

Guidance Number: 001

APPENDIX 1: Validation - Experimental Parameters Matrix

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Element	ID Test	Limit Test	Misc. Other Test	Raw Material Quantitative	Intermediate Quantitative	Compendial	
						Quan	Limit
Specificity	Y	Y	*	*	Y	Y	Y
Linearity			*	Y	Y		
Range			*	Y ¹	Y ¹		
Accuracy			*	Y ¹	Y ¹		
Repeatability			Y	Y	Y		
Intermediate Precision		Y ³	Y	Y	Y	Y ²	Y ^{2,3}
Detection Limit		Y	*				Y
Quantitation Limit			*	I	I	I	
Robustness	*	Y ³	Y	Y	Y	Y	Y ³
SST	*	*	*	Y	Y	*	*

SST = System Suitability Testing

Quan = Quantitative Test

Limit= Limits Test

I= Applicable for impurity assay only

Y= Yes. This element should be evaluated.

* = May be needed depending on intended use of the test and/or if these elements were completed as part of method development.

1. Propose Accuracy to be inferred based on specificity, precision and linearity for potency and impurities methods. Linearity and Precision must cover range of use.

2. Should also include evaluation of multiple lots (minimum 3) to demonstrate conformance to the specification. (Reference is FDA Guidance document on verification of compendial methods).

3. This is not recommended for limits methods if this element was performed as part of method development.

APPENDIX 2: Proposal for Validation Elements For Various Miscellaneous Tests

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Element	LOD	ROI	Color/Abs in Solution	Particle Size	pH	OR	Titration	RI	SG/ Density	Melting Point	KF	TIEM
Specificity						Y						
Linearity							Y&					
Range							Y					
Accuracy	Y@									M	Y#	
Repeatability	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Intermediate Precision	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Detection Limit												
Quantitation Limit	Y [§]	Y [§]					I		Y		Y [§]	Y [§]
Robustness	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
SST*											Y	

Y= Yes. This element should be evaluated.

Y[§] = Quantitation Limit may be relevant if the results are quantitative. If test is being used as a limit test
Detection Limit may be more appropriate.

M = Needed if the method of detection for the melt is automatic instead of visual.

I= Needed if test is used for quantitation of impurities.

* Normally addressed through method development.

= to demonstrate absence of side reactions.

Y& = for titration methods used as potency assays

@ If the LOD result is needed to adjust the potency value.

TIEM = Total Insoluble Extraneous Matter

RI = Refractive Index

OR = Optical Rotation.

ROI = Residue on Ignition

LOD = Loss On Drying

SG = Specific Gravity

KF = Karl Fischer