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Regulatory Requirements for Pharmaceutical Product Registration in Zambia

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Abstract

There is a significant burden of diseases in Zambia and its neighboring countries, such as malaria, HIV/AIDS, and other ailments. These health challenges necessitate a high consumption of pharmaceutical products. Currently, the majority of essential health drugs in Zambia are imported from outside of Africa. This reliance on external sources presents an opportunity for new investments in the local manufacturing of pharmaceutical products. Although Zambia may not be the largest pharmaceutical market in Africa, it possesses several advantages that make it an attractive prospect for investors. The country's demand for pharmaceutical products is consistently triggered by the prevalence of diseases, creating a stable market. By establishing pharmaceutical manufacturing facilities within Zambia, companies can cater to this demand more efficiently and reduce the country's dependence on imported medications. The health sector in Zambia is currently grappling with a substantial human resource crisis, which greatly hampers its ability to deliver essential healthcare services to the population. The shortage of healthcare professionals and the resulting strain on the healthcare system emphasize the need for increased investments in the pharmaceutical sector. By expanding local manufacturing capabilities, Zambia can improve access to essential health drugs and enhance the overall healthcare infrastructure. The primary focus of the study mentioned is to shed light on the regulatory requirements for drug registration in Zambia. Understanding and complying with these requirements are crucial for gaining easy market access and conducting pharmaceutical business in the country. The study encompasses various aspects, including the organizational structure of Zambia, the classification of medicinal products, the registration process, and the fee structure for different types of applications. By following these guidelines, pharmaceutical companies can navigate the registration process more effectively, ensuring that their products meet the necessary standards for market entry in Zambia.

Keywords: National drug policy (NDP), Zambia, pharmaceutical regulatory agency (PRA), medicinal product, basic health care package (BHCP), medicines transparency alliance (META), logistics management information system (LMIS)

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INTRODUCTION

In 1999, the Ministry of Health (MOH) formulated and implemented a National Drug Policy (NDP) in accordance with the requirements of the Basic Health Care Package (BHCP). To facilitate effective inventory management and ensure the availability of essential drugs and supplies, a three-year procurement plan was devised for the period of 2005 to 2007. Additionally, during this period, the MOH created two distinct lists, namely the 'Essential Drugs' list and the 'Tracer Drugs' list.

At present, the healthcare sector in Zambia is facing a significant human resource crisis, which severely hampers its ability to provide even basic healthcare services to the population. The government has demonstrated its dedication to counteracting this pattern, as stated in both the National Drug Policy and the Pharmaceutical Act (No.14) of 2004. Historically, the training of Zambian pharmacists primarily took place outside the country until 2003 when a program to train pharmacists at the medical school was established in alignment with the recommendations of the NDP. As a result, Zambia now produces an average of 35 pharmacists per year, marking a significant milestone.

In line with the NDP recommendations, the Zambian government has also established the Pharmaceutical Regulatory Authority to strengthen medicines control within the country. Zambia is engaged in various special projects with support from and collaboration with the following entities:

- EC/ACP/WHO partnership on Pharmaceutical Policies;
- WHO/HAI (Health Action International) Regional Collaboration for Action on Essential Medicines in Africa; and
- Medicines Transparency Alliance (META).

The regulatory agency responsible for overseeing pharmaceuticals in Zambia is known as the Pharmaceutical Regulatory Agency (PRA), which was launched in 2005 to succeed the Pharmacy & Poisons Board. The PRA is responsible for the registration and regulation of pharmacies, human and animal medicines, herbal medicines, and related substances [1]. The authority also oversees and governs the production, importation, exportation, possession, storage, distribution, supply, promotion, sale, and utilization of pharmaceuticals, herbal medicines, and associated substances [2].

ORGANIZATIONAL STRUCTURE OF MOH ZAMBIA [3–5]

The regulatory agency for Zambia is known as the Pharmaceutical Regulatory Agency (PRA) which was launched in 2005 have structure as mentioned in Figure 1, succeeding the Pharmacy & Poisons Board. The Pharmaceutical Regulatory Agency (PRA) oversees the registration and regulation of various entities, including pharmacies, medicines for human and animal use, herbal medicines, and related substances. Additionally, it is responsible for the supervision and control of activities such as manufacturing, importation, exportation, possession, storage, distribution, supply, promotion, sale, and usage of medicines, herbal medicines, and allied substances [4].

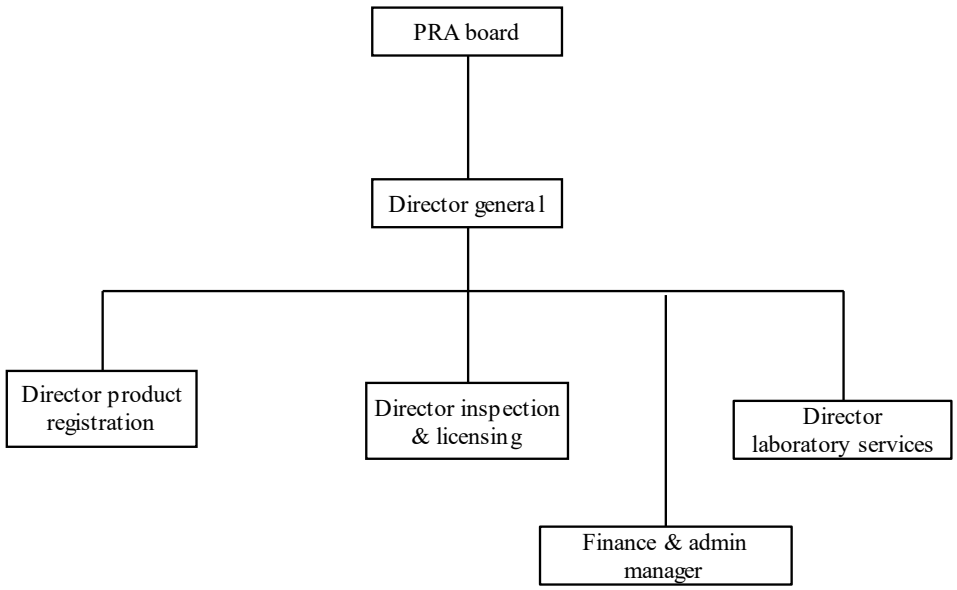

Figure 1. Zambia regulatory organizational structure.

Zambia National Drug Policy

The quality, efficiency, and effectiveness of health service delivery are heavily influenced by factors such as the presence of qualified personnel, adequate infrastructure and equipment, and the availability of essential drugs and medical supplies. It is crucial to ensure that health facilities always have a sufficient stock of essential drugs and medical supplies. To address this issue, the Ministry established and implemented a National Drug Policy (NDP) in 1999.

To ensure fairness and equal access for all citizens of Zambia, the National Drug Policy (NDP) aims to provide affordable, high-quality, safe, and effective medicines. The ultimate goal is to ensure that these medications are used appropriately and made readily available to individuals and families in their immediate vicinity.

A few activities were undertaken in the area of essential drugs and medical supplies, which included:

- The "Essential Drugs" list was developed, intended to help in the monitoring of stocks and management of procurement for critical drugs and supplies.
- In order to facilitate enforcement of the quality assurance legislation, in 2003 the National Drug Policy Steering Committee (NDP-SC) carried out a review of the Food and Drug Act and laboratory to establish their capacity to effectively enforce quality control on medicines. In order to improve on the quality of donated drugs and medical supplies, in 2004 the Pharmacy and Poisons Board, in collaboration with various stakeholders, produced Guidelines on Donation of Drugs and Medical Supplies.
- Process for establishment of a Zambian Logistics Management Information System (LMIS) continued with the establishment of the Zambian tracer drugs/medical supplies list.
- Under the newly established Pharmaceutical Regulatory Authority (PRA) structure, activities to operationalize/establish the Pharmacovigilance Unit (NPVU) have been initiated. The Unit will be responsible for introducing the concept of Pharmacovigilance in Zambia, including training and training in Adverse Drug Reaction/Events (ADR/Es) detection and its reporting.

Zambia implemented its National Drug Policy in 1999. The primary objective of the policy is to ensure that all Zambians have equal access to high-quality, safe, and effective medications that are affordable and used appropriately within their communities. Zambia recognizes the significance of regional integration in spurring the economic growth and development as well as fostering wealth creation and poverty reduction. Zambia is a member of two regional economic communities, namely the Southern Africa Development Community (SADC) and the Common Market for Eastern and Southern Africa (COMESA).

However, Zambia faces a number of challenges arising from dual Membership in both COMESA and SADC. The key challenges include:

- Duplication of policies in both COMESA and SADC (e.g. rules of origin, customs documentation etc. which tend to frustrate business people);
- Customs ethics and integrity as traders would do all it takes to ensure that they pay minimal duties;
- Inadequate capacity to establish and enforce standards; and
- Alteration of the resources and incentives: this is with respect to reduction of revenue due to lower rates or even a complete removal of customs duty. Where there has been a significant trade diversion, this loss of revenue may be permanent.

REGISTRATION SYSTEM IN ZAMBIA [5]

Below is the details steps for registration system in Zambia as summarized in Figure 2.

Preliminary review

- Completeness of application.

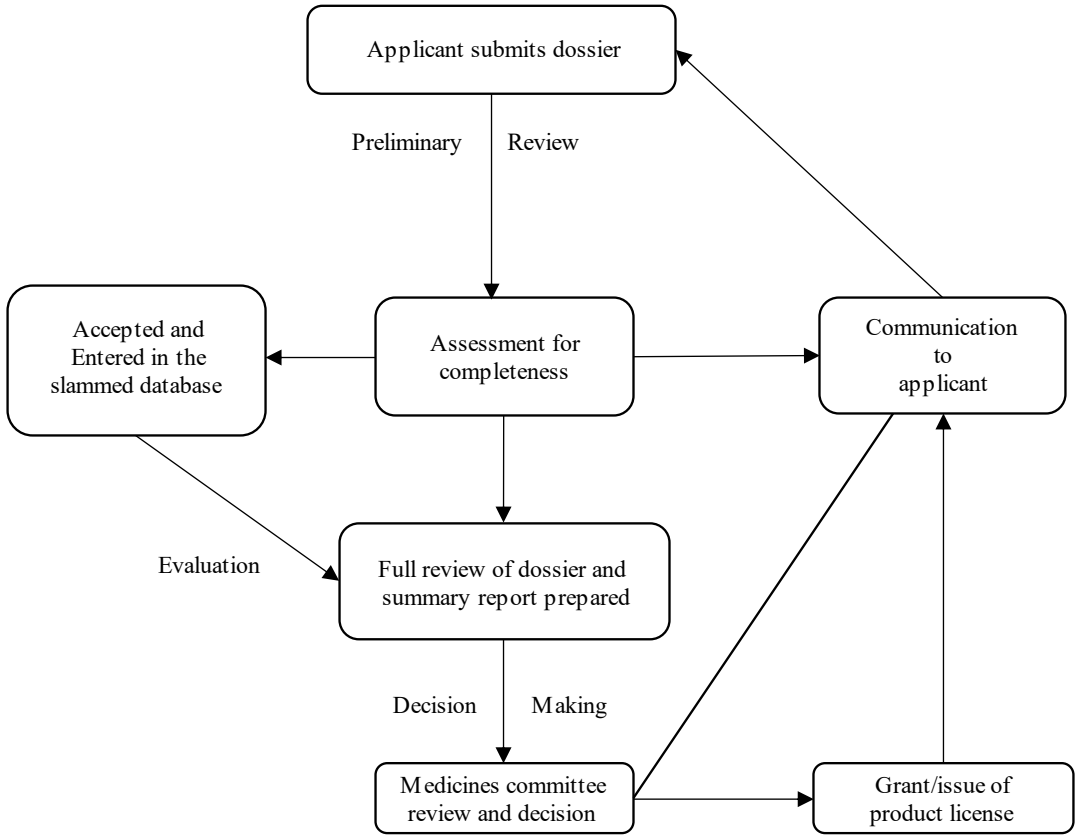

Figure 2. Zambia registration system.

- Application must be in the required format and supported by detailed technical information as may be appropriate.
- Administrative data with respect to the applicant (Prospective PLH) manufacturing site, status of manufacturer, fees paid, and samples.
- Acknowledgement and entry into PRIMS.

Evaluation

- This depends on the nature of the application, i.e. Standard application or Fast track.
- Extent of review depends on the nature of the product, i.e. locally manufactured product, Registered by stringent DRAs within and outside the region, new chemical entity or generic application.
- Due to insufficient capacities, QC is not routinely carried out as part of assessment.
- GMP inspections may be carried out on the recommendation of the Medicines Committee.
- Assessment report is prepared in the required format and presented to the Medicines Committee with the recommendations on Q, S, and E.
- Decision of the Committee may be positive, negative or deferred, pending further submission of the required information as may be directed by the Committee.
- If positive, a product license is issued and is subject to certain conditions as may be appropriate; and Applicant is required to comply with labeling requirements as stipulated under the regulations and expected to pay annual retention as required by the Act.
- If decision of the Medicines Committee is negative, the applicant is informed accordingly, and reasons given in writing for non-issuance of the product license.
- Applicant may appeal against the decisions of the Authority as per the appeal procedures.
- In cases where additional information may be required, the applicant is requested to submit within a defined timeframe, failure to which the application may be cancelled.

- Data in respect of a registered product is maintained by way of a WHO computer-assisted medicines registration program called SIAMED.
- There is a procedure for variations and all variations need to be notified to the Authority. The registration authority provides the necessary guidelines.
    - Procedures for registration and registration status of all medicines are published.
    - PRA enforces regulations through inspections.
    - Registration takes at least 1–2 years for initial registration.
    - Registration includes herbal, generic and patented medicines.
    - Registration information can be accessed by the public upon request from PRA

Post marketing surveillance

- Monitoring and Evaluation mechanism for licensed medicinal products.
- Sampling and testing of products.
- Pharmacovigilance activities: General surveillance activities to ensure adherence to licensing terms and conditions.

Product Registration Requirements [6]

The applicant is required to submit an application, a sample(s) and dossiers(s) for each product which should contain the following information:

a. The name and address of the applicant in full.
b. The name and address of the medicine.
c. The dosage form of the medicine.
d. he active constituents of the medicine.
e. The indications of the medicines and method of use.
f. The contra-indications, warnings and precautions of the medicine.
g. The composition (ingredients of the medicine and the reasons for their inclusion of if non-active as well as their specifications such as BP, USP etc.).
h. The shelf-life (this should be supported by stability studies data).
i. The containers and packaging (should give full description i.e. technical specifications).
j. The labeling should be part of the dossier and should contain the following information:
    - The name of the medicine.
    - The pharmacological properties.
    - The names and quantities of active ingredients.
    - The quantity of medicines i.e. 100 ml, 1000 tablets etc.
    - The directions for use.
    - The contra-indications, warnings and precautions.
    - The storage instructions.
    - The manufacture date.
    - The batch number.
    - The expiry date.
    - The license number.
    - The name and address of the manufacturer.
    - The method of sale, e.g. General sale, pharmacy sale only or prescription sale only.
k. The distributor's name and address.
l. An original copy of the World Health Organization (WHO) pharmaceutical certificate of quality and free sale certificate addressed specifically to Zambia.
m. The name and designation of the person signing the application.
n. Where the medicine is to be imported for Zambia for the first time.
    - The chemistry of the medicine.
    - The pharmacological data.
    - The toxicological data.

- The teratology.
- The clinical studies.
- The countries in which the sale of the medicine has been authorized.

o. The final product specifications and certificate of analysis.
p. The certificates of analysis of all the raw materials used

Registration fee: All fees payable irrespective of area in Zambian kwacha (Tables 1–6) [7].

Table 1. Pharmaceutical Licensing Fees.

No.	Description of Fees	Fee units	Amount 30 Ngwee/fee unit
(a) Complete Manufacture			
(i)	Application for grant of pharmaceutical license	64,533	19,360.00
(ii)	Re-inspection of premises for pharmaceutical license – manufacture of medicine	47,867	14,360.00
(iii)	Re-locating to new premises	64,533	19,360.00
(iv).	Inspection of Additional production line	25,400	7,620.00
(v)	Inspection of Additional production block	47,867	14,360.00
(vi)	Renewal for pharmaceutical license – manufacture	47,867	14,360.00
(b) Primary Repackage of Medicine			
(i)	Application for grant of pharmaceutical license	35,400	10,620.00
(ii)	Re-inspection of premises for pharmaceutical license – repackage of medicine	24,400	7,320.00
(iii)	Re-locating to new premises	35,400	10,620.00
(iv).	Inspection of Additional/Modification of production line	12,200	3,660.00
(v)	Inspection of Additional/Modification of production block	25,400	7,620.00
(vi)	Renewal for pharmaceutical license – repackage of medicine	25,400	7,620.00
(c) Secondary Repackage of Medicine			
(i)	Application for grant of pharmaceutical license	17,700	5,310.00
(ii)	Re-inspection of premises for pharmaceutical license – repackage of medicine	12,200	3,660.00
(iii)	Inspection of Additional/Modification of production line	7,000	2,100.00
(iv).	Inspection of Additional/Modification of production block	12,200	3,660.00
(v)	Renewal for pharmaceutical license – repackage of medicine	12,200	3,660.00
(d) Local Manufacture of Natural Remedies			
(i)	Application for grant of pharmaceutical license	35,400	10,620.00
(ii)	Re-inspection of premises for pharmaceutical license: repackage of medicine	24,400	7,320.00
(iii)	Inspection of Additional/Modification of production line	25,400	7,620.00
(iv).	Inspection of Additional/Modification of production block	25,400	7,620.00
(v)	Renewal for pharmaceutical license: repackage of medicine	25,400	7,620.00
(vi)	Re-location or export permit	25,400	7,620.00

Table 2. Marketing authorization of locally manufactured or packaged medicines or allied substances.

No.	Description of Fees	Fee units	Amount 30 Ngwee/fee unit
a	Locally Manufactured Medicines		
(i)	Human Medicines	16,667	5, 000.00
(ii)	Veterinary Medicines	16,667	5, 000.00
b	Locally Packaged Medicines		
(i)	Human Medicines	36,667	13,328.00
(ii)	Veterinary Medicines	25,867	7,760.00
c	Allied Substances	5,000	1,500.00
d	Evaluating Additional Information for an Application of a Locally Manufactured Product supplied with Inadequate Technical Information (quality safety or efficacy)	5,667	1,700.00
e	Annual Retention Fees for Locally Manufactured Medicines and Allied Substances		
(i)	Human Medicines	8,333	2,500.00
(ii)	Veterinary Medicines	8,333	2,500.00
(iii)	Allied Substances	3,333	1,000.00
f	Renewal of Marketing Authorization for locally manufactured Medicines or Allied Substances		
(i)	Human Medicines	11,667	3,500.00
(ii)	Veterinary Medicines	10,000	3,000.00
(iii)	Allied Substances	4,000	1,200.00
g	Amendment Fees for Medicines and Allied Locally Manufactured Products		
(i)	Minor amendment	1,333	400.00
(ii)	Major amendment	6,500	1,950.00

Table 3. Advertising and promotion of medicines and allied substances.

No.	Description of Fees	Fee units	Amount 30 Ngwee/fee unit
a	Advertising medicines to the general public	16,667	5,000.00
b	Promotional medicines to the health care professional fees	3,333	1,000.00
c	Exhibition of medicines at a public event fees	6,667	2,000.00

Table 4. Clinical trials involving a locally manufactured investigational product.

No.	Description of Fees	Fee units	Amount 30 Ngwee/fee unit
a	Clinical Trial Certificate involving Investigational Products without Marketing Authorization		
(i)	Human	48,333	14,500.00
(ii)	Veterinary	34,333	10,300.00
b	Clinical Trial Certificate involving Investigational Products with Marketing Authorization		
(i)	Human	46,667	14,000.00
(ii)	Veterinary	32,667	9,800.00

Table 5. Good clinical practice inspection for local sites [8–10].

No.	Description of Fees	Fee units	Amount 30 Ngwee/fee unit
(i)	GCP inspection local sites	50,000	15,000.00

Table 6. Preclearance and Other Fees for Quality Assurance and Licensing.

No.	Description of Fees	Fee units	Amount 30 Ngwee/fee unit
a	Preclearance Fees for Quality Assurance (QA) of imports for commercial consignments, Government ministries departments, Programs projects and similar institutions		1.5% of FOB invoice value
b	Preclearance Fees for Quality Assurance (QA) of imports for unregistered medicines and Allied substance for commercial consignments, Government Ministries Departments, Programs projects and Similar institutions		5% of FOB invoice value
c	Preclearance Fees for Quality Assurance (QA) of imports for Donations		1% of FOB invoice value
d	Preclearance Fees for Quality Assurance (QA) of imports for Active Pharmaceutical Ingredients (API), Bulk finished products and intermediates		1% of FOB invoice value
e	Amendment to licenses, certificates, and permits	1,500	450.00
f	Loss of licenses, certificates, and permits	1,500	450.00
g	Transfer of licenses, certificates, and permits	1,500	450.00
h	Issue of Certificate of a Pharmaceutical Product (CPP)	333	100.00
i	Application for import of Narcotic drugs and psychotropic substances	333	100.00
j	Inspection of premises for issue of a GMP certificate (local Manufacture)	20,000	6,000.00
k	Inspection and supervision for disposal of expired products	3,333	1,000.00
l	Fast track fees		Double the applicable MA applicable fee
m	Restoration of Marketing Authorization Medicines		
(i)	Medicines	20,000	6,000.00
(ii)	Allied Substances	4,000	1,200.00
n	Inspection of Register	167	50.00
o	Late submission of application for renewal of marketing authorization in respect of locally manufactured medicines and allied substances	33 per day application is late	10.00

CONCLUSION

The classification of medicines in Zambia is categorized into three groups: Prescription Only Medicines (POM), Pharmacy Only Medicines (P), and General Sales List (GSL). POMs can only be provided by a doctor or a pharmacist upon presentation of a doctor's prescription. P medicines can be supplied by a pharmacist or under their supervision without a doctor's prescription. Lastly, GSL medicines can be purchased directly from the shelves without any restrictions.

Approval for above classified medicinal products can be approved by PRA under two major applications.

1. NDA (New Drug Application), and
2. GDA (Generic Drug Application).

Registration dossiers are submitted through these pathways to receive marketing authorization; and registration dossiers should be in a regional format.

The approval process discussed in the present study covers the key parameters including timelines and regulatory requirements to be met by the different pharmaceutical products. This will help the product development including clinical, chemistry, manufacturing, and regulatory personnel to provide necessary resources required for product approval. It can be concluded that as the country is moving ahead to the area of developing to developed country, drug regulation system of country should also strengthen.

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