DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 OBJECTIVE:

To lay down a Procedure for Stability study management.

2.0 SCOPE:

2.1 This Standard Operating Procedure is applicable to carry out the Stability Study carried out at …….

2.2 The purpose of stability study is to understand any Physical, Chemical changes with time under the influence of variety of environmental factors to which drug products may be exposed during its shelf life.

2.3 To confirm that the products are assured for their efficacy and safety in marketed packs, through the cycle of warehousing, distribution, storage and use.

2.4 To monitor any changes in the manufacturing process or primary packaging and its impact on quality.

3.0 RESPONSIBILITY:

3.1 Officer/Executive QA shall be responsible for collection and storage of stability Sample.

3.2 Officer/Executive QC shall be responsible for analysis of stability sample.

3.3 Manager QA & QC/his designee shall be responsible for evaluation of stability sample.

3.4 Head QA/his designee shall be responsible for compliance of this SOP.

4.0 ACCOUNTABILITY:

Head QA (Accountable for stability management)

5.0 DEFINITION:

5.1 Stability: The ability of a pharmaceutical product to retain its physical and chemical properties within specified limits throughout its shelf life.

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

6.0 PROCEDURE:

6.1 Sample is incorporated into stability program shall be within 30 days of release of batch. In case, if the samples are not incorporated into stability program-me within schedule time, then the sample can be subjected for stability studies after re-analysis of the batch.

6.2 Subsequent time intervals shall be counted from date of incubation of sample.

6.3 Initial (zero) month is defined as the "Analysis of the product being kept on stability".

6.4 The withdrawal of samples shall be carried out within +7 days from stipulated date at accelerated condition and long-term condition.

6.5 The Sample Analysis shall be Report completed within +15 days in case of Accelerated & within 21 days in case of Long term after withdrawal of sample.

6.6 Explanation for the omission shall be mentioned in Data Sheet and authorized by Head Quality Assurance.

6.7 Selection of Batches & Stability Commitment**.**

6.7.1 First three commercial batches shall be subjected to stability study at Accelerated and Long Term.

6.7.2 On-going stability studies shall be carried out at Long Term condition and consider one batch of each product for stability study every year.

6.7.3 The samples shall be charged to stability study for following changes.

S.No.	Changes	Accelerated	Long term
1.	Change in the formulation	3 batches	3 batches
2.	Change in manufacturing process	3 batches	3 batches
3.	Change in source of API	3 batches	3 batches
4.	Change in manufacturing equipment (s) having different operating principle	NA	1 batch

6.8 Storage Conditions & Testing Frequency

6.8.1 The design of the stability testing program, based on the intended market and the climatic conditions in the area in which the drug product will be used.

6.8.2 The storage condition for the samples subjected for stability studies are:

Study Type	Storage Condition
Accelerated Stability Study	40ºC ± 2 ºC ,75 % ± 5% RH
Long Term Stability Study(Zone IVB)	30 ºC ± 2 ºC,75 % ± 5% RH

6.9 Testing Frequency

Study Type	Frequency(In month)
Accelerated Stability Study	Every Station-0,1m, 3m & 6m
Long Term Stability Study	Every Station- 0,03,06,09,12,18,24,36, & 48

6.10 Testing Procedure

6.10.1 Sample kept for stability studies at different storage conditions shall be analyzed for the parameters as per specifications and product specific stability protocols.

6.10.2 In case of Pharmacopoeia revision and In-house requirement (i.e. addition of test, change in method of analysis, change in specification) the samples already kept on stability studies shall be analyzed as per amended specification. After evaluating the results by the specification, the revised specification and STP is followed at next due frequency.

6.10.2.1 Assay : A Significant change from initial value 5%

6.10.2.2 Any degradation product (Vitamins) significant change 5 % not be applicable, it's not exceeding acceptance criteria

6.10.2.3 Related Substances/Degradation Products – exceeding its acceptance criteria.

6.10.2.4 Failure to meet the acceptance criteria for pH.

6.10.2.5 At accelerated storage, there may be changes in physical attributes and hence those are compared and evaluated w.r.t. samples kept at long term storage. The results are not considered as significant changes.

6.10.3 If significant change occurs during testing at the accelerated storage condition, the proposed shelf life period will be reviewed based on the long-term data available Storage condition may be reviewed accordingly.

6.10.4 The Head Quality Control and Head Quality Assurance review the stability data. Investigation will be carried out in case of "Out Of Specification (OOS)" as per the OOS procedure.

6.11 SEMI-PERMEABLE CONTAINER

6.11.1 Aqueous-based product packaged in semi-permeable container should be evaluated for potential water loss in addition to physical stability

6.11.2 The water loss at the low relative humidity is to multiply the rate of water loss measured at an alternative relative humidity at the same temperature, by a water loss rate ratio shown in the **table below**

Low-humidity testing conditions	Alternative testing condition	Ratio of water loss rates	Calculation
30 °C/35% RH	30 °C/75% RH	2.6	(100-35)/(100-75)
40 °C/NMT 25% RH	40 °C/75% RH	3.0	(100-25)/(100-75)

6.11.3 Loss of water in semi permeable containers changes not more than 5% of initial value.

6.11.4 Data of Loss of water in semi permeable container shall be prepared Accelerated in as per Annexure-IX.

6.11.5 Data of Loss of water in semi permeable container shall be prepared Long term in as per Annexure-X.

6.12 Guideline for Sampling

6.12.1 A calendar shall be prepared for the samples of existing products subjected for stability studies during the current year and a copy of this is provide to QA for the collection of samples.

6.12.2 After collection of samples, QA intimates to the person in-charge of stability study.

6.12.3 The quantity of samples is sufficient to carry out the repetitive analysis (if required) as per the scheduled frequency.

6.12.4 The samples for stability study shall be labeled with sticker label having information of Incubation date and sign as per Annexure- I.

6.12.5 If product is manufactured under different brand names but the formulation, strength and manufacturing process and primary packing remain same, then the samples of any one generic or brand name are collected for stability study.

6.12.6 If manufacturing formulas of the products is same but have different primary packaging systems then the three batches of each packaging are kept for stability studies at long term and accelerated storage conditions along with one control batch.

6.12.7 25% stability sample shall be loaded in stability chamber in inverted position and remaining in upright position to study the compatibility of the product with closure system.

6.12.8 Samples kept on stability studies shall be recorded in Stability Sample Inward record as per Annexure- II and are recorded in stability Scheduler program and in manual record.

6.12.9 Analysis Request for Stability study sample shall be prepared in as per Annexure Annexure-VII Stability Sample Monthly Planner shall be prepared in Annexure- IV with the help of manual record.

6.12.10 QA personnel carry out temperature mapping of the incubators once in every year. Temperature controller / indicator calibration is done by outside party once in every year.

6.12.11 Cleaning of stability chamber also shall be recorded as per Annexure-V.

6.13 Stability Study Sample Submission to Quality Assurance

6.13.1 Prepare the Stability Study Sample withdrawal & reconciliation record as per Annexure-III.

6.14 Preparation of Stability Study Reports

6.14.1 Stability Study Reports shall be prepared in Annexure -VI.

6.14.2 If analysis of stability samples not initiated as mention in this SOP due to any reason fill proper deviation report and consider sample for analysis in next station.

6.15 Storage conditions of Stability chambers

6.15.1 Stability chamber temperature & RH shall be recorded as per Chamber Software.

6.15.2 Storage condition tolerances are usually defined as the acceptable variations in temperature and relative humidity of storage facilities for stability studies.

6.15.3 The allowable tolerance in variation of temperature and humidity is ± 2°C and ±5% RH respectively from the set values. Variations due to opening of doors of the stability chamber shall be acceptable. Excursions in the range (i.e. ± 2°C and 5%) if exceeds 24 hours, calculate the mean kinetic temperature**.** For action plan in case of temperature excursion refer **point no. 6.16**

6.16 Action Plan in case of temperature and humidity excursion for more than 24 hours.

6.16.1 Officer/Executive QA shall raise the maintenance memo and intimate to Engineering

6.16.2 Prepare List of sample charged in particular stability chamber.

6.16.3 Stability Sample shall be transferred to controlled temperature area of NMT 25°C

6.16.4 After rectification of problem sample shall be transferred in particular stability chamber.

6.16.5 Stability study of products impacted due to the temperature and humidity excursion shall be increased to make up the time period consumed right from date of excursion to rectification of problem and accordingly stability study period of particular product(s) shall be increased to meet the prescribed frequency of testing mentioned in the SOP.

6.17 Destruction of Stability Samples

6.17.1 Samples left out after carrying out stability studies or, if stability study is discontinued in between, sample quantities are destroyed as per Annexure. VIII.

7.0 ABBREVIATIONS:

MRP	:	Maximum Retail Price
STP	:	Standard Testing Procedure
OOS	:	Out of Specification
w.r.t.	:	with respect to
API	:	Active Pharmaceutical Ingredient

8.0 ANNEXURE:

Annexure No.	Tittles of Annexure	Format No.
Annexure-I	Stability Study Label	
Annexure-II	Stability Samples Inward Record	
Annexure-III	Stability Sample Withdrawal & Reconciliation Record	
Annexure-IV	Stability Study Monthly Planner	
Annexure-V	Stability Chamber Cleaning Record	
Annexure-VI	Stability Study Report	
Annexure-VII	Analysis Request for Stability study sample	
Annexure-VIII	Stability Samples destruction Record	
Annexure-IX	Accelerated Data Sheet of water loss Study	
Annexure-X	Long term Data Sheet of water loss Study	

9.0 DISTRIBUTION:

Master copy - Quality Assurance

Controlled copy 01 - Quality Assurance,

Controlled copy 02 - Quality Control

10.0 REFERENCE:

ICH guideline Q1A (R2).

11.0 REVISION HISTORY:

Revision No.	Change Control No.	Details of Changes	Reason of Changes	Effective Date	Done By
00	Not Applicable	Not Applicable	New SOP		

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-I

STABILITY STUDY LABEL

STABILITY SAMPLE
ACC: Temp. 40 ˚C± 2 ˚C % &RH 75% ± 5%
Incubation Date _____ Sign_____

STABILITY SAMPLE
LT: Temp. 30˚C± 2 ˚C % & RH 75% ± 5%
Incubation Date _____ Sign_____

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-II
STABILITY SAMPLES INWARD RECORD

S.No.	Product Name	Batch No.	Pack Size	Mfg. Date	Exp. Date	Qty. of sample	Date of Charging	Charged by/Date	Page no.	Plan for Due Analysis											
										INITIAL	1 M	2 M	3 M	6 M	9 M	12 M	18 M	24 M	36 M	48 M	REMARKS

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-III

STABILITY SAMPLE WITHDRAWAL & RECONCILIATION RECORD

Date of Charging: **Location:**

Product	Batch No.	Mfg Date	Exp Date	Storage Condition ↓ →	Time station	1 M	2 M	3 M	6 M	9 M	12 M	18 M	24 M	36 M	48 M	Total Sample Quantity charged
				Long term sample	Balance quantity											
				Accelerated sample	Balance quantity											
Date of sample Qty. to be withdrawn				Long term												
				Accelerated												
Withdrawn by Sign/Date																
Received by Sign/Date																

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-IV

STABILITY STUDY MONTHLY PLANNER

MONTH:

S.No.	Product Name	Batch No.	Batch Size	Mfg. Date	Exp. Date	Due Date	Stage

Prepared by
QA officer
Sign/Date

Approved by
Head QA
Sign/Date

ANNEXURE- V
STABILITY CHAMBER CLEANING REPORT

Chamber ID No.:

S.No.	Date	Cleaning Agent	Duration		Cleaned by	Checked by	Remarks
			From	To			

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE- VI
STABILITY STUDY REPORT

Product Name				**Stability Study Type:**	**Packing Style:**
				Storage Condition:	
Generic Name				**Intervals:**	**Chamber ID:**
Batch No.				**Test to be performed:**	**Reference STP No.** **Reference SPC No.** **Protocol No.** **Sample Charging Date :**
Batch Size					
Mfg. Date		**Exp. Date**			

Tests **	**Specification**	**Intervals**									
		Initial	1m	3m	6m	9m	12m	18m	24m	36m	48m
*****											
****											
****											
*****											

Note: ***The test parameter to be defined as per individual protocol

Conclusion:	

Prepared by
QA Executive
(Sign & Date)

Checked by
QC Manager
(Sign & Date)

Approved by
QA Manager
(Sign & Date)

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-VII
ANALYSIS REQUEST FOR STABILITY STUDY SAMPLE

Date…….

Product Name: .....

Batch No. :…….. Sample Qty.: ……

Mfg. Date: …….. Exp. Date: ……...

Type of Stability : Accelerated/Real Time Study

Stage /Month: ……...

Due Date: ……..

Analysis Required: ……...

…….

Prepared by:
Officer/Executive QA
(Sign & Date)

Received by:
Officer/Executive QC
(Sign & Date)

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-VIII
STABILITY SAMPLES DESTRUCTION RECORD

Name of Product :		
Batch Number (s):		
Storage Condition (s)	30°C/75% RH	40°C/75% RH
Qty. to be destroyed		
Reason of Destruction:		
Initiated By _____ (Sign./Date)	Checked By _____ (Sign./Date)	Authorized By _____ (Sign./Date)
Total Qty. destroyed		
Destroyed By _____ (Sign / Date)	Verified By _____ (Sign / Date)	

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE- IX

ACCELERATED DATA SHEET FOR WATER LOSS STUDY

Product Name		**Alternative Storage Condition:** 40 ± 2°C, RH 75 ± 5%			
Generic Name		**Intervals: 0,1,3, & 6 months**			**Filled volume :**
Batch No.		**Mfg. Date**		**Exp. Date**	
Batch Size		**Protocol No.** **Sample Charging Date**			**Chamber ID :**

Water loss formula	**Intervals**	**Weight of container in gm**									
		1	2	3	4	5	6	7	8	9	10
% water loss= Initial weight - observed weight ----------x100x 3 Initial weight	Initial weight										
	1 M weight										
	% water loss										
	3 M weight										
	% water loss										
	6 M weight										
	% water loss										

Acceptance criteria Loss of water in semi permeable containers changes not more than 5% of initial value.

Remark – Above stability data shows that significant loss water is not observed/observed during study period. Hence the product packed in semi permeable containers can/cannot withstand low relative humidity environments.

Prepared by QA
(Sign & Date)

Approved by QA
(Sign & Date)

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Stability Management	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE- X
LONG TERM DATA SHEET OF WATER LOSS STUDY

Product Name		**Alternative Storage Condition:** 30 ± 2°C, RH 75 ± 5%			
Generic Name		**Intervals: 0,3,6,9,12,18,24,36 & 48 months**			**Filled volume :**
Batch No.		**Mfg. Date**		**Exp. Date**	
Batch Size		**Protocol No.** **Sample Charging Date**			**Chamber ID :**

Water loss formula	**Intervals**	**Weight of container in gm**									
		1	2	3	4	5	6	7	8	9	10
% water loss= Initial weight - observed weight ----------x100x 2.6 Initial weight	Initial weight										
	3 M weight										
	% water loss										
	6 M weight										
	% water loss										
	9 M weight										
	% water loss										
	12 M weight										
	……..Up to 48month weight										

Acceptance criteria Loss of water in semi permeable containers changes not more than 5% of initial value.

Remark – Above stability data shows that significant loss water is not observed /observed during study period. Hence the product packed in semi permeable containers can/cannot withstand low relative humidity environments.

Prepared by QA
(Sign & Date)

Approved by QA
(Sign & Date)