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## GUIDELINES FOR GOOD MANUFACTURING PRACTICE OF MEDICINES

This document provides guidelines for the requirements of Good Manufacturing Practice (GMP) in South Africa. This guideline is not an exclusive approach. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine. SAHPRA may amend this guideline in keeping with the latest knowledge at the time of consideration of data accompanying applications for registration of medicines. Scientifically and technically justified alternative approaches SAHPRA is committed to ensuring that all medicines gaining market approval will be of the required quality, safety and efficacy standards.

### Document History

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1	Implementation	1997
1	Chapter 9 (Validation) reformatted	January 2004
2	Adoption of PIC/S GMP Guide of July 2004	January 2006
3	Amendment of Introduction and inclusion of requirements for Quality Product Review (1.5), Risk Management (1.6), On-going stability programme (6.7), Analytical Method Validation (Annex 15 15.7) and Glossary, keeping of Reference and Retention samples (Annex 19), Quality Risk Management (Annex 20)	September 2008
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	– Inclusion of Section 2 Adoption and Adaptation of PICS GMP Guide, Section 3 Regulatory Processes and moving of Annex 16 from version 5 to Section 4	
7	– Additional guidance on the regulatory process for GMP approval – Detailing of recognised authorities for GMP reliance – Specifying the dosage form, product type and activity grouping	July 2019
8	To comply with SAHPRA documents formats	August 2022
9	Alignment with PICS Annex 16	November 2025
10	– Inclusion of Section 4.1.6 for specification of the minimum years of experience required for key personnel per license category in terms of Section 22C(1)(b) of the Medicines and Related Substances Act 101 of 1965	April 2026

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## Glossary

Abbreviation/ Term	Meaning
GMP	Good Manufacturing Practice
PICS	Pharmaceutical Inspection Co-operation Scheme
RP	Responsible Pharmacist
RPn	Responsible Person

APPROVED

## 1. INTRODUCTION

Good Manufacturing Practice (GMP) is described as a set of principles and procedures that, when followed, ensure that medicines and related substances are of high quality, safety and efficacy. The South African Health Products Regulatory Authority (SAHPRA) is an affiliated member of the Pharmaceutical Inspection Cooperation Scheme (abbreviated as PICS). The PICS aims to develop international standards between countries and pharmaceutical inspection authorities and provide harmonised and constructive co-operation in the field of GMP. The PICS affiliation is subject to initial and periodic assessment of the participating authority to ensure that it has equivalent legislation, regulatory and enforcement procedures and inspection capacity.

### 1.1 Purpose

GMP is a system that ensures medical products are consistently produced and controlled according to quality standards. It is designed to minimise the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product.

The standards set out in this guideline apply to medicines and similar products intended for human use. It is recommended, however, that the same attention be given to the manufacture of veterinary products. Administrative measures of national health authorities should be directed towards the application of these standards in practice, and any new or amended national regulations for good manufacturing practice should at least meet their level. These standards also serve as a basis for the elaboration of specific rules adapted to the individual needs of manufacturers.

### 1.2 Scope

GMP covers all aspects of production from the starting materials, premises, equipment, training and personal hygiene of staff. Detailed written procedures are essential for each process that could affect the quality of the finished product. There must be systems to provide documented proof that correct procedures are consistently followed step - by – step in the manufacturing process of a product.

## 2. LEGAL PROVISION

### 2.1 ADOPTION AND ADAPTATION OF THE PICS GMP GUIDE

Section 22C(1)(b) of the Medicines and Related Substances Act No. 101 of 1965 (Act 101 of 1965) specifies that manufacturers, importers, exporters, wholesalers and distributors of medicines and related substances (including excipients and APIs) must hold a licence. Regulation 23 of the Act specifies that there must be the ability to comply with good manufacturing, wholesaling, or distribution practices as

determined by the Authority if you want to be a licence holder. This enables the Authority to determine manufacturing practices and the relevant code of GMP to be applied by manufacturers.

As a participating Authority of PICS, SAHPRA requires that manufacturers, importers and exporters of medicines and related substances in South Africa meet the standards laid out in the PICS Guide to GMP. As such, SAHPRA has adopted the PICS Guide to GMP, and all prospective adaptations as prescribed by the PICS. Any reference to the “Responsible Person” or Authorised Person will be equivalent to “Responsible Pharmacist” within the South African context.

### 3. REGULATORY PROCESSES

#### 3.1 Principles

GMP agreements with competent international regulatory authorities support information sharing and other desirable objectives for international regulatory collaboration. These agreements do not permit automatic acceptance of the decisions of the other party but may be used to enhance regulatory oversight and significantly reduce regulatory burden without diminution of compliance.

Manufacturers of medicines (including excipients and APIs) supplied in the South African market must demonstrate compliance with the relevant code of GMP. This is usually, but not always, done through an on-site inspection and with acceptable documentary GMP evidence.

It is an offence in South Africa to manufacture, import or export medicines in South Africa without a licence and certification in terms of Section 22C of the Medicines and Related Substances Act (Act 101 of 1965).

#### 3.2 GMP Approval Guidance

GMP approval guidance for sites involved in the manufacture of products can be found below. Also note that adherence to these requirements does not guarantee a site will be deemed GMP compliant by SAHPRA. SAHPRA reserves the right to request additional documentation, schedule an inspection or reject any sites regardless of adherence to the below requirements:

- The site has been approved by a recognised regulator (see Appendix 1 below),
- The site was approved by the recognised regulator (Appendix 1) within the previous 3 years, and
- The dosage form of the product within the application is within the same dosage form grouping as the dosage form approved by the recognised regulator (see Appendix 2 below),

- The product type applied for is the same as the product type approved by the recognised regulator (see Appendix 2 below), and
- The activities applied for by the applicant are the same activities that have been approved by the recognised regulator (see Appendix 2 below).

## 4. SOUTH AFRICAN SPECIFIC REQUIREMENTS RELATED TO KEY PERSONNEL:

### 4.1 ORGANISATION AND PERSONNEL

#### 4.1.1 PRINCIPLES

The company must have an organisational chart that has been approved for use. The organogram should clearly indicate the reporting lines and level of responsibility in accordance with the functional relationships described in the individual job descriptions of the functionaries referred to.

The establishment and maintenance of a satisfactory system of quality assurance and the correct manufacture and control of medicines relies on people. For this reason, there should be sufficient personnel at all levels with the ability, suitable skills and training, experience and, where necessary, the professional or technical qualifications and appropriate managerial skills to the tasks assigned to them. Their duties and responsibilities should be clearly explained to them and recorded as job descriptions. Proper job descriptions should include the responsibilities and document in detail the policy and requirements.

All personnel should be aware of the principles of GMP that affect them and receive initial and continuing relevant training, including hygiene instructions relevant to their needs. Responsibilities should be delegated, and acceptance acknowledged in writing. Duties may be delegated to designated deputies of a satisfactory qualification level. There should be no gaps or unexplained overlaps in the responsibilities of those personnel concerned with application of GMP.

The way in which the various key responsibilities which can influence product quality are allocated may vary with different manufacturers. These responsibilities should be clearly defined and delegated. The responsibilities placed on individuals should not be so extensive as to present any risk to quality. Suitably qualified people should be designated in writing to take up the duties of key personnel during the absence of the latter.

Key personnel should be provided with adequate supporting staff. People in responsible positions should have sufficient authority to discharge their responsibilities. In particular, the people responsible for

Quality Assurance functions should be able to carry out their defined functions impartially. An official responsible for production and Quality Assurance should not be the same person and be equal in level of authority. They should not report to each other; both officials should have individual responsibility to achieve the requisite quality. The duties of the official responsible for Quality Assurance function are wider than those which may be suggested by such terms as “Chief Analyst”, “Laboratory Head”, etc.

#### 4.1.2 RESPONSIBILITIES OF KEY PERSONNEL

Key personnel include:

- a natural person who resides in South Africa, responsible to SAHPRA for compliance with the requirements of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended
- a Managing Director,
- a person responsible for Production,
- a person responsible for Quality Assurance, and
- a Responsible Pharmacist that is responsible to:
  - SAHPRA for compliance with the requirements of the Medicines and Related Substances Act, 1965 (Act 101 of 1965), and the
  - Pharmacy Council for compliance with the requirements of the Pharmacy Act, 1974 (Act 53 of 1974)

##### 4.1.2.1 Managing Director

- The Managing Director of a company entitled to carry out the business of a pharmacist must be in line with Regulation 25 of the Pharmacy Act and the relevant sections of the Medicines Act —
- Shall undertake the overall administration of the pharmacy business, which includes but is not limited to the regulation of pharmacy matters, human resources, or matters relating to processes regarding medicines or scheduled substances including procedures and record keeping and shall be responsible to the Council for any act performed by or on behalf of such company or close corporation, including any omission to perform an act required to be performed

by or on behalf of such owner which may involve disciplinary action by the Council, unless he or she can satisfy the Council that the responsibility for such act rests upon the nominee, responsible pharmacist or a pharmacist other than him or herself employed by such company or close corporation;

- shall ensure that there is compliance with good pharmacy practice as published by the Council in rules;
- shall ensure that a responsible pharmacist is appointed for each pharmacy wherein or from which the company or close corporation conducts business;
- shall be part of the decision-making process affecting the pharmacy business;
- shall supervise every pharmacist responsible, appointed by the owner of a pharmacy business, if applicable;
- shall ensure that the pharmacy owner complies with all the conditions of:
  - ownership of such pharmacy business;
  - registration of the pharmacy;
- shall ensure that no person is appointed to perform any act falling outside the scope of practice of the category in which such person is registered or which he/she is not authorized to perform in terms of the Act;
- shall report in writing any non-compliance with sub-regulations 25(2), 25(3), 25(5) or 25(6) to the management of such pharmacy business and furnish Council with a copy thereof; and
- shall not introduce or carry out any instruction or order from management about the pharmacy business of the pharmacy owner which could amount to a contravention of legislation applicable to such pharmacy business.

#### 4.1.2.2 Head of Production

The Head of Production (HOP), in addition to his responsibilities (Chapter 2) for:

- production areas, equipment, operations and records;

- the management of production personnel;
- the manufacture of products in accordance with the appropriate Master Formulation; and for
- manufacturing instructions will have other responsibilities bearing on quality, which he should share or exercise jointly with the Head of Quality Control.

#### **4.1.2.3 Head of Quality Control (HQC)**

The Head of Quality Control should have the authority to establish, verify and implement all quality control procedures such as authority over quality decisions, oversight of testing and results, approval of quality control documentation, laboratory management, validation and method control etc

In some companies the Head of Quality Assurance oversees all the quality assurance arrangements and reports to senior management.

The Head of Quality Control may report to the Head of Quality Assurance and share some of the responsibilities with him. The person responsible for Quality Assurance should be part of the decision-making process in all matters that affect the quality of products including development, laboratory, storage, distribution, vendors and third-party contractors.

#### **4.1.2.4 Shared or joint responsibilities of the Head of Production and Head of Quality Control (Chapter 2)**

It is important that both direct and shared responsibilities (e.g., validation oversight, complaint investigations, product quality review, recall management, and self-inspection) are understood by those concerned.

#### **4.1.2.5 The Responsible Pharmacist contemplated in Regulation 25 (3) of the Pharmacy Act and the relevant sections of the Medicines Act must:**

- ensure that he or she continuously supervises the pharmacy in which he or she has been appointed
- have appropriate qualifications and experience in the services being rendered by such pharmacy

- ensure that people being employed in such pharmacy and who provide services forming part of the scope of pharmacy practice of a pharmacist are appropriately registered with the Pharmacy Council
- notify the Pharmacy Council immediately upon receiving knowledge that their services as responsible pharmacists have been or will be terminated
- take corrective measures in respect of deficiencies with regard to inspection reports of the Pharmacy Council or in terms of the Medicines Act; and
- in addition to the general responsibilities also –
  - ensure that unauthorized persons do not obtain access to medicines or scheduled substances or the pharmacy premises outside of normal trading hours,
  - establish policies and procedures for the employees of the pharmacy with regard to the acts performed and services provided in the pharmacy,
  - ensure the safe and effective storage and keeping of medicine or scheduled substances in the pharmacy under his or her direct personal supervision,
  - ensure correct and effective record keeping of the purchase, sale, possession, storage, safekeeping, and return of medicines or scheduled substances and ensure the required reporting of figures of scheduled substance purchases and sales are reported to the International Narcotics Control Board (INCB),
  - ensure that all batches manufactured and released for sale, supply or export meet the requirements in terms of the marketing authorization, GMP guidelines and other legal requirements,
  - ensure that batch release considers storage- and transport conditions of bulk- and final packed product, sampling processes- and QC analysis results and where relevant, the Transmissible Spongiform Encephalopathy (TSE) status of materials used during batch manufacture is compliant with the MA terms,

- ensure that all manufacturing and testing processes remain in a validated state,
- ensure that repackaging for parallel imports and distribution purposes is approved by SAHPRA,
- Ensure that audit reports comprehensively address general GMP requirements and include accurate descriptions of inspected areas, resulting in thorough and actionable documentation ensure that tamper-evident safety features are in place to prevent product tampering,
- the required technical agreements are in place, and
- self-inspection programme is active and current.
- initiate and co-ordinate all recall activities, which should involve the Head of Quality Management;
- ensure that a letter of authorization to communicate with Council, signed by the CEO, be submitted to SAHRPA;
- compile a letter of delegation of authority in their absence;
- control the manufacturing or distribution of medicines, scheduled substances or medical devices in terms of the provisions of the Medicines Act, 1965;
- ensure that there is compliance with Good Pharmacy Practice as published by the Pharmacy Council;
- be part of the decision-making process affecting the pharmacy business;
- supervise every pharmacist appointed by the owner of a pharmacy business and ensure that the pharmacy owner complies with all the conditions of –
  - ownership of such pharmacy business
  - registration of the pharmacy
- ensure that no person is appointed to perform any act falling outside the scope

of practice of the category in which such person is registered or which he/she is not authorised to perform in terms of the Pharmacy Act, 1974 (Act 53 of 1974);

- report in writing any non-compliance with the Pharmacy Act to the management of such pharmacy business and furnish Pharmacy Council with a copy thereof;
- not introduce or carry out any instruction or order of management with regard to the pharmacy business of the pharmacy owner which could amount to a contravention of legislation applicable to such pharmacy business; and
- be responsible to SAHPRA for compliance with the provisions of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) relating to the sale, control of the manufacturing and distribution of medicines, scheduled substances or medical devices.

**4.1.2.6 A Pharmacist or other legally authorized person is responsible for:**

- independently checking and signing each dispensed material and its mass or volume;
- checking and signing the addition of each material to the mix;
- checking and signing the identity of the bulk product and printed packaging material;
- checking and signing that each packaging line or station is clear of previous product, packaging components records or materials not required for the planned packaging operations, and that equipment is clean and suitable for use before any packaging is undertaken. These checks should be recorded and each packaging line opened and closed by a pharmacist, or other legally authorized person or quality control.
- the release for sale of the finished product. This release should include the completion of a check list which will ensure that all important release criteria have been met;
- handling scheduled substances in a pharmacy. Legal requirements regarding the documentation and control of scheduled medicines should be adhered to;

- the handling of complaints. A system should be established for handling complaints, which should include written procedures indicating the person(s) (e.g. pharmacist) responsible for receiving complaints. The person responsible must have appropriate knowledge and experience and the necessary authority to decide the action to be taken;
- with the handling of adverse events. A system should be established for handling the adverse events, which should include written procedures indicating the responsible person(s) (e.g. pharmacist) through whom the reports and activities are to be channeled. The person responsible must have appropriate knowledge and experience and the necessary authority to decide the action to be taken.

#### 4.1.2.7 Consultants

Consultants advising on the manufacture, processing, packing, or storage of medicines shall have sufficient education, suitable skills, training and experience, or any combination thereof, to advise on the subject for which they are retained. Records shall be maintained stating the name, address and qualifications of any consultants and the type and period of service they provide.

### 4.1.3 LEGAL ASPECTS

#### 4.1.3.1 Definitions

##### 4.1.3.1.1 Pharmacy Act (Act of 1974) & Regulations (Pharmacy Act)

Quoted for ease of reference – the original source takes precedence.

**“direct personal supervision”** means guidance and support provided by a pharmacist whilst physically present in a pharmacy, and in accordance with rules relating to good pharmacy practice published in terms of Section 35A(b) of the Act.

**“indirect personal supervision”** means guidance and support by a pharmacist to pharmacy support personnel in a primary health care clinic or any other facility as approved by the council, and in accordance with rules relating to good pharmacy practice published in terms of section 35A(b) of the Act.

**“manufacture”** means all operations including purchasing of raw material,

processing, production, packaging, releasing, storage, quality assurance, importation, exportation of medicine and scheduled substances and related control.

**“manufacturing pharmacy”** means a pharmacy wherein or from which some or all of the services as prescribed in regulation 16 of the Pharmacy Act relating to the Practice of Pharmacy are provided and which shall sell medicine only to a wholesale pharmacy or a community pharmacy or an institutional pharmacy or to persons who are authorized to purchase medicines in terms of the Medicines Act or to an organ of State (also refer to the regulations relating to the registration of persons and the maintenance of registers – GNR 1160 of 20 Nov. 2000).

**“nominee”** means the natural person appointed and registered as such by a company entitled to carry on the business of a pharmacist in terms of the Pharmacy Act and who shall be responsible for performing the duties as prescribed in Regulation 24 of Pharmacy Act (GNR 1160 of 20 Nov. 2000).

**“responsible pharmacist”** means a natural person who is a pharmacist and who shall be responsible to the Pharmacy Council for complying with all the provisions of the Pharmacy Act and other legislation applicable to services which specially pertain to the scope of practice of a pharmacist, and the legislation applicable to the pharmacy which is under his or her personal supervision and who is registered as such in terms of the Pharmacy Act.

#### **4.1.3.1.2 Medicines and Related Substances Act (Act 101 of 1965) & Regulations (Medicines Act)**

Quoted for ease of reference – the original source takes precedence.

**“manufacture”** means all operations including purchasing of material, processing, production, packaging, releasing, storage and shipment of medicines and related substances in accordance with quality assurance and related controls.

**“medicine”** means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in – (a) the diagnosis, treatment, mitigation, modification, or prevention of disease, abnormal physical, or mental state or the symptoms thereof in man; or (b) restoring, correcting, or modifying any

somatic or psychic or organic function in man, and includes any veterinary medicine.

“**public**” includes a section of the public concerned with manufacturing, dispensing, selling, or administering, or the issue of a prescription for medicines or a Scheduled substance.

“**responsible pharmacist**” means a responsible pharmacist as defined in the Pharmacy Act, 1974.

#### 4.1.3.2 Pharmaceutical Companies

The Pharmacy Act sets certain requirements for pharmaceutical companies, the Responsible Pharmacist and pharmacists e.g.:

- the company and the Responsible Pharmacist (who must be residing in the Republic) must be registered with the Pharmacy Council
- pharmaceutical operations must be conducted under the personal supervision of a responsible pharmacist whose name is displayed over the main entrance
- certain duties and responsibilities must be performed by pharmacists e.g. manipulation, preparation or compounding of medicines, manufacturing, and the furnishing of advice with regard to medicines, distribution and the sale of medicines.

The Medicines Act further sets requirements for the following activities:

- labelling of medicines, including package inserts
- records and registers for scheduled medicines
- sale of medicines only to registered and approved customers
- registration of medicines with SAHPRA
- adherence to standards
- reporting of adverse reactions and technical errors

- advertising of medicines
- Narcotic and Psychotropic substances control

#### 4.1.3.3 Narcotics or Psychotropics

South Africa is a co-signatory to the 1961 Convention on Narcotic Drugs and the 1971 Convention on Psychotropic Substances of the International Narcotics Control Board (INCB). The said Conventions as well as the Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended require that annual returns on all sales of narcotic and psychotropic substances be submitted to the INCB in Vienna, Austria, before 28 February each year.

Manufacturers and wholesalers must keep registers of quantities of specified Schedule 5 and Schedule 6 substances that were:

- held in stock on the 01 January and 31 December of each year;
- destroyed, lost or stolen;
- acquired by importation of the substance as a raw material or as contained in a preparation, local production of the raw material and local purchasing of the raw material;
- used in the production of any other specified Schedule 5, Schedule 6, Schedule 7 or any other scheduled substances;
- used in the manufacture of preparations (medicines) containing such substances; and sold locally or exported.

These registers must be balanced on the last day of March, June, September and December of each year.

Any person wishing to manufacture specified Schedule 5, Schedule 6, Schedule 7 or Schedule 8 substances and/ or medicines containing such substances, must apply for a manufacturing permit in terms of section 22A(9)(a)(i) of Act 101 of 1965. Manufacturing permits are required for the manufacturing of all Schedule 2 preparations containing the Schedule 6 substance Cathine ((+) Norpseudoephedrine).

Importers and exporters of any specified Schedule 5 and Schedule 6 substance and/ or medicines must be licensed in terms of section 22C(1)(b) of Act 101 of 1965. In addition, permits are required to import or export such substances and/ or medicines. Import or export permits are required for all Schedule 2 preparations containing the Schedule 6 substance Cathine ((+)-Norpseudoephedrine).

Any unusual loss or theft of narcotic or psychotropic substances and/ or medicines should immediately be reported to the South African Police Services and to the office of the Registrar of Medicines.

The SAHPRA prescribes the destruction of large quantities of Schedule 2 preparations [containing the Schedule 6 substance Cathine ((+)-Norpseudoephedrine)], specified Schedule 5 and Schedule 6 substances and/ or medicines in its "Guidelines for the Destruction of Schedule 5/ Schedule 6 medicines and substances". Destruction may only take place after a written authorization by SAHPRA has been issued, specifying the quantities indicated in the request.

#### 4.1.4 QUALIFICATIONS

Each person engaged in the manufacture, processing, packing or storage of a medicine shall have the education, training and experience or combination thereof, to enable that person to perform the assigned functions.

Training shall be in the particular operations that the employee performs and in general and specific GMP and written procedures as they relate to the employee's functions. Training in GMP shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to ensure that employees remain familiar with GMP requirements applicable to them.

Each person responsible for supervising the manufacture, processing, packing or storage of a medicine shall have the education, training and experience or combination thereof, to perform assigned functions in such a manner as to provide assurance that the medicine has the quality, safety, efficacy and bioavailability that it purports or is represented to possess.

There should be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing or storage of each medicine.

#### 4.1.5 TRAINING

All Production, Quality Assurance and Stores personnel and all other personnel (e.g. maintenance, service and cleaning staff) whose duties take them into manufacturing areas, or which bear upon manufacturing activities, should be trained in the principles of GMP and in the practice (and the relevant theory) of the tasks assigned to them.

Besides the basic training on the theory and practice of GMP, newly recruited personnel should receive training appropriate to the duties assigned to them. Continuing training should also be given and its practical effectiveness should be periodically assessed.

Written training programs should be available, approved by either the head of Production or the head of Quality Control, as appropriate. Training records should be kept.

Personnel working in areas where contamination is a hazard e.g. clean areas or areas where highly active, toxic, infectious or sensitizing materials are handled should be given specific training.

To assess the effectiveness of training, checks should be carried out to confirm that designated procedures are being followed by staff at all levels.

Visitors or untrained personnel should not be taken into the manufacturing areas. However, if deemed necessary, they should be given information in advance, particularly about personal hygiene and prescribed protective clothing which may be required. They should be closely supervised.

The concept of Quality Assurance and all the measures capable of improving its understanding and implementation should be fully discussed during the training sessions.

##### 4.1.5.1 Pharmacist Intern (Industry)

After formal university education, the Pharmacist Intern must undergo a one-year internship in Industry, being trained as prescribed by the Pharmacy Act.

##### 4.1.5.2 Pharmacist's Assistant

The Pharmacist's Assistant in Industry is required to pass the Pharmacy Council's examination which enables the assistant to perform certain functions of a Pharmacist as defined by the Pharmacy Act.

##### 4.1.5.3 Pharmacy Technician - means a natural person registered as such in terms of the Act.

#### 4.1.6 EXPERIENCE

In the South African context, the full spectrum of experience requirements described in Annex 16 of the PICS Guide to GMP forms part of the legal requirements implemented through this guideline. These include the process of batch certification, reliance on GMP assessments conducted by third parties, the handling of unexpected deviations, and the release of a batch. The individual authorized to certify and release medicinal products, namely the Responsible Pharmacist, is required to meet these experience expectations within the licensing framework established under Section 22C(1)(b) of the Medicines and Related Substances Act and must demonstrate working knowledge of all PIC/S Annexes to GMP Guide relevant to the licence category and authorized activities. In addition, the minimum experience and competency requirements for other key personnel involved in manufacture, testing, packaging or distribution are also defined by licence category to ensure that all personnel supporting the batch release

##### 4.1.6.1 Manufacturing Pharmacy for Sterile Pharmaceuticals (Non-Biologicals)

The Responsible Pharmacist of a Manufacturing Pharmacy that is involved in aseptic manufacturing and terminal sterilization of pharmaceutical products must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have more than five years' post community service experience in sterile manufacturing of pharmaceutical products and demonstrate an in-depth working knowledge of Annex 1 of the PIC/S GMP Guide (PE 009-17) including but not limited to a comprehensive knowledge of GMP, pharmaceutical quality systems, aseptic processing, terminal sterilization, cleanroom behaviors, environmental monitoring, media fills, contamination control strategies, batch release systems, manufacturing processes, applicable validation and qualification of pharmaceutical technology relevant to their organization.

The Head of Production of the manufacturing pharmacy that manufactures sterile products must have more than three years' supervision experience in the pharmaceutical sterile manufacturing environment. Such an individual must demonstrate knowledge of GMP, and pharmaceutical quality systems.

The Head of Quality Control of a manufacturing pharmacy that manufactures sterile pharmaceutical products must have an appropriate qualification in chemistry and/ or microbiology. Such an individual should have three years' experience in a senior or supervisory role in a pharmaceutical or other regulated quality control laboratory environment involving sterile products. He/ she must demonstrate a sound knowledge

of GMP, pharmaceutical quality systems, microbiological and analytical quality control, sterility assurance principles, and quality control processes applicable to sterile pharmaceuticals.

The Head of Quality Assurance of a manufacturing pharmacy that manufactures sterile pharmaceutical products must have an appropriate qualification in pharmacy or chemistry or microbiology and not less than five years' experience in senior quality roles, including oversight of sterile manufacturing operations. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies, quality risk management, and regulatory expectations applicable to sterile pharmaceutical.

#### **4.1.6.2 Manufacturing Pharmacy for Non-Sterile Pharmaceuticals**

The Responsible Pharmacist of a Manufacturing Pharmacy that manufactures non-sterile products including oral solid dosage (OSD), liquids, creams and ointments (LCO) must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have no less than five years' post community service experience in manufacturing pharmacy and demonstrate an in-depth working knowledge of Annex 9 of the PICS GMP Guide (PE 009-17) as well as demonstrate a comprehensive knowledge of GMP, pharmaceutical quality systems, manufacturing processes, environmental monitoring, batch release systems, contamination control strategies, manufacturing processes, applicable validation and qualification of pharmaceutical technology relevant to their organization.

The Head of Production of the manufacturing pharmacy that manufactures non-sterile products including oral solid dosage (OSD), liquids, creams and ointments (LCO) must have more than three years' supervision experience in the pharmaceutical manufacturing environment. Such an individual must demonstrate knowledge of GMP, pharmaceutical quality systems.

The Head of Quality Control of a manufacturing pharmacy that manufactures non-sterile pharmaceutical products must have an appropriate qualification in chemistry and/or microbiology. Such an individual should have three years' experience in a senior or supervisory role in a pharmaceutical or other regulated quality control laboratory environment involving non-sterile products. They must demonstrate a sound

knowledge of GMP, pharmaceutical quality systems, microbiological and analytical quality control, and quality control processes applicable to non-sterile pharmaceuticals.

The Head of Quality Assurance of a manufacturing pharmacy that manufactures non-sterile pharmaceutical products must have an appropriate qualification in pharmacy or chemistry or microbiology and not less than three years' experience in senior quality roles, including oversight of non-sterile manufacturing operations or comparable regulated industries. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies, quality risk management, and regulatory expectations applicable to non-sterile pharmaceutical.

#### **4.1.6.3 Manufacturing Pharmacy for Biologicals and Vaccines**

The Responsible Pharmacist of a Manufacturing Pharmacy that is involved in the manufacture of biologicals and/ or vaccines must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have no less than five years' post community service experience in the manufacture of biologicals and/ or vaccines including aseptic processing, handling of biological systems, and terminal sterilization where applicable. They must demonstrate an in-depth working knowledge of Annex 1 and Annex 2B of the PICS GMP Guide (PE 009-17), a comprehensive knowledge of GMP, pharmaceutical quality systems, aseptic processing, biological manufacturing principles including upstream and downstream processes, terminal sterilization where relevant, cleanroom behaviours, environmental monitoring appropriate to biological manufacturing, media fills applicable to aseptic biological operations, contamination control strategies including biosafety and bioburden control, manufacturing processes involving biological materials, and applicable validation and qualification of biological manufacturing technologies relevant to their organization.

The Head of Production of the manufacturing pharmacy that manufactures biologicals and/ or vaccines must have more than three years' supervision experience in the pharmaceutical or biological manufacturing environment, such an individual must demonstrate knowledge of GMP, pharmaceutical quality systems, aseptic and biological manufacturing processes including cell culture, fermentation, purification or similar biological production methods, and operational control of cleanroom and

biosafety-related production activities.

The Head of Quality Control of a manufacturing pharmacy that manufactures biologicals and/ or vaccines must have an appropriate science-based qualification (e.g., chemistry and/ or microbiology) and not less than three years' experience in a pharmaceutical or other regulated quality control laboratory environment involving vaccines or biological products, such an individual should have not less three years in a senior or supervisory role related to vaccines or biologicals.

The Head of Quality Assurance of a manufacturing pharmacy that manufactures biologicals or vaccines must have an appropriate qualification, e.g., pharmacy/ chemistry/ microbiology/ serology/ molecular biology/ haematology. They must have not less than three years' experience in senior quality roles, including quality oversight in the manufacture of vaccines or biologicals. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies including biosafety and viral safety considerations, quality risk management principles appropriate for biological products, batch release systems for biologicals, and regulatory expectations related to the manufacture of sterile and biological pharmaceutical products.

#### **4.1.6.4 Manufacturing Pharmacy for Medical Gases**

The Responsible Pharmacist of a Manufacturing Pharmacy that is involved in the filling, processing of medical gases must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have not less than three years' post community service experience in the manufacture of pharmaceutical products and shall demonstrate an in-depth working knowledge of Annex 6 of the PICS GMP Guide (PE-009-17), a comprehensive knowledge of GMP, pharmaceutical quality systems, medical gas production and distribution systems, applicable quality controls, contamination and cross-contamination prevention, validation and qualification of gas supply systems. They must also demonstrate knowledge of the appropriate handling and storage of compressed and cryogenic gases. They must have an understanding of relevant pharmacopeial requirements, and pharmaceutical technology applicable to medical gases and batch release processes applicable to medical gases.

The Head of Production of a manufacturing pharmacy involved in the manufacture,

filling and processing of medical gases must have an appropriate qualification and/ or experience in a pharmaceutical or regulated manufacturing environment. Such an individual should have not less than three years' experience in a production or supervisory role related to medical gases or comparable regulated manufacturing operations. The individual must demonstrate adequate knowledge of GMP, applicable pharmaceutical quality systems, and the production processes relevant to medical gases.

The Head of Quality Assurance of a manufacturing pharmacy involved in the processing and filling of medical gases must have an appropriate qualification in pharmacy, chemistry or microbiology and/or three years' experience in quality assurance or quality management roles related to medical gases or comparable regulated manufacturing operations. Such an individual must demonstrate adequate knowledge of GMP, pharmaceutical quality systems, quality risk management, documentation control, deviation and change management, and the scope of operations of the organization.

#### **4.1.6.5 Manufacturing Pharmacy for Radiopharmaceuticals**

The Responsible Pharmacist of a Manufacturing Pharmacy that is involved in the manufacture of radiopharmaceuticals must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have not less than five years' post community service experience in the manufacture of radiopharmaceuticals or pharmaceutical products and/ or shall demonstrate an in-depth working knowledge of Annex 3 of the PICS GMP Guide (PE-009-17), a comprehensive knowledge of GMP, pharmaceutical quality systems, the handling of radionuclides, applicable quality controls, contamination control strategies, manufacturing processes and applicable validation and qualification of pharmaceutical technology relevant to their organization.

The Head of Production must have not less than three years' supervision experience in the pharmaceutical manufacturing environment or a comparable regulated manufacturing environment. Such an individual must demonstrate knowledge of GMP and pharmaceutical quality systems.

The Head of Quality Control of a Manufacturing Pharmacy that is involved in the

manufacture of radiopharmaceuticals must have an appropriate qualification in chemistry or physics and/ or experience in a pharmaceutical, radiopharmaceutical, or other regulated quality control environment. Such an individual shall have not less than three years' experience in quality control or supervisory activities related to radiopharmaceuticals, sterile pharmaceuticals, or comparable regulated products. The individual must demonstrate adequate knowledge of GMP, pharmaceutical quality systems, applicable quality control testing for radiopharmaceuticals, the handling of radionuclides for quality control purposes, and release-related controls relevant to the scope of operations of the organization.

The Head of Quality Assurance of a Manufacturing Pharmacy that is involved in the manufacture of radiopharmaceuticals must have a science-based qualification in pharmacy/ chemistry/ microbiology/ physics and/ or not less than three years' experience in quality assurance or quality management roles within pharmaceutical manufacturing or comparable regulated operations. He/ she must have had an exposure to radiopharmaceutical or sterile product manufacturing where applicable. The individual must demonstrate adequate knowledge of GMP, pharmaceutical quality systems, quality risk management, contamination control principles, deviation and change management, and batch release oversight applicable to radiopharmaceuticals and the scope of operations of the organization.

#### **4.1.6.6 Manufacturing Pharmacy for Complementary Medicines**

The Responsible Pharmacist of a Manufacturing Pharmacy that manufactures complementary medicines must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have no less than five years' post community service experience in manufacturing pharmacy and demonstrate a comprehensive knowledge of GMP, pharmaceutical quality systems, manufacturing processes, environmental monitoring, batch release systems, contamination control strategies, manufacturing processes, applicable validation and qualification of pharmaceutical technology relevant to their organization.

The Head of Production of the manufacturing pharmacy that manufactures complementary medicines must have more than three years' supervision experience in the pharmaceutical manufacturing environment. Such an individual must demonstrate knowledge of GMP, pharmaceutical quality systems.

The Head of Quality Control of a manufacturing pharmacy that manufactures complementary medicines must have an appropriate qualification in chemistry and/or microbiology. Such an individual should have three years' experience in a senior or supervisory role in a pharmaceutical or other regulated quality control laboratory environment involving non-sterile and/or complementary products. He/ she must demonstrate a sound knowledge of GMP, pharmaceutical quality systems, microbiological and analytical quality control, and quality control processes applicable to non-sterile pharmaceuticals.

The Head of Quality Assurance of a manufacturing pharmacy that manufactures complementary medicines must have an appropriate qualification in pharmacy or chemistry or microbiology and not less than three years' experience in senior quality roles. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies, quality risk management, and regulatory expectations applicable to complementary medicines.

#### **4.1.6.7 Manufacturing Pharmacy for Packaging Activities**

The Responsible Pharmacist of a Manufacturing Pharmacy that is involved in primary and/ or secondary packaging of pharmaceutical products must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have no less than five years' post community service experience in manufacturing pharmacy and demonstrate a comprehensive knowledge of GMP, pharmaceutical quality systems, manufacturing processes, environmental monitoring, batch release systems, contamination control strategies, manufacturing processes, applicable validation and qualification of pharmaceutical technology relevant to their organization.

The Head of Production of the manufacturing pharmacy that is involved in primary and/ or secondary packaging of pharmaceutical products must have more than three years' supervision experience in the pharmaceutical manufacturing environment. Such an individual must demonstrate knowledge of GMP, pharmaceutical quality systems.

The Head of Quality Control of a manufacturing pharmacy that is involved in primary and/ or secondary packaging of pharmaceutical products must have an appropriate qualification in chemistry and/ or microbiology. Such an individual should have three

years' experience in a senior or supervisory role in a pharmaceutical or other regulated quality control laboratory environment involving pharmaceutical products. They must demonstrate a sound knowledge of GMP, pharmaceutical quality systems, microbiological and analytical quality control, and quality control processes applicable to pharmaceuticals.

The Head of Quality Assurance of a manufacturing pharmacy that is involved in primary and/ or secondary packaging of pharmaceutical products must have an appropriate qualification in pharmacy or chemistry or microbiology and not less than three years' experience in senior quality roles. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies, quality risk management, and regulatory expectations applicable to pharmaceuticals.

#### **4.1.6.8 Testing Activities**

The Responsible Person of a Pharmaceutical Testing Laboratory shall have no less than five years' experience in a senior or supervisory role in a pharmaceutical or other regulated quality control laboratory environment involving pharmaceutical products. They must demonstrate a sound knowledge of GMP, pharmaceutical quality systems, microbiological and analytical quality control, and quality control processes applicable to pharmaceuticals.

The Head of Quality Assurance of a Pharmaceutical Testing Laboratory must have an appropriate qualification in chemistry or microbiology and not less than five years' experience in senior quality roles. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies, quality risk management, and regulatory expectations applicable to pharmaceuticals.

#### **4.1.6.9 Manufacturing Pharmacy for Cannabis**

The Responsible Pharmacist of a Manufacturing Pharmacy that is involved in the manufacture of the cannabis pharmaceutical products must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have no less than five years' post community service experience in manufacturing pharmacy and demonstrate a comprehensive knowledge of GMP, pharmaceutical

quality systems, manufacturing processes, environmental monitoring, batch release systems, contamination control strategies, manufacturing processes, applicable validation and qualification of pharmaceutical technology relevant to their organization.

The Head of Production of the manufacturing pharmacy that is involved in the manufacture of the cannabis pharmaceutical products must have more than three years' supervision experience in the pharmaceutical manufacturing environment. Such an individual must demonstrate knowledge of GMP, pharmaceutical quality systems.

The Head of Quality Control of a manufacturing pharmacy that is involved in the manufacture of the cannabis pharmaceutical products must have an appropriate qualification in chemistry and/ or microbiology. Such an individual should have three years' experience in a senior or supervisory role in a pharmaceutical or other regulated quality control laboratory environment involving pharmaceutical products. He/ she must demonstrate a sound knowledge of GMP, pharmaceutical quality systems, microbiological and analytical quality control, and quality control processes applicable to pharmaceuticals.

The Head of Quality Assurance of a manufacturing pharmacy that is involved in the manufacture of the cannabis pharmaceutical products must have an appropriate qualification in pharmacy or chemistry or microbiology and not less than three years' experience in senior quality roles. The individual must demonstrate comprehensive knowledge of GMP, pharmaceutical quality systems, contamination control strategies, quality risk management, and regulatory expectations applicable to pharmaceuticals.

#### **4.1.6.10 Holder of Certificate of Registration (Importer or Exporter)**

The Responsible Pharmacist for the organization that acts as a Holder of Certificate of Registration must be registered as a practicing pharmacist with the South African Pharmacy Council. Such Pharmacist shall have no less than five years' post community service experience in the regulatory environment which can include relevant cumulative experience in pharmaceutical regulatory affairs, quality assurance, GMP compliance, batch release oversight, or manufacturing quality systems, where such experience is directly relevant to the importer/ exporter role and demonstrate comprehensive knowledge of GMP, and pharmaceutical quality systems.

## 4.1.7 HYGIENE

### 4.1.7.1 Personal Hygiene

High standards of personal cleanliness should be observed by all those concerned with production processes. The special requirements for Sterile Products are covered in Annex 1.

Personnel should be instructed to use the hand-washing facilities.

Detailed hygiene programmes should be established and adapted to the different needs within the factory. These should include instructions relating to the health, hygiene practices and clothing of personnel. These instructions should be understood and followed in a very strict way by every person whose duties take him into the manufacturing and control areas. They should be promoted by management and widely discussed during training sessions.

Eating, drinking, chewing and smoking, or the storage of food, drink, smoking materials and personal medication should not be permitted within manufacturing areas or in any other area where they might adversely influence product quality. No make-up or false lashes are permitted in primary areas due to increased risk to product contamination.

Direct contact should be avoided between the operators' hands and starting materials, intermediates and products (other than when they are in closed containers), as well as with any part of the equipment that comes into contact with the products.

### 4.1.7.2 Area Control

Requirements regarding personal hygiene and protective clothing apply to all people (including visitors, maintenance personnel, senior management and inspectors) entering production areas.

All people entering production areas should wear protective garments appropriate to the processes being carried out. The garments should be regularly and frequently cleaned and not worn outside the factory premises. Changing Rooms should be provided.

Only personnel authorized by supervisory personnel shall enter those areas of the buildings and facilities designated as limited-access areas.

#### 4.1.7.3 Medical Checks

Medical checks should be performed at pre-employment and at regular intervals thereafter. Steps should be taken to ensure that no person with a disease in a communicable form, or with open lesions on the exposed surface of the body, is engaged in the manufacture of medicinal products.

Visual inspection staff should pass an annual eye examination.

Staff should be required to report infections and skin lesions, and a defined procedure should be followed when they are reported. Supervisory staff should look for the signs and symptoms of these conditions.

## 5. REFERENCES

The following related documents are referenced:

- 5.1 PICS GMP Guideline

## 6. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces previous revision (v9). It will be reviewed on this timeframe or as and when the need arises.

## 7. APPENDICES

### 7.1 Appendix 1: Recognized Regulators

- PICS Members
- WHO
- ZAZIBONA

### 7.2 Appendix 2: Dosage group, product type and activity groupings

GMP certificates submitted for reliance must be approved by a recognized regulator for the same dosage group that they are applying for. Dosage groupings are:

- Oral soluble dosages
  - Tablets
  - Capsules
  - Powders
- Liquids, creams and ointments
  - Liquids
  - Creams
  - Ointments
  - Suppositories
- Medical gasses
- Small volume parenteral
- Large volume parenteral
- Aerosols

Applicants must ensure GMP certificates submitted for reliance must be approved by a recognized regulator for the same product type that they are applying for. Product types are:

- Cytotoxics
- Hormones
- Penicillin

- Biological or Vaccines
- Cephalosporins
- Gasses
- Veterinary
- Complementary medicines

Applicants must ensure GMP certificates submitted for reliance must be approved by a recognized regulator for the same activities that they are applying for. Applicants must only select activities that are relevant to them, the list of applicable activities are:

Holder of registration certificate

- Export
- Import
- Manufacturing
- Manufacture of Active pharmaceutical ingredient (API)
- Manufacture of Excipients
- Manufacture of Finished manufacturing product (FMP)
- Packer
- Distributor
- Laboratory

### 7.3 Appendix 3: Experience Requirements in terms of Annexure 1 to the License, S22C(1)(b) of the Medicines and Related Substances Act

AUTHORISED MANUFACTURING AND MATERIAL HANDLING ACTIVITIES				
1. MANUFACTURING ACTIVITIES	RP	HOP	HQA	HQC
<b>Sterile, Non-biological Manufacture (includes filling, but not cartoning or labelling)</b>				
Large volume parenteral products				
Small volume parenteral products	5	3	5	3
Other sterile dosage forms: <b>Peritoneal Dialysis solutions, Irrigation Solutions, Blood collection and storage solutions</b>				
<b>Non-sterile Manufacture</b>				
Tablets				
Capsules				
Liquids	5	3	3	3
Semi-solids (Creams & Ointments)				
Suppositories				
Other non-sterile dosage forms: <b>Aerosol and Lozenges</b>				
<b>Biological Manufacture</b>				
Vaccines				
Sera and other immunologicals	5	3	3	3
Blood and other blood products				
Other biological products:				
<b>Medical Gas Manufacture</b>	3	3	3	3
<b>Radioactive Medicines Manufacture</b>	5	3	3	3
<b>Complementary Medicines Manufacture</b>	5	3	3	3
<b>2. PACKAGING ACTIVITIES</b>				
Packaging of bulk products and labelling				
Re-labelling or redressing	5	3	3	3
Cartoning or secondary packaging				
	RPn/QC	-	QA	-

<b>3. TESTING ACTIVITIES</b>				
Analytical				
Microbiological				
Sterility	5	-	5	-
Stability				
Animal				
Other Testing Activities: <b>Chemical</b>				
<b>4. DISTRIBUTION ACTIVITIES</b>	RP			
Bulk distribution to wholesale pharmacies (Distribution of own products only)	3			
Fine distribution to retail pharmacies and others (Distribution of own products only)				