STANDARD OPERATING PROCEDURE	
Department: Quality Control	**SOP No.:**
Title: Procedure for Stability Program	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 OBJECTIVE

To lay down a procedure for handling of stability study samples (sampling, charging, pulling out the samples, analysis and reporting).

2.0 SCOPE

This SOP is applicable for handling of stability study samples (sampling, charging, pulling out the samples, analysis and reporting) in quality control department.

3.0 RESPONSIBILITY

3.1 Quality Assurance

3.1.1 To provide the intimation to quality control department for preparation of stability study protocol.

3.1.2 To collect the stability samples from manufacturing area in its final pack as per the quantity prescribed in stability protocol and submit the samples to stability section of quality control department.

3.2 Quality Control

3.2.1 To prepare the stability study protocol.

3.2.2 To inform QA to collect required number of samples (units) for stability study as per the requirement of the stability protocol.

3.2.3 Charging of samples at condition(s) recommended in the respective stability protocol.

3.2.4 To pull out the stability samples from stability chambers as per the planner/schedule.

3.2.5 To analyze the samples as per the respective current stability specification and Standard Testing Procedure.

3.2.6 To record and compile the data generated in respective test data sheet.

3.2.7 To submit the complete report along with Analytical raw data to section Head Stability or Designee for review

3.2.8 To initiate the OOS and OOT investigation, if observed.

3.3 Section Head Stability

3.3.1 To review the stability study protocols.

3.3.2 Verification of the stability sample charged at different storage conditions.

3.3.3 To check the stability study report against Analytical raw data submitted by the analyst.

3.3.4 To carry out the OOS investigation, if initiated.

3.4 Head Quality Assurance or Designee

3.4.1 To review the stability study protocol and reports.

3.4.2 To approve the stability study protocol and stability report.

3.4.3 To review the OOS and OOT investigation if reported.

3.4.4 To inform corporate QA and R&D in case of any significant change/out of specification observation in the course of the stability study. To authorize the samples for destruction.

3.5 ACCOUNTABILITY

3.5.1 Head Quality Control/ Quality Assurance

3.5.1.1 To approve the stability study protocol and report for onward submission.

3.5.1.2 To approve the OOS and OOT investigation if initiated.

3.5.1.3 To verify the stability data if there is any significant change observed.

3.5.1.4 To ensure the compliance of standard operating procedure.

4.0 PROCEDURE

4.1 INTIMATION OF STABILITY STUDY

4.1.1 Keep initial three validation in required finished product pack form as per approved stability study protocol.

4.1.2 Keep first batch every year subsequently for long term stability study.

4.1.3 Stability needs to be re-initiated in any of the following conditions:

- First three commercial batches.
- Change(s) in the manufacturing process.
- Change in source of API.
- Change in primary packing container and closure system.
- Change in batch size/pack size.

- Installation of new equipment or major modification in existing manufacturing equipment.
- Major modification in utility system, impacting the product quality.
- Transfer of a product from one manufacturing site to another site.
- Process validation batches.
- If additional stability data needs to be generated for any specific condition/study etc or any requirement observed during annual product review.

4.1.4 Quality Assurance Department inform to Quality Control Department for initiation of stability study as per "stability study initiation request" (Annexure-I).

4.2 PREPARATION OF STABILITY STUDY PROTOCOL:

4.2.1 Section head/analyst stability shall prepare the stability study protocol as per the information provided by the Quality Assurance Department and the relevant guidelines.

4.2.2 Prepare the stability study protocol for stability study (Annexure II). The attached Annexure shall be used only for reference purpose and it may vary from study to study.

4.2.3 In case of essentially similar formulations, processing and packaging within the range of a drug product, the studies to be in the bracketing/matrixing manner and addressed appropriately in the respective protocol (for all markets).

4.2.4 Assign the protocol number to stability study protocol as follows

PRT/STB/FF/XXX/YY

Where,

PRT : Protocol

STB : Stability

FF :Product Code

XXX : Sequential No. of the product starting from 001 & so on.

YY : Revision Number (this will be the Revision number of the study for that particular product and start from 00).

4.2.5 The stability Study Protocol comprises of followings:

- Index of protocol
- Protocol approval
- Purpose
- Scope
- Responsibility
- Accountability
- Product details
- Packaging details
- Stability batches on test
- Stability storage condition
- Stability testing program
- Number of samples required at different storage conditions/test points.
- Test parameters and specifications
- Acceptance criteria
- Report preparation
- Review of stability study
- Deviation and change history
- Conclusion
- Revision history
- Attachments
- Revision history
- References

4.2.6 Calculate the sample quantity by referring the respective Specification and Standard Test Procedure and mention in the protocol.

4.2.7 The master copy of this protocol shall be maintained in QA and Control Copy of the same is issued to QC for execution of stability study.

4.3 SAMPLING OF STABILITY STUDY SAMPLES

4.3.1 In Process Quality Assurance Department (IPQA) personnel collect the samples as per the Stability Study Protocol and record the quantity of stability sample withdrawn in the batch record.

4.3.2 IPQA personnel handover the sample with "stability sample request cum intimation form" to the Quality Control Department (refer Annexure III).

4.3.3 Keep the Stability Study samples in the area having temperature less than 25^0C, before the sample are charged in the stability chamber at prescribed storage condition.

4.4 STABILITY STUDY SAMPLES CHARGING CONDITIONS

4.4.1 Stability sample shall be charged on following conditions

Conditions	Temperature	Relative Humidity (RH)
Accelerated	40°C ± 2°C	75 % ± 5 %
Long Term	30°C ± 2°C	75 % ± 5 %

4.4.2 Receive the total quantity of samples required for the study and subdivide into quantities to be charged at the required storage conditions as per the Stability Study Protocol.

4.4.3 Affix the stability sample label on the sample (Annexure-XI), for accelerated condition 40°C ± 2°C, 75 % ± 5 % label shall be in red colour and for long-term condition 30°C± 2°C, 75 % ± 5 % label shall be in green colour.

4.4.4 Charge the sample under the stability conditions up to the storage periods mentioned in the relevant Stability Study Protocols and update the location chart accordingly as per SOP.

4.4.5 Enter the charging detail in the stability sample charging log book (refer Annexure-VI), Annual Stability Planner (refer Annexure-IV) and charge the samples into the respective stability chambers.

4.4.6 Charge the finished product samples in the marketable pack, after the packing of the batch is completed. In case the batch fails to meet the acceptance criteria of finished product analysis at T0 (initial analysis), withdraw the samples from the stability chambers for discontinuation of stability study (refer Annexure IX) and destruction of stability samples as per SOP.

4.4.7 All stability study samples must be charged within 5 working days after receipt.

4.4.8 Perform the test, which are not included in FP specification at initial point if required.

4.4.9 Initial (T0) analysis of critical test parameters (as per release specification) should not exceed 30 days from the date of charging of stability sample in stability chamber.

4.4.10 If more than 30 days period is required to complete the initial (T0) analysis as per the recommended Standard Test Procedure (e.g. Preservative efficacy test), then this criteria is not applicable. In such cases all the critical tests other than the test that requires more time period must be completed within the 30 days period.

4.4.11 If the initial testing is not completed within 30 days, it is to be informed to Head Quality Assurance and decision shall be taken.

4.4.12 If required, charge the placebo at the respective stability conditions.

4.4.13 The storage conditions should be monitored and recorded, as per SOP, Short term environmental changes due to opening of doors of the storage facility are accepted as unavoidable. The effect of excursions due to equipment failure should be assessed, addressed and reported if judged to affect stability results. Excursions that exceed the defined tolerances for more than 24 hours should be described in the study report and their effects shall be assessed.

4.4.14 In case of breakdown, power failure of stability chamber, the material shall be shifted in stand by stability chamber if not rectified till 24 hours. If stand by stability chamber is not available then, fill the incidence, investigation is to be done and CAPA shall be taken. It is to be repaired within 5 days. If not repaired, the conditions are altered to lower side, the studies to be prolonged proportionately, up to a period of maximum 15 days in case of accelerated conditions and 30 days in case of long-term conditions, or else the study to be discontinued. In case of major breakdown, carry out corrective measures and evaluate the impact of breakdown of Walk-in Stability Chamber/ Stability Chamber on product.

4.5 PREPARATION OF STABILITY STUDY PLANNER

4.5.1 Analyst Stability shall make entry of sample in a Annual Stability Planner, as per Annexure-IV. And same shall be verified by Section Head Stability.

4.5.2 Based on the Annual Stability Planner (Annexure-IV), a monthly stability planner shall prepare at the end of previous month as per Annexure-V for scheduling analysis of stability study samples, same shall be verified by Section head stability/designee.

4.5.3 Annexure-IV shall be used as reference purpose only, in which the content shall remain the same and the stability data station may vary as per approved stability study protocol.

4.5.4 Addition of any batch in the stability chamber is to be updated in the Annual Stability Study Planner.

4.6 PULLING OUT OF STABILITY STUDY SAMPLES

4.6.1 Analyst Stability/Section Head Stability shall pull out the stability study samples from the stability chamber within 5 working days from the due date as per monthly Stability Planner.

4.6.2 The quantity of the samples to be withdrawn shall be as per the quantity mentioned in the protocol for each test point.

4.6.3 After the withdrawal of samples from stability chamber, support stability made entry in the pulled out log book as per Annexure-X and update the reconciliation record as per Annexure-VII.

4.7 STABILITY STUDY SAMPLE ANALYSIS

4.7.1 Allot an Analytical reference number to each stability sample (as per SOP) before analysis.

4.7.2 Handover the samples for Microbiological Analysis to the Microbiological Department.

4.7.3 Store the stability study samples after pull out from stability chamber in the laboratory at a secured designated place at temperature NMT 25^0C.

4.7.4 Section Head shall plan for the analysis of stability samples as per the planner prepared for the month.

4.7.5 GLP issue the Analytical Raw Data Sheet (ARDS) to analyst..

4.7.6 Microbiological analysis observations of stability samples shall be recorded in the respective format Analytical Raw Data Sheet (ARDS) and report shall be attached with stability data.

4.7.7 Analyze the stability samples as per approved stability specification and Standard Test Procedures.

4.7.8 Stability samples due for the analysis may be clubbed for the similar finished product and vise-versa.

4.7.9 Date of start of analysis shall be date of start of Stability Study Analysis.

4.7.10 Start and complete testing of the samples within the specified below, except Preservative Effective Test (PET). Preservative Effectiveness Testing must be completed within 5 days.

Testing to be started within	Testing to be completed within
7 days from pulled out date	15 days from pulled out date

4.7.11 In case analysis is not completed within the specified period, raise an incidence/deviation accordingly, with proper justification.

4.7.12 Record all the observation of analysis on the Analytical Raw Data Sheet (ARDS).

4.8 STABILITY STUDY DATA COMPILATION AND REVIEW:

4.8.1 Analyst stability shall compile the Analytical Raw Data Sheet (ARDS), attach all the instrument printouts/chromatograms and compile the report. Sign it on every page and submit to Section Head stability for review.

4.8.2 Section Head or designee shall check the report for its correctness and completeness and verifies Analytical Raw Data Sheet (ARDS) and all the related log books used during analysis of stability study sample.

4.8.3 Section Head shall prepare the Stability Study Report (refer Annexure-VIII) on the basis of Analytical raw data.

4.8.4 Annexure-VIII shall be used as reference purpose only which may vary as per approved Stability Study Protocol.

4.8.5 The Section Head also compare the observations of this report with earlier trends/initial value.

4.8.6 After the review of raw data and reports, Section Head hand over the same to Head QC for review.

4.8.7 Head QC shall forward the reviewed Stability Study Report to Functional Quality Assurance for review and approval from Head Quality Assurance/Designee.

4.8.8 After completion of analysis and reporting of results, destroy the remaining sample by dissolving in water or any suitable solvent as per SOP.

4.9 SIGNIFICANT CHANGE OR FAILURE:

4.9.1 In case of any significant change at Accelerated Stability Condition, inform Quality Assurance Department for further action and investigation.

4.9.2 **Significant change** at the Accelerated stability Condition is defined as:

- A 5% change in assay from initial value (T0), or failure to meet the acceptance criteria for potency.
- Any degradation in product exceeding its acceptance criterion.
- Failure to meet the acceptance criteria for appearance, physical attributes and functionality tests (e.g. Colour, phase separation, re-suspendability, caking, hardness).
- Failure to meet the acceptance criteria for P^H.
- Failure to meet the acceptance criteria for dissolution for 12 dosage units.

4.9.3 In case the stability sample does not meet the acceptance criteria, at a particular test point, investigate the respective analysis/failure as per SOP.

4.9.4 Quality Assurance Department (in consultation with R&D) decide whether to continue or discontinue the stability testing with appropriate justification (refer Annexure-IX).

4.9.5 Notify the stability failure immediately to concerned regulatory authorities in case of commercial/validation batches, if required recall the batch as per SOP.

4.10 DESTRUCTION OF STABILITY SAMPLE

4.10.1 Destroy the sample as per SOP.

- Stability study discontinued
- Unused samples remaining after completion of study for the batch.

4.10.2 Section Head Stability/Designee shall fill the sample destruction record as per SOP.

4.10.3 Head Quality/Designee shall authorize the sample destruction.

4.10.4 Stability sample/placebo shall be destroyed in the supervision of Section Head stability/designee.

4.10.5 After destruction of stability sample/placebo, destruction record shall be attached with reconciliation record/stability protocol for ready reference.

5.0 ANNEXURE (S):

Annexure I :Stability Study Initiation Request
Annexure II :Stability study Protocol

Annexure III :Stability Sample Request Cum Intimation Form

Annexure IV :Annual Stability Planner

Annexure V :Monthly Stability Planner

Annexure VI :Stability Sample Charging Log Book

Annexure VII :Stability Sample Reconciliation Record

Annexure VIII :Stability Summary Record

Annexure IX :Stability Summary Discontinuation Record

Annexure X :Stability Samples Pulled Out Log Book

Annexure XI: Label for Stability Sample

6.0 REFERENCE(S)

SOP: Operation and Monitoring of Walk-in Stability Chamber.

SOP: Allocation of Analytical Reference Number.

SOP: Disposal of Leftover Sample after Analysis.

SOP: Product recall.

SOP: Handling of Out Of Specification results.

SOP: Preparation, approval, distribution, control, revision and destruction of Standard Operating Procedure.

7.0 ABBREVIATION (S) /DEFINITION (S):

CAPA: Corrective and Preventive Action

QA: Quality Assurance

OOS: Out of Specification

R&D: Research and Development

A R Number: Analytical Reference Number

PHARMA DEVILS

QUALITY CONTROL DEPARTMENT

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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

ANNUAL STABILITY PLANNER

S.No.	Name of Product	Batch No	Mfg. Date	Exp. Date	Date of charging	Condition	3 M	6 M	9 M	12 M	18 M	24 M	36 M	48 M	60 M