

REGULATORY PERSPECTIVES OF PHARMACEUTICAL PRODUCTS IN GHANA

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REVIEW ARTICLE

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ABSTRACT

Drug Registration is a procedure of expertise of pharmaceutical product quality, efficacy and safety by the Regulatory Authority. The emergence of various formats has enabled the manufacturers of the drug to easily gain access into various markets and thus was able to place their products into the market. The choice of Ghana as one of the destinations for the market of the Drug products ensures the manufacturer a good market value. Ghana is considered as one of the growing pharmaceutical market in east Africa. Of late, generic drugs are holding a major stake in the pharmaceutical market and are gaining more and more confidence in the usage. Majority of medicines in the Ghana are generic drugs which are considered as value for the money and affordable. With Ghana Regulatory Authority is the Food and Drugs Board, which takes decision to register the product and issues Registration Certificate. This study mainly focuses on the regulatory environment, registration process involved and the regulatory requirements that are applicable for the generic drug products in Ghana.

Keywords: Ghana; FDB; Generic Drugs; NHIS.

INTRODUCTION

Main pharmaceutical policy goals in Ghana are access to essential medicines for everybody, quality assurance for all drugs on the market, a functioning and efficient supply chain as well as rational use of medicines by professionals and patients. There is also a commitment to strengthen the domestic pharmaceutical industry, outlined under health industry in the national health policy. Key challenges are: limited capacity to enforce regulation, high levels of provider indebtedness due to poor management and flaws in the payment system, a weak public sector supply chain that is increasingly being substituted by the private sector and a fragmented national private sector (manufacturing and distribution), lacking capital to make necessary investments into quality improvements. (1)

INSIGHT INTO GHANA PHARMA - CEUTICAL MARKET:

The National Health Insurance System has significantly improved access to medicines for insured patients, measured in increased utilization of facilities and rapidly growing

turnover of revolving drug funds. The risk is now that non-rational prescribing and fraud, lead to a growing medicine bill that threatens financial sustainability of National Health insurance scheme (NHIS). On the other hand, National Health insurance agency (NHIA) has the resources and purchasing power to influence provider behaviour as well as the market in terms of quality and price the government need to address the challenge of coordinating the various actors and ensure that they work together to develop, review and implement appropriate policies to address the above challenges policy options presented for key areas include: limited but efficient regulatory measures with focus on high risk products, solutions to fix the supply chain with different degrees of private sector participation, thoughts on a sustainable industrial policy for the sector, solutions to limit NHIS' drug expenditure and measures to improve rational use of drugs.

The statistics on the Ghanaian pharmaceutical market is quite weak. Unlike in larger markets that have market research companies with established data collection systems at critical points of sale, the data that are available in the

literature are based on aggregate estimates from various market participants. In 2005, the total market was estimated at 250 million USD at retail price level. Assuming a growth rate of 6-8% (drug expenditure tends to grow above overall economic growth) the total market size could be in the 300 million USD range in 2008.(2) Another factor driving growth has been the introduction of health insurance, measurably increasing utilization of healthcare facilities: more patients mean more prescriptions. The Pharmaceutical Manufacturers Association of Ghana (PMAG) is currently undertaking a survey among its members to get a better estimate of the size of the market – supported by United Nations Industrial Development Organization (UNIDO). The sales data of manufacturers and distributors are not published, but a market insider estimates that the largest players reach sales volumes in the range of > 30 million USD. The estimate of the Over the Counter (OTC) share of the total market is about 30% in value (significantly higher in volume but OTC drugs tend to be cheaper than prescription drugs). Patients' first point of call is the chemical sellers/pharmacies where there are no payments for consultation; patients tend to prefer self-medication over seeking professional advice from doctors at the onset of a disease, which can be seen as rational behaviour in places where access to healthcare facilities and cash to pay for services are limited.

Health insurance is changing this pattern and increases the rate at which patients seek initial

Table 1: Ghana Pharmaceutical Market overview (1)

Total market at retail value	300 USD
Prescription drugs total (70% of total)	210 USD
Growth rate in %	6-8%
Retail sales of domestic manufacturers (30%)	90 USD

In order to provide the context for an assessment of local pharmaceutical production in Ghana, it is first necessary to examine the situation and trends in the local and sub-region pharmaceutical market, as well as the threats

treatment in a health facility instead of self-medicating. Malaria drugs, making up a very significant share of all treatments dispensed in Ghana, are available officially without prescription, meaning they can also legally be sold by the about 10,000 licensed chemical sellers.(3) But anecdotal evidence exists that prescription drugs are also sold over the counter, as systems in place to enforce prescriptions are weak. Most of the drugs used in Ghana are generics/branded generics. But there is a significant market for originator brands mainly among wealthier patients – reflected in prescribing habits of physicians in teaching hospitals and private practice. Branded originator drugs have a reputation of better quality and higher “potency” – a widespread perception among professionals and patients in developing countries in which trust in regulatory systems is lacking. Major multinational firms have offices in Ghana: they market and distribute their leading brands in collaboration with local partners, but do not have manufacturing plants. In summary, the Ghanaian market is becoming increasingly attractive for suppliers, given the overall economic growth and increased availability of financing through NHIS. As in many African countries, Indian and Chinese firms dominate the import business with their branded generics. The domestic industry has an estimated market share of around 30%, which means 70% are imported. Some of the domestic market share is protected; import of certain generics that are domestically manufactured is not permitted.

posed to its normal functioning. In the absence of a pharmaceutical market statistical information collection system in West Africa (different stakeholders are collecting different sets of market information, but the type of

information collected needs to be developed more and coordinated), it is difficult to gather accurate data on the value, volume, imports and exports in both Ghana and the sub-region, but some general trends can be surmised.

The Ghana pharmaceutical market is made up of approximately 30% locally produced and 70% imported products; the latter originating mainly from India and China. It is estimated that 30% of the sub-region market is supplied by Nigerian manufacturers although Ghana-based manufacturers also export significant quantities to the sub-region. In contrast, Francophone countries are heavily reliant on imported medicines (local production is estimated to be approximately 5% in these countries; e.g. 94% of medicines in Cote D'Ivoire are imported), particularly from France, and reportedly this reliance on imports from France has reduced the motivation to develop a local pharmaceutical industry in the Francophone countries. (4)

The OTC sector in Ghana is considerable and consists of drugs popular with consumers such as tonics and combination analgesics. Ghana has a very large OTC sector due to several reasons, including the traditional population reliance on OTC medicines (due to inaccessibility issues concerning prescription medicines), the very recent introduction of a health insurance system in 2005 that provides prescription drug coverage, local industry focus on OTC production at the expense of essential drug production as well as heavy advertisement of OTC drugs. However, with the introduction in the past few years of major donor funding for the provision of essential drugs (and the creation of a Ministry of Health [MoH] essential drug list), the local pharmaceutical market is becoming more rational in terms of addressing the priority endemic diseases and population morbidity. Concerning the supply of medicines for priority endemic diseases to Ghana through TGF financing and the supply of:

1. Anti-retrovirals (ARVs) is heavily dependent on suppliers from India, e.g. Cipla, Ranbaxy, Haya, Emcure, Hetero, Aurobindo, and Gokals (the latter a Ghana

India-owned local distributor). In addition Ghana receives patented ARVs from Roche, GSK, BMS and Abbott. Only a few companies in the sub-region are producing ARVs.

2. Anti-malarials are largely supplied from India and China.
3. TB drugs are largely supplied through the IDA.
4. Drugs for NTDs are principally imported⁵.

Ghana has a local capacity for the production of parenteral fluids (two companies are producing - San Bao Company Limited and Intravenous Infusions Limited), however the supply of vaccines and parenteral medicines to Ghana is provided via imports through MoH and NCB as well as drug donations (e.g. quinine, parenteral antibiotics such as benzyl penicillin and Ampicillin). Ghana, like every other country in the World, also has a problem of ensuring pharmaceutical supply chain security in the face of the growing threat from counterfeit and unregistered medicines. Unregistered products are estimated to account for approximately 5% of the Ghana pharmaceutical market.

The extent of counterfeit medicines present on the Ghana pharmaceutical market is hard to estimate as no local market surveillance studies on this issue have been performed. However many products are imported from China and India (which have a well-documented fake drug industry) and also which transit through the Middle East and Nigeria; the latter which notoriously has a very large counterfeit medicine problem (a few years ago the Nigeria market was estimated to consist of over 50% counterfeit medicines, but recently this has been reduced to around 30% as a result of proactive action by the Nigerian National Agency for Food and Drug Administration and Control - NAFDAC). The Consultant was able to view a large batch of counterfeit medicines imported from China recently seized by the Ghana FDB. The standard of the fakes was of a very poor standard and easily detectable by the authorities. The situation whereby poor fake products are targeted at West Africa implies that counterfeiters consider the West African market to be an easy target in view of relatively

weak pharmaceutical regulation in the sub-region. (5)

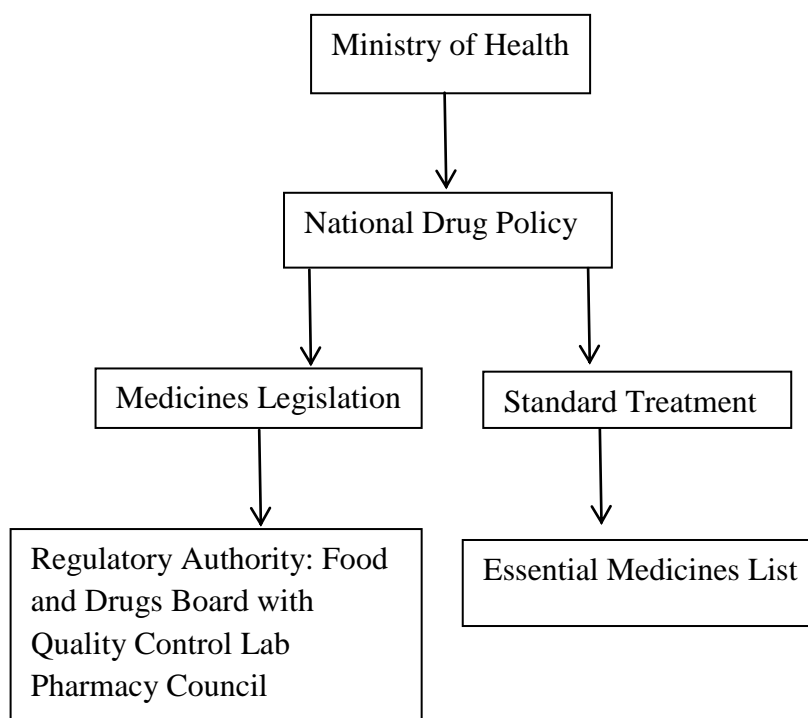


Figure 1: Framework for pharmaceutical regulation in Ghana

ORGANIZATION OF FOOD AND DRUGS BOARD:

The Ministry of Health (MOH) is responsible for ensuring the availability of health care to the people of Ghana. The Food and Drugs Board (FDB) is Ghanaian based government agency that was founded by the Food and Drugs Law 1992, Provisional National Defence Council (PNDC) Law 305B. It is accountable for the inspection, certification, importation, exportation, distribution of foods, cosmetics, medical devices and household chemicals. The board guarantees the protection of medication and foods.

FDB collaborates with WHO in various ways to increase capacity and stay on top of the technological development. (1) Three FDB experts are involved in international inspections under the framework of the WHO Prequalification Program. An assessment of FDB by WHO based on the certification scheme for regulatory agencies has been requested. FDB is managing a pharmacovigilance program with a network of

institutional contact persons in all major facilities as well as at the domestic drug manufacturers. A standard reporting form for adverse events is provided for use by these contact persons. A technical committee at the FDB hosted National Pharmacovigilance Center reviews reports on potential drugs side effects and makes recommendations for regulatory action. One major achievement of this program which was done in collaboration with the Centre for Tropical Clinical Pharmacology and Therapeutics of the University of Ghana Medical School, was the identification of side effects of a specific anti-malarial combination therapy, probably due to a formulation that led to higher than tolerated blood levels of one active ingredient in some patients. These findings led to the withdrawal of this drug from the Ghanaian market. Currently ongoing is a cohort event monitoring program covering 10,000 patients using Artemisin Based Combination Therapies (ACTs) for malaria, in collaboration with the National Malaria Program. The FDB is also working on an improvement of its public

website in an effort to strengthen communication with the general public to increase transparency and improve governance. The practice of pharmacy is regulated by the Pharmacy Council through Pharmacy Act 489. The Council has been mandated to license pharmacists and Chemical Sellers. All pharmacists have to be members of a professional society, the Pharmaceutical Association of Ghana (PSGH). The PSGH is responsible for assuring professional ethics and standards and occupies three of the nine Board seats at the Pharmacy Council. (1)

I. FDB Inspectorate Department (and GMP / GDP compliance)

- The FDB Inspectorate consists of the following units: premise inspection post market surveillance and industrial support (the latter was previously known as operational research).
- In the central Accra office there are 14 staffs. The types of inspections carried out consist of:
 - ❖ Pre-licensing inspections (for applicant manufacturers and their warehouses (Inspection of pharmaceutical distributors is carried out separately by the Ghana Pharmacy Council)
 - ❖ Routine annual premise inspections (with an unannounced follow up to see if recommendations have been implemented)
 - ❖ Post Marketing Surveillance (PMS) and
 - ❖ Advertisement monitoring and enforcement.

II FDB Drug Evaluation and Registration Department

The department operates with 10 staff. The drug registration application (Marketing Authorisation Application – MAA), dossier documentation requirements are gradually increasing as the Ghana pharmaceutical regulatory system develops. The eventual plan is to implement the ICH Common Technical Document (CTD) and eCTD dossier format and requirements, although when, is not yet certain. However, the department sometimes does receive applications in CTD format (for example, they recently received two eCTD

drug registration applications from Pfizer). Since 2004, the department has been using the WHO SIAMED database drug registration system (which inter alia greatly assists tracking the drug registration process). The number of medicinal products registered by the Ghana FDB is approximately 4,000 (including different dosage forms). The analysis of the FDB drug register revealed that the level and type of drug registrations corresponds with anticipated public health demands. 99.9% of MAA applications to the department do not get approved in the initial application (first submission) process. Thus, there is a lot of ‘back and forth’ between the department and applicants before a drug registration application is finally accepted or rejected. The minimum time frame for granting an MA is 3 months (a similar time frame exists elsewhere in the sub region), but can take over 1 year with ‘problem dossiers’, the occurrence of which is very high with respect to all MAA submissions. ‘Problem dossiers’ result from the following types of problems:

- Incomplete or missing data (e.g. no process validation, no or delayed CPP, no pharmacological analysis of raw materials, no bioequivalence studies, stability studies conducted with inappropriate climatic conditions for the region, no Drug Master File [DMF – closed and open parts] and no batch production records)
- Proposed packaging and labelling problems (‘requested legal changes’, e.g. because of the potential for brand name confusion)
- MAA drug sample quality problems. (5)

III. FDB Import and Export Control Department

The FDB operates offices in the 10 districts of Ghana as well as at Accra Kotoka international airport (4 staff) and at Tema seaport (10 staff), the only legal entry points for imported medicines and medicines manufacturing materials into Ghana. The FDB considered it necessary to open offices at these entry access points as the Ghana customs and excise is not equipped to deal with the public safety control of imported food and medicines. The Ghana

Customs and Excise is reported solely interested in meeting 'quota seizure' requirements and has little interest in exercising its duties for public health and safety protection reasons. For example, a large number of so called 'personal use' medicinal products are imported into Ghana, but the customs services are unable to deal with this problem. The FDB is in the process of also opening border town offices (particularly at its East and North borders) so as to tackle the problem of illicit border trade in counterfeit, adulterated and diverted medicines, medical devices and consumer health products. Ghana is considered to be a principle importation destination for the sub-region for several reasons. (5)

The problems associated with the control of drug importation (both manufacturing materials and finished products) into Ghana are reported by the FDB Import and Export Control Department to be quite considerable (high number of counterfeit, adulterated and diverted medicines and consumer health goods) and which is complicated by sub-region political instability (e.g. an ongoing war in Cote D'Ivoire). The largest problem that the FDB Import and Export Control Department faces is dealing with imported 'unlicensed' medicinal products (by their estimation 5-10 % of medicinal products on the Ghana market are unlicensed). 'Unlicensed', in the terms used by the FDB, covers

- (i). medicinal products brought into the Ghana market which may have acceptable manufacturing quality and are registered outside of Ghana,
- (ii). Mislabeled (deliberately or otherwise).
- (iii). Substandard ingredients.

IV. FDB Quality Control Laboratory

The FDB Quality Control Laboratory (QCL) has been operating since 2002 and consists of physico-chemical, microbiology and medical device departments and currently has 33 staff. Activities are split between food and medicines testing. The QCL is reportedly operated according to Good Laboratory Practice (GLP) standards with respect to QCL standards.

1. Every consignment of imported medicines is tested
2. Drug registration applications – a full pharmacopoeial analysis is conducted (approximately 1,000 MAA pre-registration and re-registration samples are tested per year, of which approximately 8% are found to be substandard. Previously the QCL was performing analytical checks on every product MAA, but due to resource constraints it is now focusing now on carrying out analytical checks on so-called 'problem companies' and 'problem products')
3. Samples taken in GMP inspections
4. Post marketing surveillance (PMS) sampling of medicines. In 2005 antimalarials were sampled and in 2006 a detailed study of all the different ciprofloxacin and co-amoxiclav products on the Ghanaian market was carried out (non-conforming products based on dissolution testing failure were 12 out of 33 and 5 out of 15 respectively). Non-conforming products were mainly imported. In 2007, no PMS testing was performed due to financial difficulties and the national electricity supply crisis.
5. Medical device testing – condoms, HIV testing kits, and other medical devices are routinely checked by the FDB irrespective of source.

According to the FDB QCL Director, Ghana and Nigeria are the only countries in the region that do full medicines QC testing. (5)

DRUG PRODUCT REGISTRATION REQUIREMENTS

a) Format Followed: ICH CTD

b) Administrative Documents

1. Site Registration Application / Application for GMP Inspection
2. Application form
3. WHO-GMP Certificate
4. Mfg. License
5. Free Sale Certificate
6. Certificate of Pharmaceutical Product
7. Registration Certificates of countries in which the product is already registered.

8. Site Master File

9. Letter of Authorization

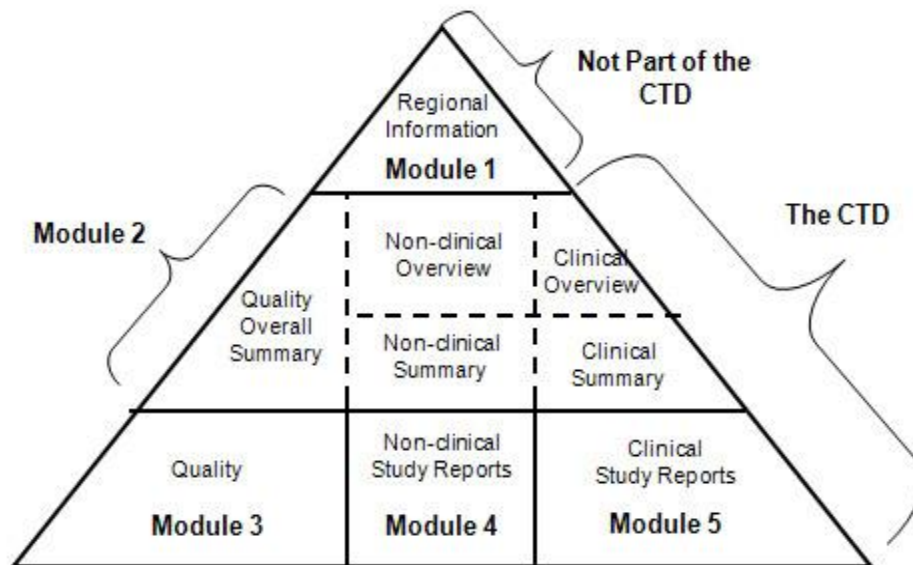


Figure 2: ICH CTD Triangle

10. Power of Attorney
11. Summary of Product Characteristics
12. Package Insert
- i) **Quality Documents**
 - a) **API Documents**
 1. Drug Master File
 2. Quality Overall Summary
 3. General Information
 4. Manufacture Of Drug Substance
 5. Characterization
 6. QC of Drug Substance
 7. Reference Standards
 8. Container Closure System
 9. Stability
 10. Manufacturing License of API manufacturer.
 11. GMP Certificate of API manufacturer.
 - b) **Excipients**
 1. Raw Material Specifications.
 2. In House COA & Vendor COA.
 - c) **Manufacture of the product**
 1. Unit Dose & Batch Formula
 2. Master Formula
 3. Manufacturing Process
 4. Packing Process
 5. Process Validation
 6. Executed Batch records
 7. Pharmaceutical Development report
 - d) **In process Product**

1. Specification & certificate of analysis.
- e) **Finished Product**
 1. Specification & certificate of analysis.
 2. In house product
 3. Finished product samples
 4. Working/Reference Standards
- f) **Stability Testing (Zone IV b)**
 1. Stability data-Accelerated & Real time
 2. Stress testing, Photo stability
 3. Stability Commitment (if any)
- g) **Packing Material**
 1. Specification's & certificate of analysis.
 2. Suitability studies
 3. Packing Material Specimen
- h) **Bioequivalence Studies**
 1. Comparative Dissolution studies
- i) **Clinical Documents**
 1. Pharmacology Studies
 2. Toxicology Studies
- j) **Other Requirements**
 1. Embassy Attestation
 2. Word format of Modules

Drug Registration Evaluation Process

Language

All applications and supporting documents shall be in English and legible. Where material is not originally in English, a copy in the original language and a full

translation should be submitted, the accuracy of the translation is the responsibility of the applicant.

GHANA REGULATORY REVIEW PROCESS FOR GENERIC DRUGS:

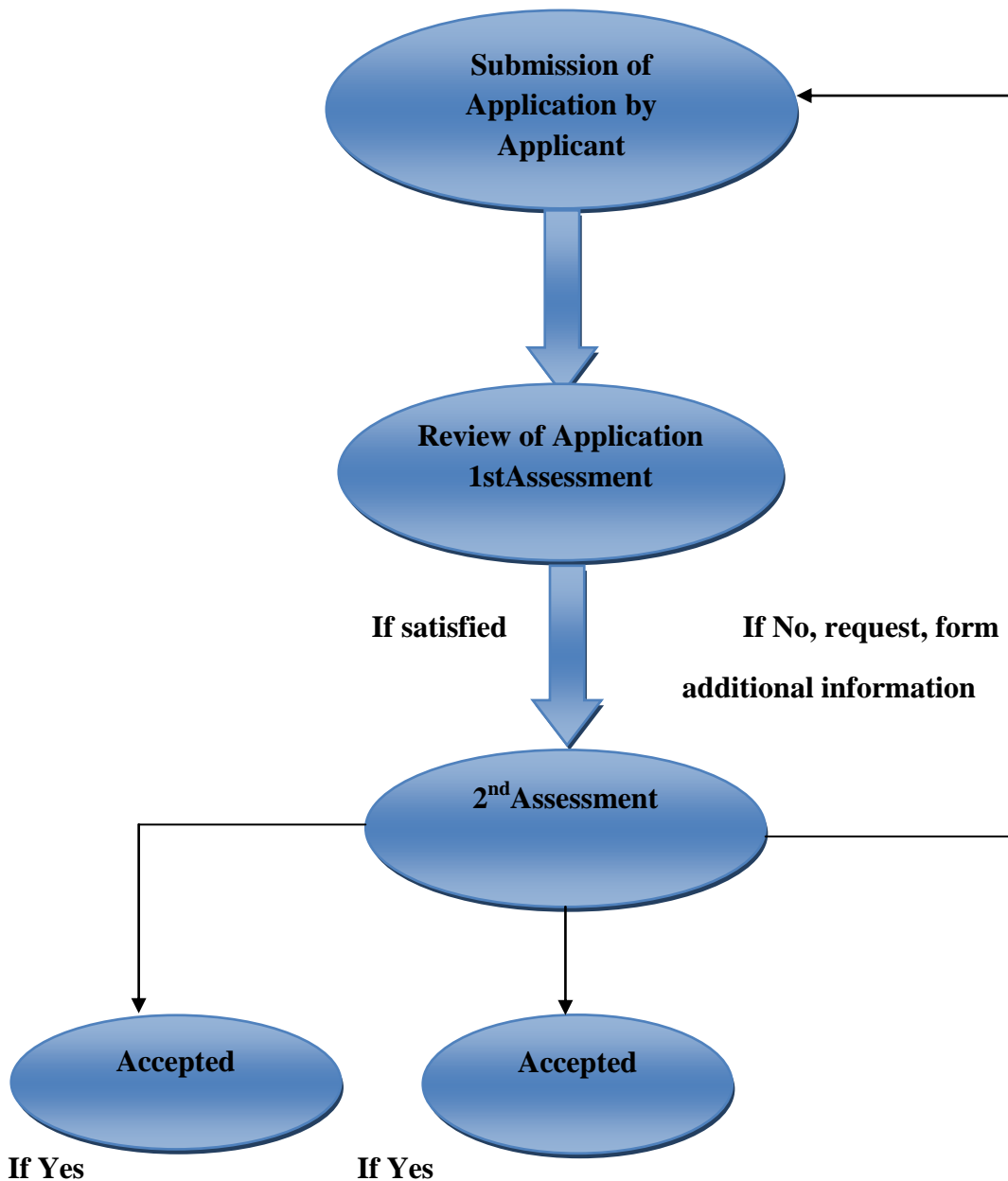


Figure 3: Ghana regulatory review process for Generic Drugs

*The queries have to be submitted within 12 months. If the queries have been reissued for a third time and the applicant provides unsatisfactory responses, the application will be **rejected**.

Timelines

The following timelines will be implemented by the FDA in processing applications for registration of products.

Processing of new applications

A Generic application will be processed within 6 months of receipt of the application. The applicant will be required to provide any

requested additional data within 12 months. In case additional time is required, a formal request must be submitted to the FDA. (6)

Fee Structure (7)

Table 2: Fee for Registration of Pharmaceutical Products

S. No	Product	Period	Rates in USD	Rates in GH
1	Local Allopathic Product	Every Three Years	--	900
2	Imported Allopathic Medicinal Products	Every Three Years	3,000	--
3.	Imported Allopathic new Chemical Entities	Every Three Years	4,500	--

CONCLUSION

The regulatory requirements of Ghana are still a matter of concern. Since, the requirements differ from one country to the other. The compilation of information to a single platform is beneficial during submission. The generic drug filing with the other necessary details like Regulatory System, Legal Framework, Evaluation Process, Timelines, Validity and fees required for the smooth filling of a dossier is discussed. Keeping in mind, the value of time and money and the requirements of the industry for the generic drug registration in Ghana, this study may facilitate the easy filing of a product dossier in Ghana.

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CONFLICT OF INTEREST

Not declared.

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Once the product is registered it is valid for 3 years.

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