pre-determined in order to properly select the validation experiment parameters before the test method is developed and the validation exercise is begun.

To begin the validation exercise, individual sites can determine from **Appendix 1 and 2** what analytical elements should be evaluated for the particular test and sample of interest.

In the case that a limited set of elements are included in the validation, it is recommended that the Method Validation Summary or protocol should address the reasons for limiting the validation to the chosen elements.

Validation of the test procedures should take into account the reactivity of the sample. If the sample can change over time, the validating scientist should attempt to find a means to quench the reaction before analysis. While this is normally a method development activity, this consideration should be evaluated by the site if method validation should occur at the sites. Once execution of the method validation has begun, deviations and experimental failures should be documented in the method validation report.

In some instances a set of experiments may be able to satisfy several validation parameters i.e. robustness, intermediate precision and repeatability could be combined and studied together instead of as isolated effects.

- For example, compendial physical tests such as LOD/ROI/pH where the analyst a sample amount are primary contributors to variation and the method is well defined in general chapters are ideal for this situation.

- An experiment could be constructed such that variations in sample size, analyst and equipment could all be studied at once.

Documentation
It is recommended that sites have local site procedures for performing test method validation. For methods in the scope of this guideline, sites may choose to prepare a protocol and obtain approval prior to commencing validation. Alternatively an SOP containing pre-approved templates or acceptance criteria guidelines could be used Because these test methods are generally lower risk than those used to test final APIs, more flexibility in documentation of validation information (e.g. use of an SOP versus a protocol) is considered acceptable.

Suggested criteria are included in this guideline on this topic; however criteria should be directly linked to the method's intended use.

Method Validation Summary Report:

It is recommended to analyse the experimental results and prepare a Method Validation Summary of the findings.

These method validation summaries may include but are not limited to:

- The performance results against criteria listed within this guideline, site SOP, or separate pre- approved protocol.
- For higher risk methods, at least two reviewer signatures are recommended to be obtained for the Method Validation Summary to be approved.

Appendix 1: Validation – Experimental Parameters Matrix.

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.