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

1.0 PURPOSE

To define a procedure for performing Annual Quality Review of Drug Product (Annual Product Quality Review).

2.0 SCOPE

2.1 This procedure applies to the quality review of the products manufactured at ……

3.0 REFERENCE(S) & ATTACHMENTS

3.1 References

3.1.1 21 CFR Part 211, 180 (e)

3.1.2 EUDRALEX, Volume 4, Chapter 1

3.2 Attachments

3.2.1 Attachment- I: Annual Product Quality Review Format

4.0 DEFINITION & ABBREVIATION(S)

4.1 Definitions

4.1.1 **Annual Product Quality Review (APQR):** An organized and comprehensive summary of all the products, analytical and customer data associated with a pharmaceutical product.

4.2 Abbreviations

4.2.1 A.R. No. : Analytical Reference Number

4.2.2 MFR: Master Formula Record

4.2.3 PMS : Packing Material Specification

4.2.4 LOD : Loss on drying

4.2.5 RSD : Relative Standard Deviation

4.2.6 SD : Standard Deviation

4.2.7 STP : Standard Test Procedure

4.2.8 API : Active Pharmaceutical Product

4.2.9 AWS : Analytical work sheet

4.2.10 GTP : General Test Procedure

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

5.0 RESPONSIBILITY:

5.1 Quality Control and Production:

5.1.1 To collect, organize and arrange to submit the respective data to Quality Assurance.

5.2 Quality Assurance:

5.2.1 To collect and organize data associated with the APQR.

5.2.2 Review of data including graphical representation to identify if there are any discrepancies or out of trends.

5.2.3 Responsible for assuring that all the requirements of APQR are fulfilled.

5.3 Quality Assurance Head:

5.3.1 To ensure implementation of the defined procedure.

5.4 Plant Head:

5.4.1 To ensure implementation of the defined procedure.

6.0 Distribution:

I. Quality Assurance
II. Quality Control
III. Production

7.0 PROCEDURE:

7.1 All batches manufactured during a calendar year i.e. from January to December shall be considered for the review.

7.2 Officer/Executive QA shall prepare trend of product parameters as per review of parameters mentioned under point 5.5.

7.3 The APQR shall be prepared and submitted before 31st March of the subsequent year.

7.4 Numbering of APQR shall be done as per the format **APQR/B/YY/NNN**

where,

APQR: Stands for Annual Product Quality Review

/ : Stands for forward slash

B : Stands for manufacturing Block:

B1 for Block 1 and

B2 for Block 2

/ : Stands for forward slash

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

YY : Stands for two digit year code e.g. 16 for 2020

/ : Stands for forward slash

NNN : Shall be serial no. starting from 001, 002 and so on

e.g. First APQR for the year 2020 manufactured at Block1 shall be numbered as APQR/B1/20/001.

7.5 Data shall be tabulated and graphed in such a way as to easily exhibit results, deviations and trends, etc.

7.6 The data shall be collected from the records and recorded in the format "Annual Product Quality Review" (Attachment-I) against the relevant points.

7.6.1 **Product Description:** Products' detailed description i.e. product name, generic name, label claim, strength, packaging types available, MMF No., batch sizes available, market, shelf life, indications, and any other specific information shall be included.

7.6.2 **Time period covered:** This shall include all batches manufactured or dispositioned (released or rejected).

7.6.3 **Manufacturing and testing procedures followed for the product:**

7.6.3.1 **MMF/BMR/BPR/PPS:** A record of MMF No. /BMR No./BPR No./PPS No. used for manufacturing and packaging of batches shall be included in APQR. If there is any change in Master Manufacturing Formula No. or Product Packaging Specification no., then reason for the change along with change control reference no. and effective batch no. shall be mentioned.

7.6.3.2 **Specifications/STP/AWS/GTP (In-process, Finished Product & Packaging component):** All the specifications/STPs/AWS/GTP followed shall be reflected for reviewed batches. If there is any change in Specification or testing procedure then the reason for change along with change control reference no. and effective batch no. shall be mentioned in APQR.

7.6.4 **Finished Product Results:** Summary of finished product results of all the batches considered while preparing the APQR shall be represented. The trend of the results shall be prepared and presented suitably. Conclusion and recommendations, if any, shall be documented as annexure to the APQR.

7.6.4.1 Tablets Finished Product: average weight of tablets, disintegration time, dissolution, relative substances and assay or any other relevant test but not be restricted to these parameters only.

7.6.4.2 Capsules Finished Product: average weight of capsules, disintegration time, and assay or any other relevant test but not be restricted to these parameters only.

7.6.4.3 Liquid Oral Finished Product: pH, weight per ml, viscosity, assay or any other relevant test and yield but not be restricted to these parameters only.

7.6.5 **In-Process Results:** Summary of in-process results of all the batches considered while preparing the APQR shall be represented. The trend of results shall be prepared and presented suitably. Conclusion

and recommendations, if any, shall be documented as annexure to the APQR.

7.6.5.1 Tablets in-process: LOD, assay and yield but not be restricted to these parameters only.

7.6.5.2 Hard gelatin capsules in-process: LOD, water content and assay but not be restricted to these parameters only.

7.6.6 **Environmental Conditions during manufacturing operation:** The data of environmental conditions during manufacturing of all the batches shall be reviewed. Conclusion and recommendations, if any, shall be documented as annexure to the APQR.

7.6.7 **Critical Equipment performance:** The critical equipment used in the manufacture of product shall be identified and overall performance of these equipment shall be evaluated by reviewing the breakdown and preventative maintenance records. The observations shall be recorded in the APQR.

7.6.8 **Qualification Status of critical equipment and utilities:** Qualification status of all critical equipment and utilities shall be checked and re-qualification done for any equipment/utility shall be recorded in the APQR.

7.6.9 **Process Deviations/Change Controls:** All product or process deviations, investigations conducted for deviations or change controls for change in procedure or product parameters shall be recorded. Any corrective actions derived from these changes and effect of these changes on product quality shall be summarized.

7.6.10 **Rejections:** The summary of rejections obtained and handling shall be summarized. Details of any complete batch rejections and cause of that rejection shall be discussed.

7.6.11 **Out of Specification:** All out of specification results for particular product (API, in-process, Finished Product and Packaging component) filed during the respective year shall be mentioned (if any).

7.6.12 **Results of Stability and Out of Trend:** Out of trend results, if any, observed during stability studies shall be cited in the APQR. Status of the progress of stability studies shall be recorded.

7.6.13 **Non-Conformance Report:** All details of non-conformance report generated in the year for particular product batch wise shall be mentioned (if any) in the Annual Product Quality Review.

7.6.14 **Product Complaints:** Summary of all product complaints shall be summarized and any trends or problematic batches shall receive additional review.

7.6.15 **Returned goods or recalled products:** Details of any returned or recalled batches shall be listed in the APQR.

7.6.16 **Yield reconciliation:** The yield of batches of the product shall be reconciled and variations along the trend shall be observed and reasons elucidated in APQR.

7.6.17 **Adverse Drug Reactions:** Data on adverse drug reactions, if any, shall be summarized in Annual

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

Product Quality Review.

7.6.18 **Maximum Retail Price:** MRP of the product shall be mentioned in APQR.

7.6.19 **Raw material (API) Manufacturer/Supplier Performance review:** the data of API shall be collected from Stores and recorded appropriately. The data shall include name of the active ingredient, manufacturer/supplier name and address, number of consignments received and batches received, number of consignments approved rejected with cause of rejection (if any). The review of manufacturer or supplier who is supplying the active ingredient shall be taken based on the approval and rejection record of the API received.

Any change in the manufacturer/vendor of the API and effective batch no. shall be recorded.

7.6.20 **Primary Packaging details:** The type of primary packaging of the product shall be described and changes, if any, in the primary packaging shall be recorded with effective batch no.

7.6.21 **Primary Packaging Material Manufacturer/Supplier Performance review:** The review of manufacturer or supplier who is supplying the primary packaging material shall be taken based on the approval and rejection record of the consignment received.

7.6.22 In case of any technical agreement from the Contract manufacturer, details regarding the same shall be included in the APQR.

7.6.23 **Conclusions and Recommendations:** The conclusion and recommendations drawn from the APQR shall be recorded which shall include

- Process in control – this conclusion shall indicate that there are no abnormalities within sets of data and confirms that the process continues to function as validated.
- Actions recommended – this conclusion shall indicate that some recommended actions should be considered, but the process is essentially functioning as designed and validated – the process continues to operate in a state-of-control.
- Corrective actions required – this conclusion shall indicate the need for immediate actions or corrections – some consideration shall be given, under this circumstance, to cease production and evaluate the impact of the problem on marketed product in case the process is not operating in a state-of-control.

7.7 During the analysis of data RSD/SD/Process capability (wherever applicable) shall be calculated. As well as related statistical analysis shall be performed (if required).

7.7.20 The standard deviation “S” is a statistical measure of the precision for a series of repetitive measurements. It is calculated from:

Where N is the number of measurements, xi is each individual measurement, and $\overline{X}$ is the mean of all

measurements.

7.7.21 The relative standard deviation (RSD) is useful for comparing the uncertainty between different measurements of varying absolute magnitude. The RSD is calculated from the standard deviation, S, and is commonly expressed as parts per thousand (ppt) or percentage (%):

$$RSD = \frac{SD}{\bar{x}} \times 100$$

7.7.22 **Process Capability:** Process capability compares the output of an in-control process to the specification limits by using capability indices:

$$CpK = \frac{(USL - \mu)}{3\ SD}$$

$$CpK = \frac{(\mu - LSL)}{3\ SD}$$

Where,

USL = Upper standard limit

LSL = Lower standard limit

CpK = Process capability factor

SD = Standard deviation

μ = Population Mean

Note: In case of one sided or unilateral specification limits, use USL or LSL (whichever applicable) for calculation of CpK.

$$s = \sqrt{\frac{\sum_{i=1}^{N} (x_i - \bar{x})^2}{N - 1}}$$

Obtained Result Interpretation criteria:

CpK < 1.00	An assessment shall be done to identify the need for improvement and action shall be recorded in conclusion and recommendation.
CpK between 1.00 and 1.33	Process is capable, but should be further monitored to check if current controls are sufficient
CpK > 1.33	Process is capable

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

7.8 A summary statement after contents page and before the APQR shall be prepared to provide an overview of the entire APQR and any key observations made.

7.9 APQR shall be reviewed by Production Head, QC Head or their designee and finally shall be approved by QA Head. The approved APQR shall be forwarded to Plant Head for notifying purpose.

8.0 REVISION HISTORY

Version No.	00	Effective Date	
Details of revision: New SOP Prepared			

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

Attachment-I

ANNUAL PRODUCT QUALITY REVIEW		
PRODUCT NAME:		
APQR No.:		**PRODUCT CODE:**
TIME PERIOD:	_____ to _____	**Page No.**

1. **Product Description:**
    a. Product Name:
    b. Generic Name:
    c. Label Claim:
    d. Strength:
    e. Packaging Types Available:
    f. MFR No.:
    g. Batch sizes available:
    h. Market:
    i. Shelf Life:
    j. Therapeutic Use:

2. **Time Period Covered for APQR:**
    a. _____ to _____
    b. Batches Manufactured: Batch Number _____ to _____

3. **Manufacturing and Testing Procedures followed:**
    a. MFR No.:
    b. PMS No.:
    c. BMR No.:
    d. BPR No.:
    e. Specifications / STP / (In-process/Bulk):

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

f. Specifications / STP / (Finished Product):
g. Specifications / STP / (Packaging component):
h. Specifications / STP / (Stability):

4. **Finished Product Results:**
5. **In-Process Results:**
6. **Environmental Conditions during manufacturing operation:**
7. **Critical Equipment Performance:**
8. **Qualification Status of Critical equipment's and utilities:**
9. **Process Deviations / Change Controls:**
10. **Rejections (Recoverable and Non-recoverable):**
11. **Out of Specification:**
12. **Out of Trend:**
13. **Results of Stability and Out of trend:**
14. **Non Conformance Report:**
15. **Product Complaints:**
16. **Returned Goods or Recalled Products:**
17. **Yield Reconciliation:**

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

18. **Adverse Drug Reactions:**

19. **Maximum Retail Price:**

20. **Raw material (API) Manufacturer / Supplier Performance review:**

Name of API	Manufacturer	Supplier	Consignment / Batches Received	Consignments Approved	Consignments Rejected	Cause of Rejection

21. **Technical Agreement, if any:**

22. **Conclusion and Recommendations:**

	Prepared By	Checked By		Approved By	Authorized By
Function	Quality Assurance	Quality Control Head	Production Head	Quality Assurance Head	Plant Head
Sign and Date					