Bioanalytical Comparability

BIOANALYTICAL COMPARABILITY BETWEEN BIOSIMILAR (TEST DRUG) AND INNOVATOR (REFERENCE) DRUG.

DR. S. GUPTA, H. CHAVDA, N. PATEL, M. ZAVERI, A. SHAH, H.SURTI
CLIANTHA RESEARCH, AHMEDABAD, INDIA.

INTRODUCTION

Biosimilar drugs are not exact duplicates of Innovator drugs and require evaluation of "similarity" of the Biosimilar compared to the innovator drug. It is important to demonstrate that the bioanalytical method can measure both the innovator and the biosimilar drug reliably and equivalently.

A one-assay approach was developed and validated to detect Biosimilar and Innovator drug. All the differences (e.g., structural and potency) were carefully evaluated and taken into consideration when developing assays that measure both the biosimilar and the innovator drug.

PROS AND CONS OF ONE ASSAY APPROACH

PROS

- To use biosimilar curve for quantification of both Demonstrate minimal difference between.
- No Between assay variability, i.e. minimization of the potential impact of assay bias on the comparison of the biosimilar and innovator drugs.
- Blinded study sample analysis possible.

CONS

- Demonstrate minimal difference between biosimilar QCs and Innovator QCs

Bioanalytical similarity between a biosimilar and reference drug was assessed during the PK assay development phase. In this phase, the similarity of assay calibration curves and quality control (QC) samples was studied in detail in order to establish target acceptance criteria for validation.

DEVELOPMENT PHASE

Confirms 'Similarity' of Calibration curves

Ensures Reference biotherapeutic and biosimilar calibration curves are parallel

Recommended statistically based approach for comparing curves

Software availability (e.g. ALLFIT, SoftMaxPro GxP)

VALIDATION PHASE

Confirms comparable reactivity of Biosimilar & Reference in common LBA

Systematic Comparison of QC results

- Intra batch evaluation
- Inter batch evaluation

Direct comparison of Biosimilar against Reference

IN STUDY VALIDATION PHASE

Study samples assayed using validated method

Plate acceptance based on recommended criteria and established system suitability requirements.

The following keys aspects of method development are expected to influence the outcome of the PK assay used to determine bioanalytical similarity.

- **Assay methodology / platform**
- **Critical Reagents**
- **Assay Design: calibrators and quality controls**
- **Assay Calibrators: Biosimilar or Innovator**

Assay Design

QC samples (HQC, MQC and LQC) prepared from Test drug and Reference drug was quantified against calibration standard prepared from Test drug and Reference drug and vice-versa. Comparability experiment was done by two different analysts on two different days.

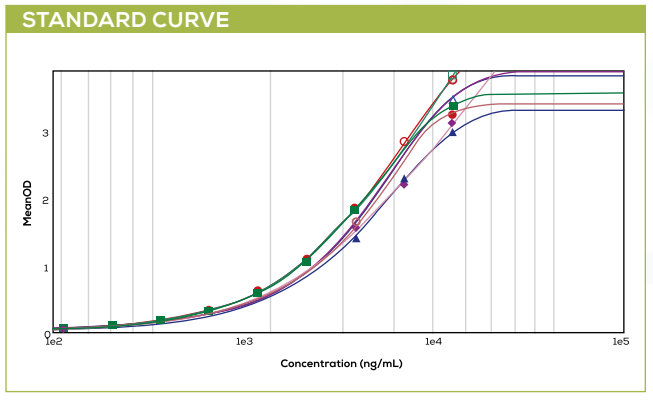
Acceptance Criteria for QC samples

- %CV of each QC samples should be ≤20% for Intra and Inter runs.
- %Bias each QC samples should be ±20% of the nominal value for Intra runs and Inter runs.

Results

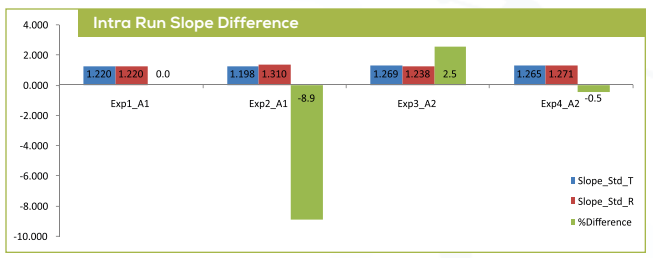
Here presented comparability data is for Adalimumab Biosimilar (Test) and Innovator (Humira) Reference drug

Calibration Standard Curve of Adalimumab Test and Reference Drug (Humira)



Intra Run Slope Difference

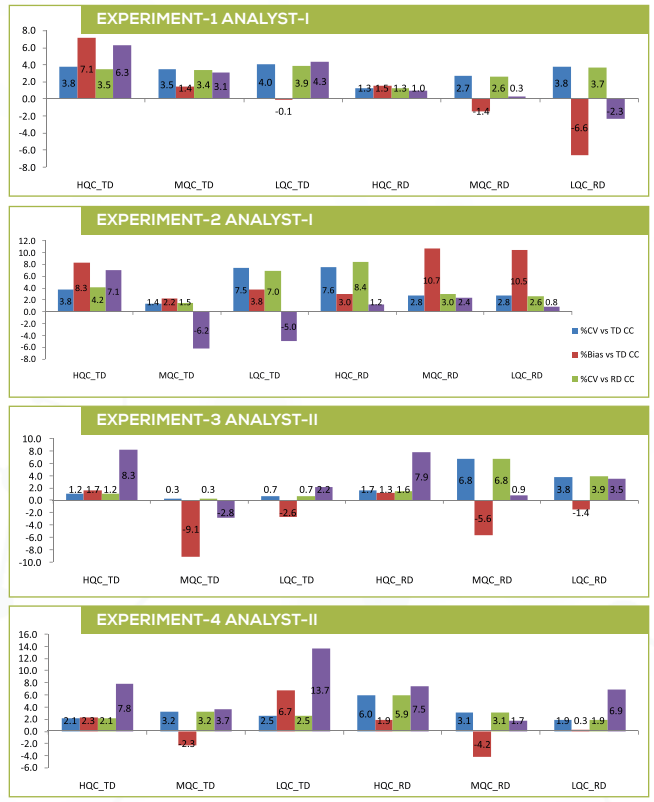
	Slope_Std_T	Slope_Std_R	%Difference
Exp1_A1	1.220	1.220	0.0
Exp2_A1	1.198	1.310	-8.9
Exp3_A2	1.269	1.238	2.5
Exp4_A2	1.265	1.271	-0.5



Accuracy and Precision of Quality Control Samples prepared from Adalimumab Test and Reference Drug (Humira)

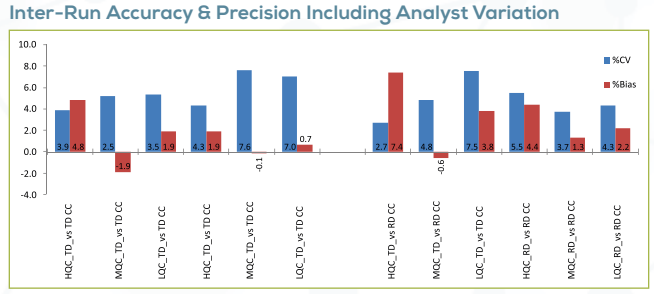
	Back Calculation of QC samples against Adalimumab (Test Drug) Calibration standards						Back Calculation of QC samples against Adalimumab (Reference Drug) Calibration standards					
	QC_Test Drug			QC_Reference drug (Humira)			QC_Test Drug			QC_Reference drug (Humira)		
	HQC	MQC	LQC	HQC	MQC	LQC	HQC	MQC	LQC	HQC	MQC	LQC
Experiment 1, Analyst 1												
Intrarun %CV	3.8	3.5	4.0	1.3	2.7	3.8	3.5	3.4	3.9	1.3	2.6	3.7
Intrarun %Bias	7.1	1.4	-0.1	1.5	-1.4	-6.6	6.3	3.1	4.3	1.0	0.3	-2.3
Experiment 2, Analyst 1												
Intrarun %CV	3.8	1.4	7.5	7.6	2.8	2.8	4.2	1.5	7.0	8.4	3.0	2.6
Intrarun %Bias	8.3	2.2	3.8	3.0	10.7	10.5	7.1	-6.2	-5.0	1.2	2.4	0.8
Experiment 3, Analyst II												
Intrarun %CV	1.2	0.3	0.7	1.7	6.8	3.8	1.2	0.3	0.7	1.6	6.8	3.9
Intrarun %Bias	1.7	-9.1	-2.6	1.3	-5.6	-1.4	8.3	-2.8	2.2	7.9	0.9	3.5
Experiment 4, Analyst II												
Intrarun %CV	2.1	3.2	2.5	6.0	3.1	1.9	2.1	3.2	2.5	5.9	3.1	1.9
Intrarun %Bias	2.3	-2.3	6.7	1.9	-4.2	0.3	7.8	3.7	13.7	7.5	1.7	6.9
Interrun %CV	3.9	5.2	5.3	4.3	7.6	7.0	2.7	4.8	7.5	5.5	3.7	4.3
Interrun %Bias	4.8	-1.9	1.9	1.9	-0.1	0.7	7.4	-0.6	3.8	4.4	1.3	2.2

Intra Run Accuracy & Precision



TD: Test Drug, RD: Reference Drug, TD CC: Test Drug Calibration Curve, RD CC: Reference Drug Calibration Curve E: Experiment, A: Analyst

Inter-Run Accuracy & Precision Including Analyst Variation



TD: Test Drug, RD: Reference Drug, TD CC: Test Drug Calibration Curve, RD CC: Reference Drug Calibration Curve

CONCLUSION

- The standard curve generated using biosimilar drug was bioanalytically similar to a standard curve generated using reference drug.
- The back calculated concentration of QC samples prepared from biosimilar drug was bioanalytically similar to the back calculated concentration of QC samples prepared from reference drug.

One bioanalytical method can be used between the biosimilar and reference drug to support PK assessments during biosimilar drug development.