GMP Clearance Guideline Papua New Guinea

1. Introduction

The Medicines and Cosmetic Act 1999 and the said Regulation 2002 with the Quality Manual for GMP Inspectorate set the basis for enforcement of the GMP Clearance Guideline.

The quality Manual for GMP Inspectorate covers GMP Clearance through Documentation Review as one of the scope of activities under the Compliance, Licensing and Inspection Unit of the Pharmaceutical Services Standards Branch.

It is an administrative requirement of the Pharmaceutical Services Standards Branch to implement standard such as the enforcement of the current Good Manufacturing Practice and collaboratively perform the administrative functions of the Pharmacy Board of Papua New Guinea.

The National Medicines Policy 2014 intends to provide a framework and direction for co-ordinating activities in the Pharmaceutical sector in Papua New Guinea. Under 3.2.3. of the National Medicines Policy 2014, it emphasises on the establishment of a Quality Assurance System for Medicines that are imported in to the country. This requires improved regulatory and quality assurance frameworks; hence, GMP Clearance through Documentation Review is on of a regulatory quality assurance framework that will pave way to ensure quality assured medicines are procured and distributed through the medical supply chain.

The PICS guide to Good Manufacturing Practices and the WHO GMP Standard will additionally be used as reference for GMP Clearance.

2. Purpose

2.1. The GMP Clearance Guideline intends to provide information and guidance to the local sponsors on the process involved and evidences required for the purpose of obtaining and maintaining Good Manufacturing Practices (GMP) Clearance for the steps of Medicinal Products including the active Pharmaceutical Ingredient (API) and biologics that are carried out overseas.

2.2. The guideline also describes the approaches and criteria that the Pharmacy Board will undertake to prequalify overseas based manufacturers by taking local sponsors (importers) accountable as agents of the overseas manufacturers as a pre-requisite for seeking marketing authorization in PNG for the Products produced by overseas manufacturers.

2.3. This GMP Clearance Guideline is also in support of the Product Registration System of Papua New Guinea. This will ensure that documentary evidence provided by that overseas based manufacturers are prequalified and compliant to the international harmonized standards such as the PICs.

The use of this GMP Clearance Guideline should be used concurrently with the Quality Manual for GMP Inspectorate and the approved Standard Operating Procedure for GMP Clearance.

What is GMP Clearance?

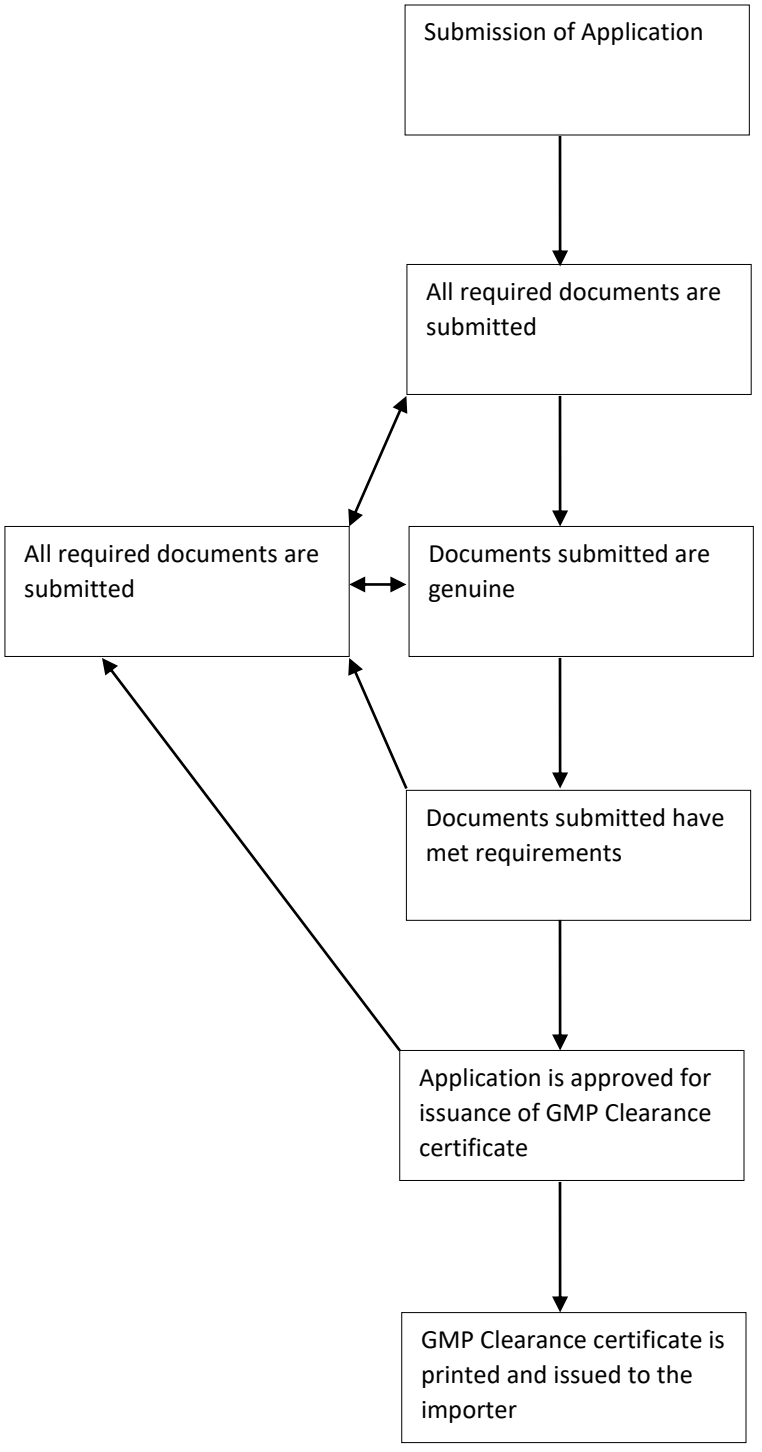
GMP Clearance is a pre-requisite for product registration in Papua New Guinea. It is a regulatory process whereby the local sponsor seeks to obtain Good Manufacturing Practice Clearance for an overseas manufacturing site used in the manufacture of medicine, Active Pharmaceutical Ingredient (AP) used in medicine intended to supply in Papua New Guinea.

Over view of GMP

Good Manufacturing Practice is a term used internationally to describe set of principles and procedures that manufacturers of medicines and biologics must follow and comply in order and to ensure that the medicines and product produced are of quality.

GMP Clearance will be performed by the Inspectorate Unit and mostly focus on Documentation Review.

Figure 2: Flow chart showing the GMP Clearance Process done by the Inspectorate Unit



Application is submitted by the registered importer of the product representing the manufacturer

Application is checked by the registration and licensing officer to ensure that the required documents are submitted

Application is assigned to a pharmaceutical inspector by the TA-CLI to do quality assessment of the documents submitted to verify that the documents are genuine. The assessment results are verified by TA-CLI

Application is endorsed by the Medicines Evaluation Committee which is chaired by the Manager-Pharmaceutical Services Standards for approval of license. The Products registration unit is informed the GMP Clearance status of the manufacturer

Application is approved for issuance of GMP Clearance certificate for the manufacturer to the registered importer by the Pharmacy Board

Once approved the application is given to the registration and licensing officer to print and issue the GMP Clearance certificate

The GMP Clearance through Documentation Review will be conducted in three phases in order to support the Product Registration System.

GMP Clearance for Product Registration in Phase I

3.0. Documentary Evidence to be submitted

3.1. Cover letter to the Licensing Authority requesting GMP Clearance of manufacturer

3.1.1. The letter should be written to the Department of Health requesting for GMP Clearance of its manufacturer. The letter has to be signed by the recognized personnel as that stated in the import application form. There should be consistency with the address of the local sponsor.

3.2. GMP Clearance Application Form completely filled, signed and stamped.

3.2.1. There will be an approved GMP Clearance Form to be filled out appropriately and should be signed by the recognized personnel and stamped by the commissioner of oaths.

3.3. Proof of Payment (Attached Original copy)

3.3.1. Payment of the GMP Clearance Application form has to be done at the Finance Department. No cash handling will be done in the office.

3.4. Registration status of the Sponsor (eligibility-if currently registered with the Pharmacy Board of Papua New Guinea).

3.4.1. It is a pre-requisite that the local sponsor must be currently registered with the Pharmacy Board of Papua New Guinea in-order to conduct pharmaceutical business in the country.

3.5. Letter of Authorization (LoA) from the manufacturer to the local sponsor. Format of the LoA will be given in the annex.

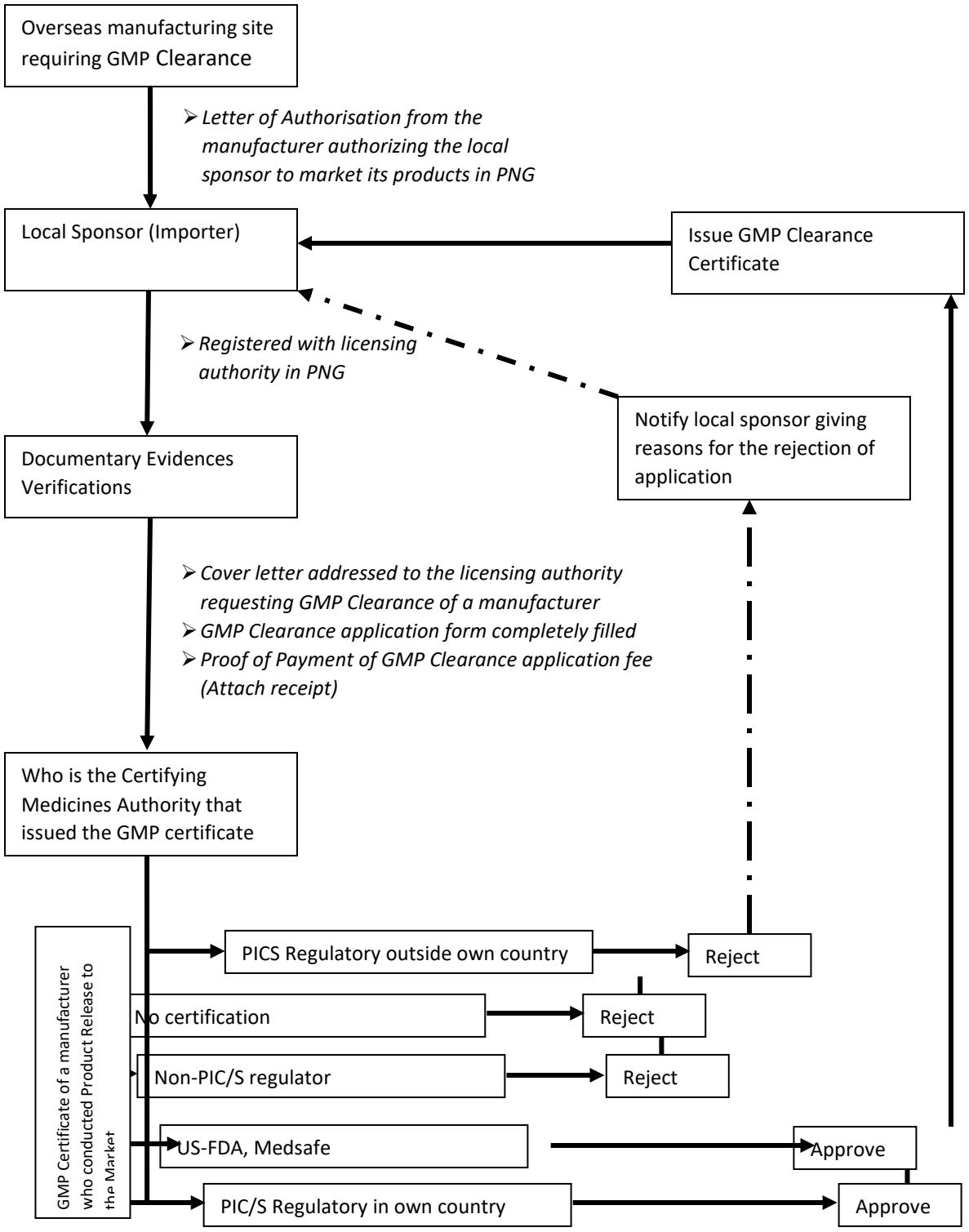
3.5.1. LoA is important as it will provide clarity to the Department of Health whether the business arrangement between the manufacturer and the local sponsor is valid of not. In the LoA, the product lines have to be clearly stated and the validity of the business arrangement must be clearly spelt out.

3.6. GMP Certificate from the product release site.

3.3.1. GMP Certificate from the product release site has to be provided. The scope of the product lines has to be clearly written in English and the stamp of the regulatory authority that approved it has to be clear. The GMP Certificate has to be valid. If about to be expired, it would be the responsibility of the local sponsor to arrange with the manufacture to get an authorization from the regulatory of that manufacturing country formally inform the Department of Health on the status of the GMP Certificate and when the approved GMP Certificate would be provided.

Procedure for Phase I

Figure 3: Phase I of the Overseas GMP Clearance Process



GMP Clearance Requirements for Product Registration Phase II

4.0. Documentary evidence to be submitted

4.1. Covering letter to the licensing authority requesting GMP Clearance of the Manufacturer (s).

4.1.1. The letter should be written to the Department of Health requesting for GMP Clearance of its manufacturer. The letter has to be signed by the recognized personnel as stated in the import application form. There should be consistency with the address of the local sponsor.

4.2. GMP Clearance Application Form completely filled, signed and stamped.

4.2.1. There will be an approved GMP Clearance Form to be filled out appropriately and should be the recognized personnel and stamped by the commissioner of oaths.

4.3. Proof of Payment (Attached original copy)

4.3.1. Payment of the GMP Clearance Application form has to be done at the Finance Department. No cash handling will be done in the office.

4.4. Registration status of the Sponsor (eligibility-if currently registered with the Pharmacy Board of Papua New Guinea.

4.4.1. It is a pre-requisite that the local sponsor must be currently registered with Pharmacy Board of Papua New Guinea in order to conduct Pharmaceutical business in the country.

4.5. Letter of Authorization (LoA) from the manufacturer to the local sponsor. Format of the LoA will be given in the annex.

4.5.1. LoA is important as it will provide clarity to the Department of Health whether the business arrangement between the manufacturer and the local sponsor is valid or not. In the LoA, the product lines have to be clearly stated and the validity of the business arrangement must be clearly spelt out.

4.6. GMP Certificate from the product release site.

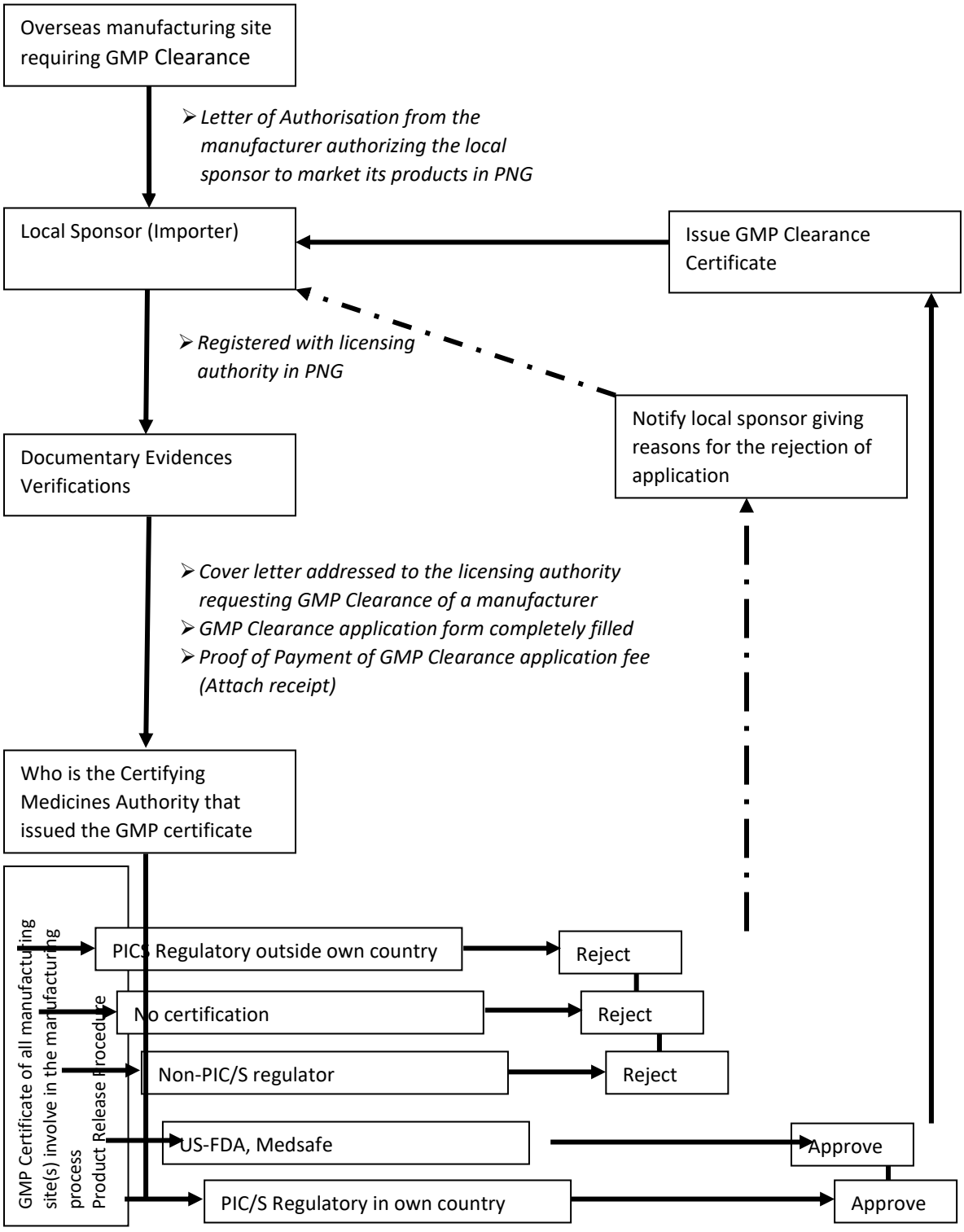
4.6.1. GMP Certificate from the product release site has to be provided. The scope of the product lines has to be clearly written in English and the stamp of the regulatory authority that approved it has to be clear. The GMP Certificate has to be valid.

f about to be expired, it would be the responsibility of the local sponsor to arrange with the manufacturer to get an authorization from the regulatory of that manufacturing country formerly inform the Department of Health on the status of the GMP Certificate would be provided.

4.7. Product Release Procedure

4.7.1. The procedure is needed to identify the release parameter and release specification. Review against compendial/pharmaceutical monographs. Check the evidence document. Eg…CoA, Batch Analysis.

Figure 4: Phase II of the Overseas GMP Clearance Process



Procedure for Phase II

GMP Clearance Requirements for Product Registration Phase III

5.0. Documentary Evidence to be submitted

5.1. Cover letter to the Licensing Authority requesting GMP Clearance of a manufacturer

5.1.1. The letter should be written to the department of health requesting for GP Clearance of its manufacturer. The letter has to be signed by the recognized personnel as that stated in the import application form. There should be consistency with the address of the local sponsor.

5.2. GMP Clearance Application Form completely filled, signed and stamped.

5.2.1. There will be an approved GMP Clearance Form to be filled out appropriately and should be signed by the recognized personnel and stamped by the commissioner of oaths.

5.3. Proof of payment (Attached original copy)

5.3.1. Payment of the GMP Clearance Application form has to be done at the Finance Department. No cash handling will be done in the office.

5.4. Registration status of the Sponsor (eligibility-if currently registered with the Pharmacy Board of Papua New Guinea)

5.4.1. It is a pre-requisite that the local sponsor must be currently registered with the Pharmacy Board of Papua New Guinea in-order to conduct pharmaceutical business in the country.

5.5. Letter of Authorization (LoA from the manufacturer to the local sponsor. Format of the LoA will be given in the annex.

5.5.1. LoA is important as it will provide clarity to the Department of Health whether the business arrangement between the manufacturer and the local sponsor is valid or not. In the LoA, the product lines have to be clearly stated and the validity of the business arrangement must be clearly spelt out.

5.6. GMP Clearance from the product release site.

5.6.1. GMP Certificate from the product release site has to be provided. The scope of the product lines has to be clearly written in English and the stamp of the regulatory authority that

approved it has to be clear. The GMP Certificate has to be valid. If about to be expired, it would be the responsibility of the local sponsor to arrange with the manufacturer to get an authorising form the regulatory of that manufacturing country to formerly inform the Department of Health on the status of the GMP Certificate and when the approved GMP Certificate would be provided.

5.7. Site Master file

5.7.1. The site master file should comply with the WHO site master file requirements.

5.8. Product Quality Review

Regular periodic or rolling quality reviews of all authorized medical products including export only products should be conducted with the objective of verifying the consistency of the exisiting process, the appropriateness of current specifications for both starting materials and finished product, to highlight any trends and to identify product and process improvements. Such reviews should normally be conducted and documented annually, taking in to account previous reviews, and should include at least:

(i) A Review of starting materials including packaging materials used in the product, especially those from new sources and in particular the reviews of supply chain traceability of active substances;
(ii) A review of critical in-process controls and finished product results;
(iii) A review of all batches that failed to meet established specification(s) and their investigation;
(iv) A review of all significant deviations or non-conformances, their related investigations, and the effectiveness of resultant corrective and preventive actions taken;
(v) A review of all changes carried out to the processes or analytical methods;
(vi) A review of Marketing Authorisation variations submitted, granted or refused, including those for third country (export only) dossiers;
(vii) A review of the results of the stability monitoring programme and any adverse trends;
(viii) A review of all quality-related returns, complaints and recalls and the investigations performed at the time;
(ix) A review of adequacy of any other previous product process or equipment corrective actions;
(x) For new Marketing Authorisations and variations to Marketing Authorisations, a review of post -marketing commitments;
(xi) The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gasses, etc;

5.9. History of Compliance

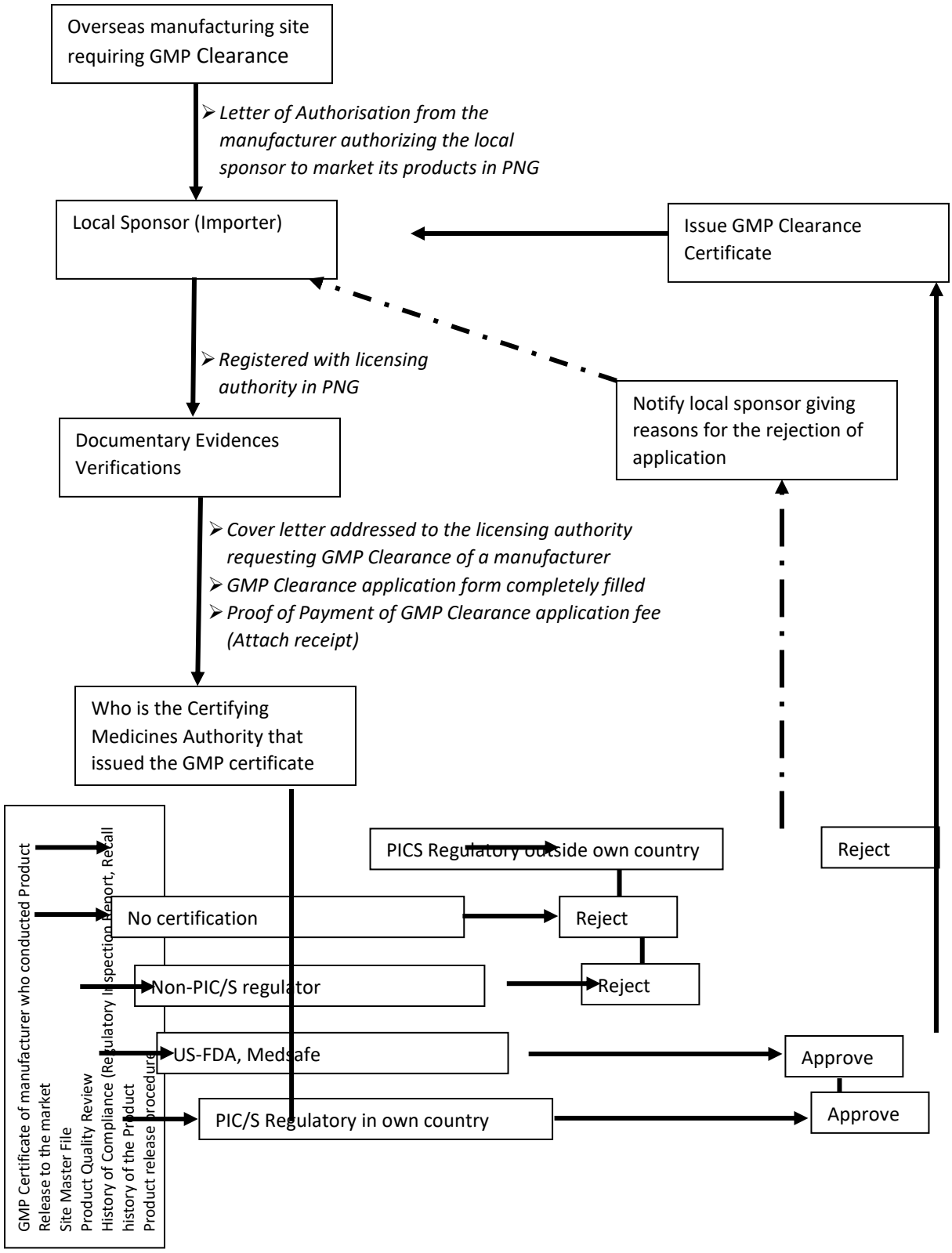
5.9.1. Regulatory inspection report; Recall history of the product.

5.10. Product Release Procedure

5.10.1. The procedure is needed to identify the release parameter and release specification. Review against compendial/pharmaceutical monographs. Check the evidences documents. eg… CoA, Batch Analysis

Procedure for Phase III

Figure : Phase III of the Overseas GMP Clearance Process



GMP Clearance

The data base

Clearance expiry

The period of GMP Clearance given to a manufacturing site is normally a maximum of the certificate expiry plus 6 months; or three years plus 6 months from the date of inspection.

The additional 6 months period facilitates the completion and assessment of Re-inspections/audits.) The expiry period may be reduced based on a risk assessment or other justification. Where a GMP Clearance has expired, or is about to expire, a new GMP Clearance application must be submitted for assessment.

5.0. Responsibilities of Sponsors (adopted from TGA GMP Clearance guideline)

The sponsors (importers) of medical products in PNG have the responsibility to adhere to the regulatory requirements set by the Department of Health of the Independent state of Papua New Guinea. For the purposes of issuing GMP Clearance for Overseas-based manufacturers, sponsors are required to submit documentary evidences to the Pharmaceutical Inspectorate Team at the Pharmaceutical Services Standards Branch of the Department of Health. The documentary evidences being provided will assist the Inspectorate team to clear the overseas manufacturing sites. Clearance of overseas manufacturing sites is very essential prerequisite to Products Registration Unit for the purposes of Registration of medicinal products prior to the issuance of marketing authorization to the sponsor. The sponsors are responsible for all the overseas manufacturing sited nominated in their GMP clearance applications at all times. Therefore, each local sponsor (importer) is required to:

5.1. Apply to the licensing authority expressing its intention to clear an overseas-based manufacturer of which it acts as an agent (sponsor) in PNG.

5.2. Provide relevant documentary evidences specified in this guideline of GMP Clearance SOPs, and/or as and when requested by the Inspectorate Unit (CLI) to assist in the GMP Clearances for the purpose of obtaining the marketing authorization to supply medicinal products in PNG.

5.3. Always maintain record or evidences of GMP Compliance of all its nominated overseas manufacturing sites used in the manufacture of the registered of listed medicines.

5.4. Advise Department of Health/Pharmacy Board of Papua New Guinea any significant changes to the manufacturing site, quality management systems (QMS), products or product range (these are changes that could potentially affect GMP compliance). These changes may also require a variation application for the sponsor’s listing or registration on the PNG Resister of Products.

5.5. Monitor regulatory actions taken by any competent overseas regulatory agency (i.e. recalls, unacceptable inspection findings, warning letters) that involve any overseas manufacturers used by the sponsor.

5.6. Notify the Department of Health/Pharmacy Board of Papua New Guinea as soon as possible should the overseas manufacturing site is no longer used and is not intended to be maintained as an alternative manufacturer.

6.0. Responsibilities of the GMP Inspectorate

The responsibility of the GMP Inspectorate Unit of the Pharmaceutical Services Standards Branch is to:

6.1. Set policies, standard, and evidence and /or criteria necessary for GMP Clearance in the country.

6.2. Receive and conduct through assessments of Documentary Evidences being provided by sponsors(s) of overseas-based manufacturing sites for the purpose of GMP Clearance.

6.3. Request additional information as and when required

6.4. Recommend to the Pharmacy Board of Papua New Guinea Licensing Authority and applicant from a sponsor of an overseas-based manufacturing site to be issued or reject issue of GMP Clearance to support Products Registration in PNG.

6.5. Maintain the GMP Clearance Database of all manufacturers.

6.6. Conduct on-site GMP inspections as and when necessary

6.7. Review GMP Clearance guidelines, SOPs and Policies as and when required to align with current best practices of Good Manufacturing Practices.