STANDARD OPERATING PROCEDURE	
Department:	**SOP No.:**
Title: Procedure for Procurement, Standardization, Storage & Usage of Reference Standard and Working Standard	**Effective Date:**
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1.0 OBJECTIVE:

To lay down procedure for procurement, Standardization, storage & usage of Reference standard and Working standard in quality control laboratory.

2.0 SCOPE:

This SOP is applicable to

2.1 Procurement and storage of Reference Standard / Impurity standard

2.2 Usage and destruction of Reference Standard.

2.3 Standardization of working standard

2.4 Usage and Destruction of working standard.

3.0 RESPONSIBILITY:

Officer, Sr. Officer, Executive – Quality control

Head – Quality control

4.0 PROCEDURE:

4.1 Reference standards are categorized in two types:

A. Pharmacopoeial Reference Standard: These are for the standards mentioned in the Pharmacopoeia i.e. USP, BP, Ph.Eur and Indian pharmacopoeia.

B. Non Pharmacopoeial Reference Standard: These are standards, which are not mentioned in any Pharmacopoeia.

4.1.1 **Working Standard**:

Working standard shall be developed in-house and Standardized against the Reference Standard or collect from ARD laboratory along with certificate of analysis.

4.2 Procurement and storage of Reference standard / Impurity standard :

4.2.1 Pharmacopoeial Reference Standards / Impurity standards shall be procured from the respective agencies or representative of agencies or ARD.

4.2.2 Non-Pharmacopoeial Reference standards are procured from the manufacturer of specific substance or from ARD laboratory.

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4.2.3 Reference standard / Impurity standard are procured whenever In case of

1) New lot number of pharmacopoeial reference standard / impurity standard is released by the agencies.
2) Non-Pharmacopoeia reference standard is expired.
3) New product is introduced in the facility.

4.2.4 Keep track of the release of new lot numbers of reference standard / impurity standard in the publications of agencies or in web site of respective agencies.

4.2.5 On receipt, check the integrity of seal of pharmacopoeial reference standard / impurity standard vial and label details.

4.2.6 After receiving the reference standard / impurity standard, record the details in the reference standard inward register as per Annexure – I. If more than one reference vial received in such case affix the vial numbering label shall be: X/Y

Where,

X = Sequential number for vial

Y = Total number of vial

For example if two vial of reference standard received than vial numbering for first vial will be ½, for second vial will be $^{2}/_{2}$ etc.

4.2.7 Whenever the potency/purity is not mentioned on the label consider the same as 100%.

4.2.8 Reference standard (Non-pharmacopoeial) shall be obtained from manufacturer or ARD laboratory along with certificate of analysis.

4.3 Usage & Destruction of Reference Standard / Impurity standard :

4.3.1 Record the date of opening for the testing or for the Qualification of working standard in reference standard logbook as per Annexure - II.

4.3.2 If the reference standard vial store at 2° C to 8° C or freezer, take the reference standard vial and keep it in the desiccator to attain room temperature. (For 2° C to 8° C about 20 minutes and for freezer about 45 minutes).

4.3.3 During usage of reference standard/impurity standard, precautions should be taken such that contents of the vial are not contaminated with other products or any spillage should not occur.

4.3.4 Seal the reference standard / impurity standard vial after usage & keep in the designated place.

4.3.5 Ensure that reference standard / impurity standard quantity is sufficient for next qualification. If not indent for further procurement.

4.3.6 If the reference standard/impurity standard is expired (for non-pharmacopoeial) and /or replaced (for pharmacopoeial) by a new lot of reference standard/impurity standard dispose off the previous lot by solubilizing in a suitable solvent and discarding the solution and record the same in reference standard log book & as per Annexure - II.

4.4 Standardization of working standards:

4.4.1 Reference standard is received in less quantity therefore working standard is developed against reference standard.

4.4.2 If non-pharmacopoeial reference standard / working standard / impurity standard is received in sufficient quantity from the ARD/Vendor/Other location, then the same standard can be used for routine analysis, otherwise working standard shall be developed against reference standard.

4.4.3 Obtain the required quantity of material from pre-approved batch from store. Qualify the material as per Standardization procedure. If the material is not available in the stores, obtain the material from approved vendor and evaluate the material as per the procedure.

4.4.4 If the material is available and crossed the retest period. This material shall be retested for critical analysis like Related substances, Water/LOD, Polymorphism etc. If these tests comply with the specification, this material shall be used for working standard qualification.

4.4.5 Collect approximately 100g sample from the selected batch. The sample quantity may be changed as per requirement and availability of material.

4.4.6 After receiving material, details of the same shall be entered and allotted working standard number in the Inward register as per Annexure – III.

4.4.7 Working standard number shall be assign as per following procedure:

XYYZZAABBBCC

Where,

X = Location code (For example)

YY = WS (Working standard)

ZZ = Last two digit of current year (For current year 2015 will be 15)

AA = Current Month of current year (For current month of current year is 09)

BBB = Sequential number of working standard prepared at location (For example for first standard prepared in current year then number is 001) and further numbering shall be 002….003…..004……so on)

CC = Version number (If same batch number of material requalified then version number will change from 00 to 01, 01 to 02 ....so on)

For example:

MWS150300100

Where,

M = Location Code for General block

WS = Working standard

15 = Last two digit of current year

03 = Month of current year

001 = Sequential number of working standard prepared.

00 = Version number

4.4.8 For working standard Standardization perform the following tests.

a. Description

b. Identification

c. Water Content / Loss on drying

d. Assay / Potency

e. Any additional test, if required.

4.4.9 Above tests shall be carried out as per the standard testing procedure mentioned for respective material.

4.4.10 Record the analysis in the working standard test data sheet as per Annexure - IV.

4.4.11 System suitability shall be performed, as per respective pharmacopoeia/STP.

4.4.12 Perform the assay with triplicate sample preparation and report the average value (as is basis).

4.4.13 The % RSD of 3 assay values should not be more than 1.0 %.

4.4.14 If the assay (on as is basis) of any working standard is more than 100 %, potency shall be reported as 100 % on certificate of analysis.

4.4.15 After completion of analysis batch shall be considered as Standardization working standard and prepare the certificate of analysis of qualified working standard. The format of COA should be as per the Annexure - V.

4.4.16 Preserve the working standard vials in a clean & dry amber coloured vial at 2°C to 8°C or as per the storage condition of the material.

4.4.17 Transfer the working standard in 13 vials containing about 5.0 g per vial or as per requirements.

4.4.18 In case of unavailability of material, or for not frequently manufacturing product vial may contain less than 5 g of standard and total no. of vials may also be reduced.

4.4.19 Each vial shall be properly sealed and labeled as per Annexure - VI.

4.4.20 The remaining quantity of standard shall be stored in TLHB with label. If working standard is required by any customer, material from this shall be supplied.

4.5 **Usage and destruction of WS:**

4.5.1 GLP Section will issue the number of vial as per requirement or at least 13 vials. Issuance note as per Annexure VII.

4.5.2 Working standard number of vial received from the ARD/Vendor/location the details of standards enter as per format given in Annexure – VII.

4.5.3 Concerned person shall issue One vial per month to analyst. Issued vial shall be use up to last date of the same month. For second next vial shall be issued 1st working day of the each month and use up to last date of the same month. In case working standard exhaust for given month, next vial shall be issue and use up to last date of the same month.

4.5.4 Vial opening date, validity for the month and destruction etc required information shall be recorded in format given as per Annexure – VII. Individual vial validity for the month shall be affix on vial label at the time of issuance.

4.5.5 If the working standard vial store at 2° C to 8° C or freezer, take the working standard vial and keep it in the desicator to attain room temperature. (For 2° C to 8° C about 20 minutes and for freezer about 45 minutes).

4.5.6 After attaining room temperature weigh the required quantity of the working standard and closed the vial immediately and keep in the designated place again.

4.5.7 Remaining quantity (if any) of issued vial at the end of validity shall be destroyed by dissolving in suitable solvent.

4.5.8 Destroy all remaining amount of working standard and vial at the end of the validity period or after development of the new working standard. Record the destruction of working standard as per Annexure – VII respectively.

4.6 Frequency of WS development:

4.6.1 A maximum of 12 months validity period shall be assigned to working standard. The validity of the standard shall not exceed the expiration date of material.

4.7 Impurity standard received from the ARD/Vendor/ Other location the details of standards enter as per format given in annexure – VIII.

5.0 ANNEXURE (S):

Annexure – I : Reference standard log book

Annexure – II : Reference standard usage/destruction record

Annexure – III : Working standard log book

Annexure – IV : Working standard analysis record.

Annexure – V : Working standard Certificate of Analysis.

Annexure – VI : Specimen Label for Working standard.

Annexure – VII : Working standard Usage Record.

Annexure – VIII : Impurity standard record.

6.0 REFERENCE (S):

USP <11> / Ph. Eur. 5.12/BP Supplementary Chapter IV M

USP catalog

EDQM catalog

SOP: Preparation, Approval, Distribution control, revision and destruction of Standard operating Procedure (SOP).

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7.0 ABBREVIATION (S)/ DEFINITION (S):

ARD : Analytical Research and Development

USP : United State Pharmacopoeia

BP : British Pharmacopoeia

Ph. Eur. : European Pharmacopoeia

TLHB : Triple Laminated Hand Bag

LOD : Loss on drying

RSD : Relative Standard Deviation

EDQM : European Directorate for the Quality of Medicines & HealthCare

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REVISION CARD

S.No.	REVISION No.	REVISION DATE	DETAILS OF REVISION	REASON (S) FOR REVISION	REFERENCE CHANGE CONTROL No.
1	00	-	-	New SOP	-

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ANNEXURE I

REFERENCE STANDARD LOG BOOK

S.No.	Name of Reference standard and Respective pharmacopoeia	Lot No./B.No. of Reference standard	Date of Receipt	Quantity Receipt	Checked By	Remarks

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ANNEXURE II

REFERENCE STANDARD USAGE/DESTRUCTION RECORD

Name of Reference Standard:

Batch No./LOT No.: **Valid up to:**

No of vial (In number) & Total quantity received (in mg)	Issue of Vial No. /Date	Date of used	Used quantity (in mg)	Balance quantity (in mg)	Used for	Used By	Checked By	Destroyed by/Date

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ANNEXURE III

WORKING STANDARD LOG BOOK

S.No.	Name of Material	A. R. No.	Mfg. Date	Exp. Date	Quantity	Working Standard No.	Potency (As is basis)	LOD/ Water	Valid up to	Qualification Status	Date of Standardization	Standardized By

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ANNEXURE IV
WORKING STANDARD ANALYSIS RECORD

Batch No.		**AR No.**	
Source		**Ref. Std. No.**	
Specification No.		**Standard Test Procedure No.**	

Description :	
Observation :	
Observed by / Date :	Checked by / Date:

Identification:	Instrument ID:
Observation :	
Analysed by / Date :	Checked by / Date :

LOD / Water Content :	
Water Content :	
Balance ID: EQI/QCD	Instrument ID : EQI/QCD/
Karl Fischer factor = Sample weight : Volume of Karl Fischer reagent consumed :	

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Observation :

Analysed By / Date :	Checked By / Date :

Loss on drying :

Balance ID: EQI/QCD	Oven ID: EQI/QCD/

Weight of LOD bottle :

Weight of bottle + sample :

Weight of sample :

Weight of bottle + sample (After drying):

Loss in weight :

% Loss on drying = $\frac{\text{Loss in weight in g X 100}}{\text{Weight of sample in g}}$ = _____

=

Observation:

Analysed by / Date:	Checked by / Date:

Assay

A) By HPLC

Balance ID: EQI/QCD/	HPLC ID: EQI/QCD/

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pH Meter ID: EQI/QCD/	

Reference standard / Working standard : _____

Batch / Lot No.: _____ Purity : _____ Validity: _____

Reference standard / Working standard : _____

Batch / Lot No.: _____ Purity : _____ Validity: _____

n of mobile phase :

reparation:

/eight: _____ mg Dilution:

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Sample preparation:

I) Sample weight : _____ mg Dilution :

II) Sample weight : _____ mg Dilution :

III) Sample weight : _____ mg Dilution :

Chromatographic condition:

Column No.

System suitability :

Standard and Sample area :

Chromatogram	Standard Area Response	Sample (I) Area Response	Sample (II) Area Response	Sample (III) Area Response
1				
2				
3				
4				
5				
6				
Mean				

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% RSD	

Bracketing standard area: % RSD:

Calculation (% Assay) :

Sample I :

Sample II :

Sample III :

Sample No.	Potency (% w/w, on as is basis)	Assay (% w/w, on dried or on anhydrous or solvent free basis)
Sample I		
Sample II		
Sample III		
Mean %		
% RSD of potency (Not more than 1.0%):		

Analysed by/ Date :	Checked by/ Date :

B) By Chemical :

Balance ID: EQI/QCD/	Instrument ID: EQI/QCD/

Name of Volumetric solution:

Volumetric solution No.: Validity:

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Determination of Assay:

I. Sample weight : _____ Volume consumed: _____

II. Sample weight : _____ Volume consumed: _____

III. Sample weight : _____ Volume consumed: _____

Calculation :

Sample I :

Sample II :

Sample III :

Sample No.	Potency (% w/w, on as is basis)	Assay (% w/w, on dried or on anhydrous or solvent free basis)
Sample I		
Sample II		
Sample III		
Mean %		
% RSD of potency (Not more than 1.0%):		
Analysed by/ Date :	Checked by/ Date :	
4.0 Assay		
C) By UV		

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Balance ID: EQI/QCD/	UV ID: EQI/QCD/
pH Meter ID: EQI/QCD/	

Reference standard / Working standard : _____

Batch / Lot No.: _____ Purity : _____ Validity: _____

n of Diluent:

reparation:

/eight: _____ mg Dilution:

Sample preparation:

I) Sample weight : _____ mg Dilution :

II) Sample weight : _____ mg Dilution :

III) Sample weight : _____ mg Dilution :

Standard Absorbance:

1	2	3	4	5	6	Mean

% RSD =

Bracketing standard absorbance: % RSD:

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Sample Absorbance	Sample (I)	Sample (II)	Sample (III)
1			
2			
Mean			

Calculation : % Assay :

Sample I :

Sample II :

Sample III :

Sample No.	Potency (% w/w, on as is basis)	Assay (% w/w, on dried or on anhydrous or solvent free basis)
Sample I		
Sample II		
Sample III		
Mean %		
% RSD of potency (Not more than 1.0%):		

Analysed by/ Date :	Checked by/ Date :

Remark: The sample complies/Does not comply with specifications as per above-mentioned tests.

Checked By : Date :	Approved By : Date :

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ANNEXURE V
WORKING STANDARD CERTIFICATE OF ANALYSIS

WORKING STANDARD CERTIFICATE OF ANALYSIS

Reference SOP No.:

Product			
WS No.			
Name of Mfg.			
Batch No.		Ref. Std. No.	
Effective date		Valid up to	

Storage Condition & Packing configuration :

S.No.	TEST	SPECIFICATIONS	RESULTS
1.	**Description**		
2.	**Identification**		
3.	**Loss on Drying/ Water** (% w/w)		
4.	**Assay** (% w/w, On anhydrous/ dried basis/ solvent free basis)		
5.	**Potency** (% w/w, on as is basis)		

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Remarks: The sample complies with specifications as per above mentioned tests & qualified as working standard.		
Analyzed By : **Date**	**Checked By :** **Date**	**Approved By :** **Date**

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ANNEXURE VI
SPECIMEN LABLE FOR WORKING STANDARD

WORKING STANDARD			
Name			
WS No.		**Potency (As is basis)**	
Effective date		LOD/Water	
Valid up to		Vial No.	___of____
Storage :		**Vial Valid up to**	

ANNEXURE VII
WORKING STANDARD USAGE RECORD

S.No.	Name of WS	WS No.	Potency (As is basis)	Water/ LOD	Received /Preparation Date	Valid Up to	No. of vials Received/ Prepared Vials	Usage of Vials													
								Vial No.	1	2	3	4	5	6	7	8	9	10	11	12	13	Remarks
								Opening date														
								Valid up to														
								Destroyed by Sign /date														
								Opening date														
								Valid up to														
								Destroyed by Sign /date														

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ANNEXURE VIII
IMPURITY STANDARD RECORD

S.No.	Name of Impurity Standard	Batch No. / Lot No.	Potency	Received Date	Valid up to	Quantity Received	Checked by	Remarks