PHARMA DEVILS

QUALITY CONTROL DEPARTMENT

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

1.0 OBJECTIVE:

To lay down a procedure for good GC practice.

2.0 SCOPE:

This SOP is applicable for good GC practice at Quality Control laboratory.

3.0 RESPONSIBILITY – Execution - Executive QC.
Checking - Assistant Manager QC.

4.0 ACCOUNTABILITY - Manager Quality Control

5.0 PROCEDURE:

5.1 USAGE OF SOLVENTS AND GASES:

5.1.1 Use GC grade solvents (in case of non availability of GC grade solvents use AR grade solvents) and water for injection or any high purity water (suitable for GC analysis) for the preparation of solutions.

5.1.2 High purity carrier gas shall be used.

5.1.3 In case of carrier gas change in between of analysis than check the reproducibility of area/ ratio by repeating the previous injection, which should be ±4 % against the previous injection

5.1.4 Glassware shall not be rinsed with solvent for the cleaning in the GC analysis

5.2 SYSTEM SET AND USAGE OF THE COLUMN:

5.2.1 Follow the Instrument Operating Procedure for operation and make necessary entry in the "Instrument Usage log book."

5.2.2 Attach the column and make necessary entry in the "column Usage log book".

5.2.3 Make entry of column details and GC set – up in "GC Condition and System Suitability Format" (Annexure –I).

5.2.4 Follow the procedure of SOP for column conditioning.

5.2.5 Condition the column as per SOP on GC Column SOP or more until baseline gets stabilised or as specified in the individual Pharmacopoeia.

5.2.6 Inject System Suitability solution / Standard solution and set the appropriate integration parameters.

5.2.7 Check the peak shape, Retention time, Resolution , Asymmetry , Theoretical Plates from the first injection (System Suitability solution / Standard solution)and if required make necessary

modification in system as per guidelines provided in 5.3 & 5.4 step for the System Suitability.

5.2.8 Start sample analysis only if, the System Suitability parameters are within specified limits.

5.2.9 Fill the details of System Suitability parameters in "GC Condition and System Suitability Format" (Annexure – I).

5.2.10 After the completion of analysis , condition the column as per SOP on GC Column, SOP and make necessary entry in the "column Usage log book". And "Instrument Usage log book".

5.3 SYSTEM SUITABILITY CRITERIA UNLESS OTHERWISE SPECIFIED IN THE PHARMACOPOEIA FOLLOW THE FOLLOWING PARAMETERS:

5.3.1 Relative Standard Deviation of 5 replicate injection of standard preparation should not be more than 2.0%. In case of RSD limit is more than 2.0%.inject six replicate injection of standard preparation.

5.3.2 Relative Standard Deviation of 3 replicate injection of standard preparation should not be more than 1.0%.

5.4 ALLOWABLE MODIFICATION IN CHROMATOGRAPHIC SYSTEM AS BELOW:

Following are the general criteria, which provides the extent of allowable variation to get the system suitability. The adjustments are allowed only to improve the quality of the chromatography and must not to compensate for column failure or to extend the use of deteriorated column.

5.4.1 Stationary phase : Column length : ± 70 %

(Ex . : If specified length is 30 m then allowable limit for adjustment is 9 m – 51 m)

5.4.2 Column internal diameter : ± 50 %

(Ex . : If specified internal diameter is 0.5 mm then allowable limit for adjustment is 0.25 m – 0.75 mm)

5.4.3 Film thickness : Maximum reduction of 50 % , Increase up to 100% permitted.

(Ex . : If specified Film thickness is 5 microns then allowable Maximum reduction is 2.5 microns and increase up to 10 micron).

5.4.4 Particle Size : Maximum reduction of 50 % , No Increase permitted

(Ex . : If specified Particle Size is 5 microns then allowable Maximum reduction is 2.5 microns).

5.4.5 Flow rate : ± 50 %

(Ex . : If specified Flow rate is 40 ml / min. then allowable limit for adjustment is 25 – 60 ml / min).

5.4.6 Column temperature ± 10 %

(Ex . : If specified Column temperature is 100 º C then allowable limit for adjustment is 90 º C – 110 º C).

5.4.7 Injection volume can be reduced but care should be taken that it should not affect the detection of peaks and repeatability of area.

Injection volume may be increased to as much as twice the volume specified but care should be taken that it should not affect adversely to baseline, peak shapes, resolution, linearity and retention time.

5.4.8 For the times specified for the temperature to be maintained or for the temperature to be changed from one to another , an adjustment of up to ± 20 % is permitted.

5.5 GC INJECTION PATTERN:

5.5.1	**Stage: In - Process**			
S.No.	**Sample ID**	**No. of Injection**	**Remarks**	**System Suitability Criteria**
1.	Blank	1	To be observed for any peak at RT of principal peak.	No peak at RT of principal peak.
2.	Resolution or System Suitability solution	1	If finished product/RM/Stability samples are to be clubbed	For the confirmation of peak Resolution or System Suitability criteria
3.	Standard	3 or 5	If finished product/RM/Stability samples are to be clubbed inject 5 Standard preparation	RSD: NMT 1.0 % (for 3 injections) & NMT 2.0 % (for 5 injections)
4.	Sample - 1	2	For “Assay” duplicate injections of each sample preparation.	

5.	Sample - 2	2		
6.	Sample - 3	2		
7.	Sample - 4	2		
8.	Sample - 5	2		
9.	Sample - 6	2		
5.5.2	**Stage: Trial Study**			
1.	Blank	1	To be observed for any peak at RT of principal peak.	No peak at RT of principal peak.
2.	Resolution or System Suitability solution	1	For the confirmation of peak Resolution or System Suitability criteria	As per requirement.
3.	Standard	3 or 5	If finished product/RM/Stability samples are to be clubbed inject 5 Standard preparation	RSD: NMT 1.0 % (for 3 injections) & NMT 2.0 % (for 5 injections)
4.	Sample - 1	2	For “Assay” duplicate injections of each sample preparation.	
5.	Sample - 2	2		

6.	Sample - 3	2		
7.	Sample - 4	2		
8.	Sample - 5	2		
9.	Sample - 6	2		
5.5.3	**Stage : finished product/Raw Material /Stability**			
1	Blank	1	To be observed for any peak at RT of principal peak.	No peak at RT of principal peak.
2	Resolution or System Suitability solution	1	For the confirmation of peak Resolution or System Suitability criteria	As per requirement.
3	Standard	5	System Suitability check	RSD: NMT 2.0 % & other parameters to comply as per Pharmacopoeia.
4	Sample - 1	2	For “Assay” 10 injections of sample should be bracketed by duplicate injection of std. preparation.	
5	Sample - 2	2		

6	Sample - 3	2		
7	Sample - 4	2		
8	Sample - 5	2		
9	Sample - 6	2		
10	Standard	2	Bracketing standard. For Calculation of Sample No. s 01 to 06 consider mean area of standard injection No. s 4,5,6 & 7	RSD: NMT 2.0 % for the standards 4,5,6 & 7
11	Sample - 7	2	For raw material and stability samples each, 5- sample preparation(i.e. 10 sample injections)should be bracketed by duplicate standard injection.	
12	Sample - 8	2		
13	Sample - 9	2		
14	Sample - 10	2		

15	Sample - 11	2		
16	Sample - 12	2		
17	Standard	2	Bracketing standard. For Calculation of Sample No. s 07 to 12 consider mean area of standard injection No. s 6,7,8 & 9	RSD: NMT 2.0 % for the standards 6, 7, 8 & 9
In case of more injections are required, follow the above procedure.				
5.5.4	**Stage : Stability /finished product Degradation tests**			
1	Blank	1	To be observed for any peak at RT of principal peak.	No peak at RT of principal peak.
2	Placebo	1	To identify the Placebo peak / s	
3	Sample - 1	2	For the Degradation Calculation.	As per the Pharmacopoeia.
4	Sample - 2	2		
5	Sample – 3	2		
6	Sample – 4	2		
7	Sample - 5	2		
5.5.5	**Stage: Related substances / chromatographic purity for RM / FP**			
1	Blank	1	To be observed for any peak at RT of	No peak at RT of principal peak.

			principal peak.	
2	Resolution solution	1	System Suitability check	As per the Pharmacopoeia.
3	Placebo	1	To confirm the Placebo peak / s	
4	Lowest concentration solution	1	Set the sensitivity/ peak response using Lowest concentration as defined in procedure.	Peak obtained from Lowest concentration solution should detect and quantitative
5	Specific impurity solution	3	System Suitability check	RSD: NMT 3.0 % & other parameters to comply as per Pharmacopoeia.
6	Diluted test solution	3	System Suitability check. If more than one sample lots are to be analyzed then inject Diluted test solution of any one lot and identify it properly.	RSD: NMT 3.0 % & other parameters to comply as per Pharmacopoeia.
7	Test solution -1	2	Calculate the impurity %by comparing the area with that obtained from Diluted test solution / Specific impurity solution	
8	Test solution -2	2		
9	Test solution -3	2		

5.5.6 No standard bracketing for in – process sample but if finished product or other samples are clubbed with in – process sample then follow standard bracketing.

5.5.7 For the analysis of validation samples like process validation, cleaning validation (Swab sample and mock sample) follow the injection pattern of "finished product" or specified in validation protocol, except single sample injection for cleaning validation sample preparation.

5.5.8 For in – process sample if RSD of triplicate standard injection is not within the limit then inject two more standard injection and Calculate the RSD of five replicate injection and RSD shall be NMT 2.0%

5.6 CHECKING OF CHROMATOGRAMS:

5.6.1 In the Blank / Placebo chromatogram identify the Diluent / Placebo peak if present and exclude the Diluent / Placebo peak for impurity calculation in related substances and chromatographic purity test.

5.6.2 Check that the integration parameters like width, threshold values are selected appropriately for proper peak marking and detection.

5.6.3 In the System Suitability chromatogram identify the peaks, its RRT , Tailing Factor, peak shape and report the values as applicable.

5.7 CALCULATION AND DOCUMENTATION:

5.7.1 The custom report shall cover the following information:

5.7.1.1 Name Of product / Raw Material
5.7.1.2 Test Performed
5.7.1.3 B.No. / AR No.
5.7.1.4 Method path
5.7.1.5 Sequence path
5.7.1.6 Data path
5.7.1.7 Date of acquisition
5.7.1.8 Name of instrument used
5.7.1.9 Analyst

5.7.2 The peak table in custom report shall cover the following information, however select other data as per requirement.

5.7.1.1 Retention time
5.7.1.2 Area
5.7.1.3 Area%
5.7.1.4 Tailing factor
5.7.1.5 Theoretical plates

5.7.3 Ensure System Suitability parameters from the first standard injection and on completion of

specified no.of standard injection calculate the System Suitability parameters of fifth / sixth injection.Record the values in the "GC Condition and System Suitability Format" (Annexure-1)

5.7.4 In case of discontinuation, mention the reason for discontinuation in usage log for traceability.

5.7.5 Take print out of integration parameters on method print.

5.7.6 Documentation related to "GC chromatogram Check list" format.

5.7.6.1 Put the "3" mark for indicating the completion of that stage or put 'NA' where it is not applicable.

5.7.6.2 If any parameter in GC chromatogram Check list is not complied or not carried out take authorization of Head – QC.

5.7.6.3 Analysis shall be done as per the guidelines provided in the "GC chromatogram Check list" format.

5.7.6.4 Document any deviation in QC – Deviation Formats and take authorization of Head – QC.

5.7.6.5 Put "GC DATA" stamp on the first chromatogram of actual analysis (i.e. Blank) and attach duly filled "GC Condition and System Suitability Format" (Annexure -1) if required, "GC chromatogram Check list" format and "Sequence print out"along with the chromatograms.

5.7.6.6 Put all the chromatograms in plastic folder and attach with the relevant B.No. / AR No. document.

5.7.6.7 In case where more than one batch / lot of samples are clubbed for analysis, attach all chromatograms with one batch / AR No. document and give cross reference in all other batch / AR No. document.

5.8 General guidelines:

5.8.1 Column change in between the analysis.

5.8.1.1 Put remark on the last chromatogram of the previously used column regarding change over reason and change over column no.

5.8.1.2 Make entry in the "column Usage log book" and keep the previously used column for flushing.

5.8.1.3 Put remark for discontinuation of the column in the previously used column usage log.

5.8.1.4 Preserve all the chromatograms in serial and attach with the analytical reports. DONOT DESTROY ANY CHROMATOGRAM OBTAINED WITH THE PREVIOUS COLUMN.

5.9 Carrier gas change over:

5.9.1 Put remark for discontinuation of the Carrier gas.

5.9.2 Preserve all the chromatograms obtained from first Carrier gas and Put remark "Trial" on the chromatograms.

5.10 Run time and replicate injection:

5.10.1 In the test for Assay, run all Standard and Sample chromatograms until peak is completely eluted and integrated or otherwise specified in the Pharmacopoeia..

5.10.2 In chromatographic Purity / Degradation / Related Substances / Stability sample analysis, run the chromatogram 2.5 times RT of principal peak or as specified in individual Pharmacopoeia. In case of specific impurity analysis, run the chromatogram as specified in monograph.

5.10.3 In the test for Related Substances/ chromatographic Purity / Degradation product where the impurity % is to be calculated by area normalization method by injecting only sample preparation.

5.10.3.1. Inject sample preparation in triplicate and calculate the System Suitability parameters specified in the procedure.

5.10.3.2 If the System Suitability parameters are not specified in the procedure calculate RSD of principal peak , it should be below 2.0 %

5.10.3.3 If RSD of triplicate injection is not less than 2.0 % then inject additional 2 injections of sample preparation and calculate RSD of principal peak, it should be below 3.0 %

5.10.3.4 Calculate the % Impurity from all the sample injections.

5.10.4 If Degradation / Related Substances is to be calculated from Assay, take separate print out of sample chromatogram by setting the width and threshold appropriately to detect all the peaks.

5.10.5 In the test for chromatographic Purity / Degradation product, identify the Blank peak as "B" , Placebo peak as "P" , and Prinicipal peak as "PP" in the chromatogram of sample preparation.

6.0 SAFETY & PRECAUTIONS:

Not Applicable

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7.0 REVISION HISTORY:

Revision No.	Reason for Revision	Superseded from & Date

8.0 DISTRIBUTION:

Copy No.	Issuance Record				Withdrawal Record		Destruction Record	
	Date	Dept. issued	Name / Signature of receiver	Issued By Name / Signature	By	Sign/ Date	By	Sign/ Date

9.0 REFERENCES:

Not Applicable

10.0 ABBREVIATIONS & ANNEXURES:

SOP : Standard Operating Procedure

QA : Quality Assurance

No. : Number

QC : Quality Control

ANNEXURE – I : GC Condition And System Suitability Format

ANNEXURE – II: GC Chromatogram Check List

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ANNEXURE – I

GC CONDITION AND SYSTEM SUITABILITY FORMAT

Product : **B.No. / AR No. :**

Test : **Method Ref: IP/ BP / USP / IH :**

PARAMETERS		TEST CONDITIONS	APPLIED CONDITIONS
1.0 COLUMN:			**No.:**
Type			
Dimensions			
Film thickness / Particle size			
2.0 GC SET – UP :			
Carrier gas / Flow rate			
Purge flow			
Injector temperature			
Detector / Detector temperature			
Linear velocity / Pressure			
Injection Volume			
Column temperature	Initial		
	Initial Hold		
	Rate – 1		
	Temperature – 1		
	Hold time		
	Rate – 2		
	Temperature – 2		
	Hold time		
	Rate – 3		
	Temperature – 3		
	Final Hold		
Split Ratio			

Head Space vial temperature		
Head Space syringe temperature		
Syringe rinse mode		
Sensitivity / Sampling rate		
Run time		
3.0 INTEGRATION PARAMETERS :		
Width		
Threshold / slope		
Integration off		
Valley to valley		
Others (if any)		
4.0 SYSTEM SUITABILITY:		
Reference Chromatogram No.:		
RSD		
Theoretical plates		
Tailing Factor		
Resolution		

Analysed By:	**Date:**
Checked By:	**Date:**

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ANNEXURE – II

GC CHROMATOGRAM CHECK LIST

Product / Sample : _____ **AR No. :**_____
Test : _____ **B. No. :**_____
Reference H.B. No.:_____ **Page No. :** _____

1. Integration Parameters should be printed on method print. ☐
2. Chromatograms should be un serial of Blank , Standard and Sample from the first injection (including trials). If not should be authorized ☐
3. Cancellation of any chromatogram should be justified and authorized. ☐
4. Each chromatogram should be properly identified.(eg. Trials , Blank , Standard and Sample) ☐
5. Chromatograms should be checked for the proper peak shape and baseline and identify peaks in one standard and one sample chromatogram. ☐
6. System Suitability Parameters should be filled in the respective format and should be within limit , before sample injection ☐
7. In chromatographic Purity / Degradation / Related Substances / Stability sample analysis, run the chromatogram 2.5 times RT of principal peak or as specified in individual Pharmacopoeia. ☐
8. First chromatogram of actual analysis (Blank) should be stamped with “GC Data” stamp. ☐
9. Method and integration Parameters should be same through out the analysis. ☐
10. Any type of Reintegration should be authorized. ☐
11. Samples should be bracketed by Standards as per the system. If not, should be authorized. ☐

REMARKS:

Analyst: **Checked:**