Streamlining Bioanalytical Processes with QC in Real Time

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ABSTRACT

All bioanalytical (BA) LC-MS/MS labs strive to provide quality data in a timely manner. One important means of assuring adequate quality is performing quality control (QC) checks on the data and laboratory procedures. Traditionally, QC is performed after data has been acquired, with errors identified and addressed after they occur. At that point, issues can only be resolved by resource-intensive investigative processes. Both of these options are undesirable and impact productivity and efficiency in the bioanalysis laboratory. The present study was undertaken to identify options for overcoming this retrospective analysis in current QC processes. Incorporating QC checks into the workflow prevents re-work or written justification.

Methods

The electronic lab notebook (ELN) solution *E-WorkBook Suite* (IDBS, Bridgewater, NJ) was configured to support several BA laboratory workflows. In addition to providing an audit-tracked and paperless environment, the ELN was specifically configured to detect deviations from SOPs and approved BA methods.

- A Balance Check workflow was created to enforce QC processes in the instrument standardization and verification steps. The ELN system was used to register balances and weight sets, along with their associated parameters (range, calibration expiration date, etc.). The template was configured to alert the user to any QC violations during the process of balance verification.

- A Common Reagents workflow was created to support preparation of common laboratory reagents and stock solutions. The system was used to detect and record possible SOP deviations. Specifically, the ELN-based workflow was utilized to preemptively identify :
  - Lapsed reagent expiration dates
  - Use of incorrect reagents
  - Erroneous calculations of analyte parameters, such as purity constraints or dilution factors

- ELN-based templates contained embedded laboratory and business rules to prevent most potential laboratory errors from occurring

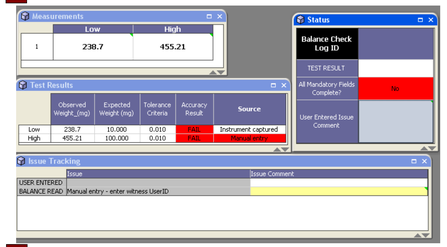
1 Selection of instrument assets drives business rules (calibration date, asset parameters)

Balance Check

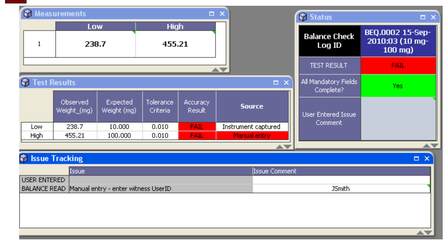
	Entry	Field Status
Test Date	15-Sep-2010	
Site	US	
Target Mass	70.000	
Target Mass Unit	mg	
Balance Asset Id	BAL0001	
Expiration Date	07-Jun-2010	Balance calibration has expired
Balance Type	Analytical	
Weight Range Low (mg)	10.000	
Weight Range High (mg)	1000.000	
Weight Set Asset Id	TSTWS0002	
Weight Set Expiration Date	31-Dec-2009	
Nominal 1	1 mg	
Nominal 2	5 mg	
Nominal 3	10 mg	
Nominal 4	25 mg	
Nominal 5	100 mg	
Nominal 6	250 mg	
Nominal 7	750 mg	
Select Low Check	Nominal 2	Check Weight Low must be greater than Balance Weight Range Low (mg)
Select High Check	Nominal 3	High check weight must be greater than Target Mass
Check Weight Low	5 mg	
Check Weight High	10 mg	

2 System registers whether measurements are captured directly from the instrument

a.



b.



3 Query for valid COA records returns analyte data and enforces a valid balance check record

Material Information

	Entry	Field Status
Date	15-Sep-2010	
Lot Number	ABC	
CoA	CoA ABC-342-b1-000025	
CoA Reference	/Root/BA Group 2/BA Solution Workflows/ CoA ABC-342-b1-000025 (v4)	
Material Name	Losartan	
Material_Type	Small Molecule	
Exhausted Status	No	
Potency Value	0.89	
Specificity Value		
Protein_Content A280 (mg/mL)		
Production Date		
Expiration Date	28-Sep-2011	
Target Mass	5	
Target Mass Unit	mg	
Select Balance	BAL0003	
Balance Model	Mettler Toledo	
Balance Weight Range High	100	
Balance Weight Range Low	1	
Weight Range Units	mg	
Balance Check Reference	Balance Check Hyperlink	A balance check must be performed
Reagent Prep Generic Name		
Diluent Prep Reference		

4 Real Time Issue Tracking : System captures deviations from defined SOP. Deviation from previously defined business rules are captured, and require user comment to proceed.

Issue Tracking

	Issue	Issue Comment
USER ENTERED	User Entered Issue	Standard Mass is defective
1	Balance range does not bracket Target Mass	
2	Balance calibration has expired	
3	Check Weight Low must be greater than Balance Weight Range Low (mg)	
4	High Check weight must be greater than low check weight	

RESULTS

Each ELN template was validated before use, incorporating business and scientific rules to ensure that the task could be consistently and completely recorded in an error-free manner, making post-analysis QC redundant. The validated ELN functionality allowed 'audit by exception.' As a result, the system prevented the real-time use of expired reagents by checking the database to confirm that it was approved for use in the analytical method and was not expired. Failure to rectify either deviation prevented the analyst from proceeding with the method. This approach was extended to the use and control of equipment, standards, methods, document templates, and general lab processes, enabling faster QC audits and final reporting.

CONCLUSIONS

The utility of an ELN in supporting common bioanalytical laboratory processes was successfully tested.

Once configured within the system, each workflow produced no auditable findings and supported the hypothesis that QC processes can indeed be incorporated during real time operations.

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