PHARMA DEVILS

QUALITY CONTROL DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Control	**SOP No.:**
Title: SOP for Stability Studies of Drug products	**Effective Date:**
Supersedes: Nil	**Review Date:**
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1.0 OBJECTIVE:

To lay down the procedure for Initiation, Monitoring, and Evaluation of Stability Study of Drug Products.

2.0 SCOPE:

This SOP shall be applicable for the Initiation, Monitoring, and Evaluation of Stability Study of Drug Products manufactured.

3.0 RESPONSIBILITY:

3.1 Preparation - Executive QC.

3.2 Checking - Assistant Manager QC.

3.3 Approval - Manager QC

4.0 PROCEDURE:

4.1 After receipt of the samples from QA Dept verify the details on the sample against the received "INTIMATION FOR STABILITY STUDY" as per ANNEXURE-I. Acknowledgement of the receipt shall be done by executive and above in QC and one copy of the same shall be returned to QA Dept.

4.2 Executive and above shall check the finished product release date and ensure that the incubation date is within 7 days of the finished product release date. The initial finished product analysis result shall be considered as initial (0 month) stability data. If stability study is initiated after more than 30 days of initial analysis date, reanalysis must be done for"0" month (only instrumental test which are listed in the stability protocol). If the finished product analysis is carried out by non stability indicating method then "0" month (initial) analysis shall be carried out by stability indicating method and the result of the stability indicating method shall be entered in the stability summary report as "0"month.

4.3 Executive and above shall make entry in the "MASTER STABILITY SCHEDULE" register as per Annexure-II at the time of receipt of stability sample. On sample incubation, concerned person shall make entry for "SAMPLE KEPT ON" "STABILITY STATION"&"REMARKS" in "MASTER STABILITY SCHEDULE".

4.4 Based on the "master stability schedule" stability co-ordinator shall make an entry in the "monthly stability schedule" register as per Annexure-III at the time receipt of stability samples. After completion of analysis stability co-coordinator shall make entry for

"ANALYZED BY/DATE", "ANALYSIS REFERENCE", "DOCUMENT NO.", "REMARKS" in "MONTHLY STABILITY SCHEDULE"

4.5 Stability co-ordinator shall divide the sample quantity according to the sample required per station for Accelerated & Long term conditions against the stability protocol

4.6 Prepare "STABILTY SAMPLE LABEL" (Refer Annexure-IV) and affix it on the sample container. Incubate the samples as per the required storage conditions mentioned in the intimation slip for stability study (Annexure-I)

4.7 Stability co-ordinator shall make entry for "product", "B.No.","Quantity", "kept On", "Condition in stability sample reconciliation and destruction form (Annexure -V).

4.8 According to the "MONTHLY STABILITY SCHEDULE" concerned person shall schedule the analysis planning for the product being analyzed.

4.9 Stability co-ordinator shall arrange for the photocopy and issuance of the Stability Protocol for the due product from the "Operation copy for photocopying" after it is received from QA.

4.10 Due dates are calculated considering that every month consists of 31 days. The sample-withdrawal date shall be three days before and after the due date. During closure periods (Holidays and factory closure) sampling will be performed after the due date. And if the sample analysis is not planned till then, then it should be stored in the refrigerator.

4.11 Stability co-ordinator shall withdraw the samples as per the quantity specified in each station in the stability protocol.

4.12 Stability coordinator shall make entry of the sample withdrawn in "Stability Sample Bin Card " for "Qty drawn, "Qty drawn date/by", "Station no. /due on", "Qty Balance","Remarks". (Annexure-V).Finally the form is signed for prepared by, reviewed by & approved by, by the respective departments. Then record for "Remaining samples destroyed by and "Witnessed by" is duly signed by the respective authorities.

4.13 In case if sample is required for the additional testing (in case of station missing or any significant Change), entry of the same for the withdrawal shall be made in "STABILITY SAMPLE RECONCILIATION AND DESTRUCTION FORM" duly authorized by Head QC.

4.14 In case if any stability station is missed, Analysis for next subsequent stability station or any other station shall be conducted and the real time of analysis shall be mentioned in the stability summary Report (Annexure-VIII).Missed stability station shall be mentioned as "Missed station" in stability summary report.

4.15 Analysis shall be done as per respective Standard Test Procedure and enter the raw data in

the respective protocol.

4.16 Analysis must be completed within 10 days from the sample withdrawal dates for the accelerated study and within 21 days for long term stability study. Analysis, which requires extended time, shall be justified. Microbiological testing must be completed within 30 days from the withdrawal date.

4.17 Handling of Significant changes and Failure:

4.17.1 Significant changes are defined as follows:

(A) 5% potency loss from the initial assay value of the batch.

(B) Any specified degradant exceeding its specification limit.

(C) The product exceeding its pH limits.

(D) Failure to meet specification for appearance and physical properties.

4.17.2 In case any significant change occurs, Head QC & QA or his Designee shall evaluate the data and confirm significant changes / failure, & shall suggest an additional testing as follows.

4.17.2.1In case significant change occurs in accelerated condition, samples from real time shall be withdrawn in triplicate for analysis.

4.17.2.2In case significant change occurs in long term stability condition, additional testing with different analysts in triplicate shall be carried out and if all results are reproducible then product storage condition needs to be reevaluated.

4.17.2.3 Head Quality Assurance shall discuss with technical group comprising of Plant Head, Head Production and Head QC to take joint decision for recall/ revision of formulation /revision in product storage conditions.

4.17.2.4If sample does not meet the specifications, Head QC or his Designee shall investigate the out of specification (OOS) results and final conclusion shall be given by Head Quality Assurance.

4.18 On completion of analysis of all tests, the stability co-ordinator shall give the stability report for checking along with the raw data to the designated person.

4.19 After checking and approval of stability reports the concerned person shall enter the results in the stability summary report (Annexure-VI) and remarks shall be given by comparing the results obtained with the evaluation parameters and from previous stability summary report.Real time study should be mentioned in summary report in case of delayed time analysis.

4.20 The stability co-ordinator shall prepare placebo of the particular product if required for analysis from BMR of that product. (Stability co-ordinator shall calculate the required

quantity of each inactive ingredient and mix properly, keep in glass bottles (for liquids) and mark on the placebo preparation label for product, storage at, kept on and placebo ref. no.)

4.21 The same no. is given for each Placebo Ref no. as the master batch record no. which is given in BOM of Product. Keep the placebo at long term storage condition.

4.22 In case of any abnormal observation in physical appearance of placebo, discard it and prepare the fresh placebo.

4.23 The stability co-ordinator shall make entry in placebo preparation register for each preparation as per Annexure-VII .

4.24 On completion of stability schedule analysis (all stations) of the product batch, Head of Quality Control Department or his Designee shall give remarks by evaluating all results generated against the remarks.

4.25 On receipt of approval from QA, the stability co-ordinator shall file the report along with initiation for stability (Annexure-I), Stability sample Bin Card (Annexure-V) and raw data of analysis in to a respective product stability data file.

4.26 On completion of stability schedule analysis (All station) stability co-ordinator shall destroy the excess sample and make an entry for the remaining sample in stability sample reconciliation and destruction form.

4.27 In case if stability study needs to be discontinued then the concerned person shall fill the stability discontinuation authorization form (Annexure-VIII).

4.28 The stability co-ordinator shall submit the stability discontinuation authorization form to the Head QC for review and to the Head QA for authorization. After the authorization of the same the concerned person shall attach the stability summary report and file in the respective file along with the stability sample reconciliation and destruction form.

4.29 In case of any change in specification and test procedure, revise the protocol and analyze the next station with revised document. Study the impact and take the necessary action.

4.30 Reconciliation of incubated samples shall be carried out quarterly to cover all the samples once in an year. The stability co-ordinator shall fill the observations as per Annexure-X and any deficiency shall be reported to Head QC.

4.31 Selection of batches:

4.31.1 The initial validation batches shall be kept for stability study (Real time, Intermediate, Accelerated).

4.31.2 If the stability study of three batches has been completed for a particular product with

existing formulation which is found stable, keep minimum one batch for long term stability study every year and perform the test as per respective stability protocol.

4.32 Sample requirement :

4.32.1 The actual sample quantity required for stability study shall be calculated & the record shall be maintained on Annexure X

4.33 Temperature and humidity monitoring:

4.33.1 The actual temperature and humidity should be monitored during stability storage to avoid any excursions.

4.33.2 The excursions during the storage conditions should be reported & if it is more than 24 hours then the suitable corrective & preventive action shall be taken.

4.33.3 If the temperature exceeds 10°C more than the set value because of malfunctioning of the equipment, then the study may be discontinued.

5.0 SAFETY AND PRECAUTION:

Not Applicable.

6.0 REVISION HISTORY:

Revision No.	Reason for Revision	Superseded from & Date

7.0 REFERENCES:

Not Applicable.

8.0 ABBREVIATIONS:

SOP : Standard Operating Procedure

QA : Quality Assurance

No. : Number

QC : Quality Control

Qty. : Quantity

°C : Degree Centigrade

BOM : Bill of Material

BMR : Batch Manufacturing Record

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9.0 ANNEXURE

Annexure-I: Intimation for stability study

Annexure-II: Master stability schedule

Annexure-III: Monthly stability schedule

Annexure-IV: Stability sample label

Annexure-V: Stability sample Bin Card

Annexure-VI: Stability summary report

Annexure-VII : Placebo preparation register

Annexure-VIII : Stability discontinuation authorization

Annexure-IX : Stability sample inventory log

Annexure X: Sample Quantity for stability study

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Annexure-I

INTIMATION FOR STABILITY STUDY

Product Details

Name of Product :
Generic Name :
Batch No. (s) :
Batch Size :
Mfg. Date :
Exp. Date :

Packaging Details :

Packaging Material Details :
Packaging Description :

Sampled Quantity for Study :

Target Market (Please √) **Export** □ **Domestic** □

Purpose: (Please √)

□ **Optimization Batch** □ **Change Request Form/Deviation No.:**

□ **Validation Batch** □ **Other (Please Specify)**

Sample to be kept for:

TYPE OF STUDY	CONDITION	TIME INTERVAL
ACCELERATED		
INTERMEDIATE		
LONG TERM		

Prepared By	Reviewed By	Approved By
Quality Assurance	Quality Control	Quality Assurance

Annexure-II

MASTER STABILITY SCHEDULE

S. No	Sample received by/date	Product name	B.No	Mfg date	Exp date	Purpose of stability	Stability condition	Sample qty.	Sample kept on	Remark	Stability station										
											1	2	3	6	9	12	18	24	36	48	60

Annexure-III
MONTHLY STABILITY SCHEDULE

MONTH___________________ **YEAR**______________

S. No	Product name	B.NO.	Stability condition	Stability station	Master stability schedule Ref. No.	Due date	Analyzed by/date	Analysis reference document No.	Remark

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Annexure-IV
STABILITY SAMPLE LABEL

STABILITY SAMPLE LABEL	
PRODUCT	
B.NO	
STORAGE AT	
KEPT ON	
QUANTITY	
STATION	
SIGN/DATE	
Format No:	

Size:

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Annexure-V
STABILITY SAMPLE BIN CARD

Product : **Batch No. :**

Quantity : **Kept On :**

Condition :

Qty. Drawn	Qty. Drawn		Station		Qty. Balance	Remarks
	Date	By	No.	Due On		

Prepared By	Reviewed By	Approved By
QUALITY CONTROL	QUALITY CONTROL	QUALITY ASSURANCE

Remaining Sample destroyed by: **Witnessed By:**

Date : **Date :**

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Annexure-VI
STABILITY SUMMARY REPORT

Product Name		**Batch No.**	**:**		
Label Claim		**Batch Size**	**:**		
Date of Initiation		**Stability Testing Protocol No.**	**:**		
Stability Intimation Form		**Shelf-life**	**:**		
Storage / Test Conditions		**DOSAGE FORM / PACKAGING**	**:**		
		Date of	**:**		
		Expiry date	**:**		
TEST	**Description**	**Related Substances**	**Assay**	**Others Test**	**Remarks**
SPECIFICATION LIMITS / TIME INTERVAL					
Month					
Month					
Month					
Month					
Month					
Month					
Month					
Month					
Conclusion :					

Prepared By	Reviewed By	Approved By
QUALITY CONTROL	**QUALITY CONTROL**	**QUALITY ASSURANCE**

Annexure-VII
PLACEBO PREPARATION REGISTER

Product : **Placebo Reference No. :**

Placebo Prepared On : **Kept On :**

Condition :

S.No.	Name of Inactive Material	AR Number	Quantity Required	Actual quantity drawn	Prepared by	Reviewed by	Remarks

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Annexure-VIII
STABILITY DISCONTINUATION AUTHORIZATION

Product Name	
Batch No.	
Stability Condition	
Stability Station Remaining	
Qty. to be dispose	
Reason for discontinuation:	
Reference:	
Recommendation:	

Prepared By and Date : **Verified By and Date :**

Authorized By and Date : **Qty. Destroyed By and Date:**

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Annexure-IX
STABILITY SAMPLE INVENTORY LOG

S.No.	Date	Product Name	B.No.	Condition	Qty. in Bin Card	Actual Qty.	Difference	Remarks

Remarks:

Carried out by/date	**Reviewed by/date**	**Authorized by/date**

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Annexure X
SAMPLE QUANTITY FOR STABILITY STUDY

S.No.	Name of Product	Unit Pack size	Quantity Required		
			Real time	Intermediate	Accelerated

Prepared by: **Checked by:** **Approved by:**