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"IN-PROCESS QUALITY CONTROL (IPQC): A REVIEW"

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ABSTRACT

All Pharmaceutical Industry aims to make products with good quality products so this can be done by allowing In-Process Quality Control (IPQC) Approaches. The importance of IPQC to carry out complete testing before, after and during the manufacturing process is completed for the Products or to Monitor and improve effectively the whole applied process at the every stage of the finished pharmaceutical products by according to Standard Operating Procedures (SOPs). This article proposes to establish clearly written in-process methods for critical points at all stages of the product their documentation and review.

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INTRODUCTION

The Pharmaceutical Industry, as a vital segment of the health care system conducts research, manufacturing and marketing of pharmaceutical products used for the treatment and diagnosis of diseases. The development of a drug product is a lengthy process involving drug discovery, laboratory testing, animal studies, clinical trials and regulatory registration. To further enhance the effectiveness and safety of the drug product after approval, many regulatory agencies such as US FDA, TGA, ENVISA etc. also require that the drug product be tested for its identity, strength, quality, purity and stability before it can be released for use. For this reason, pharmaceutical validation and process controls are important in spite of the problems that countered. The quality of the product is the foundation of pharmaceutical industries and is achieved from careful attention to a number of factors including selection of materials, selection of product, manufacturing process design and development, control of the process variables, in-process control and end-product testing. [1, 2]

Quality can be defined as the suitability of the goods or services to the determined qualifications. Or Quality refers to the characteristic of a product from both qualitative & quantitative point of view.

In-process quality control allows the producer to follow all changes that occur during applied technological procedures. It gives the producer security that the finished products fulfills all quality requirements, most of all that all the products should be safe.

In-process quality control is the process that is carried out before, after and during the manufacturing of the finished pharmaceutical product (FPP).[3] In-process materials should be tested for identity, strength, quality and purity as appropriate and approved or rejected by the quality control unit during the production process.

In-process control gives an assurance to the manufacturer that the finished pharmaceutical product fulfils all the quality requirements. All operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, labelling and re-labelling, to completion of the finished product are controlled.

The FPP are the products of all categories which has undergone all stages of manufacturing process, including packaging in its final container and labelling.

The control on the all operations should be established in the form of written procedure which clearly describes to follow the IPQCs and tests. These Step by Step Written procedures are known as Standard operating procedures (SOPs). [4]

OBJECTIVES OF IN-PROCESS QUALITY CONTROL [5]

- To optimize the whole applied technological procedure.
- To monitor control and improve effectively the whole applied operations at the every stage of the finished pharmaceutical products.
- Inspection of raw material, equipment, environment, process, testing with respect to specification, packing and so on.
- Quality control & Process Control.

IN PROCESS CHECKS SHALL INCLUDES FOLLOWING PROCESS CONTROLS [5]

- Cleanliness of the area and line clearance
- Checking of the status labels on the area and process containers.
- Equipment/instrument: Calibration, verification and checking of the status labels.
- Checking and verification of material used as Material Name, Material Code, Control No. or A.R. No.
- Time limits at all stages of process.
- Checking of sieve/filter integrity.
- Check vendor while goods are received and it should be according to approved vendor.
- Online review of batch record at every stage of process.
- Product attributes Like Weight, Hardness.
- Verification of yield at various stages of manufacturing process.
- Periodic check of control samples.
- Measured values obtained from the room environment like Temperature, Humidity.

AT MANUFACTURING OPERATION STAGE

Weighing or measuring of active pharmaceutical ingredients, excipients, diluents or vehicle should be done under the suitable conditions which do not affect their conformity of use. Appropriate and calibrated equipment / instrument should be used for the above purpose.

Weighing, measuring, or subdividing operations should be done in presence of QA & production authorized personnel. Prior to use in manufacturing process, IPQC & production personnel should verify all the materials against the batch manufacturing record. Materials should be appropriately controlled to prevent unauthorized use. Following information being available on the label:-

- Material Name, Material Code, Control No. or A.R. No
- Weight or volume of material in the new container,
- Re-test date if required.

When the product from one process is transferred to other process, the yield should be compared with set targets, if problems or deviations are observed the remarks and reasons are mentioned. If the deviation is not within the acceptable limits further manufacturing process should be continued only after QA / QC clearance and proper records should be maintained either by computer control systems, or alternative means. [6]

AT SAMPLING STAGE

Planning of sampling should be done as per the Standard Operating Procedures (SOP) which describes the sampling methods. Sufficient quantity of samples should be collected for Analysis. Sampling plans and procedures will be changed for in-process materials, intermediates, bulk products or products of different category it should be based on the required testing parameters for different dosage forms. Sampling procedures should be established to ensure the quality of the samples after collection.[7] Samples are tested to verify conformance with specifications by quality control personnel.

IN-PROCESS TEST STAGE

In-process tests should be performed on the sampled material. The quality control dept. will be responsible for the testing. Samples are tested by quality control personnel to verify conformance with specifications within the acceptable limits.

These tests are only used for the purpose of adjusting process parameters within an operating range, e.g., hardness and friability of tablet cores which will be coated, individual tablet weights are not included in the specification. Some tests conducted during the manufacturing process, (e.g., pH of a solution), the IPQC limit of pH is also within the appropriate range.

The examples of applicable in-process controls testing are given in the (Table-1).

The acceptable limit comply to specifications for above stage will be set by the manufacturing site which should be establish according to available data of development stage, validation stage, stability studies and compendia.[5]

The limit set for the in-process tests are only for the purpose of monitoring and/or adjusting the process.

Out-of-specification (OOS) investigations are not necessary for the in-process tests.

AT PACKING STAGE [5]

QA Personnel should give clearance for the finished dosage forms at all the critical points of packing operation stages according to the written procedure.

The packing of batch should be performed in following sequence:-

- Check environmental monitoring it should be performed and record must be maintained.
- Check the area of cleanliness, all unwanted material of previous batches should be absent.
- Check that the blisters are free from knurling defects, strips for alignment defects & empty pockets.
- Check that the packing materials are received from approved vendors.
- Check that the packing material should be tested by quality control dept and status labels.
- Check the status labels on equipment, area & in-process containers.
- Check the Name, Strength, Volume and Composition on the printed packing material.
- Check the over printing quality on the primary & secondary packing material
- Check the Batch coding details on primary and secondary pack (B. No, Mfg. /date, Exp. /date, M.R.P. /bar code, etc.)
- Check the Text matter on the printed label, foil, carton & shipper etc.
- Check the Pharmacopeia status of the material used in the preparation of product.
- Check the Mfg. License number printed on the packing material.
- Check the mandatory information printed according to drugs act and rules on pre-printed packing materials.
- Check and confirm that the Storage condition details are available in the packaging materials are according to particular product and same condition should be available on all printed items.
- Check the directions for use are available on the packaging items and warnings or caution against wrong administration is provided in the packing items.
- Ensure checkers are performing their activity in a proper way.
- Verify the records for online entries.
- Sampling should be done according to SOPs.

Testing must be completed by Quality Control Personnel before packing and record should be maintained. The above In-process control checks and interpretations of the results of all stages become the part of Batch Manufacturing Record. These records should be maintained by authorized IPQC and Production person with their initials and become the part of Batch Manufacturing Record. The final packed finished control samples are kept as representative samples.

The packed Finished Goods transfer to quarantine area and submit the filled BMR, BPR and Finished Goods Transfer Note to QA Personnel for verification.QA authorizes to release the batch for dispatch after reviewing all the records.

The Quality Assurance (QA) department plays an important role at the different stages of manufacturing of finished pharmaceutical product. One of them is IPQC checks of critical points.

The Good Manufacturing Practices follow to eliminate the risks at every stage of manufacturing process Good Documentation Practices and Good Review Practices should be follows during the In-process checks to maintain the records. [8]

Table -1: In-process Control Parameters.

Stage	Control Variables
Granulation	Moisture, Blend Uniformity, Bulk & tapped Density, Particle size Distribution.
Solid Oral Products (Tablets, Capsules)	Appearance, Average Weight, Weight Variation, Hardness, Thickness, Friability, Disintegration
Semi-solids	Appearance, Viscosity, Homogeneity, pH,
Liquids Oral Products	Appearance, Clarity Of Solutions, pH, Specific Gravity, Weight Per mL
Parenterals- Injectables (liquid-SVP & LVP)	Appearance, Clarity, Fill Volume, pH, Filter Integrity Tests, Particulate Matter, Shape Of Container, Sealing Quality Of Container, Leak Testing Of Container, Pre-Filtration or Post-Sterilization, Bio-Burden Testing, Bacterial Endotoxin Tests.
Parenterals-Injectables (Dry powder Injection)	Appearance, Clarity after reconstitution, Weight, Average weight, Weight variation, Particulate matter, Shape of container, Sealing quality of container, Leak testing of container.
Dry powder inhalers	Assay of API-excipient blend, Moisture, Weight variation of individually contained doses.
Transversal dosage forms	Assay of API-adhesive mixture, Weight per area of coated patch without backing.
Metered dose inhalers	Fill weight or volume, Leak testing, Valve delivery.
Yield	Verification with the set target at every stage

CONCLUSION

In-Process Quality Check is designed to provide early warning for quality or to her problems arising during production. Monitoring processes for a finished product, manufacturing of an Active Pharmaceutical Ingredients is the first step to ensuring quality in pharmaceutical manufacturing & having reliable and reproducible methods will enable the production plant to guarantee the consistency of drugs batch after batch. These in-process controls are necessary to ensuring the quality of the product. Furthermore, it may simplify the characterization of such processes and their chemical profile. So in this, in- process methods quality control and validation are deals with several of criteria that are discussed in this review.

By the in-process checks QA gives assurance that the product conforms to its specification and ensure that the quality of product is built up within the product.

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