Ministry of Health & Family Welfare
Government of India

厚生労働省
Ministry of Health, Labour and Welfare
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(JMHLW)

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Updates of GMP and Quality Management (India)

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CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
CDSCO CDSCO
MINISTRY OF HEALTH, GOVERNMENT OF INDIA

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独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

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Why GMP

- ✓ GMP is aimed primarily at managing and minimizing the risks inherent in pharmaceutical manufacture which cannot be detected by testing so as to ensure the quality, safety and efficacy of products
- ✓ To minimize or eliminate chances of contamination, cross-contamination, mix-ups, and errors.
- ✓ To ensure that products are consistently produced and controlled to the quality standards.

Guiding Principle of GMP

- Quality is Built into a Product not just tested into a Product
- GMP is Minimum Mandatory Standard
- It is the expectation of patient/Consumers that each batch of medicines they take meet quality standards and is therefore safe and effective
- GMPs provide for systems that assure proper design, monitoring, and control of manufacturing processes and facilities.
- Adherence to the GMP regulations assures the identity, strength, quality, and purity of API and formulations by requiring that the pharmaceutical manufacturers of medical products adequately control manufacturing operations.
- This includes establishing strong quality management systems, obtaining appropriate quality raw materials, establishing robust operating procedures, detecting and investigating product quality deviations, and maintaining reliable testing laboratories

Schedule M

- GMP was first incorporated in Schedule M of the Drugs and Cosmetics Rules in the year 1988.
- Revised in the tune of WHO TRS 823 in 2001.
- There is a necessity to further revise the main principle and concept of GMP mentioned in Schedule M to fulfill international regulatory commitment.
- A Gap Analysis of Schedule M with WHO GMP norms was carried out.
- The Central Government has published a draft notification vide **G.S.R. 999(E) dated 05.10.2018** to upgrade and synchronize the Schedule M of the Drugs and Cosmetics Rules, 1945 in compliance with WHO-GMP standards.

Revised Schedule M-2018 (Draft)

- Part-I Good Manufacturing Practices for Pharmaceutical Products _ **Main Principles**
- Part –II Specific Requirement for manufacture of **Sterile Products , Parenteral Preparations(SVP & LVP), and Sterile Ophthalmic Preparations**
- Part-III: **Specific Requirement for manufacture of products containing hazardous substances such as Steroids (Anabolic and Androgenic), Sex Hormones and Cytotoxic Products**
- Part IV: Specific Requirement for manufacture of **Biological Products**
- Part V : Specific Requirement for manufacture of **Radio Pharmaceuticals**
- Part VI : Specific Requirement for manufacture of **Phyto Pharmaceuticals**

Revised Schedule M-2018 (Draft)

- Part-VII: Specific Requirements for manufacture of **Investigational Pharmaceutical Products for Clinical Trials in Humans**
- Part –VIII: Specific Requirements for manufacture of **Oral Solid Dosage forms (Tablets and Capsules)**
- Part -IX : Requirement for manufacture **of Oral Liquids (Syrups, Elixir, Emulsions and Suspensions)**
- Part- X: Specific Requirements for manufacture of **External Preparation (Ointments, Creams, Emulsions, Solutions , Lotions, Dusting powders and identical Products)**
- Part XI : Specific Requirements for manufacture of **Metered Dose- Inhalers (MDI)**
- Part XII: Specific Requirements for manufacture of **Active Pharmaceutical Ingredients (API)**
- Part XIII: Requirements of Plant and Equipment.

Revised Schedule M-2018 (Draft)

Part-I: Good Manufacturing Practices for Pharmaceutical Products-Main Principles

1. Pharmaceutical Quality System
2. Quality Risk Management
3. Good Manufacturing Practices for Pharmaceutical Products
4. Sanitation and Hygiene
5. Qualification and Validation
6. Complaints
7. Product Recall
8. Change Control
9. Product under Loan License or Contract and Contract Analysis and other activities
10. Self Inspection, Quality Audit ,Vendor/supplier's audit and approval
11. Personnel

Revised Schedule M-2018 (Draft)

Part-I: Good Manufacturing Practices for Pharmaceutical Products-Main Principles

12. Training
13. Personal Hygiene
14. Premises
15. Equipment
16. Materials
17. Reference Standards
18. Waste Materials
19. Documentation
20. Good Practices in Production
21. Good Practices in Quality Control
22. Computerized System

Appendix I– Site Master File

Revised Schedule M-2018 (Draft)

Pharmaceutical Quality Management System

- Manufacturer should assume responsibility for Quality of Pharmaceutical products, so that the product is fit for intended use.
- Senior Management must be engaged and responsible to institutionalize Quality system Principles with commitment of staff at all levels right from manufacturing till the product is distributed.
- Quality System should be designed to incorporate current Good Manufacturing Practices and Quality Risk Management comprehensively.
- Pharmaceutical Quality system- applies to the life cycle stages i.e. from manufacturing of IMP (Investigational Medicinal product), Technology transfer to Commercial production till the discontinuation of a product).

Revised Schedule M-2018 (Draft)

Pharmaceutical Quality Management System

- The product quality system can extend to the pharmaceutical development life-cycle stage and shall facilitate innovation and continual improvement and strengthen the link between pharmaceutical development and manufacturing activities
- Continual Improvement in Process and Product Quality with knowledge of process and product Quality trend.
- Deviations (identified in Quality system , Process, operations, Quality controls) are timely detected , logged , investigated to find out right root cause /most likely root cause , CAPA identified , implemented and CAPA effectiveness monitored.

Revised Schedule M-2018 (Draft)

Pharmaceutical Quality Management System

- **Periodic Management Review :** Regular Participations of Senior Leadership in review of causes of escalation such as -non-conformances, deviation , complaint trends , Product Quality defects , Quality System trends to identify opportunity for continual Improvement Actions and resolution to Process issues and improvement in Product Quality System.
- Continual Improvement in Process and Product Quality with knowledge of process and product Quality trend.
- There should be Quality Risk Management established in organization to identify the risk factors at all levels , and at each life cycle stages , and to mitigate the risks by implementing CAPA for Quality improvement.

Revised Schedule M-2018 (Draft)

Product Quality Review

- Regular, periodic or rolling quality reviews of all medicinal products, including export-only products, should be conducted with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements.

- The manufacturer shall evaluate the results of the review and an assessment shall be made as to whether corrective and preventive actions or any revalidation shall be undertaken, under the product quality system.

- Corrective and preventive actions shall be completed in a timely and effective manner, according to documented procedures.

Draft Schedule M-2018

Product Quality Review

- There shall be procedures for the on-going management and review of these actions, and the effectiveness of these procedures shall be verified during self-inspection.

- Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, or sterile products, where scientifically justified. There shall be a technical agreement in place between the various parties that defines their respective responsibilities in producing the quality review.
- The authorized person responsible for final batch certification shall ensure that the quality review is performed in a timely manner and is accurate.

Revised Schedule M-2018 (Draft)

Change Control

- A formal change control system shall be established to evaluate all changes that may affect the production and control of the product.
- Written procedures shall cover the identification, documentation, appropriate review, and approval of changes in raw materials, specifications, analytical methods, facilities, support systems, equipment (including computer hardware), processing steps, labelling and packaging materials and computer software.
- The potential impact of the proposed change on the quality of the intermediate or API or finished product shall be evaluated.
- When implementing approved changes, measures shall be taken to ensure that all documents affected by the changes are revised.
- After the change has been implemented there shall be an evaluation of the first batches produced or tested under the change.

Revised Schedule M-2018 (Draft)

- **Stability studies:** Detailed guidance on planning, conducting and reporting of stability study

- **Computerised System Validation:**
  - GMP-related computerized systems shall be validated.
  - The depth and scope of validation depends on the diversity, complexity and criticality of the computerized application.

Regulation on Joint inspection

- The Ministry of Health & Family Welfare published the gazette notification vide G.S.R. 1337(E) dated 27/10/2017 prescribing the provisions of joint inspection by the inspectors appointed by the Central and State Government for grant of manufacturing licenses and for periodic inspections of not less than once in three years or as needed as per risk based approach.

- Jointly conducted by inspectors, CDSCO Zonal offices with Drugs Inspectors of respective states in accordance with checklist and procedures developed as cGMP requirements for inspection in line with WHO norms

- Inspections are planned, conducted and reported as per written procedures established between the states and zonal offices through guidance documents, circulars and in accordance with Drugs and Cosmetics Act and Rules.

- There is a procedure of Central Inspection Plan and risk-based inspection procedures established for vaccines as per SOPS and guidance documents developed in line with PICs and WHO guidance for GMP inspectorate

Joint inspection during Covid 19

- Inspections were conducted in hybrid mode through desktop review and participation of local inspectors at the site for urgent permission whenever needed

- Inspections were initiated in early development stages of the products including vaccines for verification of data submitted as part of dossier submission for conduct of clinical trial or for marketing authorisation permission

- Early engagement and continuous monitoring at the development stages to technology transfer to commercial production through onsite inspections enabled CDSCO in expedited review and accelerated approval process for drugs, vaccines and other biological products

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Thank You

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