Standardization of Cell Culture Monitoring Analyzers to Eliminate Bridging Studies and Reduce Tech Transfer Time

Genentech — *A Member of the Roche Group*

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ABSTRACT

- Standardization of cell culture monitoring analyzers was applied in Roche's antibody manufacturing processes to align throughout the Roche and Genentech network.
- An assessment was performed in the Genentech Oceanside Lab and Pilot Plant to assess comparability of parameters monitored in Roche and Genentech manufacturing processes.
- An evaluation of Roche Custom Biotech (RCB) analyzers was performed to replace a multi-functional membrane technology
- Results suggested the data collected from Roche analyzers can be considered equivalent to the obtained measurements from the membrane analyzers.
- This poster will discuss the results of data comparison between different analyzers with respective Chinese hamster ovary (CHO)-based cell culture processes.

MATERIALS AND METHODS

Cell Culture Parameter A and B

- Cell Culture Samples from Molecule X at three stages for 2 different bioreactors:
  - Seed Train, before and after solera
  - Inoculum Stage (N-X), day 1 and day 2
  - Production stage, day 1, day 8, day 14
- Evaluation:

Specificity:
Manually analyzed results of every measurement and compared the result with the RCB analyzer

Parameter	Acceptance Range	Formula
Specificity (%) A	94.0 % - 106.0 %	$\dfrac{A_{RCB\ analyzer}}{A_{manual}} \times 100$
Specificity (%) B	94.0% - 106.0 %	$\dfrac{B_{RCB\ analyzer}}{Sum\ (B_{RCB\ analyzer} + incorrect\ B)} \times 100$

Accuracy by Method Comparison:
Reported values from the Previous Membrane Analyzer vs Roche Custom Biotech Analyzers.

Parameter	Acceptance Range	Formula
Accuracy by method comparison (%) A	94.0 - 106.0 %	Mean of the Relative % difference between RCB Analyzer value and the corresponding value from the previous membrane analyzer.
Accuracy by method comparison (%) B	80.0 - 120.0 %	Mean of the Relative % difference between RCB Analyzer value and the corresponding value from the previous membrane analyzer.

Cell Culture Parameter C

- Cell Culture Samples from Molecule X at three stages:
  - ≥ 10 samples: Seed Train Culture (Passage)
  - ≥ 25 samples: Inoculum Culture (N-X)
  - ≥ 25 samples: Production Culture

- Evaluation:

Accuracy by Method Comparison
Calculated difference between the new method and the true value and report the mean difference:

$$\Delta C = C\ (New) - C\ True\ Value\ (Reference)$$

Acceptance Criteria:

$$Mean\ difference\ (New - Reference) \leq \pm 0.05$$

OBJECTIVE

- To standardize cell culture analytical instruments across Roche organizations.
  - Save additional resources, cost and time needed for bridging comparison studies.
  - Improve collaboration for development, technology transfers and across company validation studies.
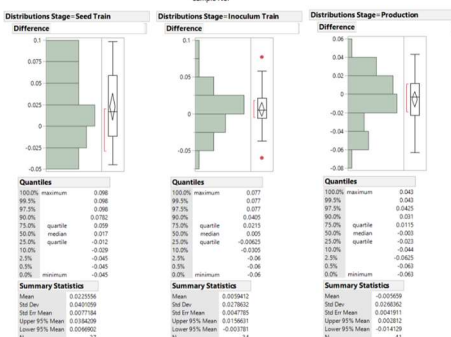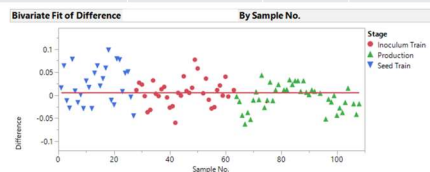

RESULTS

Cell Culture Parameter A and B

Parameter	Acceptance Criteria	Results	Evaluation
SPECIFICITY			
Specificity (%) A	94.0 – 106.0 %	Seed_bs: 101.5 % Seed_as: 101.1 % N-X_d1: 102.7 % Prod_d1: 100.3 % Prod_d8: 100.4 % Prod_d14: 101.1 %	Pass
Specificity (%) B	94.0 – 106.0 %	Seed_bs: 99.2 % Seed_as: 98.5 % N-X_d1: 99.1 % Prod_d1: 99.5 % Prod_d8: 100.0 % Prod_d14: 99.5 %	Pass
ACCURACY BY METHOD COMPARISON			
Accuracy by method comparison (%) A	94.0 - 106.0 %	97.8 %	Pass
Accuracy by method comparison (%) B	80.0 - 120.0 %	81.0 %	Pass

Cell Culture Parameter C

| Parameter	Acceptance Criteria	Results	Evaluation
Mean Difference	$\leq \pm 0.05$	0.01	Pass
95% CI for mean difference of all samples	Report	0.00-0.01	Reported

CONCLUSIONS

- Results of 100.3 % – 102.7 % for parameter A and 98.5 % – 100.0 % for parameter B demonstrate specificity of the method for Molecule X. The mean relative % difference was 97.8 % for parameter A and 81.0 % for parameter B.
- Results of a mean difference of 0.01 reported between the RCB Analyzer and Previous Membrane Analyzer demonstrated accuracy by method comparison.

COMPANY COST SAVINGS

	Previous Membrane Analyzer	Roche Custom Biotech Analyzer	Total Savings
Equipment	$ 7,965,000.00	$ 3,407,769.14	$ 4,557,230.86
Annual PM	$ 752,250	$ 696,427.00	$ 55,823.00
Consumables	$ 1,910,700.00	$ 1,206,600.00	$ 704,100.00
Total Overall Savings: $5,317,153.86			

Roche Custom Biotech Net Present Value (NPV) ($M)
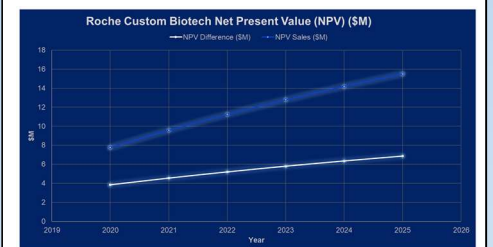
Year	2020	2021	2022	2023	2024	2025
Equipment sale ($)	$3,407,769					
PM annual sale ($)		$696,427	$696,427	$696,427	$696,427	$696,427
Consumables sale ($)	$1,206,600	$1,206,600	$1,206,600	$1,206,600	$1,206,600	$1,206,600
Savings	$4,557,231	$55,823	$55,823	$55,823	$55,823	$55,823
Cost / depreciation ($)	($1,405,374)	0	0	0	0	0
Sale and savings with WACC	$7,766,226	$9,571,618	$11,235,573	$12,769,173	$14,182,629	$15,485,353
NPV	$15,485,353					

OVERALL BENEFITS

- ✓ Reduces technology transfer and development time across the Roche and Genentech network
- ✓ Simplifies data sharing across all network sites
- ✓ Eliminates bridging studies
- ✓ Newer technology increases accuracy and precision
- ✓ Processes multiple samples at once
- ✓ Faster sample analysis
- ✓ Less frequent calibrations
- ✓ Decreased equipment cost
- ✓ Increased reliability of service
- ✓ Decreased consumable cost
- ✓ Decreased service cost

REFERENCES

- Report # 300-9999-TER-040 v 2.0; Evaluation of the Roche Custom Biotech Analyzers
- VAL-0205995; Method Suitability Test and Validation Protocol: Viability and VCD determination
- VAL-0210100; Method Suitability Test and Validation Report: Viability and VCD determination
- VAL-0205973; Method Suitability Test Protocol: pH Determination
- VAL-0210099; Method Suitability Test and Validation Report: pH determination

ACKNOWLEDGEMENT