Programme	**-**	B. Pharm
Course	**-**	Industrial Pharmacy II
Course Code	**-**	BP 702 (T)
Sem	**-**	VIIth
Year	**-**	2020 -21
Unit	**-**	1
Topic	**-**	Pilot plant scale up techniques
Sub- Topic	**-**	SUPAC guidelines, Introduction to platform technology.

Part –B

GUIDANCE FOR INDUSTRY

SUPAC: "Scale-Up and Postapproval Changes"

INTRODUCTION: This guidance provides recommendations to pharmaceutical sponsors of new drug applications (NDAs), abbreviated new drug applications (ANDAs), and abbreviated antibiotic drug applications (AADAs) who intend to change

- The components or composition,
- The site of manufacture,
- The scale-up/scale-down of manufacture,
- The manufacturing (process and equipment) of a modified release solid oral dosage form during the post approval period.

The guidance defines as below:

1. Levels of change,
2. Recommended chemistry, manufacturing, controls (CMC) tests for each level of change,
3. Recommended in vitro dissolution tests and/or in vivo bioequivalence tests for each level of change;
4. Documentation that should support the change.

This guidance specifies application information that should be provided to the Center for Drug Evaluation and Research (CDER) to ensure continuing product quality and performance characteristics of a modified release solid oral dose formulation for specified Postapproval changes.

GENERAL STABILITY CONSIDERATIONS:

The effect SUPAC-type changes have on the stability of the drug product should be evaluated. For general guidance on conducting stability studies, applicants are referred to the FDA Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics.

For SUPAC submissions, the following points also should be considered:

1. In most cases (except those involving scale up), stability data from pilot scale batches will be acceptable to support the proposed change.
2. Where stability data show a trend toward potency loss or degradant increase under accelerated conditions, it is recommended that historical accelerated stability data from a representative prechange batch be submitted for comparison. It is also recommended that under these circumstances, all available long-term data on test batches from ongoing studies be provided in the supplement. Submission of historical accelerated and available long-term data would facilitate review and approval of the supplement.
3. A commitment should be included to conduct long-term stability studies through the expiration dating period, according to the approved protocol, on the first or first three (see text for details) production batches and to report the results in the annual reports.

COMPONENTS AND COMPOSITION — NONRELEASE CONTROLLING

EXCIPIENT:

This section of the guidance focuses on changes in nonrelease controlling excipients in the drug product. For modified release solid oral dosage forms, consideration should be given as to whether the excipient is critical or not critical to drug release. The sponsor should provide appropriate justifications for claiming any excipient(s) as a nonrelease controlling excipient in the formulation of the modified release solid oral dosage form. The functionality of each excipient should be identified. Changes in the amount of the drug substance are not addressed by this guidance. Changes in components or composition that have the effect of adding a new excipient or deleting an excipient are defined at level 3 (defined below), except as described below in Section III.A.1.a. Waiver of bioequivalence testing for a change in composition which involves only a different color, flavor or preservative may be permissible as described in 21 CFR.

Introduction to platform technology:

Definitions:

Platform technology / platform process: a common or standard method, equipment, procedure or work practice that may be applied to the research, development or manufacture of different products / or the approach of developing a production strategy for a new drug starting from manufacturing processes similar to those used by the same manufacturer to manufacture other drugs of the same type.

- QbD: Quality by Design
- IND: Investigational New Drug
- IMPD: Investigational Medicinal Product Dossier
- EBE: European Biopharmaceutical Enterprises
- Mab or mAb: Monoclonal antibody
- HCP: Host cell protein
- CHO: Chinese hamster ovary
- GS-NS0: Glutamine synthetase-NS0

Introduction: A platform technology or process may be generally defined as a common or standard method, equipment, procedure or work practice that may be applied across multiple products under development or manufacture. For example, 'platform' may be used to refer to an expression system such as Chinese Hamster Ovary (CHO) cells, a high throughput screening system based on robotics, an analytical method such as capillary electrophoresis, a drug product formulation, a mode of cell culture such as perfusion culture, a process unit operation such as affinity chromatography or even a complete process comprising multiple unit operations.

The main benefits of an established platform technology / process such as this include;

- Reduction of process development effort, time and costs.
- Prior platform data informs risk assessments on new process weak-points, and focuses development effort where most needed.

- Consistency in process performance and product quality (especially important when developing a particular class of products, e.g., monoclonal antibodies
- Simplification of technology transfer activities to production facilities
- Improved asset utilization: one facility / same equipment for multiple products
- Documentation preparation can be simplified; e.g., only minor adjustments to production batch records may be required from one process (product) to the next
- Ability to translate learning from one product to another as process database grows.
- Greater significance of a 'multi-product' dataset as compared to a 'one-off' study on a single product
- Raw materials and consumables are standardized allowing the use of materials with safety profiles proven to be acceptable, cost reductions through volume purchasing and waste reduction as inventory stocks may be used across several different products
- Reduction in time and resources leading up to and including pre-clinical and clinical studies
- Reduction in failure rates during manufacturing due to accumulated process experience
- Reduced personnel training burden owing to similar processes and equipment
- Improved speed through repetition
- Routine procedures for in-process and batch release testing lead to reduction of errors
- Platform specifications' for early-phase clinical programs
- Broad database and experience to speed troubleshooting of manufacturing processes
- Preparation of INDs/IMPDs/marketing authorization applications may be facilitated more readily: pre-populated templates may be created which reduce the time necessary for manufacturers to author and prepare the submissions

References:

1. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-second report. Geneva, World Health Organization, 2008 (WHO Technical Report Series, No. 948).
2. Good manufacturing practices for sterile pharmaceutical products In: WHO Expert Committee on Specifi cations for Pharmaceutical Preparations. Thirty-sixth report. Geneva, World Health Organization, 1992 (WHO Technical Report

Series, No. 957, 2010), Annex 4; WHO Technical Report Series, No. 961, 2011) Annex 6.