	(private)ltd

STANDARD OPERATING PROCEDURE

Title: **ANNUAL PRODUCT REVIEW OF FINISHED PRODUCTS**

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Signature	**Signature**	**Signature**

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1. PURPOSE

The purpose for this proposed GMP requirement is to provide reliable procedures for a drug manufacturer to review the quality standards for each drug product.

2. SCOPE

This procedure is applicable to all products manufactured in mylab (Pvt)Ltd.

3. RESPONSIBILITY

QC Manager ,Production Manager,Q A officer,Q.C Officer

4. INTRODUCTION

Annual Product Quality Review:

Annual product review is an evaluation conducted annually to assess the quality standard of each drug product with the view to verify the consistency of existing process and to check the appropriateness of current specifications and to highlight any trends in order to determine the need to change any drug product specifications or the manufacturing processes or control Procedures

It is an effective quality improvement tool to enhance the consistency of process and the overall quality of the product. It will capture broader view of product data, capturing trends and will help to determine the need of any revalidation or any changes.

Importance of Annual Product Quality Review:

O It verifies the consistency of the existing manufacturing processes.
O It determines the quality and process defects of the products.
O It determines the defects and possible improvements of the methods and process.
O Trend of yield, analytical results, and manufacturing parameters of the product are also highlighted.
O It reviews the quality of the raw material and packaging material which is used for the product.
O To determine the consistency of the quality of the product the in-process parameters and the finished product results are reviewed.
O Quantity of the final product is reviewed by trending the yield of every batch.
- Out of specification parameter helps to determine the product defects.

O If any of the batch is failed, then it is also included in the Annual Product Quality Review to determine the batch rejection of the product.
O For the determination of the stability of the product, stability study and its trend are performed.
O It also helps to determine if there is any re-validation of the process and the effect of any improvement made previously.
O The determination of the Corrective and preventive actions and their impact on product quality are also reviewed

Basic Contents of Annual Product Quality Review:

Such reviews should normally be conducted and documented annually, taking into account previous reviews, and should include at least:
i. A review of starting materials including packaging materials used in the product, especially those from new sources.
ii. A review of critical in-process controls and finished product results.
iii. A review of all batches that failed to meet established specification(s) and their investigation.
iv. A review of all significant deviations or non-conformances, their related investigations, and

the effectiveness of resultant corrective and preventative actions taken.
V .A review of all changes carried out to the processes or analytical methods.
vi. A review of Marketing Authorisation variations submitted/granted/ refused, including those for third country (export only) dossiers.
vii. A review of the results of the stability monitoring programme and any adverse trends.
viii. A review of all quality-related returns, complaints and recalls and the investigations performed at the time.
ix.A review of adequacy of any other previous product process or equipment corrective actions.
x.The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc
xi Annual product review shall be carried out for each product manufactured in the previous

calendar year.

Xii Annual Product Review report should be completed by the month of January.

Xiii Annual product review records shall be maintained in QC department

Regulatory requirements for the preparation of Annual Product Quality -Review

PARAMETERS	DATA TO BE REVIEWED
Starting material: A review of starting materials including packaging materials used in the product, especially those from new sources.	**STARTING MATERIALS:** Firstly identify all starting and packaging materials received in the year and used for manufacturing of the product. It should then contain the name of the suppliers/manufacturers of the materials. It should contain suppliers certificate of analysis (CoA) or certificates of compliance All analytical tests should be performed for the starting materials. If there are any changes to process for production of the product or any changes related to specifications for the starting materials should also be included. If there are any significant deviations observed in the results or any trending done, then it should also be mentioned in the annual product quality review. **FOR PACKAGING MATERIAL:** It should include all the written procedures describing sufficient detail about identification, storage, handling, sampling, examination, and/or testing of labelling and packaging materials. All the labelling and packaging materials shall be representatively sampled and examined before using it for packaging or labeling of a drug product. Any labeling or packaging materials which meet the appropriate written specifications should be approved and then only released for use and if it does not meet the specifications then they shall be rejected to prevent their use in operations for which they are unsuitable and these all results should be clearly mentioned in annual product quality review. All the record should be maintained for each shipment received of each different labeling

	and packaging material indicating receipt, examination or testing, and whether accepted or rejected and the result should be reviewed and included in APQR. Labels and other labeling materials for each different drug product, strength, dosage form, or quantity of contents shall be stored separately with suitable identification. The use of appropriate electronic or electromechanical equipment to conduct a 100-percent examination for correct labeling during or after completion of finishing operations should also be included. If any automated technique, including differentiation by labeling size and shape, that physically prevents incorrect labeling is used for product development then the name of the technique should also be included. It should also contain the inspection rejection Rate.
In-process controls and quality control testing: A review of critical in-process controls and finished product results	This part of APQR should include the written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. These written procedures, including any changes in the procedures should be drafted, reviewed, and approved by the appropriate organizational units and also by the quality control unit and then only mentioned in the APQR. The trend in-process tests results and also the QC tests results in both manufacturing and packaging processes and microbiology considerations should also be included. The trending should include the following test results: □ Physical variations such as weight/volume, □ Rejected products such as breakages,particulates, etc. should also be includedin the APQR. □ The yield obtained during the manufacturing process.
Manufactured batches (intermediates, bulk, finished products and campaign batches) : A review of all batches that failed to meet established specification(s) and their investigation.	The list of deviations and non-conformances observed with the product when it is reviewed should be mentioned. Then the next is to identify the deviations associated with the product and also the reports of Corrective and Preventive Actions (CAPA) taken. The reasons for the failure of the batches should be included.
Process or testing changes: A review should be done for all changes carried out to the processes, and if any change is carried out for the analytical methods.	If there is any change in the process to manufacture the pharmaceutical product, then the changes should be clearly mentioned in this section of annual product quality review.

	The changes in any of the manufacturing processes, analytical methods, labelling, packaging, etc. should be mentioned in this section. The steps include: • First identify the batches which are affected. • Then provide a justification for the change. • Review the effectiveness/impact of the change on the batch under review.
Marketing authorisations: A review of Marketing Authorisation variations which are submitted or refused or granted and also those for third country (export only) dossiers.	This section of Annual Product Quality Review should include the list of marketing authorisation variations found including the third country export only dossiers. It should also include the number of products submitted/granted/refused. If any changes are made to the product then it requires submission of variations to the marketing authorisations. The number of products registered locally or overseas should be sent to the marketing authorisation. The above variations should be submitted and if not submitted then a conclusion should be documented.
Stability programme: A review of the results of the stability monitoring programme and any if any adverse trends found should be reviewed and included.	The review of the results of any long term and on-going stability of the bulk product and the marketed product should be done. And the results of long term stability and on going stability of the bulk product and finished product should be included. Also include the product information such as its manufacturing date, shelf-life, etc.
Returned product: A review should be done for the quality-related returns and the salvaged products and also the investigations should be performed at the time.	The batch number(s) which are returned should be mentioned. The reason for the return should be mentioned. The associated investigation report number should be written.
Complaints and/or adverse events reported: A review should be done for the quality related complaints and also the investigations should be performed at the time.	The batch number of the product should be identified and written. The reason for complaint should be noted. The complaints obtained should be reported and the manufacturing should be stopped. The associated investigation report number should be written. Current status of the product should be mentioned.
Recalls: A review of all quality related recalls should be performed.	The number of batches/product recalled should be written. The reason for recall should be mentioned.Associated investigation report number should be mentioned. The Current status of the product is mentioned.

Review of past PQR responses: A review of adequacy of any other previous product process or equipment corrective actions.	The focus of this requirement is on previous PQRs and the status and effectiveness of associated actions: review and report on previous PQR CAPAs and change implementation status assess effectiveness of actions taking into account the current PQR findings
Equipment qualification: The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc.	List and review the following for critical equipment/instruments and utilities in production and laboratory departments associated with the product in review: Qualification/requalification status and the next qualification due date of equipment used in the production processes and QC laboratory Reference to relevant qualification reports Review changes made to equipment and utilities which resulted in requalification and assess for subsequent impact to product quality
Contractual agreements: A review is done for any contractual arrangements made to ensure that they are up to date.	The contracts should be reviewed for the services associated with the product in review and report: The Name and address of the contract acceptor should be written. The availability and details of the written contract is mentioned. The types of services provided, For e.g. testing or maintenance and calibration services.

CONCLUSION:

Thus Annual product Quality Review is an evaluation conducted annually to assess the quality standard of each drug product with the view to verify the consistency of existing process and to check the appropriateness of current specifications to manufacture the pharmaceutical product. Thus it is necessary to study the regulatory requirements for the preparation of Annual Product Quality Review to manufacture the pharmaceutical product according to the GMP requirements and which is safe and effective to the public. Hence to study the regulatory requirements is essential.

5. PROCEDURE

1.0 Annual Product Review process, recommends review of all the batches that are manufactured in the previous year from January 1st to December 31st. And the batches include both approved as well as rejected batches.
2.0 The configuration of an annual product review report can vary based on different products and a company's specific documentation requirements.
3.0 However, a company should follow a standard template to ensure that all required aspects are evaluated.
4.0 As an APR is an evolving document. It should be of few sections with minimal requirements to an elaborate document with agenda containing information or data relevant to the product.
5.0 An Annual product review report should contain the following informations.
5.1 Finished product testing results.
5.2 Critical in-process controls.
5.3 Quality and yield review of all batches (OOS) & and CAPA taken

5.4 Deviations and CAPA taken against each deviation, effectiveness of CAPA on later manufactured batches.
5.5 Review of reprocessed/ reworked batches and reason for reprocess/ rework of the batches.
5.6 Changes proposed, approved and implemented that are directly or indirectly related to the product, in-case if a change control is raised related to a multi-product facility should be mentioned in the annual product review report of all the products that are manufactured in the facility.
5.7 Validations (Process or Analytical method) if get triggered by the changes made.
5.8 Repacking made
5.9 Regulatory filings made, or updates made in the existing DMF that owed to the changes made
5.10 Stability studies of all batches .
5.11 Return goods, complaints, recalls, noted for the product.
5.12 Critical equipment qualifications.
5.13 Quality agreements made for the product.
5.14 Effectiveness of CAPA mentioned in the previous year APR.
5.15 Unresolved or open issues of previous year APR.
5.16 Review of starting materials including packaging materials used for the product.
5.17 Retain sample review
5.18 Each numbered sub-section typically should be followed by a comment or observation and finally should have a cumulative summary of the report.
5.19 And the document should finally be reviewed by all the concerned departments, approved by the Q.A Officer & QC Head.

6. Quality Record(s)/Form(s)

The following Quality Records shall be generated and managed in accordance with the

Procedure for Control of Company Quality Records

ANNEXURE:

Annexure 1 Annual Product Review Report

Annexure 2 Annual product quality attributes trend analysis review

Annexure 3 Annual product critical process monitoring trend analysis review
(Post production stability study review (all batch under ongoing stability study)

Annexure 4 Annual product critical process monitoring trend analysis review

(Non conformance /out of specification review)

Annexure 5 Annual product critical process monitoring trend analysis review
(Regulatory changes/Drug act review)

Annexure 6 Annual product critical process monitoring trend analysis review
(Major changes review (Change In Facility,Equipment,Batch Size,Vendor,Process,Composition)

Annexure 7 Annual product critical process monitoring trend analysis review
(Market complaint review)

Annexure 8 Annual product critical process monitoring trend analysis review
(Product Return /Recall Review)

Annexure 9 Annual Product Review Summary Report