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SCHEDULE M
GMP & MANUFACTURING

Pharmaceutical Manufacturing Compliance Handbook

A Comprehensive Working Manual for Pharmaceutical Manufacturers in India

A Practitioner's Handbook for the Pharmaceutical Industry

BHATT & JOSHI ASSOCIATES

Advocates & Legal Consultants

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FOREWORD

The Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945, together with Schedule M (Good Manufacturing Practices), Schedule U (Records), and directions issued under Section 33-P of the Act, constitute one of the most comprehensive — and most demanding — regulatory frameworks applicable to any industry in India. Compliance failures carry criminal consequences: prosecution, licence suspension, and personal liability of directors and qualified persons. Yet the rules themselves are spread across hundreds of pages of subordinate legislation, schedules, and administrative guidelines, making day-to-day compliance difficult for manufacturers without dedicated legal and regulatory teams.

This handbook, published by Bhatt & Joshi Associates, is designed as a step-by-step working manual — tracing the lifecycle of a pharmaceutical manufacturer from the pre-licensing stage, through grant of licence, ongoing GMP compliance, quality control obligations, batch record keeping, and the critical post-manufacture obligations of information updating, product recall, and handling regulatory inspections. Special attention is given to sterile and parenteral products (including injectable preparations), which attract additional and more stringent requirements.

PART I — THE REGULATORY ARCHITECTURE

Chapter 1: The Legislative Framework

1.1 Principal Legislation

The pharmaceutical manufacturing sector in India is primarily governed by:

The Drugs and Cosmetics Act, 1940 ("the Act") — the parent statute defining offences, penalties, powers of inspectors, and the licensing framework

The Drugs and Cosmetics Rules, 1945 ("the Rules") — the subordinate legislation laying down all procedural and technical requirements

Schedule M (appended to the Rules) — Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products

Schedule U (appended to the Rules) — Particulars to be Shown in Manufacturing Records

Schedule F, F(1), F(2) — Special conditions for biological products, large volume parenterals, and sterile preparations

Schedule L-I — Good Laboratory Practices

Schedule Y — Requirements and guidelines for import and manufacture of new drugs

Directions under Section 33-P — Central Government policy directions to State Drug Controllers, including DCC prosecution guidelines

1.2 Constitutional and Administrative Structure

India's pharmaceutical regulatory framework operates on a dual-authority model:

Ciprofloxacin Injection (Schedule C(1)) falls under CDSCO/CLAA jurisdiction — the licence is issued in Form 28/28D after State inspection and CLAA approval.

1.3 Key Definitions

A working manufacturer must be familiar with the following statutory definitions:

"Standard quality" [Section 3(b)(i)]: Compliance with standards of strength, quality and purity specified in the Second Schedule (which incorporates the Indian Pharmacopoeia by reference)

"Not of Standard Quality" (NSQ) [Section 16]: A drug that does not comply with the prescribed standard

"Adulterated" [Section 17A]: A drug that contains a filthy, putrid or decomposed substance; is injurious to health; or contains any substance not permitted

"Spurious" [Section 17B]: A drug which is an imitation of or substituted for another drug, or bearing wrong label

"Manufacture" [Section 3(f)]: Any process or part-process for making, altering, ornamenting, finishing, packing, labelling, breaking up, or otherwise treating or adapting any drug with a view to sale or distribution

"Competent technical staff" [Rule 76(1)]: The Rule 76-qualified whole-time employee under whose active direction and personal supervision manufacture is conducted

PART II — OBTAINING A MANUFACTURING LICENCE

Chapter 2: Pre-Licensing Requirements and Eligibility

Before filing any application for a manufacturing licence, a pharmaceutical company must first satisfy several threshold conditions that are checked during pre-grant inspection.

2.1 Premises Requirements

The applicant must have dedicated manufacturing premises used exclusively for the production of drugs — no other manufacturing activity is permitted within the same premises. The premises must satisfy the requirements of Schedule M including:

Adequate floor area for each manufacturing operation

Separate areas for each category of drug (oral solids, liquids, parenterals, etc.)

Separate quality control/testing laboratory, physically independent of the production area

Adequate environmental controls (temperature, humidity, air pressure differentials)

Change rooms, airlocks, and appropriate flooring/ceiling/walls (smooth, cleanable, no crevices)

Separate storage areas for raw materials, packaging materials, quarantined goods, released goods, and rejected materials

For sterile and parenteral products, additional classified clean room infrastructure is required (see Chapter 17).

2.2 Equipment and Plant

The applicant must provide and maintain adequate plant and equipment appropriate to the drugs intended to be manufactured. Rule 76(3) requires the applicant to provide:

Adequate space, plant and equipment as specified in Schedule M

A testing laboratory with equipment to carry out all IP tests for the drugs being manufactured, or a documented arrangement with an approved institution

2.3 Competent Technical Staff — Rule 76(1)

This is the most critical pre-licence requirement. Before any licence can be issued, the applicant must have on its payroll a qualified whole-time employee who will take personal supervision of manufacture. Rule 76(1) requires this person to be:

The licence in Form 28 is granted in the name of the company AND names the specific competent person. This is not a mere formality — the named person carries criminal liability under Section 34 of the Act for any offences committed during manufacture under their supervision.

Additionally, Rule 76(4) requires the testing/QC unit head to be:

Independent of the head of the manufacturing unit

A graduate in Medicine, Science, Pharmacy or Pharmaceutical Chemistry

With experience in drug testing considered adequate by the licensing authority

The production head and the QC head must be different persons. This statutory separation is fundamental to GMP and to the legal protection of individual officers.

2.4 Quality Management Documentation

Before grant of licence, the applicant must also have in place:

Master Formula Records (MFR) for each product to be manufactured

Standard Operating Procedures (SOPs) for all manufacturing, testing, cleaning, and environmental monitoring operations

A written Pharmaceutical Quality System (PQS) as required by Schedule M, Para 1

Chapter 3: The Application Process

3.1 Which Form? — A Decision Matrix

Ciprofloxacin Injection (Schedule C(1)) requires an application in Form 27 leading to a licence in Form 28 (or Form 28D if LVP).

3.2 Application Fees

Note: Fees for Form 27/28 licences (Schedule C/C(1)) are prescribed separately and subject to revision. Always verify current fees from the State licensing authority at the time of application.

3.3 Application Contents — Key Documents Required

Every application must include:

Site Master File (brief description of premises, operations, products)

Floor plan / layout of manufacturing premises with dimensions

List of equipment with capacity

Qualifications and experience certificate of the proposed Rule 76 competent technical person

Appointment letter and undertaking from the competent technical person

List of drugs proposed to be manufactured with their Schedule classification

Stability data and bioequivalence data (for specified categories under Rule 76(10))

New Drug approval letter from DCGI (for drugs falling under Rule 122E — new drugs)

Undertaking in Form 51 confirming non-conflicting brand/trade name (for branded products) under Rule 76(11)

NOC from local authority (in some States)

Chapter 4: Pre-Grant Inspection — Rule 79

No manufacturing licence under Part VI-B of the Rules is granted without a physical inspection of the premises.

4.1 Scope of Inspection

Under Rule 79, before a licence is granted, the licensing authority or CLAA shall cause the establishment to be inspected by one or more Inspectors (with or without an expert in the relevant field). The Inspector must:

Examine all portions of the premises, plant, and appliances

Inspect the process of manufacture intended to be employed

Inspect the means employed for standardising and testing the drugs

Enquire into the professional qualifications of technical staff proposed to be employed

Examine and verify all statements in the application

Assess the applicant's capability to comply with Schedule M GMP requirements and Schedule U record-keeping requirements

4.2 Inspector's Report — Rule 80

Under Rule 80, the Inspector must forward a detailed descriptive report on each aspect of inspection with recommendations to the licensing authority or CLAA. This report is the primary document on which the licensing decision is made.

4.3 Outcome — Rule 81

PART III — THE MANUFACTURING LICENCE — CONDITIONS AND OBLIGATIONS

Chapter 5: Understanding Your Licence (Form 28)

The manufacturing licence issued in Form 28 is not a one-time clearance — it is a continuing relationship between the licensee and the licensing authority. The licence incorporates by reference:

The special conditions in Schedule F or Schedule F(1) applicable to the specific drug category

The general conditions in Rule 78

All subsequent amendments to the Rules which come into force four months after Gazette publication

Every holder of a Form 28 licence must keep a copy of the current D&C; Rules and all relevant schedules accessible to staff and updated.

Chapter 6: General Conditions of Licence — Rule 78

6.1 The Twelve Core Obligations

Rule 78 sets out the mandatory ongoing conditions for every Form 28 licence. Violation of any condition is an offence under the Act. The key conditions are:

Condition (a) — Adequate Staff, Premises and Plant:

The licensee must provide and maintain adequate staff and adequate premises and plant for the proper manufacture and storage of the licensed substances at all times. This is not a snapshot obligation — it is continuous. Any reduction in qualified staff, any dilapidation of premises, or removal of required equipment while manufacture continues is a breach.

Condition (b) — Schedule M Compliance:

The licensee must provide and maintain staff, premises, and equipment as specified in Rule 76 and as required by Schedule M.

Condition (c) — Batch Testing and Records:

The licensee must test each batch of raw material and each batch of the final product — either in their own QC laboratory or in a laboratory approved by the licensing authority. Records must be maintained as specified in Schedule U.

Records of substances with a potency/expiry date: retained for 2 years from expiry

Records of other substances: retained for 5 years from date of manufacture

Condition (d) — Inspection Access:

The licensee must allow any Inspector appointed under the Act to enter (with or without prior notice) any premises where manufacture is carried on, and to inspect the premises and process of manufacture.

Condition (e) — Records Inspection and Information:

The licensee must allow Inspectors to inspect all registers and records and supply such information as required to ascertain compliance with the Act and Rules.

Condition (f) — Reporting Changes in Expert Staff and Premises [CRITICAL]:

This is addressed in detail in Chapter 9 (Information Update Obligations).

Condition (g) — Batch Samples on Request:

On request, the licensee must furnish to the licensing authority samples from any batch in such quantity as may be considered adequate, along with full protocols of tests applied.

Condition (h) — No Sale Pending Authority's Clearance:

Where directed by the licensing authority or controlling authority, the licensee must not sell or offer for sale any batch in respect of which a sample has been requested until a clearance certificate is issued.

Condition (i) — NSQ Batch Recall:

On being informed by the licensing authority or controlling authority that any part of a batch has been found NSQ, and on being directed, the licensee must withdraw the remainder of that batch from sale and recall all issues already made from that batch, as far as practicable.

Condition (j) — Preservation During Storage:

No drug manufactured under the licence shall be sold unless precautions necessary for preserving its properties have been observed throughout the period after manufacture. This condition is directly relevant to injectable sedimentation cases — improper storage conditions breaking this condition are the responsibility of the storage holder, not the manufacturer.

Condition (m) — Reference Samples:

The licensee must maintain reference samples from each batch in a quantity at least twice what is needed for all prescribed tests:

For drugs with an expiry date: retain until 3 months beyond expiry

For drugs without an expiry date: retain for 3 years from date of manufacture

Condition (p) — Schedule M and Schedule L-I Compliance:

Full compliance with Schedule M (GMP) and Schedule L-I (Good Laboratory Practices).

Chapter 7: Duration and Renewal of Licence

7.1 Regular Manufacturing Licences (Form 28)

The Form 28 manufacturing licence does not expire on a fixed calendar date — it remains valid as long as the licensee pays the retention fee at the prescribed intervals and does not violate the licence conditions. However:

Any change requiring amendment to the licence (e.g., adding products, changing premises, changing competent person) requires a fresh application/amendment

Violation of conditions can result in show-cause, suspension, or cancellation under Rule 85

7.2 Loan Licences (Form 28A / Form 28DA)

Loan licences remain valid if the licensee deposits the retention fee before the expiry of every five-year period from the date of issue. A loan licence is automatically cancelled or suspended if the Form 28/28D licence of the host manufacturing facility is cancelled or suspended.

PART IV — INFORMATION UPDATE OBLIGATIONS (RULE 78(f))

Chapter 8: The Mandatory Update Obligations — A Compliance Calendar

This chapter is perhaps the most underutilised and yet most legally consequential part of this handbook. Rule 78(f) is the most commonly violated licence condition in Indian pharmaceutical manufacturing. Its breach not only creates regulatory liability but — critically — also affects the criminal liability defence available to individual officers and directors under Section 34 of the Act.

8.1 What Must Be Reported — Rule 78(f)

Under Rule 78(f), the following changes must be reported to the licensing authority:

In several State licence forms (Form 28 conditions), the reporting window is specified as within one month of the change, and the licensee must appoint a qualified replacement within one month.

8.2 How to Report — Procedure

File a written intimation to the State Licensing Authority (for State-licensed items) or to CDSCO/CLAA (for Schedule C/C(1) licensed items) stating the name of the outgoing expert, the date of change, and the name/qualifications of the replacement

Attach the qualifications and experience certificate of the new Rule 76 competent person

Attach the appointment letter of the new competent person (indicating date of joining and designation as "Competent Technical Person" under Rule 76)

Attach the resignation/separation letter of the outgoing expert (if applicable)

Apply for amendment of the licence (Form 28 amendment) to reflect the change in named competent person — many licensing authorities require a fresh Form 27 application or a specific amendment application

Pay the prescribed amendment/inspection fee as required by the SLA

8.3 What Gets Recorded in the Form 28 Licence

The Form 28 licence specifically names:

The manufacturing company (licensee)

The licensed premises (address)

The drug(s) licensed for manufacture

The name of the competent person under whose supervision manufacture is to be conducted

Any change to any of these elements requires either an amendment or a fresh licence. Operating under an outdated Form 28 (naming an expert who has left) while actually operating under a new expert who has not yet been approved — is a dual breach: of Rule 78(f) and of the substance of Rule 76(1).

8.4 Legal Consequences of Failure to Report

Failure to update Rule 78(f) information creates the following cascading legal risks:

Licence condition breach — The manufacturing licence is technically operating in violation of a condition. The licensing authority may initiate proceedings for suspension or cancellation under Rule 85

Manufacturing under unlicensed supervision — If the old expert has left and no replacement is approved, the manufacture is arguably without proper supervision — potentially an offence under Section 18(c) of the Act

Criminal liability exposure for current officers — If an NSQ complaint is filed for a batch manufactured during the transition period (when the old expert had left but no replacement was approved), both the old expert and current management are exposed

Inability to use the "designated person" defence — In proceedings under Section 34, the defence requires proof that the accused was the Rule 76 competent person at the time of the offence. Failure to maintain clean records of staff changes makes this defence difficult to establish with documentary evidence

PART V — GOOD MANUFACTURING PRACTICES (SCHEDULE M)

Chapter 9: The Pharmaceutical Quality System (PQS) — Schedule M, Part I, Para 1

The Schedule M GMP framework, as overhauled in alignment with WHO and ICH standards, places the Pharmaceutical Quality System (PQS) at the apex of all manufacturing compliance obligations.

9.1 PQS — Senior Management's Responsibility

Senior management bears the ultimate responsibility to ensure that:

An effective PQS is in place, adequately resourced, and that roles, responsibilities, and authorities are defined throughout the organisation

The PQS is documented — a Quality Manual or equivalent documentation is mandatory

The PQS is subject to periodic management review — at least annually — with involvement of senior management, to identify opportunities for continual improvement

9.2 What the PQS Must Ensure

Schedule M lists the minimum performance requirements of the PQS:

Product and process knowledge is managed through the entire lifecycle

Each production batch has been produced and controlled in accordance with licence requirements before any authorised person certifies it for release

Arrangements exist for management of outsourced activities (contract testing, loan licence manufacturing)

Satisfactory arrangements exist for storage, distribution, and handling so that quality is maintained throughout shelf life

There is a procedure for self-inspection or quality audit to regularly appraise the PQS

Deviations, suspected product defects, and other problems are reported, investigated, and recorded with root cause analysis, CAPA (Corrective and Preventive Actions), and monitoring of CAPA effectiveness

9.3 Product Quality Review — Annual Requirement

Schedule M Para 2.3 requires regular (at least annual) rolling quality reviews of all pharmaceutical products, covering:

Starting materials and packaging materials (especially new sources)

Critical in-process controls and finished product results

All batches that failed specifications and their investigation

All significant deviations, NCRs, and effectiveness of CAPAs

All changes to processes or analytical methods

Results of the stability monitoring programme and adverse trends

All quality-related returns, complaints, and recalls

This annual Product Quality Review (PQR) document is a key document demanded by inspectors during GMP inspection. Its absence or inadequacy is a critical GMP deficiency.

Chapter 10: Quality Risk Management (QRM) — Schedule M, Para 2

Quality Risk Management is a systematic process for assessment, control, communication, and review of risks to product quality, applicable both proactively

(before manufacture) and retrospectively (after events).

The two key principles of QRM are:

Evaluation of risk to quality must be based on scientific knowledge and experience with the process, ultimately linked to the protection of the patient

The level of effort, formality, and documentation of QRM must be commensurate with the level of risk

Practical implication for manufacturers: Every manufacturing deviation, OOS (Out of Specification) result, customer complaint, or NSQ finding from a Drug Inspector should trigger a formal QRM assessment — not merely a corrective action. The QRM documentation demonstrates due diligence and is the primary defence material if prosecution is initiated.

Chapter 11: Personnel Requirements — Schedule M, Para 11

11.1 Key Personnel and Independence

The Schedule M GMP framework requires:

Key positions occupied by full-time personnel

Heads of production and quality units must be independent of each other — this mirrors the Rule 76(4) statutory requirement

In large organisations, functions may be delegated but responsibility cannot be delegated

11.2 Qualifications of Key Personnel

Key personnel responsible for supervising production and quality units must possess qualifications and experience as prescribed under Rule 76 and must have education in an appropriate combination of: chemistry, chemical engineering, microbiology, pharmaceutical sciences and technology, pharmacology and toxicology, physiology, or related sciences.

11.3 Responsibilities of the Head of Production

The Head of Production has the following specific responsibilities:

Ensure products are produced and stored in accordance with documentation to achieve required quality

Approve instructions relating to production operations including in-process controls

Ensure production records are evaluated and signed by a designated person

Check maintenance of department, premises and equipment

Ensure process validations and calibrations of control equipment are performed and recorded

Ensure initial and continuing training of production personnel

11.4 Responsibilities of the Head of Quality Units

The Head of QC/QA has the following specific responsibilities:

Approve or reject starting materials, packaging materials, intermediate, bulk and finished products against specifications

Evaluate batch records

Ensure all necessary testing is carried out

Approve sampling instructions, specifications, test methods, and other QC procedures

Approve and monitor contract analyses

Ensure validations of analytical procedures and calibrations

Supervision of regular internal audits/self-inspections

Participation in validation programmes

11.5 Training

A written training programme must be established and documented for all personnel whose duties take them into manufacturing areas or control laboratories. Key requirements:

Newly recruited personnel: basic GMP theory and practice training plus role-specific training before duties are assumed

Continuous training must be assessed for practical effectiveness periodically

Training records must be kept — name, date, subject, trainer, assessment result

Personnel in clean areas, areas with highly active/toxic/infectious materials: additional specific training required

Visitors and untrained personnel in production/QC areas: must be supervised and given advance hygiene briefing

11.6 Personal Hygiene — Non-Negotiable Standards

All personnel must undergo health checkups before and during employment; personnel conducting visual inspections must have periodic eye checkups

Personnel with illness or open lesions that may affect product quality must not be allowed to handle materials until the condition is resolved

All personnel must wash and sanitise hands before entering production areas

Direct skin contact with the product by production staff must be avoided

Chapter 12: Premises Requirements — Schedule M

Manufacturing premises for pharmaceutical products must be:

Used exclusively for pharmaceutical production — no other manufacturing

Laid out, designed, constructed, and maintained to prevent contamination and cross-contamination

Of adequate size to permit logical placement of equipment and flow of materials and personnel

Surfaces: smooth, washable, free from crevices, able to be effectively cleaned and disinfected

Environmental controls: temperature, humidity, and air pressure appropriate to the drug being manufactured

Separate, clearly demarcated areas for: raw material storage (quarantine / released / rejected), production, in-process storage, packaging, finished goods storage, QC laboratory, and reject/returned goods

The QC laboratory must be physically separated from the production area

Chapter 13: Change Control — Schedule M, Para 8

A formal written Change Control System (CCS) is mandatory for evaluating all changes that may affect the production and control of the product.

13.1 What Requires Change Control

Raw material specifications or suppliers

Analytical methods

Facilities, support systems, equipment (including computer hardware/software)

Processing steps and batch sizes

Labelling and packaging materials

Any change to validated processes

13.2 Change Control Procedure

Raise a Change Request — document the proposed change with justification

Impact Assessment — evaluate the potential impact on product quality, stability, process validation status

Classification — minor or major change (major changes may require regulatory notification/approval before implementation)

Review and approval — by appropriate organisational units and quality units

Implementation — all documents affected must be revised before implementation

Post-change evaluation — evaluate the first batch produced/tested under the change; consider accelerated stability testing if expiry dates may be affected

PART VI — STERILE PRODUCTS AND INJECTABLES — SCHEDULE M, PART II

Chapter 14: Specific GMP for Sterile/Parenteral Products

This chapter applies to all manufacturers of sterile products including small volume injectables (SVIs), large volume parenterals (LVPs), and sterile ophthalmic preparations. All Part I GMP requirements apply mutatis mutandis, plus the following additional requirements.

14.1 Clean Room Infrastructure — Grade Classification

Manufacturing operations for sterile products are divided into two categories:

Terminally sterilised products — manufactured in controlled conditions, then sterilised in final container

Aseptically processed products — one or more stages conducted aseptically

Clean areas are classified into four grades — A, B, C, and D — based on airborne particulate counts:

Grade A zones require unidirectional (laminar) air flow systems providing a uniform air speed of approximately 0.45 m/s.

14.2 Sterility Assurance

Sterility testing is the last in a series of control measures — it must not be relied upon as the sole assurance of sterility.

For terminally sterilised products: sterility is assured by validation of the sterilisation cycle

For aseptically processed products: assurance is by "media fill" (process simulation) runs

Samples for sterility testing must be representative of the whole batch including containers filled at the beginning and end of the batch and after any significant interruption

14.3 Endotoxin/Pyrogen Testing

For injectable products, Water for Injection (WFI) and intermediate and finished products must be monitored for endotoxins using a validated pharmacopoeial method. For large-volume parenterals, this monitoring is always required in addition to the finished product monograph tests. Any sample failing the endotoxin test must be investigated.

14.4 Environmental Monitoring for Sterile Areas

An environmental monitoring programme must be in place for microbial contamination and airborne particulate counts in all classified clean rooms. Results must be recorded and reviewed periodically. Any exceedance of alert/action limits must trigger investigation and CAPA.

PART VII — QUALITY CONTROL — STANDARDS AND TESTING

Chapter 15: The Role of the QC Department

The Quality Control department is not a gatekeeping function — it is an integrated part of GMP. Under Schedule M, the QC department's responsibilities include:

Approval or rejection of all starting materials, packaging materials, intermediates, bulk, and finished products against specifications

Evaluating and approving batch manufacturing records before batch release

Ensuring all testing is carried out — in-house or through approved contract testing laboratories

Approving all sampling instructions, specifications, test methods, and QC procedures

Establishing, implementing, and maintaining the quality system

Supervision of internal audits and self-inspections

No batch of product may be released for sale or supply prior to certification by the Authorised Person (AP).

15.1 The Authorised Person (AP) — Batch Release

The AP is the named individual responsible for compliance with technical and regulatory requirements related to finished product quality and for the approval of each batch for sale.

Before certifying any batch for release, the AP must ensure:

The licence and approval requirements for the product have been met for that batch

GMP requirements have been followed throughout

Principal manufacturing and testing processes have been validated

All necessary checks and tests have been performed

Any planned changes or deviations have been notified

All production and QC documentation has been completed and endorsed

Appropriate audits and self-inspections have been carried out

15.2 Indian Pharmacopoeia Tests — The Standard

For drugs listed in the Indian Pharmacopoeia (IP), the IP test methods and acceptance criteria constitute the legally prescribed standard under the Second Schedule to the Act. Key tests for injectable products:

Critical note on particulate matter testing: IP 2.15.1 (visible particles) requires the product to be "essentially free from visible particles" — the term "particles" in pharmacopoeial usage refers to foreign/extrinsic particles. The IP and WHO GMP guidelines distinguish between intrinsic particles (drug substance — e.g., ciprofloxacin crystals from pH/temperature-dependent precipitation) and extrinsic/foreign particles (glass, rubber, metal, fibre). Only extrinsic particles represent a product defect in the classical GMP sense. Any QC deviation report on injectable particulate matter must therefore specify whether the particles were identified, and if so, whether they are intrinsic or extrinsic.

PART VIII — BATCH MANUFACTURING RECORDS — SCHEDULE U

Chapter 16: Schedule U — Mandatory Records for Every Batch

Schedule U prescribes the exact particulars that must be maintained for every batch manufactured. For parenteral preparations (injectable products), the following records are mandatory:

16.1 Batch Manufacturing Record (BMR) — Parenterals

Every batch of parenteral preparation must have a BMR capturing:

Serial Number, Name of Product, Reference to Master Formula Record

Batch/Lot size; Batch Number/Lot Number

Date of commencement and completion of manufacture

Names of all ingredients, specifications, quantity required for batch size, and quantity actually used — with initials of the responsible person who weighed/measured and countersignature of the competent technical staff supervising the operation

Control numbers of raw materials used

Date, time and duration of mixing; pH of solution (if applicable)

Date and method of filtration

Sterility test reference on bulk batch

Records of volume check on filling

Date of filling

Records of tests employed — (a) sealing/leak-proof check of ampoules; (b) check for the presence of foreign particles; (c) pyrogen test; (d) toxicity test

Records of sterilisation instruments and apparatus (indicators)

Records of cleaning and sterilisation of containers and closures

Records of sterilisation (time, temperature, pressure) for heat-sterilised parenterals

Number and size of containers filled; quantity rejected

Theoretical yield, actual yield, and percentage yield

Reference to Analytical Report numbers — stating whether of standard quality or otherwise

Specimen of labels, cartons, batch coding (batch number, manufacture date, expiry date)

Signature with date of competent technical staff responsible for manufacture [Rule 76(1) person]

Precautions taken to ensure aseptic conditions

Counter-signature of head of testing unit or person-in-charge of testing — for having verified documents and having released the product for sale, quantity released and date of release [Rule 76(4) person]

Records of transfer to warehouse

Separate records of rejected batches and batches withdrawn from market

Records of reprocessing (if any)

The BMR is the single most important document in any regulatory investigation or prosecution. It records who supervised manufacture, who tested the batch, what tests were conducted, what the results were, and whether the batch was released. Gaps, alterations, or missing signatures in the BMR are treated as serious GMP violations.

16.2 Raw Material Records

Records for each raw material must show:

Date of receipt; invoice number; supplier name and address; batch number; quantity received; pack size

Date of manufacture and date of expiry (if any)

Date of analysis; analytical report number; release/rejection status; special remarks

Quantity issued; date of issue; name and batch number of products for which issued; disposal of stocks

16.3 Analytical Records for Parenteral Products

The analytical record for each batch must contain:

Analytical report number; batch number; date of receipt of sample

Protocols of all tests applied with results (description, visual/clarity inspection, particulate matter check, assay, sterility, endotoxin, pH, fill volume)

Reference to IP test method used for each test

Final conclusion — "of standard quality" or "not of standard quality" with reason

PART IX — LABELLING REQUIREMENTS

Chapter 17: Mandatory Label Particulars — Rules 96 and 97

Every drug manufactured for sale must have a label complying with Rules 96 and 97 of the D&C; Rules.

17.1 Schedule-Based Label Warnings — Rule 97(1)

Ciprofloxacin Injection is a Schedule H drug. The Rx symbol in red must appear conspicuously on the top-left corner of the label, and the Schedule H caution must appear in a red rectangular box.

17.2 Additional Mandatory Label Elements for Injectables

Product name (proper/brand name)

Name and address of manufacturer

Batch number and date of manufacture

Date of expiry

Storage conditions (e.g., "Store below 25°C", "Protect from light")

Net content/volume

Route of administration ("For Intravenous Infusion", etc.)

Schedule designation (Schedule H)

For ciprofloxacin: the caution "Do not use if solution contains visible particles" — this is also a pharmacopoeial label requirement

17.3 Brand Name Undertaking — Rule 76(11)

If the drug is to be marketed under a brand/trade name, the manufacturer must furnish an undertaking in Form 51 confirming that the proposed brand name does not already exist in the Trade Marks Registry, the CDSCO central brand name database, literature, or internet, and will not cause confusion or deception in the market.

PART X — PRODUCT RECALL — SCHEDULE M, PARA 7

Chapter 18: Product Recall System

18.1 Mandatory Recall Infrastructure

Every pharmaceutical manufacturer must have a prompt and effective product recall system documented as a Standard Operating Procedure. The key elements are:

A designated recall coordinator with authority to initiate recall at the required level in the distribution chain

Recall operations must be capable of being initiated at short notice

Recalled products must be stored in a secure, segregated area pending final disposition

The licensing authority must be informed of any intention to recall because a product is, or is suspected of being, defective

Distribution records must be readily available showing wholesalers and direct customers to enable complete traceability

18.2 Recall Records

Progress monitoring and recording throughout the recall process

Records must include disposition of the product (destroyed, re-processed, returned to manufacturer)

A final report must be issued including reconciliation between quantities delivered and quantities recovered

Effectiveness of recall arrangements must be evaluated periodically (mock recalls are recommended)

18.3 When Recall Triggers a Rule 78(i) Obligation

When the licensing authority or controlling authority directs a recall (after finding a batch NSQ), the Rule 78(i) obligation is triggered. The licensee must:

Withdraw the remainder of the batch from sale

Recall all issued quantities from the market "as far as may be practicable"

Document all steps taken and quantities recovered

Report completion to the licensing authority

PART XI — COMPLAINTS HANDLING AND DEVIATION MANAGEMENT

Chapter 19: Complaints — Schedule M, Para 6

A formal written system for handling complaints about drug quality is mandatory.

19.1 Complaint Management Procedure

Receipt and logging — all complaints from any source (patients, healthcare professionals, regulators, distributors) must be recorded with date, complainant details, product details, batch number, nature of complaint

Investigation — root cause analysis of every complaint; retain reference samples and BMR for the specific batch

Classification — is the complaint indicative of a systemic problem or a one-off? Does it require regulatory notification?

CAPA — implement corrective and preventive actions; monitor effectiveness

Response — communicate investigation outcome to complainant where appropriate

Recall trigger assessment — if the complaint suggests a potential safety or NSQ issue with a batch in distribution, assess whether recall is needed

All complaint records must be maintained and available for inspection.

PART XII — SELF-INSPECTION AND AUDITS

Chapter 20: Internal Quality Audits

Schedule M requires that a procedure for self-inspection or quality audit regularly appraises the effectiveness and applicability of the PQS.

20.1 Frequency and Scope

At least annual comprehensive self-inspection covering all aspects of GMP

More frequent targeted audits for specific areas of concern

Audits must be conducted by qualified and experienced staff — ideally from departments other than the area being audited

Results must be documented and presented to senior management

20.2 Audit Areas to Cover

Personnel (qualifications, training records, hygiene)

Premises (maintenance, cleanliness, environmental monitoring)

Equipment (qualification, calibration, cleaning records)

Documentation (SOPs, BMRs, analytical records — completeness and accuracy)

Production (process compliance, in-process controls, deviations)

QC (testing compliance, OOS handling, stability programme)

Change control records

Recall and complaint handling systems

Supplier and contract manufacturer management

PART XIII — INSPECTIONS BY DRUG AUTHORITIES

Chapter 21: Handling Drug Inspector Inspections

21.1 Inspector's Powers

Under Rule 78(d) and (e), a Drug Inspector may enter any licensed manufacturing premises with or without prior notice and has the right to:

Inspect premises, plant, and process of manufacture

Inspect all registers and records maintained under the Rules

Take samples of the manufactured product (using procedures under Rules 56–58)

Require information as necessary to ascertain compliance

Important: Under Schedule C(1) drug licences, the Inspector has power to inspect the plant and process of manufacture and the means employed for standardising and testing the substance.

21.2 Sample Taking — Statutory Procedure

When a Drug Inspector takes a sample:

The purpose of sampling must be intimated in writing in Form 17 (Rule 56)

The sample must be divided into four parts: one sent to the Government Analyst, one retained by the Inspector, one given to the manufacturer, and one kept as a counter-sample

The manufacturer's sample enables exercise of the right to seek retesting under Section 25(3)

Practical advice: Never allow an Inspector to take samples without compliance with the Form 17 intimation requirement. The statutory sampling procedure is mandatory, and failure to follow it vitiates the Government Analyst's report for prosecution purposes.

21.3 Government Analyst's Report and Your Rights

The Government Analyst's report under Section 25 carries evidentiary status:

The Government Analyst's report is evidence of the facts stated therein

The report of the Central Drugs Laboratory (CDL) is conclusive evidence — superseding the Government Analyst's report

Within 28 days of receipt of the Government Analyst's report, the manufacturer must dispute it in writing if contested, and seek retesting at the CDL

21.4 Right to Retesting — Section 25(3) and (4)

Upon receipt of the Government Analyst's report declaring a drug NSQ, the manufacturer's rights are:

Within 28 days — dispute the report and apply (through the Drug Inspector or the court) for the retained sample to be sent to the CDL for retesting

The CDL report, when obtained, supersedes the Government Analyst's report and is conclusive

If the shelf life of the drug expires before retesting can be completed, this deprivation of the right to retesting renders the prosecution null and void (State of Haryana v. Brij Lal Mittal, (1998) 5 SCC 343; Medicamen Biotech Ltd. v. Rubina Bose,

(2008) 7 SCC 196)

CRITICAL COMPLIANCE REQUIREMENT: Always exercise the right to retesting within 28 days. Missing this window waives the most powerful procedural defence available to manufacturers.

PART XIV — OFFENCES, PENALTIES, AND CRIMINAL LIABILITY

Chapter 22: Schedule of Offences and Penalties

22.1 Section 34 — Vicarious Liability of Company Officers

When an offence is committed by a company, every person who at the time of the offence was in charge of and responsible to the company for the conduct of business is deemed guilty unless they prove the offence was committed without their knowledge or they exercised due diligence.

This provision requires careful management of records to establish:

Who was the Rule 76 competent technical person at the time of manufacture of the specific batch

Whether that person was actually in charge at the time of the offence

Whether there was any delegation and whether it was properly documented

The Supreme Court in Sunil Bharti Mittal v. CBI, (2015) 4 SCC 609 and Gunmala Sales (P) Ltd. v. Anu Mehta, (2015) 1 SCC 103 has held that non-executive directors cannot be held vicariously liable without specific averments about their role in the offence, and that unimpeachable documents (Form 28, board resolutions, appointment letters) can be used in quashing petitions to establish absence of nexus.

22.2 Section 19(2)(b) — The Unavoidable Intermixture Defence

For prosecutions relating to extraneous matter or impurities, Section 19(2)(b) provides a statutory defence:

This defence requires documentary evidence that the manufacturer:

Did not introduce the extraneous substance intentionally

Could not have reasonably prevented the intermixture

Was not aware of the intermixture at the time of sale/distribution

Contemporaneous batch records (BMR) documenting all in-process controls, cleaning records, and environmental monitoring are the best evidence for this defence.

PART XV — LICENCE SUSPENSION, CANCELLATION, AND RESTORATION

Chapter 23: Adverse Regulatory Actions

Under Rule 85 of the Drugs Rules (and Section 18B of the Act), a manufacturing licence may be suspended or cancelled if:

The licensee has failed to comply with any condition of the licence

Any statement in the application was false or misleading

The licensee has been convicted of an offence under the Act

It is in the public interest to do so

The procedure requires:

Show Cause Notice — the licensee must be given an opportunity to be heard before any adverse order

Order with Reasons — suspension/cancellation order must give reasons

Opportunity of hearing — right to be heard is mandatory; violation renders the order voidable

APPENDIX A — KEY FORMS REFERENCE TABLE

APPENDIX B — KEY SCHEDULES CROSS-REFERENCE

APPENDIX C — INFORMATION UPDATE OBLIGATIONS — QUICK REFERENCE CHECKLIST

Use this checklist every time there is a change in your manufacturing unit:

Staff Changes:

■ Has the Rule 76(1) competent technical person (production supervisor) changed? → File intimation under Rule 78(f) within one month; apply for Form 28 amendment; attach qualifications and appointment letter of new person

■ Has the Rule 76(4) QC/testing head changed? → Same procedure as above

■ Has any other key GMP personnel changed (Head of QA, Authorised Person)? → Update internal PQS documentation; update GMP training records; consider whether regulatory notification is needed

Premises Changes:

■ Has any material alteration to the approved manufacturing premises been made? → File Rule 78(f) intimation; consider whether fresh inspection/licence amendment is required

■ Has any new manufacturing area been added? → Fresh application may be needed for expanded premises

Product Changes:

■ Adding a new drug product to the licence? → Fresh application for licence amendment; pre-grant inspection for new product category may be required

■ Changing manufacturing process, batch size, or equipment for an existing product? → Initiate Change Control; assess if regulatory notification to licensing authority is required before implementation

Documentation:

■ Annual Product Quality Review (PQR) completed for all products? → Due annually

■ Self-inspection/audit conducted? → Due at least annually

■ Stability monitoring samples placed and reviewed? → Ongoing

■ Training records updated for all personnel? → Ongoing; new staff before duties assumed

■ Reference samples maintained? → Check retention conditions and dates

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