Checklist for Analytical Method Validation (Chemical)

TEST	ASSAY/RELATED SUBSTANCES		
PARAMETER	**No.**	**DOCUMENTS REQUIRED**	**AVAILABILITY**
Specificity	1	Testing Method	
	2	Acceptance criteria	
	3	Chromatogram/spectrum for following solutions:-	
		a) Standard	
		b) Sample	
		c) Blank/Placebo	
		d) Spike solution	
		e) System suitability tests	
	4	Impurities available	
		a) Peak purity for PDA detector or spike solution for non-PDA detector	
		b) Relative Retention Time (RRT)	
		c) Resolution (R) where applicable	
	5	Impurities not available	
		a) Stress data (minimum data for humidity, heat and light)	
		b) Peak purity	
		c) Relative Retention Time (RRT)	
		d) Resolution (R) where applicable	
Linearity	1	Testing Method	
	2	Acceptance criteria	
	3	Minimum five (5) levels of standard solutions	
	4	Data for linear regression equation, Y-intercept, slope, r^2 and linearity graph	
Range	1	For the assay of drug substances: 80% - 120% of working concentration (WC)	
	2	For the determination of an impurity: from the reporting level of an impurity to 120% of the specification	
Accuracy	1	Testing Method	
	2	Acceptance criteria	
	3	Minimum three (3) levels of concentration in triplicates covering the specified range	
	4	Result : reported as percent recovery by the assay of known added amount of analyte in the sample, OR as the difference between the mean and the accepted true value together with the confidence intervals	
Precision (Repeatability)	1	Testing Method (using sample/product as the test solution)	
	2	Acceptance criteria	
	3	Minimum three (3) levels of concentration in triplicates covering the specified range , OR	

		minimum six (6) replicates at 100% of the WC	
	4	Result : SD, RSD and confidence Interval	
Precision (intermediate precision/ ruggedness)	1	Testing Method (using sample/product as the test solution)	
	2	Acceptance criteria	
	3	Minimum three (3) levels of concentration in triplicates covering the specified range , OR minimum six (6) replicates at 100% of the WC	
	4	Cover at least 2 parameters among variation of analyst, date and equipment	
	5	Result : SD, RSD and confidence Interval	
Detection Limit	1	Testing Method : visual observation / signal-to-noise / standard deviation of the response and the slope	
	2	If based on standard deviation of the response and the slope method	
		a) Minimum five (5) levels of standard solutions	
		b) Peak area values for all concentrations	
		c) Data for linear regression equation, Y-intercept, slope, r^2 and linearity graph.	
	3	Calculation/formulation where applicable	
	4	Related Chromatogram(s) at LOD	
	5	Value of detection limit	
Quantitation Limit	1	Testing Method : visual observation / signal-to-noise / standard deviation of the response and the slope	
	2	if based on visual observation method, accuracy and precision data at LOQ must be provided	
	3	If based on calibration curve method	
		a) Minimum five (5) levels of standard solutions	
		b) Peak area values for all concentrations	
		c) Data for linear regression equation, Y-intercept, slope, r^2 and linearity graph.	
	5	Calculation/formulation where applicable	
	6	Value of quantitation limit	
System Suitability Testing	1	RSD, tailing factor, theoretical plate	
	2	Resolution (if two or more components)	
Robustness (not mandatory)	1	Testing Method	
	2	Acceptance criteria	
	3	Result : refer acceptance criteria for accuracy and precision (repeatability)	

Table A: Checklist for Assay/Related Substances

TEST	DISSOLUTION		
PARAMETER	**No.**	**DOCUMENTS REQUIRED**	**AVAILABILITY**
Specificity	1	Testing Method	
	2	Acceptance criteria	
	3	Chromatogram/spectrum for following solutions:-	
		f) Standard	
		g) Sample	
		h) Blank/Placebo	
		i) Spike solution	
		j) System suitability tests	
Linearity	1	Testing Method	
	2	Acceptance criteria	
	3	Minimum five (5) levels of standard solutions	
	4	Data for linear regression equation, Y-intercept, slope, r^2 and linearity graph.	
Range	1	Dissolution testing: ± 20% over the specified range Example 1: if the specification is NLT 75% *(Q)* of the labelled amount is dissolved in 45 minutes, the validated range would be 60 – 100% of the label claim Example 2: if the specification for a controlled released product cover a region from 20% after 1 hour, up to 90%, after 24 hours, the validated range would be 0 – 110% of the label claim	
Accuracy	1	Testing Method	
	2	Acceptance criteria	
	3	Minimum three (3) levels of concentration in triplicates covering the specified range	
	4	Result : reported as percent recovery by the assay of known added amount of analyte in the sample, OR as the difference between the mean and the accepted true value together with the confidence intervals	
Precision (Repeatability)	1	Testing Method (using sample/product as the test solution)	
	2	Acceptance criteria	
	3	Minimum three (3) levels of concentration in triplicates covering the specified range , OR minimum six (6) replicates at 100% of the WC	
	4	Result : SD, RSD and confidence Interval	
Precision (intermediate precision/ ruggedness)	1	Testing Method (using sample/product as the test solution)	
	2	Acceptance criteria	
	3	Minimum three (3) levels of concentration in triplicates covering the specified range , OR minimum six (6) replicates at 100% of the WC	
	4	Cover at least 2 parameters among variation of analyst, date and	

		equipment	
	5	Result : SD, RSD and confidence Interval	
System Suitability Testing	1	RSD, tailing factor, theoretical plate	
	2	Resolution (if two or more components)	
Robustness (Not Mandatory)	1	Testing Method	
	2	Acceptance criteria	
	3	Result : refer acceptance criteria for accuracy and precision (repeatability)	

Table B: Checklist for Dissolution

Note:

1. The following validation parameters are required for **COMPENDIAL METHOD** (assay/related substances/dissolution):
   a) Specificity
   b) Precision (intermediate precision)
   c) System Suitability tests
2. Please arrange the documents in sequence according to the checklist provided.

Commonly Acceptance Criteria

PARAMETER	ACCEPTANCE CRITERIA
Specificity	Absence of interfering peaks in the placebo, impurity demonstrate specificity
	Pass peak purity test (particularly for related substances test)
Linearity	$r^2 \geq 0.995$
	y-intercept at 100% working concentration ≤ 2%
Accuracy	Measured recovery within 95% - 105% or mean difference ± 2% & CI
Precision (Repeatability)	RSD ≤ 2.0% & CI
Precision (intermediate precision/ ruggedness)	RSD ≤ 2.0% & CI or mean difference ± 2% & CI
Detection Limit	LOD peak must be visible
	If based on standard deviation of the response and the slope method, DL = 3.3 Ó/S
	If based on signal to noise, S/N= 3:1 or 2:1
Quantitation Limit	if based on visual observation method, accuracy and precision data at LOQ must be ± 20%
	If based on standard deviation of the response and the slope method, DL = 10 Ó/S
	If based on signal to noise, S/N= 3:1 or 2:1
System Suitability Testing	RSD ≤ 2%
	Theoretical plate/column efficiency, N ≥ 2000
	Tailing factor < 2
	Resolution > 2
Robustness (not mandatory)	Refer acceptance criteria for accuracy and precision (repeatability)