
pSMILE
SAFETY·QUALITY·RESULTS
Correlation and Parallel (LOT to LOT) Testing
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pSMILE Contract

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Project Title: Patient Safety Monitoring in International Laboratories

Correlation Testing

- Is a measure of the extent to which two variables are related
- Required for both Qualitative and Quantitative Assays
- Required for all laboratories performing research funded by the NIH Division of AIDS (DAIDS)

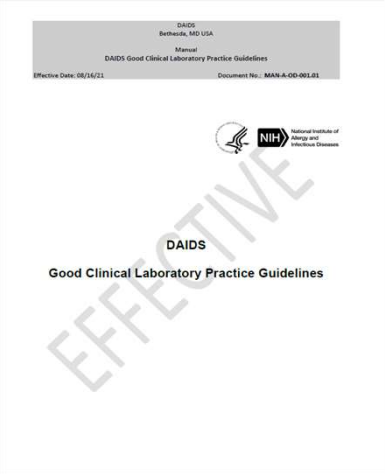
DAIDS Requirement for Correlation

DAIDS GCLP Guideline States,

- If a laboratory uses more than one instrument to perform the same test, the primary and backup instruments must be compared to each other to determine the consistency of results

- For qualitative tests, verifying the successful EQA performance or use of participant specimens for the backup lab/instruments should be sufficient

- For quantitative tests, correlation testing should be performed on a semi-annual basis at minimum, where applicable



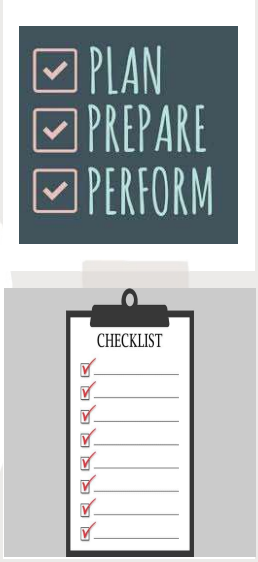
Planning and Preparing for Correlation

Ensure all instruments for correlation testing have

- All maintenance activities completed
- Acceptable Validation and Calibration
- Internal Quality Control results within acceptable range and no biases, shifts, and trends observed
- Acceptable EQA performance

Recommendations

- Create a checklist to track completion of all items listed above
- Ensure laboratory personnel performing the testing have been trained and follows SOP
- Use Correlation Worksheet and document dates and other relevant information



Sample Selection

- The use of fresh human samples is recommended.
- If fresh samples are not available, the use of EQA, linearity, and commercial controls may be necessary to ensure low, normal, and high specimens are tested
- Qualitative Assay
  - Positive and Negative – 2 samples (Indeterminate/Trace sample if that is a possible reportable result)
- Quantitative Assay
  - Low, Normal, and High – At least 3 samples that span the reportable range

Sample Analysis

Samples

- Should be processed according to the stability requirements of the analyte
- Should be protected from evaporation and analyte degradation during the time between measurements
- Can be run on both instruments at the same time or within 2 hours of collection is recommended
- If analysis is not possible within the time frame, ensure samples are stored appropriately. Transport samples to backup laboratory as soon as possible
- Should be run in duplicates, at a minimum, on both instruments

Acceptability Criteria/Tolerance limit

•Determine the tolerance limit for your correlation ratio

• pSMILE recommends a tolerance limit of ≤ 3 when you begin monitoring correlation ratio. If dissimilar methods are compared, this limit may have to be increased

• Using ≤ 3 as a tolerance limit for your correlation ratio is equivalent to using ≤ 3SD in your QC evaluation. In other words, if your correlation ratio is equal to 3, the results from your instruments are more than 3SD apart from each other

Example of Correlation Results

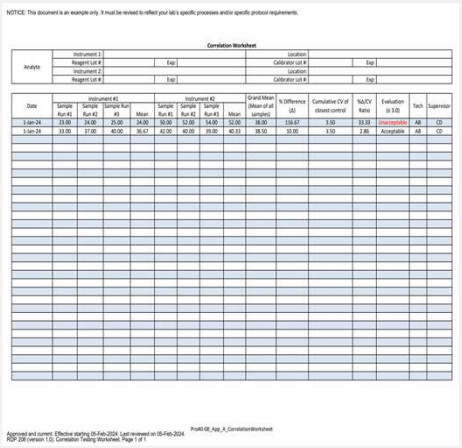
Analyte	Instr. 1 Mean	Instr. 2 Mean	Grand Mean	Δ	%Δ	Cume CV	%Diff/CV ratio	Accept. % Diff/CV Ratio	Pass/ Fail
Glucose	92.5	89	90.75	3.5	3.9	2.5	1.5	≤3	PASS
Glucose	58.5	57.5	58	1	1.7	2.5	0.7	≤3	PASS
Glucose	136.5	128.7	132.6	7.8	5.9	2.5	2.4	≤3	PASS
Glucose	302.5	276.5	289.5	26	9.0	2.2	3.6	≤3	FAIL
Glucose	214.5	207	210.75	7.5	3.6	2.2	1.4	≤3	PASS

Evaluation of Correlation Results

- Do Final Evaluation : Is the percent ratio 3.6% less than 3%? No so this is not acceptable so you will need to rerun your Correlation studies
- Possible reasons for failure
  - Different methodologies/Instrumentation
  - Calibration differences including a lot of calibrator or assigned values
  - Age of calibrator (Open stability)
  - Imprecision of one of the methods
  - Reagent lot or shipment (storage)
  - Reagent stability (On-board)

Documentation

- Use Correlation Worksheet
- Document dates, instrument IDs, reagent lot numbers, expiration dates, assay values
- Ensure calculations are correct
- Evaluation and acceptability criteria are present
- Document reasons for failure and actions taken to resolve the issue
- Technician and supervisor initials
- All documents should be reviewed and approved by the Laboratory Director or Designee



NOTICE: This document is an example only. It must be revised to reflect your lab's specific processes and/or specific protocol requirements.

Correlation Worksheet

Analyte:	Instrument 1		Location:				
	Reagent Lot #		Exp:		Calibrator Lot #		Exp:
	Instrument 2		Location:				
	Reagent Lot #		Exp:		Calibrator Lot #		Exp:

Date	Instrument #1				Instrument #2				Grand Mean (Mean of all samples)	% Difference (Δ)	Cumulative CV of closest control	%Δ/CV Ratio	Evaluation (≤ 1.0)	Tech	Supervisor
	Sample Run #1	Sample Run #2	Sample Run #3	Mean	Sample Run #1	Sample Run #2	Sample Run #3	Mean							
1-Jan-24	23.00	24.00	25.00	24.00	50.00	52.00	54.00	52.00	38.00	116.67	3.50	33.33	Unacceptable	AB	CD
1-Jan-24	33.00	37.00	40.00	36.67	42.00	40.00	39.00	40.33	38.50	10.00	3.50	2.86	Acceptable	AB	CD

Approved and current. Effective starting 05-Feb-2024. Last reviewed on 05-Feb-2024. Pro40-08_App_A_CorrelationWorksheet
RDP 208 (version 1.0). Correlation Testing Worksheet. Page 1 of 1

Questions?

Parallel testing

DAIDS GCLP states “For each new lot of reagents, the laboratory must document that samples are tested in parallel with each current lot and that comparable results are obtained before or concurrently with their use as applicable.”

Qualitative Assays

Example - Rapid HIV, UHCG

- A minimum of 3 samples
  - Positive
  - Negative
  - Indeterminate/Trace if kit reports
- Type of samples
  - Patient samples are preferred
  - EQA
  - Quality Control - Preferably from previous kit lot; new kit lot controls can be used but must be tested on previous lot
- Samples should be run on both the old and new lot
- Designated personnel should review the results to confirm that the results are within defined acceptability limits.
- Negative results should be negative, positive results should be positive on the new lot.

Quantitative Assays

Example - Chemistry Analytes

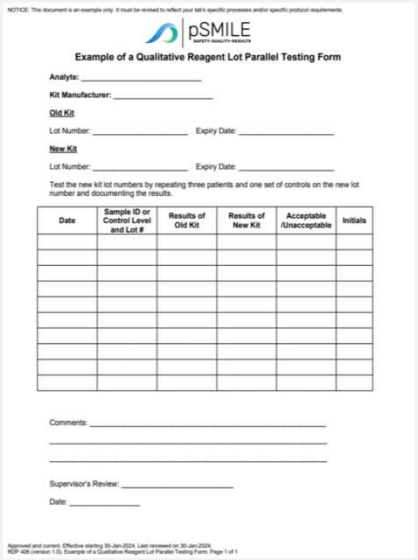
- A minimum of 3 samples that span the analytical measurement range
- Type of samples
  - Patient samples are preferred
  - EQA
  - Quality Control
- Samples should be run on both the old and new lot
- Designated personnel should review the results to confirm that the results are within defined acceptability limits.
- Suggested acceptability limits are within +/- 1SD or within +/-10%

Current Lot – New Shipment of Reagents

- 3 Patient samples is still recommended
- Current lot of QC material can be used to check a new shipment of the same reagent lot
  - There should be no change in potential matrix interactions between the QC material and different shipments of the same lot reagents.

Documentation

- Use Parallel Testing Form
- Document lot numbers of old and new reagents and expiration dates
- QC values on both runs
- Results obtained from old and new lots
- Criteria for acceptance
- Document reasons for failure and actions taken to resolve the issue
- Initials of testing personnel and reviewer
- Final report should be reviewed by Laboratory Director or Designee



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Example of a Qualitative Reagent Lot Parallel Testing Form

Analyte: _____

Kit Manufacturer: _____

Old Kit

Lot Number: _____ Expiry Date: _____

New Kit

Lot Number: _____ Expiry Date: _____

Test the new kit lot numbers by repeating three patients and one set of controls on the new lot number and documenting the results.

Date	Sample ID or Control Level and Lot #	Results of Old Kit	Results of New Kit	Acceptable /Unacceptable	Initials

Comments: _____

_____

_____

Supervisor's Review: _____

Date: _____

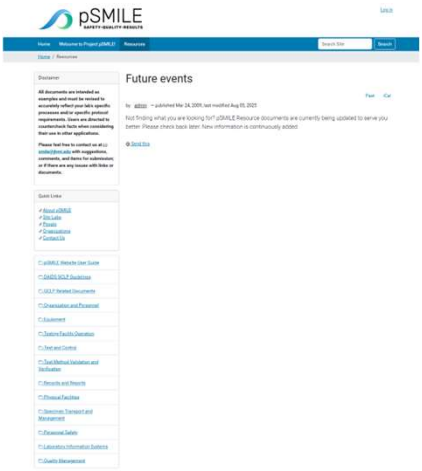
Approved and current. Effective starting 30-Jan-2024. Last reviewed on 30-Jan-2024.
RDP 406 (version 1.0). Example of a Qualitative Reagent Lot Parallel Testing Form. Page 1 of 1

Things to Remember

- Patient samples are preferred, however if lack of patient samples, it may be necessary to use QC, EQA, linearity, and other standards
- An attempt should be made to span analytical measurement range
- Volatility of the analyte correlated (storage and transport)
- Use manufacturer designed materials specifically for validation/correlation

pSMILE Procedures on Resources

- All Documents used and discussed today are on www.psmile.org under Resources section
  - Correlation Testing for Quantitative Assays
  - RDP 208 Correlation Testing Worksheet
  - Parallel Testing and Reagent Lot Validation Guidelines
  - Example of a Qualitative Reagent Lot Parallel Testing Form
  - Examples of Coagulation, Hematology, Chemistry Reagent Lot Parallel Testing Form



Exceptions to Consider

- **Coagulation** – There is a specific procedure for new lots of coagulation reagents. Refer to the coagulation-specific procedures that are available at www.pSMILE.org

- **Viral Load** – Do not use this procedure for the parallel testing of new lots of reagents for HIV RNA, HIV DNA and other viral load tests. Refer to recommendations provided by the VQA.

- **Flow Cytometry** - Do not use this procedure for the parallel testing of new lots of Flow Cytometry reagents for CD4, CD8 and other cell markers. Refer to recommendations provided by the IQA.

SOP should include

- Type of samples to use for Comparison testing and Parallel testing
- Frequency
- Acceptability criteria
- How to document acceptability and failures
- What to do if comparison and parallel testing passes
- What to do if comparison and parallel testing fails and actions taken
- Supervisory review process

References

DAIDS Good Clinical Laboratory Practice Guidelines, Version 4.1, 2021

Clinical Laboratory Standards Institute (CLSI) Verification of Comparability of Patient Results Within One Health Care System Workbook. 1st ed. CLSI workbook EP31-ED1-WB. 2022.

Clinical Laboratory Standards Institute (CLSI) Measurement Procedure Comparison and Bias Estimation Using Patient Samples. CLSI EP09c 3rd Ed. 2018.

College of American Pathologists (CAP) 2023. Commission on Laboratory Accreditation, Laboratory Accreditation Program; All Common Checklist

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