

Procedure/Method Statistical Work-up/Validation Study Guidelines: Microbiology

Work-up guidelines and definitions (change in method/instrument):

Work-up Element:	Definition: CLSI or International Federation of Clinical Chemistry (IFCC)	Minimum Data Requirements: (where appropriate):	Applicability:	
			Qualitative	Quantitative
1. Imprecision <ul style="list-style-type: none"> • within run • between run 	The variation in analytical results demonstrated when a particular specimen or aliquot is analyzed multiple times or on multiple days. Imprecision is expressed quantitatively by a statistic such as standard deviation or coefficient of variation.	Within run – use preferably a patient sample or pool close to the decision levels with a minimum of 10 data points. Between run – 20 results from 20 separate runs on 2 levels over a 10-day minimum time period using appropriate Q.C. material.		✓
2. Patient Correlation	The correlation coefficient is a means to look for a relationship, not agreement, between pairs. Two methods may have a perfect correlation throughout the measuring range but may not agree in value i.e.: one may be double the value of the other.	40 data points are recommended with a minimum of 20 having 50% of the data points outside the reference intervals, if possible. Correlations should involve comparison with an acceptable reference method or laboratory.	n=20 ✓	n=40 ✓
3. Linearity	(IFCC) The range of concentration or other quantity in the specimen over which the method is applicable without modification (CLSI) when analytical results are plotted against expected concentrations; the degree to which the plotted curve conforms to a straight line is a measure of the system linearity.	4 data points each in duplicate as a minimum requirement, but 5 data points are preferred (over reportable range). Linearity studies are expected on an initial method work-up and further studies as defined by the College guidelines i.e.: troubleshooting. .		✓
4. Reference range validation	It is common convention to define the reference range or interval of a laboratory test as the central 95% interval bounded by the 2.5 and 97.5 percentiles of the selected patient population. Validation of an established reference range requires a minimum of 40 samples.	The minimum requirement is 40 data points for confirmation of an established reference range and 120 for the establishment of a new reference range.		✓

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Work-up guidelines and definitions (change in method/instrument) -continued

Work-up Element:	Definition: CLSI or International Federation of Clinical Chemistry (IFCC)	Minimum Data Requirements: (where appropriate):	Applicability:	
			Qualitative	Quantitative
5. Accuracy	Closeness of the agreement between the result of a measurement and the accepted reference value (true value of the analyte)	3 data points using acceptable reference material i.e.: CEQAL or CAP.	✓	✓
6. Sensitivity	Measure of the ability of an analytical method to detect small quantities of the measured component. When concern is performance at very low concentration it is useful to determine the detection limit as influenced by imprecision.	Sensitivity studies are only required for those methods which have clinical relevance at values close to "0" e.g.: PCR.	✓ When clinically relevant	✓ When clinically relevant
7. Specimen Stability	The conditions of handling and storage which permits the measurement and reporting of a clinically relevant result.	Data required for specimens known to be time sensitive. Usually associated with rejection criteria, e.g. specimens > 24 hours in transit, or arrived in inappropriate media.	✓ Storage and transport dependent	✓ Storage and transport dependent
8. Interference	The effect of any component of the sample on the accuracy of the measurement of the desired analyte.	Document the manufacturer's interference information. The method should include a disclaimer or a process for dealing with a lipemic, icteric or hemolyzed sample.	✓ Methods with known interferences	✓ Methods with known interferences
9. Organism Identification		20 patient isolates worked up by the new identification test in parallel with an acceptable reference method or laboratory. In addition, for specimens likely to possess complex flora, up to 20 common contaminants should be included as negative controls. See patient correlation above.	✓	✓ Semi-quantitative only
10. Antibiotic Sensitivity		Appropriate CLSI standard organisms should be tested in triplicate, e.g. see accuracy above.	✓	✓ Semi-quantitative only

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Quantitative:

Work-up requirements when an instrument is moved from site “A” to site “B”: (It is assumed that the instrument has been in recent use with acceptable performance).

Work-up Element:	Minimum data requirements:
1. Imprecision studies, Q.C. only.	As above
2. Patient correlation.	10 data points, where feasible

Qualitative or semi-quantitative:

If site B has no previous experience

Work-up Element:	Minimum data requirements:
1. Organism identification	10 patient isolates, up to 10 contaminants
2. Antibiotic susceptibility	As above