates percent difference or percent change based on the user selecting comparison or stability, respectively. The stability time interval is calculated from solution preparation and sample injection time-date stamps.

Key Instrumentation and Software

- Thermo Scientific TSQ Vantage mass spectrometer
- Watson LIMS v 7.4 SP2 and TSQ Module v 1.0
- IDBS E-WorkBook 2010 v 8.3.1

Results

Figure 1. Scan the fresh and aged stock solutions to be compared

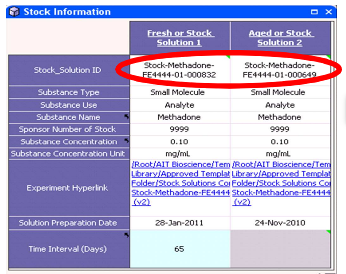


Figure 2. In ELN, create dilutions of both stock solutions (with IS) and scan these into the experiment

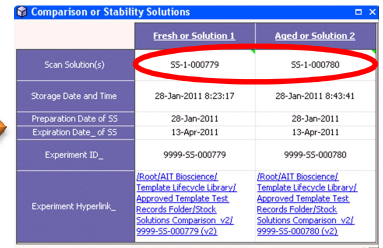
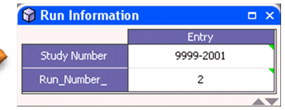


Figure 3. Enter Watson LIMS run designation



While the math is quite simple, this process provides numerous significant features. The ELN template does not allow the user to change data or to inadvertently input incorrect data. The ELN uses a direct database link to access the Watson response data and at the same time electronically capture the exact time and date that various steps took place, thereby determining the exact length of time for which stability is determined. This information can be used subsequently to prevent the use of expired stock solutions based on the most current stability data.

Figure 4. Instantaneous query of Watson LIMS database to retrieve analyte and IS response

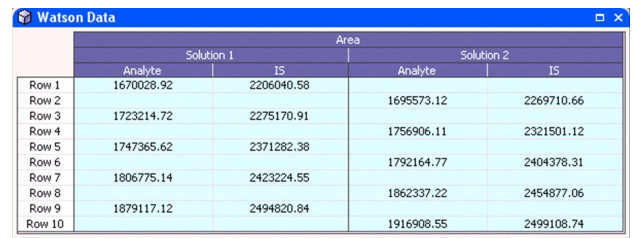


Figure 5. ELN calculation of response ratios.

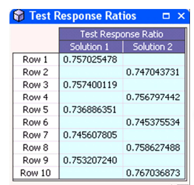


Figure 6. Status determined by embedded business logic using SOP criteria

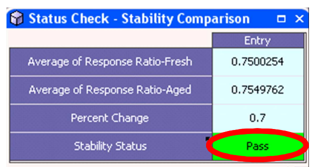
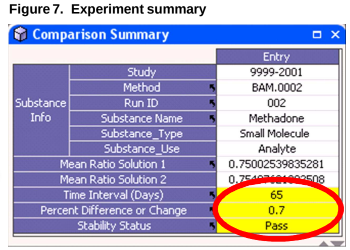


Figure 7. Experiment summary



Conclusions

Because the template and network database systems have been validated, there is no need for further secondary review of the stability or comparison data. Data processing is standardized, while the potential for human error is significantly decreased. During run preparation, fields requiring user entry in the template can be completed rapidly by barcode scanning or via dropdown menus within a few minutes. Following data acquisition, comparison results are obtained in seconds using a database link to the Watson data. The template then displays the final Pass or Fail status of the stock stability experiment entirely based on whether the data meet the business rules (SOPs) for acceptance criteria. While this is a general example of the process, similar workflows have been designed and validated to reduce human error and tabulate data for a report as needed for stability tests in matrix, carryover evaluations, selectivity, matrix factor, recovery, and specificity.