BIO & PHARMA ANALYTICAL TECHNIQUES

Chapter 1 Introduction

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Chapter Description

- Aims
  - Explain Process Analytical Techniques (PAT) and the benefits to pharmaceutical industry

- Expected Outcomes
  - Discuss on the significance of process analytical technology (PAT) in industry
  - Analyze the role of PAT in pharmaceutical manufacturing
  - Apply the benefits of PAT in pharmaceutical industry

- References
  - Ravindra Kamble, Sumeet Sharma, Venus Varghese and KR Mahadik (2013) Process Analytical Technology (PAT) in Pharmaceutical Development and its Application, *Int. J. Pharma. Sci. Rev. Res.* 23(2). 212-223.

Process Analytical Technology (PAT)

- BACKGROUND:

❑ Conventional pharmaceutical manufacturing – accomplished using batch processing with laboratory testing.

❑ Recently, there are some improvement in:
  - ❑ Pharmaceutical development
  - ❑ Quality assurance
  - ❑ Manufacturing

❑ Efficient pharmaceutical manufacturing process → effective health care system.

PAT

DEFINITION:

- "A system for designing and controlling manufacturing through timely measurements of critical quality and performance attributes for raw and in-process materials and also processes with the goal of ensuring final product quality"(FDA).

Introduction

- PAT - applied to manufacturing processes long time ago.
- FDA implemented it into an initiative focusing on improving several aspects of the pharmaceutical industry.
- Initially, the PAT initiative was intended for traditional pharmaceutical manufacturers.
- However, FDA's PAT guidance now clearly states - it applies to all manufacturers of human and veterinary drug products.

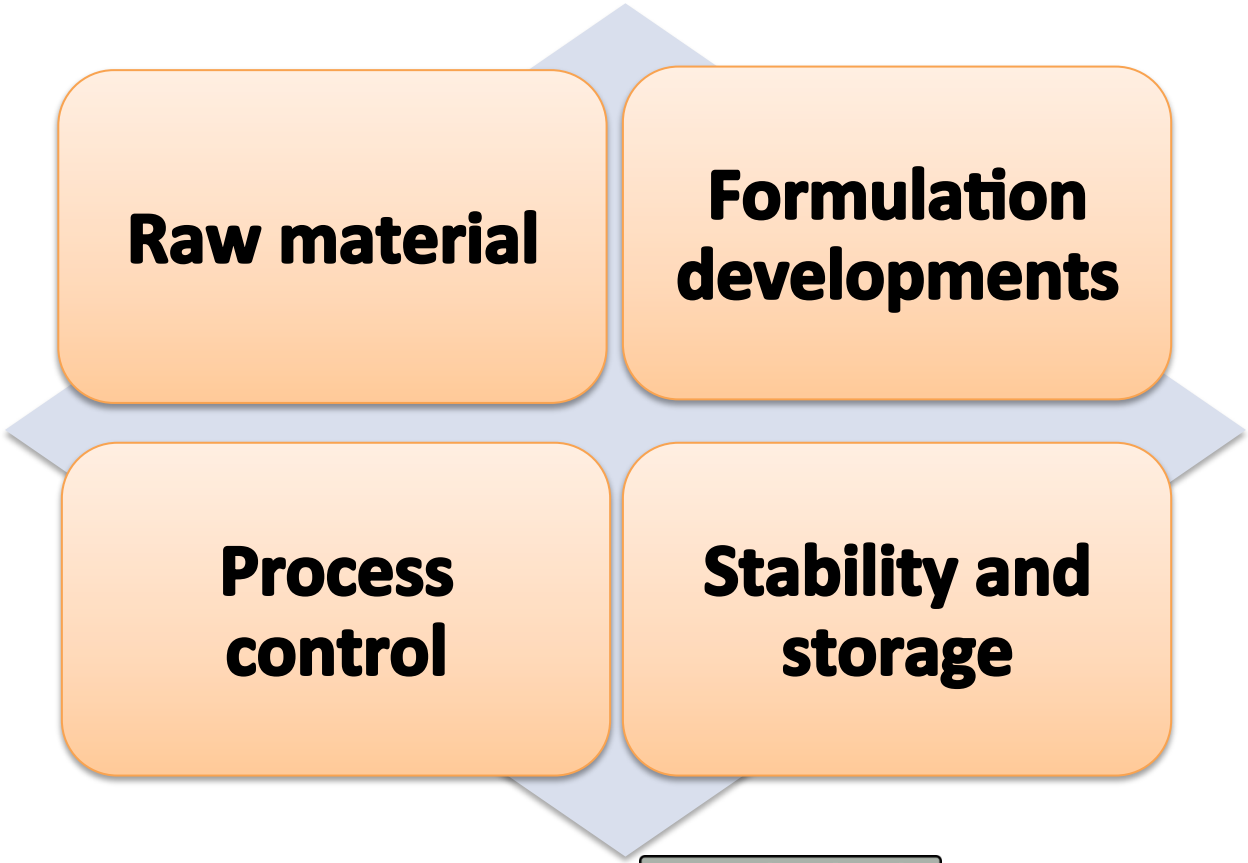
PAT

- PAT focuses on:
  - **Building quality -** product and manufacturing processes
  - **Continuous process** improvement

- PAT involves:

  Testing the quality *of the finished drug product* → ***building quality*** *into products by testing several intermediate steps.*

What PAT DOES in pharmaceutical manufacturing???



Raw Materials

- **Raw material testing –** ensures raw materials → **suitable for their intended use**.

- Conducting raw material analysis can:
  - **prevent costly production problems**
  - **diminish quality variations.**

- Raw material qualification → **defined in GMP procedures** and placed under strict change control.

- The **status of a raw material** is related directly to:
  1. **Reason of usage** in the process
  2. **potential risk** in the raw material → impact the **product's identity, purity, potency, toxicity or efficacy.**

- USP-NF, the Japanese Pharmacopoeia and the European Pharmacopoeia → provide standardized test methods.

- Pharmacopoeia monographs → establish minimum standards for identity, purity and quality requirements for raw materials.

- Some qualify a raw materials supplier by performing an initial detailed vendor audit

- Annual qualification consisting of full pharmacopoeial monograph testing.

Raw Material Testing:

Most common pharmacopoeial raw material tests include:

- Titration (purity assays)
- Loss of drying (moisture contents, organic volatile impurities)
- Karl Fisher titration (moisture content)
- IR spectrophotometry (identification)
- HPLC (assay, impurities)
- GC (assay, impurities)
- TLC (identity, impurities)

Raw Materials Contamination

- The raw materials used may also lead to microbiological contamination. Thus, the control of bio-burden, endotoxins and viral contamination (animal origin), is of special regulatory concern.
- Ex:
  - Committee for Proprietary Medicinal Product (CPMP) [part of the EMEA] – **published a guidance for use of bovine serum** in the manufacture of medicinal products.
  - CPMP – establishes the **general control requirements for utilisation of bovine serum** in the manufacture of a human biological medicinal product.

Viral Contamination

- The risk of viral contamination - common to all biotechnology products (derived from cell lines).

- Safety of these products can be ensured by:
  1. Application of a virus testing program
  2. Assessment of the virus removal and inactivation

     - The processes need to be proven effective and validated. **Proper validation** will include both DNA and RNA viruses {single/double-stranded configurations}

Formulation development

- Influencing factors: the purification, stability requirements, API stability (T, P)
- Generally, the final formulation is either liquid (concentrates)/ solid (powder, tablets)
- Standard tests: Content uniformity, dissolution, purity/ impurity, residual solvents, related substances.

Process Control

- Process monitoring/measurements is one of the key issues when applying PAT → to improve processing efficiency and guarantee end-product quality.

Stability

- Stability studies - an important study of pharmaceutical development which allows evaluation of API stability or drug product stability under the influence of a variety of environmental factors (T, humidity and light).

- Applied to various phases; raw material selection, pre-clinical enabling stability on API's through to phase III and phase IV clinical trials, end products storage.

- Results from these studies - recommended storage conditions, retest intervals and shelf lives to be established.

- ICH guidelines Q1A and Q1B (stability studies)

Objectives of Stability Testing

- to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors
- To establish a retest period for the drug substance
- To establish a shelf life for the drug product
- To establish recommended storage conditions

Recommended Stability Test

Photostability

Accelerated stress studies (high T and humidities

Cycling chamber

Additional non-standard T/ humidity conditions **upon request**

Transport/dispatch testing under controlled conditions

Benefits of PAT

- Get better understanding of each process
- Reproducibility in batch-to-batch production
- Less batch failures
- Enhanced operating efficiency
- Reduce cycle time
- Greater utilization of production equipment

Conclusion of the Chapter

1. PAT encourage manufacturer's to implement high technologies to ensure high quality of end products
2. PAT helps in reducing the cost and operation time
3. Cut shorter the batch release time by providing QC data
4. Reduce the risk and errors

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Any Question?

Please refer to:

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