Revised GMP Guidelines and requirements under Schedule M

GMP and Requirements of Premises, Plant and Equipment for Pharmaceutical Products

- **GMP and the Requirements under Schedule M have been revised vide G.S.R. 922(E) dated 28.12.2023 to make it harmonized with WHO Guidelines.**
- **Manufacturing premises should be exclusively used for production of drugs.**
- **It will come into force for implementation as under:—**

Category of manufacturers	**Time line for implementation**
Large manufacturers (Turnover> 250 crores)	Six months from the date of publication of these rules
Small and Medium manufacturers (Turnover≤ 250 crores)	Twelve months from the date of publication of these rules.

PART1 : Main Principles

1. Pharmaceutical Quality System

- Manufacturer must assume the responsibility for the quality.
- Senior management has the ultimate responsibility.
- Consistency in the quality
- Product and process knowledge
- Products are designed and developed taking into account GXP
- Materials from approved vendors
- Production and release as per conditions of license and other applicable regulations

Pharmaceutical Quality System contd..

- Notification of changes to the LA
- Approval of planned changes from LA where required,
- Continual improvement in the quality
- Regular review of quality
- Root cause analysis of defective products
- Periodic management review
- Quality Manual

2. Quality Risk management

- **QRM:**
  - Assessment of risk, Control of risk, Communication of risk, Review of risk

Product quality review

- Starting materials, critical in-process control and finished product results.
- Review of all batches that had failed.
- Review of non-conformance related investigation and corrective and preventive action taken.
- Review of complaints and recalls etc.
- Qualification status of equipment such as heating, ventilation and air-conditioning, water and compressed gases.
- Even for exported products
- Annually
- Technical agreements, up-to-date.

3. Good Manufacturing Practices

Definition: Part of quality management which ensures that products are consistently produced and controlled according to the quality standards appropriate to their intended use and as required by the licence

Aim:

Managing and Minimizing Risk

4. Sanitation

Existing :

Covers only Workers and manufacturing premises

New:

High level of sanitation and hygiene for personnel, premises, equipment/ apparatus, production materials and containers.

5. Qualification and Validation

Qualification and Validation:

Existing:

Validation covers only manufacturing process, testing and cleaning

New:

Also covers Premises, Utilities and equipment

Qualification and Validation:

Existing: No provision for qualification

New:

Premises, Utilities, equipment, process (DQ, IQ, OQ, PQ)

6.Compliance and Adverse reactions

Existing:

- Serious Adverse drug reactions to be reported to Licensing Authority

New:

- Faulty manufacture, product deterioration, serious quality problems to be reported to Licensing authority
- Pharmacovigillance system should be in place

7. Product Recall

Existing:

- No provision to inform to LA

New:

- Comprehensive system specified for promptly and effective recall
- To be informed to LA

8.Change Control

Existing:

- Only in case of significant changes

New:

- Changes in RM, PM, Specifications, Analytical methods, Facilities, Utilities, Equipment, processing steps, labeling Software etc.
- Minor, Major and Critical Changes based on nature and extent

9.Production

Existing:

No details of Contract giver, contract acceptor, Contract analysis

New:

- Role and Responsibilities of Contract giver, Contract Acceptor
- Agreement
- Technology Transfer

10.Self Inspection, Quality Audits and Supplier Audit and approval

Existing:

- Frequency-performed routinely and in specific occasions i.e. recall or inspection by LA

New:

- At least once in a year
- Suppliers audit and approval (approved list of RM and PM)

11.Personnel

New:

- Organization chart
- Personnel should be motivated to support maintenance of high quality standards
- Role and responsibilities of Key personnel (Heads of production, QC)
- Qualification of key personnel (as specified under Rules)
- Functions may be delegated, but not responsibilities
- Visitors entry procedures into production area
- Approved training program

12.Premises

Detailed requirements about premises including

- Production areas,
- Weighing areas,
- Ancillary areas,
- Storage area,
- Production areas,
- Quality areas,
- Equipments,
- Materials,
- Reference standards etc. have been prescribed.

13. Equipment

- Validated Cleaning procedures

14.Materials

New:

- Validated Computerized storage systems
- PM – not to test all batches, but based on vendor approval and statistical data analysis
- Identity test for each container of Starting material (Exception- dedicated facilities)
- Reworking of rejected products (new batch number)
- Part of earlier batches into a batch of the same product at defined stages of manufacture
- Extension of retesting date (Para 10.9 of Schedule M)

15.Reference Standard

New:

- IP RS/IS should be procured from IPC
- Procedure for working standard

16.Waste Materials

- By and large similar provisions

17. Documentation

Exist:

- MFR, SOP in hard copy for verification

New:

- Audit trail- to ensure existence of documented evidence, traceability
- MFR – Hold time permitted for Intermediates and in-process materials
- Validation Master Plan

18. Good Practices in Production

- Detailed requirements about Good practices in production have been provided.
- Deviation control
- Prevention of cross contamination, measures to be taken
- Timeline for storage of equipment after cleaning
- Any significant deviation from the expected yield shall be recorded and investigated
- Line clearance for packaging operations

19. Good Practices in Quality Control

- Detailed requirements about Good practices in QC have been provided.

- The detailed requirements of stability studies of finished products and, when necessary of starting materials and intermediate products, establishing shelf life including written programme for ongoing stability determination have been specified.

- Stability shall be determined prior to marketing and following any significant changes e.g. changes in in-process, equipment or packaging materials.
- Part testing, in case CoA from the reliable manufacturer
- Retention sample of other materials – Minimum of two years
- Retest date

20. Computerised Systems

- Detailed requirements about validation of GMP related computerized system.
- IQ and OQ of Hardware and Software
- Proper backup system

Applicability of WHO Guidelines

The guidelines published by WHO on following aspects relating to GMP through their Technical Report Series from time to time may be considered for general guidance purposes:-

i. Guidelines on the principles of airflow directions, air filtration standards, temperature, humidity and related parameters.

ii. Good manufacturing Practices (GMP) guidelines regarding the design, installation and operation of pharmaceutical water systems including guidance about which quality of water to use for specific applications, such as the manufacture of active pharmaceutical ingredients (APIs) and dosage forms.

iii. Guidelines on design, installation, qualification and maintenance of the Heating, Ventilation, Air Conditioning (HVAC) systems of the manufacturing plant.

iv. GMP guidelines for validation.

v. Guidelines on packaging of pharmaceutical products

Specific requirements

PART-II :Specific Requirements for Manufacture of Sterile Products

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PART-III :Specific Requirements for Manufacturing of Pharmaceutical Products Containing Hazardous Substances Such as Sex Hormones, Steroids (Anabolic, Androgenic) or Cytotoxic Substances

PART-IV: Specific Requirements for Manufacture of Biological Products

PART-V : Specific Requirements for Radiopharmaceutical Products

PART VI: Specific Requirements for Phytopharmaceuticals

PART-VII: Specific Requirements for the Manufacture of Investigational Pharmaceutical Products for Clinical Trials in Humans

The parts related to oral solids, oral liquids, topical preparations, active pharmaceutical ingredients and meter-dose inhalers are same in the proposed rules as present in the existing Schedule M of the Drugs and Cosmetics Rules, 1945.

Conclusion

- Continual improvement in the quality
- Facilitate Innovation
- Promote exports
- At par with Global Standards
- Built trust and confidence on quality
- Reduce NSQ and product failures
- Reduce Recall


Thank you