

Electronic Laboratory Notebook as a tool to Facilitate Scientific Data Analysis and Review in Regulated and Non-Regulated Bioanalysis

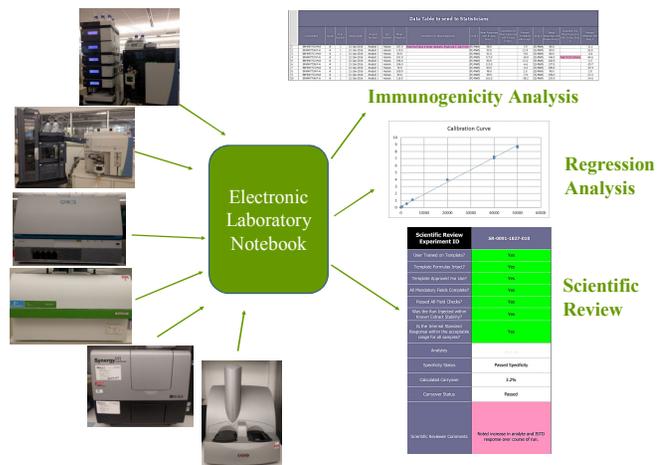
Jessica White¹, April Pisek¹, Jennifer Vance¹, Ashley Brant^{1*}

¹AIT Bioscience, Indianapolis, IN



Purpose

To illustrate the utility of the Electronic Laboratory Notebook (ELN) in facilitating scientific data analysis and review in regulated and non-regulated bioanalytical studies.



Methods

Since 2011, an Oracle-based ELN (IDBS E-Workbook 10.1.3) has been the backbone of operations at AIT Bioscience. The validated templates and workflows allow real-time electronic data collection and quality control checks. The variety of templates and workflows serve regulated and non-regulated work for both small and large molecule bioanalysis. This work describes the additional benefits of the ELN in streamlining and facilitating scientific data analysis and review.

Immunogenicity Analysis

Uses analyst-defined experimental design to calculate all data needed for statistical determination of cut-point. Deactivation status automatically omits deactivated samples from analysis and carries through related notes.

| Study Design | Run 1 | Run 2 | Run 3 | Run 4 | Run 5 | Run 6 | Run 7 | Run 8 | Run 9 | Run 10 |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|
| 1 | A | B | C | D | E | F | G | H | I | J |
| 2 | A | B | C | D | E | F | G | H | I | J |
| 3 | C | D | E | F | G | H | I | J | A | B |
| 4 | C | D | E | F | G | H | I | J | A | B |
| 5 | A | B | C | D | E | F | G | H | I | J |

Automated calculation of ANOVA precision statistics for entire experiment.

| Run | Sample | Concentration | Response | Standard Deviation | CV (%) |
|-----|--------|---------------|----------|--------------------|--------|
| 1 | 100 | 100 | 100 | 10 | 10% |
| 2 | 200 | 200 | 200 | 20 | 10% |
| 3 | 300 | 300 | 300 | 30 | 10% |
| 4 | 400 | 400 | 400 | 40 | 10% |
| 5 | 500 | 500 | 500 | 50 | 10% |

| ANOVA Statistics | F-Value | P-Value | MSD |
|------------------|---------|---------|--------|
| Between Groups | 18.0 | 0.0001 | 100.00 |
| Within Groups | 0.5 | 0.4838 | 20.00 |
| Total | 18.5 | 0.0001 | 120.00 |

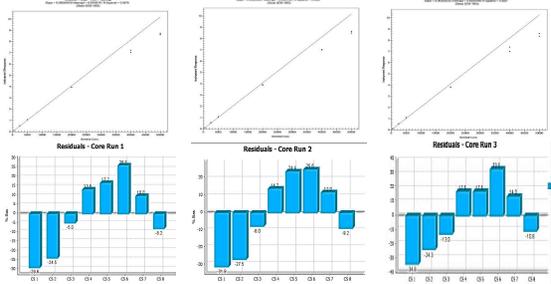
| Specificity - Sent to Statistics | Sample | Response | Standard Deviation | CV (%) |
|----------------------------------|--------|----------|--------------------|--------|
| 1 | 100 | 100 | 10 | 10% |
| 2 | 200 | 200 | 20 | 10% |
| 3 | 300 | 300 | 30 | 10% |
| 4 | 400 | 400 | 40 | 10% |
| 5 | 500 | 500 | 50 | 10% |

| Data Table to send to Statistics | Sample | Response | Standard Deviation | CV (%) |
|----------------------------------|--------|----------|--------------------|--------|
| 1 | 100 | 100 | 10 | 10% |
| 2 | 200 | 200 | 20 | 10% |
| 3 | 300 | 300 | 30 | 10% |
| 4 | 400 | 400 | 40 | 10% |
| 5 | 500 | 500 | 50 | 10% |

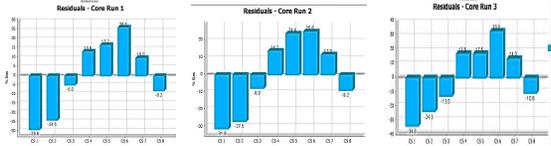
Regression Analysis

Links data from Watson for core runs and determines residuals allowing for selection of best fit by a regulatory-acceptable pre-defined methodology.

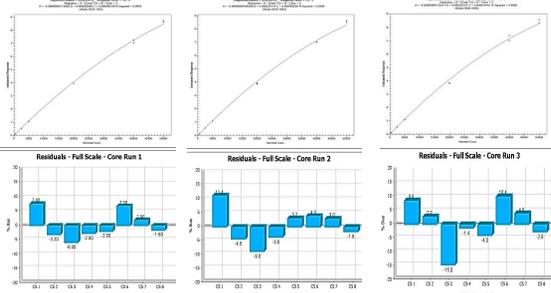
Linear Fit Calibration Curves



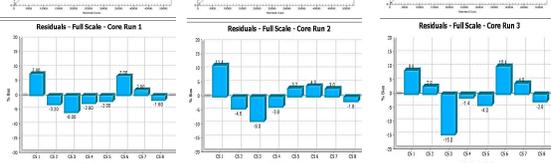
Linear Fit Residuals



Quadratic Fit Calibration Curves



Quadratic Fit Residuals



Scientific Review

A combination of manual review of the chromatography for MS transitions, retention times and integrations along with automated determination of extract stability, specificity, carry-over status and sample impact, and internal standard response.

| Scientific Review Experiment ID | SR-001-1827-012 |
|--|------------------------------------|
| Template Formulas Used? | Yes |
| Template Approved for Use? | Yes |
| All Mandatory Fields Completed? | Yes |
| Were the Runs Specified when Approval Entered (Sample)? | Yes |
| Is the Internal Standard Consistent with the Specified Sample? | Yes |
| Analysis | Pass |
| Specificity Status | Passed Specificity |
| Calculated Carryover | 3.5% |
| Carryover Status | Passed |
| Scientific Reviewer Comments | Run meets all acceptance criteria. |

Abnormal Internal Standard flagged

| Run | Sample | Concentration | Response | Standard Deviation | CV (%) | Internal Standard Response |
|--------|--------|---------------|----------|--------------------|--------|----------------------------|
| Run 1 | 100 | 100 | 100 | 10 | 10% | 100.00 |
| Run 2 | 200 | 200 | 200 | 20 | 10% | 200.00 |
| Run 3 | 300 | 300 | 300 | 30 | 10% | 300.00 |
| Run 4 | 400 | 400 | 400 | 40 | 10% | 400.00 |
| Run 5 | 500 | 500 | 500 | 50 | 10% | 500.00 |
| Run 6 | 600 | 600 | 600 | 60 | 10% | 600.00 |
| Run 7 | 700 | 700 | 700 | 70 | 10% | 700.00 |
| Run 8 | 800 | 800 | 800 | 80 | 10% | 800.00 |
| Run 9 | 900 | 900 | 900 | 90 | 10% | 900.00 |
| Run 10 | 1000 | 1000 | 1000 | 100 | 10% | 1000.00 |
| Run 11 | 1100 | 1100 | 1100 | 110 | 10% | 1100.00 |
| Run 12 | 1200 | 1200 | 1200 | 120 | 10% | 1200.00 |
| Run 13 | 1300 | 1300 | 1300 | 130 | 10% | 1300.00 |
| Run 14 | 1400 | 1400 | 1400 | 140 | 10% | 1400.00 |
| Run 15 | 1500 | 1500 | 1500 | 150 | 10% | 1500.00 |
| Run 16 | 1600 | 1600 | 1600 | 160 | 10% | 1600.00 |
| Run 17 | 1700 | 1700 | 1700 | 170 | 10% | 1700.00 |
| Run 18 | 1800 | 1800 | 1800 | 180 | 10% | 1800.00 |
| Run 19 | 1900 | 1900 | 1900 | 190 | 10% | 1900.00 |
| Run 20 | 2000 | 2000 | 2000 | 200 | 10% | 2000.00 |
| Run 21 | 2100 | 2100 | 2100 | 210 | 10% | 2100.00 |
| Run 22 | 2200 | 2200 | 2200 | 220 | 10% | 2200.00 |
| Run 23 | 2300 | 2300 | 2300 | 230 | 10% | 2300.00 |
| Run 24 | 2400 | 2400 | 2400 | 240 | 10% | 2400.00 |
| Run 25 | 2500 | 2500 | 2500 | 250 | 10% | 2500.00 |
| Run 26 | 2600 | 2600 | 2600 | 260 | 10% | 2600.00 |
| Run 27 | 2700 | 2700 | 2700 | 270 | 10% | 2700.00 |
| Run 28 | 2800 | 2800 | 2800 | 280 | 10% | 2800.00 |
| Run 29 | 2900 | 2900 | 2900 | 290 | 10% | 2900.00 |
| Run 30 | 3000 | 3000 | 3000 | 300 | 10% | 3000.00 |

Carry-over Impact calculated by sample

Extract stability checked against the validation.

Specificity automatically calculated.

Results

A key to the successful use of an ELN in the bioanalytical lab is ensuring the flexibility to operate in both regulatory and non-regulatory environments and provide real-time quality control checks. Previous communications focus on the design and structure of our ELN to meet this need.

With the front-end quality control in place, efforts turned to the organization and turn-around time for back-end scientific data analysis and review. Workflows and templates have been created to facilitate 3 major tasks in data analysis and review. Each of these back-end processes rely on direct datalinks from multiple instrument platforms (TSQ Vantage and TSQ Quantiva mass spectrometers, MSD and Biotek plate readers, and PE Gamma Counter) to Watson LIMS.

- Regression analysis tool for method validation:** Imports all validation runs and performs root mean squared analysis for both linear and quadratic fitting with multiple weightings to find the optimal regression.
- Immunogenicity analysis template:** Allows for the collection of confirmatory and domain ADA cut points data. Generates descriptive statistics and presents complete dataset in a format compatible with statistical software.
- Scientific review template:** Calculates carry-over, internal standard statistics and extract stability compliance and flags outlying results.

Having all of the required data imported and the cumbersome calculations handled by these templated workflows frees up the scientific staff's time to focus on critical assessment of the data. Furthermore, it simplifies auditing and reporting of the results.

Conclusion

By providing real time quality control in the lab as well as streamlined scientific data analysis and review using Watson LIMS data links, the ELN is a powerful tool for high quality, audit-ready bioanalytical data.