SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

SA GUIDE TO GOOD MANUFACTURING PRACTICE FOR MEDICINES

This document is intended to serve as guidance on the requirements for Good Manufacturing Practice (GMP) in South Africa. This guideline is not intended as an exclusive approach. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine. SAHPRA may make amendments in keeping with the knowledge which is current at the time of consideration of data accompanying applications for registration of medicines. Alternative approaches may be used but these must be scientifically and technically justified. SAHPRA is committed to ensure that all medicines gaining market approval will be of the required quality, safety and efficacy standards.

Version 1	Implementation	1997
Version 1	Chapter 9 (Validation) reformatted	January 2004
Version 2	Adoption of PIC/S GMP Guide of July 2004	January 2006
Version 3	Updates to Sections in line with PIC/S Guide updates	September 2008
	Released for comment	31 January 2009
Version 4	Amendments to Annexes 3 & 7	March 2009
	Released for comment	30 June 2009
Version 5	Consolidation of comments on versions 3 & 4	November 2010
Version 6	Adoption and acknowledgement of future adaptations of the PIC/S Guide to GMP	December 2017
Version 7	Amendments to section 3 and addition of Annex 17 & 18	July 2019

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1 INTRODUCTION

Good Manufacturing Practice (GMP) describes a set of principles and procedures that, when followed, ensure that medicines and related substances are of high quality, safety and efficacy. SAHPRA is a participating authority of the Pharmaceutical Inspection Cooperation Scheme (jointly known as PIC/S). PIC/S aims to develop international standards between countries and pharmaceutical inspection authorities, to provide harmonised and constructive co-operation in the field of GMP. PIC/S 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.

2 ADOPTION AND ADAPTATION OF THE PIC/S GMP GUIDE

Section 22C(1)(b) of the Medicines and Related Substances Act 1965 (Act 101 of 1965) specifies that manufacturers, importers, exporters, wholesalers and distributers of medicines and related substances must hold a licence. Section 35, Regulation 23, of the Act specifies that to hold a licence there must be the ability to comply with good manufacturing, wholesaling, or distribution practices as determined by the Authority. This allows for the Authority to determine manufacturing practices and the relevant code of GMP to be applied by manufacturers.

As a participating authority of PIC/S, SAHPRA requires that manufacturers, importers and exporters of medicines and related substances in South Africa meet the standards laid out in the PIC/S Guide to Good Manufacturing Practice (GMP). As such, SAHPRA has adopted the PIC/S Guide to GMP and all prospective adaptations as prescribed by the PIC/S. Annex 16 of the PIC/S guide to GMP pertains to country specific requirements and should be replaced with the SA specific Annex 16 as detailed in Section 4 of this guideline. Any reference to the “Responsible Person” will be equivalent to “Responsible Pharmacist” within the South African context.

The Guide for medicinal products is divided into two parts and a number of annexes:

- Guide to Good Manufacturing Practice for Medicinal Products – Introduction
- Guide to Good Manufacturing Practice for Medicinal Products – Part I
- Guide to Good Manufacturing Practice for Medicinal Products – Part II
- Guide to Good Manufacturing Practice for Medicinal Products – Annexes

There is a different code of GMP for Human Blood:

- Guide to Good Manufacturing Practice for Plasma Establishments

A different system, known as conformity assessment, is used to ensure that medical devices are of high quality, safety and performance.

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 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, 1965 (Act 101 of 1965).

3.2 GMP approval guidance

GMP approval guidance for sites involved in the manufacture of products can be found below. Please 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 (Appendix 1) AND
- 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 (Appendix 2) AND
- The product type applied for is the same as the product type approved by the recognised regulator (Appendix 2) AND
- The activities applied for by the applicant are the same activities that have been approved by the recognised regulator (Appendix 2)

4 ANNEX 16 – SOUTH AFRICAN SPECIFIC REQUIREMENTS: ORGANISATION & PERSONNEL

4.1 PRINCIPLES

The company must have an organisation chart. The organogram should clearly indicate the reporting lines and level of responsibility, and should be authorised and be 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 rely upon people. For this reason, there should be sufficient personnel at all levels with the ability, training, experience and, where necessary, the professional / technical qualifications and managerial skills appropriate 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 Good Manufacturing Practice (GMP) that affect them and receive initial and continuing 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 any one individual should not be so extensive as to present any risk to

quality. Suitably qualified persons 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. Persons in responsible positions should have sufficient authority to discharge their responsibilities. In particular, the person responsible for Quality Assurance should be able to carry out his defined functions impartially. The person responsible for Production and the person responsible for Quality Assurance, should be different persons of equal level of authority, neither of whom should be responsible to the other, but who both have a responsibility for achieving the requisite quality. The duties of this person responsible for Quality Assurance are wider than those which may be suggested by such terms as "Chief Analyst", "Laboratory Head", etc.

4.2 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).
- the person responsible for Production,
- the person responsible for Quality Assurance, and
- the Responsible Pharmacist, 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)

Head of Production

The Production Manager, in addition to his responsibilities (Chapter 2) for

- production areas, equipment, operations and records
- the management of production personnel; and for
- the manufacture of products in accordance with the appropriate Master Formulation and Manufacturing instructions,

will have other responsibilities bearing on quality, which he should share or exercise jointly with the person responsible for Quality Control.

Head of Quality Control

The person responsible for Quality Control should have the authority to establish, verify and implement all quality control procedures (Chapter 2).

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

The person responsible for Quality Control may report to the Quality Assurance Manager 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.

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 are understood by those concerned.

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 in fact 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 persons 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 his/her services as responsible pharmacist 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 unauthorised 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;
- initiate and co-ordinate all recall activities, which should involve the head of Quality Management;
- ensure that a letter of authorisation to communicate with Council, signed by the CEO, be submitted to the SAHRPA;
- compile a letter of delegation of authority in her / his 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, if applicable
- 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.

A **Pharmacist or other legally authorised 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, other legally authorised 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;
- dealing with complaints. A system should be established for dealing with complaints, which should include written procedures indicating the responsible person(s) (e.g. pharmacist) through whom the complaints are to be channeled. The responsible person must have appropriate knowledge and experience and the necessary authority to decide the action to be taken;
- dealing with adverse events. A system should be established for dealing with 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 responsible person must have appropriate knowledge and experience and the necessary authority to decide the action to be taken.

Consultants

Only in exceptional circumstances should persons engaged part time or in a consultative capacity be appointed to key positions. Consultants advising on the manufacture, processing, packing, or storage of medicines shall have sufficient education, 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.

4.3 LEGAL ASPECTS

4.3.1 Definitions

4.3.1.1 Pharmacy Act (Act 53 of 1974) & Regulations (Pharmacy Act)

Quoted for ease of reference – the original source takes precedence

“direct personal supervision” means guidance and support by a pharmacist whilst physically present in a pharmacy

“indirect personal supervision” means guidance and support by a pharmacist in accordance with a standard operating procedure approved by the Pharmacy Council whilst absent from the pharmacy.

“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 authorised 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 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.

4.3.1.2 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

4.3.2 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 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

4.3.3 Narcotics/Psychotropics

South Africa is 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) 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 1st of January and the 31st of December 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 each year.

Any person wishing to manufacture specified Schedule 5, Schedule 6, Schedule 7 of 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 authorisation by SAHPRA has been issued, specifying the quantities indicated in the request.

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

4.5 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 sensitising 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.

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.

Pharmacist's Assistant (Industry)

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.

4.6 HYGIENE

4.6.1 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.

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.

4.6.2 Area Control

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

All persons 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 authorised by supervisory personnel shall enter those areas of the buildings and facilities designated as limited-access areas.

4.6.3 Medical Checks

Medical checks should be performed 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 Appendix 1 – Recognised regulators

Country	Organisation	Acronym
Argentina	Instituto Nacional de Medicamentos (*National Institute of Drugs*)	INAME
Australia	Therapeutic Goods Administration	TGA
Austria	Austrian Agency for Health and Food Safety	AGES
Belgium	Agence Fédérale des Médicaments et des Produits de Santé (*Federal Agency for Medicines and Health Products*)	AFMPS
Canada	Health Canada - Regulatory Operations and Regions Branch (*Sante Canada - Direction générale des opérations réglementaires et des régions*)	RORB
Chinese Taipei	Taiwan Food and Drug Administration	TFDA
Croatia	Agency for Medicinal Products and Medical Devices of Croatia (*Agencija za lijekove i medicinske proizvode*)	HALMED
Cyprus	Pharmaceutical Services	CyPHS
Czech Republic	Státní Ústav pro Kontrolu Léčiv (*State Institute for Drug Control*)	SUKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv (*Czech Institute for State Control of Veterinary Biologicals and Medicines*)	ISCVBM
Denmark	Danish Medicines Agency	DKMA
Estonia	State Agency of Medicines	SAM
Finland	Finnish Medicines Agency	FIMEA

France	Agence nationale de sécurité du médicament et des produits de santé (*French National Agency for Medicines and Health Products Safety)*	ANSM
	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (*French Agency for Food, Environmental & Occupational Health Safety*)	ANSES
Germany	Bundesministerium fur Gesundheit (*Federal Ministry of Health*)	BMG
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten (*Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices*)	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων (*National Organization for Medicines*)	EOF
Hong Kong SAR	Pharmacy and Poisons Board of Hong Kong	PPBHK
Hungary	National Institute of Pharmacy and Nutrition (NIPN)	NIPN
Iceland	The Icelandic Medicines Agency	IMA
Indonesia	National Agency for Drug and Food Control	NADFC
Iran	Iran Food and Drug Administration	IFDA
Ireland	Health Products Regulatory Authority	HPRA
Israel	Institute for the Standardization and Control of Pharmaceuticals	ISCP
Italy	Agenzia Italiana del Farmaco	AIFA
Japan	Ministry of Health, Labour and Welfare	MHLW
	Pharmaceuticals and Medical Devices Agency	PMDA
	Japanese Prefectures	-
Korea (Republic of)	Ministry of Food and Drug Safety	MFDS
Latvia	Zāļu Valsts Aģentūra (*State Agency of Medicines*)	ZVA
Liechtenstein	Amt für Gesundheit (*Office of Healthcare*)	AG
Lithuania	State Medicines Control Agency	SMCA
Malaysia	National Pharmaceutical Regulatory Agency	NPRA

Malta	Medicines Authority Malta	MAM
Mexico	Federal Commission for the Protection Against Sanitary Risks (*Comision Federal para la Proteccion contra Riesgos Sanitarios*)	COFEPRIS
Netherlands	Inspectie Gezondheidszorg en Jeugd (*Health and Youth Care Inspectorate*)	IGJ
New Zealand	Medicines and Medical Devices Safety Authority	Medsafe
Norway	Norwegian Medicines Agency	NOMA
Poland	Chief Pharmaceutical Inspectorate	CPI
Portugal	Autoridade Nacional do Medicamento e Produtos de Saúde IP (*National Authority of Medicines and Health Products IP*)	INFARMED IP
Romania	National Agency for Medicines and Medical Devices	NAMMD
Singapore	Health Sciences Authority	HSA
Slovak Republic	State Institute for Drug Control	SIDC
Slovenia	Agency for Medicinal Products and Medical Devices	JAZMP
South Africa	Medicines Control Council/South African Health Products Regulatory Authority	MCC/SAHPRA
Spain	Agencia Española de Medicamentos y Productos Sanitarios (*Spanish Agency for Medicines and Medical Devices*)	AEMPS
Sweden	Medical Products Agency	MPA
Switzerland	Swiss Agency for Therapeutic Products	Swissmedic
Thailand	Food and Drug Administration	Thai FDA
Turkey	Turkish Medicines and Medical Devices Agency	TMMDA
Ukraine	State Service of Ukraine on Medicines and Drugs Control	SMDC
United Kingdom	Medicines and Healthcare Products Regulatory Agency	MHRA
	Veterinary Medicines Directorate	VMD
United States of America	United States Food and Drug Administration	US FDA
WHO PQ	World Health Organisation Prequalification	WHO PQ
Zazibona	Zazibona work sharing agreement	Zazibona

6 Appendix 2 – Dosage, product type and activity groupings

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

- Cytotoxics
- Hormones
- Penicillin
- Biological/Vaccines
- Cephalosporins
- Gasses
- Veterinary
- Complementary medicines

Applicants must ensure GMP certificates submitted for reliance must be approved by a recognised 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 section

- Manufacture Active pharmaceutical ingredient (API)
- Manufacture Finished manufacturing product (FMP)
- Packer
- Distributor
- Laboratory

5 UPDATE HISTORY

Date	Reason for update	Version & publication
1997	PIC/S Guide to GMP Adopted	v1 1997
Jan 2004	Chapter 9 (Validation) reformatted	v1 January 2004
Jan 2006	Adoption of PIC/S GMP Guide of July 2004	v2January 2006
Sep 2008	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)	v3 September 2008
Mar 2009	Amendments to Radiopharmaceuticals (Annex 3), Herbal Medicinal Products (Annex 7)	v4 March 2009
1 Nov 2010	Consolidation and implementation of comments on versions 3 and 4)	v5 Nov 2010
Dec 2017	• Adoption of PIC/S Guide to Good Manufacturing Practice (GMP) – 1 January 2017, PE 009-13 • Amendment of Introduction • Deletion of Chapters 1 – 9, Annexes 1 – 15 and 17 – 20, Addendums I and II and Glossary • Inclusion of Section 2 Adoption and Adaptation of PIC/S GMP Guide, Section 3 Regulatory Processes and moving of Annex 16 from version 5 to Section 4	v6 Dec 2017

Date	Reason for update	Version & publication
July 2019	• 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	v7 July 2019