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# Assessment of Regulatory Compliance of Small-Scale Pharmaceutical Manufacturing in Addis Ababa city, Ethiopia

**By**

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**ADDIS ABABA ETHIOPIA**


# ASSESSMENT OF REGULATORY COMPLIANCE OF SMALL SCALE PHARMACEUTICAL MANUFACTURINGSIN ADDIS ABABA CITY, ETHIOPIA

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## Abstract

**Introduction**: There is growing concern that most of the developing world's supply of medicines are of poor quality.Manufacturing facilities need to be compliant with regulatory requirement, which comprises a set of safeguards and procedures at each stage of the production process to ensure that the manufactured product is of the desired quality, safety and efficacy.

The aim of this study was to assess regulatory compliance of small-scale pharmaceutical manufacturing found in Addis Ababa city, Ethiopia.

**Method:** A cross-sectional observational and questionnaire based study was conducted to assess regulatory compliance of small-scale local pharmaceutical manufacturing companies and the major challenges faced by the manufacturing for implementation of regulatory requirements.

**Result:**Our study indicated that the overall implementation status of regulatory requirements in the local pharmaceutical manufacturing companies is far below the minimum standard set by WHO and national regulatory Authority. From the total regulatory element requirement only 26.1% were implemented by local small scale pharmaceutical manufacturers. Major challenges faced by the local small scale pharmaceutical manufacturing industry for the implementation of regulatory requirement were: human resource capacity constraints, limited investment, Limited support from Governments and other stakeholders and poor Infrastructure.

**Conclusion:** The results of this study will help policy makers and regulatory bodies, pharmaceutical industries, and other stakeholders to design appropriate interventional strategy to improve the quality of products in the local pharmaceutical manufacturing companies.

**Recommendation:**Government and other stakeholders has a central role to play in nurturing the infant pharmaceutical industry through support supervision, facilitating access to technology and business finance, and promoting market access at the national, regional and international levels.

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## Acronyms

API:ActivePharmaceutical Ingredient

AU:AfricaUnion

EFDA: Ethiopia Food and Drug Authority

GDP: Good Documentation Practice

GLP:Good Laboratory Practices

GMP: Good Manufacturing Practice

GTP: Growth and Transformation Plan

MRA: Medicine regulatory authority

QA: Quality Assurance

QC: Quality Control

R&D Research and Development

SOP: Standard Operating Procedure

WHO: World Health Organization

UNIDO: United nation industrial development organization

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# 1. Background

In monetary terms, over 90 percent of global pharmaceutical production takes place in a few high-income countries (WHO,2004), although the industry is globalizing in order to improve stocks of raw materials to be used in global production and also to improve skills and research capability (Floyd D,2008).

The experience of developing countries with pharmaceutical production entails the lack of ability to independently produce the drugs that they need (Olliaro et al,2001). Even in developed countries, variation exists in capabilities, the level of R&D and the know-how leaving developing countries very far behind.

Ethiopia is one of the most populated countries of Africa with high demand of pharmaceutical products. The manufacturing of pharmaceutical products in Ethiopia is quite small.

Local manufacturing is considered as a potential solution to the "access" problem and the local industry desperately needs support via capacity building in order to enable them to meet the required quality standards. Government and international agencies involved in promoting local production have a critical role to play in providing the necessary support to facilitate the transfer of technical knowledge and investment (AU, 2012).Manufacturing facilities need to be compliant with GMP requirements, which comprise a set of safeguards and procedures at each stage of the production process to ensure that the manufactured product is high quality, effective and safe (WHO,2003).

Detailed written procedures and documentation of implementation and practice are crucial aspects as they monitor whether GMP is being followed consistently at every stage of the manufacturing process. Quality control and assurance are required, not only for producing the final products but also for the processing of raw materials and products at different stages of the production chain( WHO,2003).

Implementation of a Good Documentation Practice for pharmaceutical products will facilitate compliance with GMP and requirements. It is again emphasized that documentation is a very

important aspect of GMP and will enhance the visibility of the quality assurance function(WHO,2003).

The regulatory authority should be able to ensure all pharmaceutical value chain players involved in clinical research, laboratory work, manufacturing, importation and exportation, wholesaling, distribution and retail sale of products conform with acceptable international standards available(Global fund, 2007).

Small scale pharmaceutical manufacturer is a manufacturer involved in processing or production of products for external use only, including sanitary items, cosmetics, antiseptic, and medical supplies and other related products using none sophisticated technology (EFMHACA, 2014).

EFMHACA developed directive for small scale pharmaceutical manufacturing facility to ensure products manufactured in small scale medicine establishments are up to the required safety, quality, and efficacy. In addition, the authority set and defines minimum requirements with respect to practices, premises, professionals and products of the small scale medicine establishments, and to ensure adherence to current Good Manufacturing Practice and Good Laboratory Practice (EFMHACA, 2014).

Therefore, in this study we assessed the regulatory compliance of small scale local pharmaceutical manufacturer based on EFMHACA and WHO directives (Establishment directive for small scale medicine establishment directive 2014 and WHO Technical Report Series, No. 961, 2011, Annex 3).

## 1.1. Statement of the problem

The Ethiopian local pharmaceutical production is still limited. Estimates on the share of the market held by local producers of pharmaceuticals are 20% of the market (MOH and MOI, 2015). There is no active pharmaceutical ingredient production in Ethiopia (Von Rosenstiel, 2007). There are very low pharmaceutical products exports while the majority of drugs used by domestic needs are imported. The pharmaceutical industry contributes very low to the country foreign currency. (Floyd, 2008).

Local pharmaceutical production capacity is affected by many factors such as lack of access to input materials(active ingredients) needed for the production, skilled labor, technology, the qualities of a given company( management, leadership within the company, assessment of market size, marketing, government incentives, access to finance, etc. influence the feasibility and profitability(WTO,2001).

Ensuring the quality of healthcare can only be possible when equal emphasis is given to the different aspects of the healthcare system including the quality of pharmaceutical products. Since medicines are critical elements in healthcare; the pharmaceutical manufacturing company is a vital segment of healthcare system. Poor quality of medicines is not only a health hazard but also a waste of money for both government and consumers (Sharma, *et al*., 2011; Nigam, 2012).Medicines produced should be fit for their intended use. To meet this principle, quality assurance of product by in process and finished product inspection and testing is difficult. Medicines must be manufactured to the highest quality levels. Quality assurance systems must be implemented. In the pharmaceutical manufacturing companies, GMP elements perform this task (Rachan, *et al*., 2012).

Compliance to the local and any other international regulatory requirements increases production capacity of local pharmaceutical manufacturing factories due to reduction of product failure, boosts pharmaceutical product export and foreign exchange earnings, assure quality of produced products, and avoid double standard market authorization process by the regulatory authority and improve the overall healthcare out-come. Local production, if it results in substandard drugs, can also decrease consumer trust in authentic combinations, with serious implications for public health(Global Fund, 2007)

Every pharmaceutical site needs good hygiene and sanitation over 24 hours and 365 days a year.70 % of the failure in sanitation and hygiene can be attributed to the lack of orientation and inadequate training (Gupta, 2012). However, data on the implementation of any of the quality assurance requirements in the local pharmaceutical industries are lacking in Ethiopia. As shown in the internal report of EFMHACA from 2017 to 2018 six regulatory measures were taken on local pharmaceutical manufacturing facility because of product quality defects(EFMHACA,2018).From 2017 to2018 eighteen different products were recalled from the market due to product quality defect only, and among product quality defects three of them were due to miss labeling of the product which directly related with documentation problem and the others were substandard products. (EFMHACA, 2018).

Poor practices on the process of production can result in contamination or in products that do not possess the strength, quality, and purity required by regulatory authority. EFMHACA internal report of 2017 shows that, in one year only 25 small scale pharmaceutical manufacturer were notified to recall their product from the market because of quality problem (EFMHACA internal Report, 2018). Therefore, regulatory requirement compliance of the local pharmaceutical manufacturer indicates the quality of the product in the market; because, the compliance of the company directly related to the quality of the product on the market. Based on the finding of this research, by improving the regulatory compliance of the local pharmaceutical manufacturer we can improve the quality of locally produced product and decrease the cost associated with poor quality of medicine manufactured by local pharmaceutical manufacturers.

Therefore, this study was focused on the regulatory compliance status of small-scale pharmaceutical manufacturers with respect to personal, premises, documentation, sanitation and hygiene and explore major challenges for the implementation of the regulatory requirements in these pharmaceutical manufacturing industries.

## 1.2. Significance of the study

Most of the local manufacturers operate below their capacities and supply only about 20% of the local market. In 2014, local pharmaceutical companies supplied products to the value of US$ 44.2 million. Local manufacturers have limited product portfolios and are thought to be able to supply only 90 of more than 380 products on the national essential medicines list. Around 35–40% of their total output is supplied to the private sector at a price premium of 10%. The annual private pharmaceutical market in Ethiopia is estimated to be worth US$ 100 million.

knowing the regulatory compliance of the local pharmaceuticals and challenges for the sector that have influenced the growth of the local pharmaceutical industry so far enables the concerned organization to act on the challenge identified that could provide support for further industry development. Identifying, existing challenges would allow Ethiopia to define its strengths in development of pharmaceutical sector.

It is intended that, the findings of this work will be used for industrial capacity building sectors, pharmaceutical regulatory sectors, pharmaceutical investors and other related stakeholders.

Moreover, we believe that, the results of this study will help policy makers and regulatory bodies, pharmaceutical industries, and other stakeholders to design appropriate interventional strategy to improve the quality of products in the local pharmaceutical manufacturing companies. Besides, there is no data on the regulatory compliance of the local pharmaceutical manufacturing companies and this study attempts to fill this information gap.

## 1.3. Literature review

The African Union (AU) has raised the issue of local pharmaceutical production of generics, encouraging countries in the continent to set their objectives to support local production of essentially needed medicines. Of course, the lack of access to essential medicines in Africa is more severe than in other parts of the world, including access to drugs for HIV/AIDS, malaria and tuberculosis (AU, 2007).

Global pharmaceutical market 2008 ($ billion) by region (% share) Source: Data from IMS Health (www. imshealth.com) had indicated that North America 40.33%,Europe 32.01%, Africa 11.74%, Japan 9.91% and Latin America 6.01%. In the Middle East, Turkey is one of the largest pharmaceutical producers, importing less than one percent of the drugs needed locally and producing both finished products and active pharmaceutical ingredients for local use and export (J Med Syst, 2001).

Local production and related technology transfer in low- and middle-income countries often operate in a difficult environment. Although the same challenges are not equally present in all countries, many factors have been identified as commonly occurring. Several factors influence the feasibility of producing pharmaceuticals in a given country. Most importantly, access to active ingredients needed for the production or skilled labor and know how impacts have on the business potential. In addition, the qualities of a given company, such as management, leadership within the company, assessment of market size, marketing etc, influence the feasibility and profitability (WTO, 2001).

Pharmaceuticals are products that need special technical manufacturing capabilities throughout the whole process, following comprehensive guides of good manufacturing practice (GMP). Weak adherence by manufacturers to GMP standards and weak medicine regulatory authorities result in products of non-assured quality (AU, 2009). Local producers find it difficult to meet regulatory standards, including those for WHO prequalification, and medicine regulatory authorities in Africa are not considered to be meeting their own national or international standards (UNIDO, 2014).

Pharmaceuticals regulatory system was used as independent study variables because of the fact that pharmaceuticals are products that need special technical manufacturing capabilities throughout the whole process, following comprehensive guides of good manufacturing practice (GMP). There must be a body to regulate and supervise such activities, which is usually a public institution. Medicines as such are special commodities; their production, distribution and marketing require adequate control and supervision (Floyd D.2008). Therefore, study variables will be including level of pharmaceutical regulation of pharmaceutical market in Ethiopia, National regulation authority's resources, delivery capacity, institutional performance or the capacity to ensure pharmaceuticals to reach international quality standards and monitoring systems (AU, 2007,2009).

Capacity is needed in the area of R and D, training people in pharmaceutical sciences, in drug discovery and development and other areas. Lack of a collaborative culture among manufacturers, academics and industry practitioners, lack of access to knowledge, and lack of incentives that reward modes of collaborative conduct contribute to a lack of collaborations, which impacts industry development (Berger, etal.,2010).

Ethiopia is one of the most populated countries of Africa with a high demand for pharmaceutical products. The manufacturing for pharmaceutical products in Ethiopia is quite small. The industrial base is not well developed and the manufacturing companies have relatively low production capacities. Usually, local manufacturers tend to be given preference in the case of procurement from the government. The prices of the locally manufactured products are actually higher than imported products. (WTO, 2001).

In 2001, a Kansas City-based pharmacist was discovered to have adulterated 72 different drugs, including many oncology medications, to increase profits. According to law enforcement estimates, the pharmacist diluted approximately 98,000 prescriptions for 4,200 patients over an 11-year time period ( Draper R. , 2012.)

A 2011 outbreak of Serratiamarcescens bacteremia, which infected 19 patients at six Alabama hospitals, 9 of whom died, was caused by contaminated total parenteral nutrition bags from a compounding pharmacy (US FDA compounded products recall, 2012)

The FDA became aware of 55 product quality problems associated with compounded medicines between 1990 and 2001. The agency therefore conducted a limited survey of 29 different compounded medicines sourced from 12 compounding pharmacies, testing 8 different drugs of various dosage types (oral, injectable, topical, etc.) against established quality standards. Ten out of 29 samples (34 %) failed quality testing, mostly for sub-standard potency ranging from 59 to 89 % of the target dose. By comparison, the FDA noted that the failure rate for over 3,000 FDA-approved commercial products tested from 1996 to 2001 was less than 2% (US FDA Survey of Compounded Drug Products,2013)

The FDA conducted a follow-up survey in 2006 and found that 12 of the 36 compounded products (33 %) failed quality testing (US FDA Survey of Compounded Drug Products. 2012).Most of the failures were again related to potency, ranging from 68 to 268 % of the labeled dosage.

The FDA concluded that, the compounding processes used at pharmacies most likely the cause for quality failures and reiterated that this rate of failure raises public health concerns for compounded drugs. Annual testing of randomly selected compounded drugs by the Missouri Board of Pharmacy covering the years 2005–2009 showed failure rates between 11.6 and 25.2 %, with potency ranging from 0 to 450 % of the labeled dosage (26 Missouri Board of Pharmacy Compounding Report. FY2006– 2009.)

The Ohio State Board of Pharmacy performed similar testing of compounded drugs in 2007, which found potency results ranging from 27 to 87 % of the labeled dosage and 1,380 doses of fungally contaminated products. Thousands of the purportedly sterile compounded products that were examined had not undergone appropriate sterility testing . (Sasich LD, SukkariSR. ,2008). Over the period 2008–2010, the Texas State Board of Pharmacy found an overall potency failure rate of 23 % for compounded drugs ( Texas State Board of Pharmacy, Business Meeting Minutes, November 9, 2010)

A 2007 Centers for Disease Control and Prevention (CDC) report described three deaths from cardiac arrest in the Pacific Northwest, which were traced to intravenous colchicine compounded by a pharmacy in Texas. Subsequent investigation found that, the compounded preparation contained 4 mg/mL of colchicine rather than the labeled 0.5 mg/mL dose (Texas

State Board of Pharmacy, 2010).Regulatory approval is one of the barriers to market entry in international markets. To enter international markets pharmaceutical firms require complying with the norms of concerned country's' regulatory authority. The norms are related to approval of manufacturing plant that will be used to manufacture pharmaceutical products for international markets (Gray 2004, Hill and Johnson 2004, Timmermans 2004). The products to be manufactured in this plant are then required to be registered with respective countries' regulatory authorities to sell it in the foreign markets. In most countries, the production and distribution of drugs is almost exclusively undertaken by the private sector, largely consisting of extremely powerful multinational corporations. Regulation of the industry is essential to ensure the production of safe and efficacious drugs. Recent efforts to improve access to medicines in the developing world has led to a focus not only prices and international barriers to trade, but on national drug regulatory agencies (DRAs), in their role in registering drugs for use (Gray 2004, Hill and Johnson 2004, Timmermans 2004).

In Ethiopia, Local pharmaceutical industries dependson import of most raw materials. They imports over 95% of the required raw materials. In Ethiopia the pharmaceutical industry is still at infancy stage of development. For example, there is a big disparity between the three East African countries on the level of development in the pharmaceutical industry. Kenya is at the forefront in the number of established industries and has other supporting industries such as packaging, printing, pharmaceutical active ingredient wholesalers etc. While Kenya is the main exporter of pharmaceuticals into Uganda and Tanzania, the local Kenyan pharmaceutical production can only meet 30-35% of the national demand.(Satyanvesh, 2013).

The U.S. Pharmacopeial Convention (USP) reports results of data collected from medicines quality monitoring (MQM) activities spanning the period of 2003–2013 in 17 countries of Africa, Asia, and South America. Approximately 71% of the samples reported came from Asia, 23% from Africa, and 6% from South America. The samples collected and tested include mainly antibiotic, ant malarial, and anti tuberculosis medicines. A total of 848 samples, representing 5.6% of total samples, failed the quality test. The failure proportion per region was 11.5%, 10.4%, and 2.9% for South America,

Africa, and Asia, respectively. Eighty-one counterfeit medicines were reported, 86.4% of which were found in Asia and 13.6% in Africa.

Additional analysis of the data shows the distribution of poor-quality medicines per region and by therapeutic indication as well as possible trends of counterfeit medicines.(USFDA, 2013).

Study which was conducted in Nigeria indicated the availability of high quality human resources with the capability to conduct research and generate new knowledge useful for enhancing pharmaceutical industries to comply the local and international cGMP requirements. Even though all stakeholders have equal responsibility, this study shows that the National Academic institutions are placed in first line (Siyanbola, et.al, 2012).

A study in Nigerian pharmaceutical manufacturing companiesshow that academic-pharmaceutical manufacturing company interaction is the basis for pharmaceutical manufacturing company's competitiveness and advance (Siyanbola, *et al.,* 2012). Academia-pharmaceutical manufacturing company interaction, in the context of this study, is limited to "university-pharmaceutical manufacturing company interaction" and "research institute-pharmaceutical manufacturing company" interactions. This study identified that the research institutes should support the local pharmaceutical manufacturing companiesin areas such as: in- house R&D department, consultancy service on cGMP requirements and man power training. The identified interaction of universities with manufacturing companies include: support of the in-houseR&D, give emphasis to cGMP in their curriculum, organize and participate in GMP training and provide consultancy service.

In General even if there is a gap in the study areaglobally, summery of literature review shows that regulatory in compliance of local manufacturer were observed in different country and there was no study regarding to regulatory compliance in Ethiopia and this study will pave the way for future study in the sector.

# 2. Objectives

### 2.1.1. General objective

- To assess the regulatory compliance of small-scale local pharmaceutical manufacturing companies found in Addis Ababa, Ethiopia based on national and WHO Requirements.

### 2.1.2. Specific objectives

- To assess implementation status of regulatory requirement specifically documentation, personnel, practice and quality assurance system.
- To identify challenges faced by the small-scale pharmaceutical industries for the implementation of the requirements.

# 3. Methodology

## 3.1. Study design

A cross-sectional quantitative study was conducted to assess regulatory compliance of small-scale local pharmaceutical manufacturing companies and to assess major challenge faced by thesmall scale manufacturing industries for implementation of regulatory requirements from September 2019 to May 2020 in Addis Ababa, Ethiopia.

## 3.2. Study area and scope

Ethiopia has currently 11 large pharmaceutical manufacturing company and 46 small scale pharmaceutical manufacturing facilities. In Ethiopia pharmaceutical supply chain consists of manufacturers, Importers, whole sellers and retail outlets. Ethiopia has around 540 medicine and medical supply importers and Distributors. The study was conducted in 18 local small-scale pharmaceutical manufacturing companies in Addis Ababa, Ethiopia between September 2019 to May 2020. Addis Ababa is the capital city of Ethiopia where majority of small-scale pharmaceutical manufacturing facilities found in Addis Ababa City.

## 3.3. Source and Study Population

Eighteen pharmaceutical manufacturing companies that were producing medicines, reagents and disinfectants were assessed. Technical staff members working in selected small-scale pharmaceutical manufacturing companies who directly or indirectly involved in the implementation of regulatory requirements within their respective companies were included in the study.

## 3.4. Inclusion and exclusion criteria

### 3.4.1. Inclusion criteria

- Small scale pharmaceutical manufacturing companies found in Addis Ababa city that were producing medicines, reagents and antiseptics during the study period included in the study.

### 3.4.2. Exclusion criteria

- Large pharmaceutical manufacturing companies that were producing medicine, reagent and disinfectants.

- Small-scale pharmaceutical manufacturing companies that was not functional during the study period.

## 3.5. Data collection instruments

- Checklist was prepared based on EFMHACA minimum standard requirements and used to assess extent of regulatory compliance according to regulatory requirement of EFMHACA and WHO. Observations of the small-scale pharmaceutical manufacturing companies were made by trained data collectors using the checklist**.(Annex I)**
- In order to investigate challenge for the implementation of regulatory requirements, a pre-tested semi-structured self- administered questionnaire was prepared**.(Annex II**) Pre-test were done with 5 technical staff members working in a small scale pharmaceutical manufacturing companies in Addis Ababa city. Based on the pre-test, appropriate modifications were made before the actual data collection. All the data were collected by the principal investigator.

## 3.6. Data Entry and Analysis

- After data collection, each checklist and self-administered questionnaires was checked for completeness and given appropriate code. Then, data cleaning were performed to check if there were any missed values and inconsistency. Finally, the data from the checklist and self-administered questionnaires were entered into a computer and analyzed using a Statistical Package for the Social Sciences software (SPSS, version 22). Findings are presented in the form of tables, graphs and descriptive summaries. Implementation status for each specific requirements are rated as Full implementation for company which shows evidence for the implementation of the requirements, partial Implementation was rated for company have evidence of implementation of some requirements and Not Implementation for company which does not Implement any requirement Elements.

## 3.7. Variables

### 3.7.1. Dependent variable

- These studies propose to asses several concepts as outcomes and represent the central dependent variables. The dependent of variables were implementation status of regulatory requirements by local small scale pharmaceutical manufacturing.

### 3.7.2. Independent variables

## 3.8. The proposed independent variables years of operation, personnel qualification, product type/range Operational definition

- **Active pharmaceutical ingredient**: biologically active component of a drug product to be used in medicine manufacturing
- **Good Manufacturing Practice (GMP):** is a subset of the quality assurance (QA) system in pharmaceutical industries which assures the quality, efficacy and safety of medicines. World Health Organization(WHO) defines Good Manufacturing Practices as "that part of QA which ensures that products are consistently produced and controlled to the quality standards appropriate for their intended use and as required by the marketing authorization"(WHO, 2003). It covers all aspects of the manufacturing process.
- **Fully implemented**: Implementation of all specific regulatory requirements set by EFMHACA directive and WHO Guideline.
- **Not implemented**: Among numbers of regulatory requirements elements related to specific requirements set by the regulatory Authority/WHO when none of the requirements elements is not implemented.(Example if all requirements elements related to personnel are not implemented)
- **Partially implemented**: Among numbers of regulatory requirements elements related to specific requirements set by the regulatory Authority/WHO, when some elements are implemented and some elements are not implemented.(Example if some requirements elements related to personnel are implemented and some are not implemented).
- Pharmaceuticals**: drug**s **that used for cu**re human disease

- **Regulatory compliance**: Full implementation of the requirements of premises, equipment, personnel, documentation, sanitation and hygiene
- **Small-Scale pharmaceutical**: manufacturer classified as small scale by the Authority (EFMHACA) and involved in processing or production of products for external use only, including sanitary items, cosmetics, antiseptic, and medical supplies and other related products using none sophisticated technology.

## 4. Ethical consideration

The research has the ethical clearance from the School of Pharmacy ethical review committee (**Reference No**. **ERB/SOP/95/04/2019**) and a letter from EFMHACA. Permission from each small-scale pharmaceutical manufacturing company was also obtained before cascading the research. Verbal consent was also obtained from the study participants after explaining the purpose of the study, benefit of participating in the study, why and how they were selected for the study, and what was expected of them. Participants were assured about the confidentiality of the information they provide in the course of the study and were informed that personal and pharmaceutical company identifiers will not be used.

Because of confidentiality, issue with respect to regulatory compliance of pharmaceutical company, code was used for each company, and all information is secured and used only for research purpose.

## 5. Results

During the study period, there were eighteen small scale pharmaceutical manufacturing companies, all of them have been working for a minimum of 1 year to 24 years. All the selected small scale pharmaceutical manufacturing companies produced only human medicines, reagents and disinfectants. The entire local small scale pharmaceutical manufacturer included in the study has manufacturing license from the regulatory authority. All of the company involved in the study were owned by private, and one was a joint venture with foreign investor.

Only technical professionals were included in study. Total of 18 participants were included, each of them were recruited from different local pharmaceutical manufacturing companies. Of the participants, more than half (61.1%) were male with similar age distribution with a cut of 40 years and mean age of 41.63 ± 12.54 years, majority (61.1%) were having 6-15 years of lifetime working experience and at least 5 years working experience in their current pharmaceutical company. Above 75 % of the study subjects have highest academic achievement of BSc degree and nearly half of them were working as a production manager(Table 1).

**Table 1: Distribution of respondents according to different characteristics (N=18)**

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Sex | Male | 11 | 61.1 |
| | Female | 7 | 38.9 |
| Age in years (n=16) | ≤40 | 8 | 50.0 |
| | >40 | 8 | 50.0 |
| Total number of years of experience | ≤5 | 3 | 16.7 |
| | 6-15 | 11 | 61.1 |
| | >15 | 4 | 22.2 |
| Years of experience at current pharmaceutical company | ≤5 | 11 | 61.1 |
| | >5 | 7 | 38.9 |
| Primary responsibility at the | Production | 8 | 44.4 |

| | | | |
|---|---|---|---|
| current | manager | | |
| | Quality control | 4 | 22.2 |
| | Chief executive officer | 2 | 11.1 |
| | Technicalmanager | 2 | 11.1 |
| | General Manager | 2 | 11.1 |
| Highest academic qualification | BSc degree | 14 | 77.8 |
| | MSc | 3 | 16.7 |
| | PhD | 1 | 5.6 |

In the current study, regulatory compliance requirements were grouped in to 8 composite questions encompassing two or more regulatory compliance elements. With respect to specific regulatory requirements; full implementation was higher (55.6%) on requirement related to documentation of storage of reference/retention samples and requirement related to availability of responsibility of personnel followed by availability of procedure/SOP for receiving and storage of raw materials, sufficient testing of raw material. Availability of adequate and qualified personnel was mentioned in 50% of participants and the rest response was described in Table 2.

**Table 2: Participants response on regulatory compliance elements**

| Regulatory compliance element | Specific requirement | FI N (%) | PI N (%) | NI N (%) |
|---|---|---|---|---|
| **1**.Require | Procedure/SOP for receiving | 9 (50.0) | 0 (0) | 9 (50.0) |

| | | | | |
|---|---|---|---|---|
| met related to raw materials | and storage of raw material | | | |
| | List of approved raw material suppliers | 5 (27.8) | 6 (33.3) | 7 (38.9) |
| | Specification for each raw material | 3 (16.7) | 10 (55.6) | 5 (27.8) |
| | Sufficient testing of raw material. | 9 (50.0) | 7 (38.9) | 2 (11.1) |
| 2.Requirement related to analytical method | In- house analytical methods availability | 0 (0) | 16 (88.9) | 2 (11.1) |
| | System suitability test for compendia analytical procedure | 0 (0) | 9 (50.0) | 9 (50.0) |
| **3**.Requirement related to stability study | The availability of stability study program | 8 (44.4) | 3 (16.7) | 7 (38.9) |
| | The availability of stability study protocol | 8 (44.4) | 3 (16.7) | 7 (38.9) |
| | The availability of written stability study procedure | 8 (44.4) | 1 (5.6) | 9 (50.0) |
| | The availability of prospective and concurrent stability studies | 8 (44.4) | 1 (5.6) | 9 (50.0) |
| **4**.Requirement related to personnel | The availability of personnel qualification program | 2 (11.1) | 13 (72.2) | 3 (16.7) |
| | The availability of adequate and qualified personnel | 9 (50.0) | 7 (38.9) | 2 (11.1) |
| | The availability of schedule for | 7 (38.9) | 7 (38.9) | 4 (22.2) |

| | | | | |
|---|---|---|---|---|
| | training of personnel | | | |
| | Induction training program | 6 (33.3) | 5 (27.8) | 7 (38.9) |
| | Continuous training program | 7 (38.9) | 0 (0) | 11 (61.1) |
| | Refreshment training program | 7 (38.9) | 0 (0) | 11 (61.1) |
| | Responsibility of personnel available and clearly stated | 10 (55.6) | 8 (44.4) | 0 (0) |
| **5.**Requirement related to Manufacturing | The availability of SOPs for all manufacturing processes | 8 (44.4) | 10 (55.6) | 0 (0) |
| | The availability of Batch manufacturing record | 4 (22.2) | 13 (72.2) | 1 (5.6) |
| | The availability of Batch packing record | 2 (11.1) | 7 (38.9) | 9 (50.0) |
| | Logbooks for major equipment which state product name, calibration status, maintenance status, cleaning status including date and name of persons who performed? | 2 (11.1) | 12 (66.7) | 4 (22.2) |
| **6**.Requirement related to QC | Availability of method of analysis in the QC | 4 (22.2) | 12 (66.7) | 2 (11.1) |
| | Availability of SOPs for each analytical procedures | 6 (33.3) | 8 (44.4) | 4 (22.2) |
| | Availability of SOPs for sampling | 8 (44.4) | 6 (33.3) | 4 (22.2) |
| | Availability of specifications | 3 | 11 | 4 |

| | | | | |
|---|---|---|---|---|
| | for all materials within QC and user | (16.7) | (61.1) | (22.2) |
| | Certificate of analysis mention the reference of SOP used | 3 (16.7) | 10 (55.6) | 5 (27.8) |
| | Analysis performed by GLP qualified personnel | 4 (22.2) | 11 (61.1) | 3 (16.7) |
| **7.**Requirement related to QA | BMR and analytical records being reviewed by QA | 4 (22.2) | 9 (50.0) | 5 (27.8) |
| | Availability of SOPs for designing, revising, handling and controlled documents in QA unit | 2 (11.1) | 9 (50.0) | 7 (38.9) |
| | Internal quality/GMP compliance audits | 2 (11.1) | 9 (50.0) | 7 (38.9) |
| | Rejection , reuse and recall of products | 7 (38.9) | 8 (44.4) | 3 (16.7) |
| | Complaints handling | 4 (22.2) | 12 (66.7) | 2 (11.1) |
| | Storage of reference/retention samples | 10 (55.6) | 6 (33.3) | 2 (11.1) |
| **8.**Requirement related to sanitation and | Are all personnel, prior to and during employment, should undergo health examinations | 2 (11.1) | 10 (55.6) | 6 (33.3) |
| | Are all personnel trained in the practices of personal hygiene | 2 (11.1) | 9 (50.0) | 7 (38.9) |

| | | | | |
|---|---|---|---|---|
| hygiene | Are personnel instructed to wash their hands before entering production areas? | 2 (11.1) | 7 (38.9) | 9 (50.0) |
| | Are all personnel trained in the practices of avoiding direct contact between the operator's hands and materials/products, to ensure protection of the product from contamination | 5 (27.8) | 9 (50.0) | 4 (22.2) |

*Abreviations: FI-fully implemented; PI-partially implemented; NI-not implemented.*

In this study percent positive response (PPR) was calculated for each regulatorycompliance dimention. Responses of fully implementation are only considered as positive response. Accordingly, PPR was found to be heigh (44.4) on questions that assesed documentation related to stability study followed by documentation related to personel (38.1%) as shown in Fig 1.

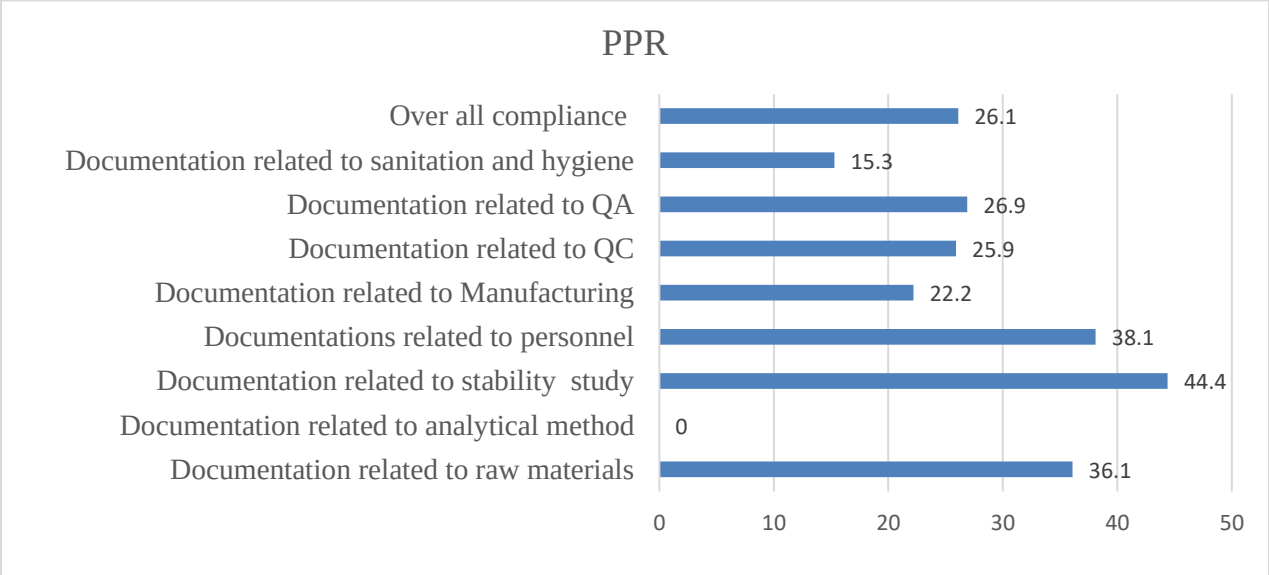


**Figure 1: Percent positive response of regulatory comliance dimentions**

Analysis of our data showed that, competitions from similar imported finished products, high cost of drugs production, lack of overall co-ordination among drugs manufacturers and other stakeholders, inadequate infrastructure and manufacturing equipment, and inadequate government incentives are challenge to all local pharmaceutical manufacturers.

In addition to the above mentioned challenges regulatory authority reluctance is also reported in 14 companies as depicted in Fig 2.

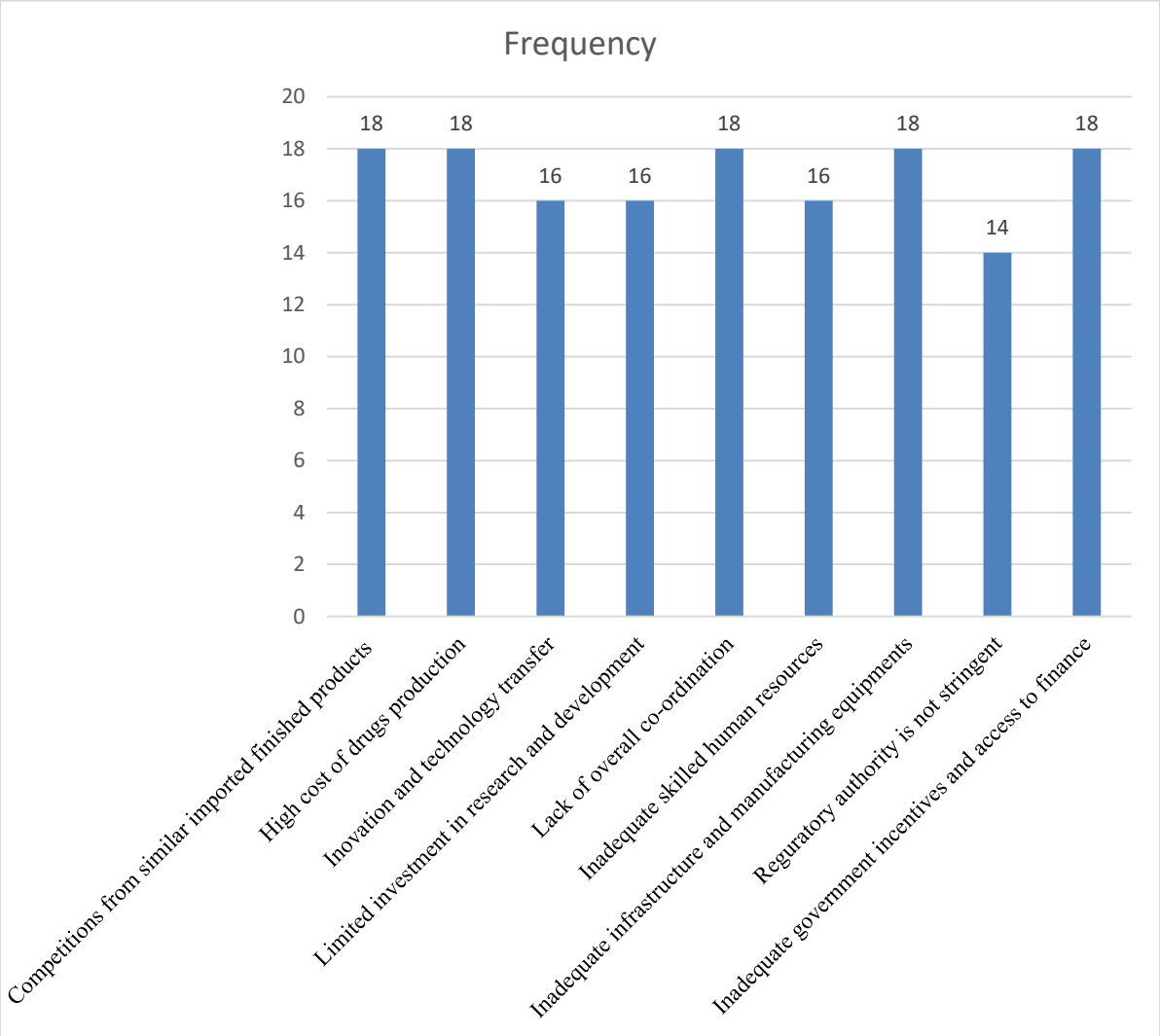


**Figure 2: Challenges of local pharmaceutical manufacturers**

High cost of drugs production is associated with many factors. Majority of participants (88.9%) disclosed that, locally manufactured drugs tend to be more expensive due to: high cost of imported input materials and all pharmaceutical ingredients including API were imported from abroad. Half (50%) of participants agreed that, Ethiopia being a landlocked country makes importation very expensive. Unsustainable API supply and variation of price of API are also factors making locally produced drugs to have high costs as reported by 7(38.9 %) participants.

Many challenges related to inovation and technology transfer were also reported which includes;limited local expertise and capabilitiesby 16(88.9%) participants, and 14 (77.8%) of them mentioned that, there is poor personnel qualification and skill. About 11(61.1%) subjects reported that, their company suffer economic hardship, and there is inadequate technology transfer practice and experience. Old equipements and inapprioprate premises were also mentioned in 6(33.3%) participants, and there is also inadequate enforcement by regulatory body according to the respondents(27.8%).

As reported by 18 participants, there is lack of overall co-ordination among drugs manufacturers and other stakeholders. Of them, 14(77.8%) agreed that there is poor University-Industry Linkage, lack of collaborative linkages and lack of policy coordination between various relevant ministries, departments and institutions, especially between those for trade, science, technology and innovation on the one hand and health on the other hand. Poor coordination between factories, government agencies, and development partners (Business Corporation) is also reported in 13(72.2%).Only1 subject said that the long inspection time needed warants fast tracking system with limitted co-ordination to be practiced in the institution.

According to the respondents, inadequate skilled human resources are related with many factors. Of which, 15(83.3%) participants said that there are gaps of academic institutions to produce human resources as need by the local pharmaceutical industry, there were gaps on pharmaceutical industry education curriculum (66.7%). Similar number of participants mentioned that, there exists lack of organizing and training

programs for local pharmaceutical manfacturers staff. More than half (55.6%) said that, there is difficulty of getting technicians locally for equipment and utilities maintenance.44.4% of them reported the lack of providing consultancy service and skilled technical personnel with sufficient know-how of the highly sensitive pharmaceutical manufacturing technology and to undertake R&D is in limited in Ethiopia. In addition, 5 (27.8) of them mentioned that, there is high turnover of the few available skilled personnel.

Many participants reported that, there is a challenges related to inadequate infrastructure and manufacturing equipments . Of which,utilities and equipment maintenance problems in 14(77.8%) of subjects, electric power interruptions and the high cost of running generators (72.2%) and very old manufacturing equipments and premises as reported by 38.9% participants. Table 3 summerizes the proposed corrective measures to be taken by relevant government body to strengthen local pharmaceutical companies. Of these, many (72.2%) of them emphasized on training of personnel on GMP.

**Tabe 3: Participants proposed corrective measures to be taken by relevant government body.**

| Proposed corrective measures | N(%) |
|---|---|
| Establishing a strong drug regulatory system is perhaps the most essential to enforce execution of GMP requirements and Drugs quality assurance system. | 11(61.1) |
| Timely correct specific deficiencies | 11(61.1) |
| Training of personnel on GMP | 13(72.2) |
| Provide competent and skilled Auditors because there were gaps regarding effective functioning of national drug regulatory authorities | 11(61.1) |
| Independent pharmaceutical capacity building body which support local pharmaceuticals | 8(44.4) |

The existence of gaps to understand and un-willingness of banks in providing lines of credit or loans at reasonable interest rates for the special needs of local pharmaceutical manufacturer is reported as a major challenge related to inadequate government incentives and access to finance in many (83.3%) respondents. In addition, about 2/3$^{rd}$ participants mentioned difficulties in accessing dollars, half of them mentioned bureaucratic hustle in every government offices and lack of good governance as a challenge. On top of this, there were no Ethiopian government law that forbids import of drugs, which are sufficiently locally manufactured (38.9%), inadequate technical and financial support from the government (33.3%) and financial constraint on most of local manufacturers as reported by 3(16.7%) study subjects.

# 6. Discussion

This study attempted to provide an insight on the status of regulatory compliance of small-scale local pharmaceutical manufacturing companies found in Ethiopia. We tried to assess the implementation status of regulatory requirements. Apart from assessing the implementation of regulatory requirements, this study also explored challenge of the small-scale local pharmaceutical manufacturing companies to implement these regulatory requirements.

## 6.1. Regulatory requirement elements implementation status

The regulatory requirement element includes; implementation of requirement related to ( raw materials, analytical method, stability study, personnel, manufacturing, QC,QA, and sanitation and hygiene).

The results of the study showed the presence of inadequate implementation of regulatory requirements within the manufacturing companies. Based on the study, the implementation status of the requirements was less than 50%. Within the implementation status, documentation related to quality assurance was less implemented in the studied local small-scale pharmaceutical industries.

Of the companies, 9(50%) of them have no procedure/SOP for receiving and storage of raw material and none of the company have fully implemented regulatory requirement for system suitability test for compendia analytical procedure. Only 44 % of the companies included in the study have written stability study procedure. Among the company included in the study, only 22% have personnel qualification program and schedule. Only 44% of the company include in the study have written SOPs for all manufacturing processes. 22% of the small scale pharmaceutical company have fully implemented regulatory requirement for method of analysis in the QC. Quality assurance activity was implemented only by 50 % of the selected pharmaceutical company.

The pharmaceutical sector is a complex one, involving many different stakeholders such as; the manufacturers themselves, national regulators, government ministries, wholesalers and others. The role of different stakeholders can be seen with regard to the scourge of counterfeit drugs, which cause huge health problems and also represent a threat to

legitimate manufacturers who effectively have to compete with these substandard products (UNIDO, 2010).

The role of the regulatory authorities is to ensure the quality, safety, and efficacy of all medicines marketed in their country. This includes; the process of manufacturing, distribution, and promotion of drugs in addition to regulating and monitoring the drugs.

Improperly functioning health regulatory systems have been observed in a range of low and middleincome countries (e.g. Zimbabwe, Tanzania, and Lao PD) (Hongoro and Kumaranayake 2000, Stenson et al 1997, Kumaranayake et al 2000). Hongoro and Kumaranayake (2000) identified capacity as a key factor influencing the ability of regulation to achieve its stated goals. Regulatory agencies often face crippling manpower shortages that severely curtail their ability to perform designated tasks. A comparative 10-country study of drug regulation concludes that 'the shortage of qualified staff is the main problem faced by regulatory authorities' (Ratanawijitrasin and Wondemagegnehu 2002).

## 6.2. Challenges faced by local industry for the implementation of regulatory requirement element

In this study, some of the challenges that were perceived to hinder compliance of regulatory requirements as required by national and international regulatory bodies have been explored.Analysis of data showed that: competitions from similar imported finished products, high cost of drugs production, lack of overall co-ordination among drugs manufacturers and other stakeholders, inadequate infrastructure and manufacturing equipment, and inadequate government incentives were some of thechallenges in all local pharmaceutical manufacturers, while regulatory authority reluctance is reported by only 14 companies.

Besides, the major challenges that were identified by the study were:high costs of production, lack of innovation & technology transfer, limited investment in research & development, lack of skilled human resources, limited local expertise & capabilities, inadequate infrastructure & manufacturing equipments, insufficient drug regulatory authority due to deprived capacity, market related challenges-competition , insufficient incentives (Limited funding) & lack of access to finance especially for hard currency and lack of overall co-ordination among drugs manufacturers & other stakeholders.Literature emanating from the World Bank support these research findings and it indicates that; barriers to business and industrial concerns in

developing countries, particularly for sub-Saharan Africa, are: a shortage of skilled labor, a weak financial sector (banking/non-banking), diminished flows of foreign direct investment, the fact that smaller firms face more problems than larger firms with financing and inflation and weak legal and regulatory systems and enforcement(Schiffer M. and Weder, B. (2001), (Beltchika, N., Stryker, J., Mwase, A., &Kazembe, G. (2001).

- **Innovation and technology transfer:**

Innovation and technology transfer was identified as one of the challenges for pharmaceuticals manufacturing development, as it is the basis for pharmaceutical manufacturing industrial growth. Several studies done in different countries support this result. For example, Schartinger, et al., (2002) argue that, knowledge interactions among firms, public research institutions and technology policy are key determinants of innovation success. Literature emanating from (World Trade Organization (WTO), 2001) indicated that, the promotion of the local technological base through transfer of technology between countries to their mutual advantage facilitates local pharmaceutical manufacturing development (Henry D, Lexchin N, 2002). Several empirical studies and literatures also continue to show innovation and technology transfer is major factor for local pharmaceutical industry development. For example, Bayh-Dole Act, 1980, passed by the United States to incentivize patenting, licensing, and technology transfer of university research is one of the earliest and clearest examples of efforts to foster entrepreneurialism and innovation. Since the 1980s, similar policies and strategies have spread to countries around the globe, including developing countries. The shortage of trained professionals and the expertise, quality laboratories, and financial resources hampers innovation and the development of new chemical molecules (DiMasiJA(2001) , DiMasi, J.A., Hansen, R.W. and Grabowski, H.G. (2003).

- **Co-ordination among drugs manufacturers and other stakeholders:**

The major challenging agenda identified with respect to this challenges was; lack of a collaborative culture among academics, various relevant ministries and industry practitioners for science, technology and innovation to meaningful and sustainable local pharmaceutical manufacturing industry development in Ethiopia. Study show that, cooperation has been identified as the basis for rapid industrial growth and competitiveness (Lundvall, 1992).

Collaborative linkages can take various forms and involve different intensities of engagement and these include R&D, training and curriculum development, and consultancy (Martin, 2000). Enterprises and other actors may commission a specific research project, sponsor a university chair in an area of interest, or engage in joint R&D with universities (Kaplan, W.A., Laing, R. (2004). Other universities focus on providing consultancy and business services, such as testing and certification (Basant and Chandra, 2007). Leadership, dedicated posts, clear strategic direction, and policies for managing the effective governance of industry linkages are also important for promoting a more directed institutional approach to building industry linkages (Kruss, 2008). A study in Nigeria on31pharmaceutical manufacturing companies show that, academic-pharmaceutical manufacturing company interaction is the basis for pharmaceutical manufacturing company's competitiveness and advance (Siyanbola, et al., 2012).

- **Availability of skilled human resources:**

Study emanating from literature showed that availability of skilled technical personals, and the qualities of a given company, such as; management, leadership within the company, assessment of market size, marketing etc., influence the feasibility and profitability of local pharmaceutical manufacturers industry development(See Klaus Liebig,2006).This study indicates that there are inadequate skilled human resources in Ethiopia. Accordingly, skilled technical personals with sufficient know-how of the highly sensitive pharmaceutical producing technology and to undertake R&D is inadequate in Ethiopia. Different study suggest that, relevant professionals such as; researchers, laboratory technicians and drug regulators and inspectorsare mandatory for strengthening pharmaceutical R&D, production and delivery in any country required for the development of local manufacturing industry (World Trade Organization (WTO) (2001), Henry D, Lexchin N. (2002). According to the respondents, the second human resource challenge is the high turnover of the few available skilled personnel. They reported that, there is a major challenge in retaining skilled staff even after training them at a high cost due to their limited numbers and the willingness of other employers to pay them more. Study which was conducted in Nigeria indicated that, the availability of high quality human resources with the capability to conduct research and generate new knowledge is useful for enhancing pharmaceutical industries development (Siyanbola, et al., 2012).

### Availability of Infrastructure and manufacturing equipments:

Our study showed that availability of physical infrastructure were poor. The electric power interruptions were one of the challenges; moreover, the cost of running generators is high. Respondent indicated also utilities and equipment maintenance problems were affecting the local pharmaceutical manufacturer performance. In addition, Ethiopia, like other landlocked country has long recognized significant challenges. Studies indicated that, Poor infrastructure and high transport costs are often identified as key constraints for industrial development in low-income countries (Bloom and Sachs, 1998). As noted by Collier (2000), manufacturing firms are intensive users of transport infrastructure services; therefore, poor quality, or high cost of the service will be at a comparative disadvantage for the manufacturer. Tybout (2000) argues that poor infrastructure is an important reason why markets for manufactured goods in low-income countries are often small and fragmented (Schiffer M. and Weder, B. (2001).

- **Market related challenges-Competition:**

Based on respondents of market players, two salient observations can be made about the relative performance of local manufacturers in the domestic market. Firstly, imported generics have a larger market share than locally-produced medicines. Some recognize the differences between product offerings by different local producers and importers and accept that some locally-produced medicines are also of poor quality and some imported "branded generics" are indeed of high quality. Studies show that, the vast majority of tenders are issued by international donors provided that bidding for such tenders requires compliance with international quality standards (GMP standards); because, weak adherence by manufacturers to GMP standards results in products of non-assured quality. Studies found from literature indicate that, local producers find it difficult to meet GMP standards, including those for WHO prequalification in Africa are not considered to be meeting their own national or international standards(World Health Organization 2011) ,(African Union, 2007).

- **High costs of production and market competition:**

Other major challenge identified was; local pharmaceutical manufacturer have struggled to compete for two reasons. Firstly, the high costs of active pharmaceutical ingredients (APIs) and other input materials in Ethiopia has left most unable to compete on price with Asian

generic manufacturers and unable to access the most in-demand therapy areas. Secondly, local pharmaceutical manufacturers have struggled to implement good manufacturing practices (GMP) and ensure quality production. There was studies supporting the finding and states as a number of firms, especially those selling exclusively on the domestic market, complained about weak domestic demand for their goods due to competition from imports, lack of income growth and lack the skills to successfully compete in a more liberalized economy (Beltchicka,N., Stryker,J. Mwase,A., and Kazembe,G.(2001). Studies show that, all pharmaceutical manufacturers in Ethiopia process imported active pharmaceutical ingredients (APIs) and others inputting materials (SatyaMarg,G.(2014). The cost of production is therefore a significant challenge, which has inhibited the development of local pharmaceutical manufacturing industry. Studies show that, firms that manufacture drug products cannot be competitive without being able to minimize production cost while maintaining appropriate quality standards (UNIDO, 2016). For a number of reasons, manufacture of medicines in many developing countries will be relatively more expensive than their import, at least in the short run (Beltchika, N., Stryker, J., Mwase, A., &Kazembe, G. (2001)Incentives (Limited funding) andaccess to finance:

According to our finding, local pharmaceutical manufacturers have encountered inadequate incentives and access to finance. Studies indicated that, the vast majority of drug companies in developing countries like Ethiopia could not afford the costs of R&D for developing new chemical entities, assuming they have the technical capacity and the know-how because of developing a new drug from basic research is a complex, risky, capital-intensive and timeconsuming activity (DiMasi J., 2001). Several studies indicated that real growth of local pharmaceutical manufacturing industry occurs when there is adequate expenditures of funds for research and development, and for capital equipment and other activities. Therefore, access to finance is an obstacle often mentioned when it comes to the economic development of local pharmaceutical manufacturing includinganysector (DiMasiJA(2001), Schiffer M. and Weder, B. (2001).

- **Capacity of National Drugs Regulatory Authority (NDA):**

According to our study, weaknesses in inspection, including of medicine imports, is one of the reason for reported increase in substandard and counterfeit medicines on the market.

Respondents indicated that, there was low NDA's capacity to check both local and foreign manufacturers to ensure that they are complying with manufacturing standards. Assessments conducted on African drug regulatory authorities by WHO have highlighted significant challenges to effective functioning of national drug regulatory authorities, the key ones being human resource gaps and weak or absent legal and regulatory frameworks. The current trend is towards harmonization of regional drug regulation, based on the obvious benefits that would accrue from pooling individual country capacities (Berger, M; Murugi, J; Buch, E; IJsselmuiden C; Moran, M; Guzman, J; Devlin, M; Kubata, B, 2010).

Strong regulation is essential to reduce the penetration of these counterfeit products that could benefit the local pharmaceutical industry as well as the public health. Quality requires upgraded skills and equipment (UNIDO, 2010). The challenge of counterfeit requires the involvementof local companies to invest in high quality production and supported by the relevant government ministries. Consequently, the establishment and enforcement of quality standards by regulators is a critical element in solving the conundrum (UNIDO, 2010).In 2004, WHO estimated 90% of African Medicines Regulatory Authority (MRAs) lacked capacity to carry out medicines regulatory functions, and more than forty African MRAs were largely non-functional. This was due to lack of clear legislative framework, dispersion of regulatory responsibility, lack of resources, lack of experienced and qualified staff, lack of political support, lack of appreciation for importance of medicine regulation. (Guzman, 2010).

# 7. Strength and limitation

## 7.1. Strength

- Try to assessregulatory compliance of small scale pharmaceutical manufactures which is neglected area of study and identify major challenges faced by the company for the implementation of regulatory requirement.

## 7.2. Limitation

- The assessment did not cover perspective from regulatory body and perspective of client.

# 8. Conclusion

Our study indicated that the overall implementation status of regulatory requirements in the local pharmaceutical manufacturing companies is far below the minimum standard set by WHO and national regulatory Authority. From the total regulatory element requirement only 26.1% were implemented by local small scale pharmaceutical manufacturers. From the total regulatory requirements set related to raw materials, 36.1% requirement were implemented, requirement related to stability study 44.4% were implemented, , requirement related to personnel 38.1% were implemented, requirement related to manufacturing operation 22.2%r were implemented, requirement related to QC 25.9 were implemented, requirement related to QA 26.9, requirement related to sanitation and hygiene 15.3% were implemented.

Finally, the major challenges faced by the local pharmaceutical manufacturer industry in the implementation of regulatory requirements were highlighted and discussed, significant challenges: including human resource capacity constraints, limited access to foreign currency, and raw material procurement difficulties are some of the major challenges.

## 9. Recommendation

To improve implementation of regulatory requirement elements by small-scale pharmaceuticals manufacturers in Ethiopia, the challenges need to be addressed at the firm and national levels.

Government and other stakeholders has a central role to play in nurturing the infant pharmaceutical industry through support supervision, facilitating access to technology and business finance, and promoting market access at the national, regional and international levels.

Strengthening regulation of the pharmaceutical sector is also recommended for ensuring quality of products. This is necessary to encourage the local pharmaceutical manufacturers to lay out new lines of medicines and this encourages R&D into new medicines. Also at the regional level, harmonization of regulation to improve inspection and market approvals in the regional market (East Africa) is highly recommended.

Governments should facilitate transfer of technology in close collaboration with other countries, international organizations, foreign companies and local enterprises through policy incentives that are specifically designed for the acquisition.

Local small scale pharmaceuticalmanufacturers should carry out self-audits to determine their capacity and technological needs to inform the search for partnerships and collaborations for technological transfer, quality improvement, and cost minimization.

Promotion of partnerships and collaborations is other key issue for local small-scale pharmaceutical manufacturers. Synergy of collaboration between the government, academia, industry-university linkages and the medical profession and consumer groups in the pharmaceutical manufacturing industry is also highly recommended.

We recommend for future to conduct qualitative study on the challenge of pharmaceutical manufacturer found in Ethiopia.

## 10. References


African Union, 2007, April.Pharmaceutical manufacturing plan for Africa.In Third Session of the African Union Conference of Ministers of Health (pp. 9-13).

African Union, 2009, May. Local pharmaceutical production in Africa.In 4TH Session of the African Union conference of ministers of health, Addis Ababa, Ethiopia (pp. 4-8).

Beltchika, N., Stryker, J.D., Mwase, A.A., Kazembe, G.J. and Kwengwere, P.L., 2001. Barriers to Business Expansion in Malawi's New Policy Environment.

Bennett, S., Quick, J. and Velasquez, G., Public-private roles in the pharmaceutical sector implications for equitable access and rational drug use. DAP Series no. 5.

Berger, M., Murugi, J., Buch, E., IJsselmuiden, C., Moran, M., Guzman, J., Devlin, M. and Kubata, B., 2016.Strengthening pharmaceutical innovation in Africa.Council on Health Research for Development (COHRED).

Briguglio, L.P., 1998. Small country size and returns to scale in manufacturing. World Development, 26(3), pp.507-515.

Brunetti, A., Kisunko, G. and Weder, B., 1997. Institutional obstacles to doing business: region-by-region results from a worldwide survey of the private sector (Vol. 1759).

Centers for Disease Control and Prevention,CDC, 2007. Deaths from intravenous colchicine resulting from a compounding pharmacy,2007. MMWR.Morbidity and mortality weekly report, 56(40), pp.1050-1052.

COMESA Member States (2011).Implementation of the WTO Decisions on TRIPS Public Health .Available on www.cardno.com,[Accessed 10 March 2018].

DiMasi, J.A., 2001. Risks in new drug development: approval success rates for investigational drugs. Clinical Pharmacology & Therapeutics, 69(5), pp.297-307.

Dhahir HI. Arab pharmaceutical industry: present and future. Proceedings of the 2ND Drug Sym.S.A.Pharmac.deve.Countr(1982).pp131-140.

Draper, R., 2003. The toxic pharmacist. The New York Times Magazine, pp.83-83.

Ethiopia Food, Medicines and Health Care Administration and Control Authority, 2012.GMP guidelines for pharmaceutical products, Addis Ababa.

Ethiopia Food, Medicines and Health Care Administration and Control Authority, 2018. Report of product quality defect on small scale pharmaceutical manufacturing facility, unpublished

Floyd D. (2008), the changing dynamics of the global pharmaceutical industry-assessing the key factors driving the growth of the pharmaceutical industry.

Good manufacturing practices for pharmaceutical products: main principles. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh report. Geneva, World Health Organization, 2003, Annex 4 (WHO Technical Report Series, No. 908).

Global Fund, "Global Fund Grants for Malaria: Summary of Lessons Learned in the Implementation of ACT Policies in Ghana, Nigeria, and Guinea-Bissau," Arlington, VA: Rational Pharmaceutical Management Plus, June 2007.

Hajjou, M., Krech, L., Lane-Barlow, C., Roth, L., Pribluda, V.S., Phanouvong, S., El-Hadri, L., Evans III, L., Raymond, C., Yuan, E. and Siv, L., 2015. Monitoring the quality of medicines: results from Africa, Asia, and South America. The American journal of tropical medicine and hygiene, 92(6_Suppl), pp.68-74.

Henry, D. and Lexchin, J., 2002.The pharmaceutical industry as a medicines provider. The Lancet, 360(9345), pp.1590-1595.

J Med Syst (2001), the performance and problems of the Turkish pharmaceutical industry: is there a need to develop a national drug policy? pp 309–18

Kisa, A., 2001. The performance and problems of the Turkish pharmaceutical industry: is there a need to develop a national drug policy?. Journal of medical systems, 25(5), pp.309-318.

Kaplan, W.A., Laing, R., Waning, B., Levison, L. and Foster, S., 2003. Is local production of pharmaceuticals a way to improve pharmaceutical access in developing and transitional countries? PP 35-47

Lancet 2002, Trouiller P, OlliaroTorreeleOrbinski Laing Ford 359(9324):2188–2194. P, E, J, R, N. Drug development for neglected diseases: a deficient market and a publichealth policy failure.

Löfgren H. The global biopharma industry and the rise of Indian drug multinationals: implications for Australian generics policy. Aust New Zealand Health Policy 2007; PP 4-10.

Naidoo, S. (2012), High growth rates expected for the Ethiopian pharmaceutical market, but it's not all smooth sailing –Unpacking the challenges.Mountain View: Frost & Sullivan Market Insight; (http://www. frost.com/prod/servlet/market-insightprint.pag?docid=267359592, accessed 26 June 2015).

National strategy and plan of action for pharmaceutical manufacturing development in Ethiopia (2015–2025)

National Pharmaceutical Control Bureau, Malaysia.Annual reports and awards.Annual report 2007.Petaling Jaya: National Pharmaceutical Control Bureau, Malaysia, 2007.

Olliaro PL, Vijayan R, Inbasegaran K, Lang CC, Looareesuwan S. Drug studies in developing countries. Bull World Health Organ. 2001; 79(9)894

Petaling Jaya (2007), National Pharmaceutical Control Bureau, Malaysia. Annual reports and awards. Annual report 2007. National Pharmaceutical Control Bureau, Malaysia.

Prof. John Ssebuwufu , Director, Research &Programmes , Association of African Universities (AAU) , Strengthening University-Industry Linkages in Africa: A Study of Institutional Capacities and Gaps, Email: info@aau.org, shesra@aau.org, Web site: http://www.aau.org.

Rachana P, Rana A, Nimrata S, Rajni B. (2012) Reveiw: introduction and general overview of pharmaceutical process validation: Int.J.Pharm 3:60-64.

Sasich, L.D. and Sukkari, S.R., 2008.Unknown risks of pharmacy-compounded drugs. The Journal of the American Osteopathic Association, 108(2), p.86.

Sharma T, Solanki N, Mahatam O. (2011) Process validation: An essential in pharmaceutical industries. IJPRD 3:133-142.

Satyanvesh (2011).Role of quality assurance in generic product development (documentation review process validation). Department of quality assurance, Kleu's college of pharmacy, Belgaum.

Shretta, R., 2007. Global Fund Grants for Malaria: Summary of Lessons Learned in the Implementation of ACTs in Ghana, Nigeria, and Guinea-Bissau. Arlington, VA: Management Sciences for Health.

Ssebuwufu, J., Ludwick, T. and Béland, M., 2012. Strengthening university-industry linkages in Africa: a study on institutional capacities and gaps.Association of African Universities.

Sloan FA, Hsieh C-R. (2007), Conclusions and policy implications. In: Sloan FA, Hsieh C-R, editors. Pharmaceutical Innovation: Incentives, competition, and cost-benefit analysis in international perspective. New York: Cambridge University Press; 2007.

Schiffer M. and Weder, B. (2001), "Firm Size and the Business Environment: Worldwide Survey Results". International Finance Corporation, editor. Discussion Paper No. 43.

Siyanbola O., Oladipo G., Oyewale A., Famurewa J. and OgundariO.(2012 ) Academia-Industry Interactions in Nigeria Pharmaceutical Innovation System .Procedia - Social and Behavioral Sciences 52 : 279 -289.

Trouiller, P., Olliaro, P., Torreele, E., Orbinski, J., Laing, R. and Ford, N., 2002. Drug development for neglected diseases: a deficient market and a public-health policy failure. The Lancet, 359(9324), pp.2188-2194.

Tybout, J. (1998), Manufacturing Firms in Developing Countries How Well Do They Do, and Why? World Bank, Washington, D.C., Policy Research Working Paper No. 1965

Tybout, J.R., 2000. Manufacturing firms in developing countries: How well do they do, and why?. Journal of Economic literature, 38(1), pp.11-44.

United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP). (2007), Fact sheet: ensuring access to essential drugs. Bangkok: United Nations Economic and Social Commission for Asia and the Pacific.

United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP). Fact sheet: ensuring access to essential drugs. Bangkok: United Nations Economic and Social Commission for Asia and the Pacific, 2007.

United Nations Industrial Development Organization (UNIDO).Jordanian pharmaceutical sector. Vienna: United Nations Industrial Development Organization. Available at: http://mediterraneanexchange.unido.org /upload/3423_Pharmaceutical%20sector.pdf.

United States Food and Drug Administration. The special risks of pharmacy compounding. 2012. http://www.fda.gov/ForConsumers/ ConsumerUpdates/ucm107836.htm. Accessed Sept 2019.]

United States Food and Drug Administration. Meds IV pharmacy, IV compounded products recall: outbreak of Serratia marcescens bacteremia in Alabama hospitals. March 30, 2011. 2011.http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm249099.htm. Accessed Aug 2012. 18. Tainted TPN Cases Put Focus on h797i Rules, Pharmacy Practice News, June 2011, Volume 38. 2011. http://issuu.com/mcmahon group/docs/ppn0611_de. Accessed Nov 2018

United States Food and Drug Administration. Limited FDA Survey of Compounded Drug Products.2001.http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Pharmacy Compounding/ucm155725.htm. Accessed Mar 2018.)

US Food and Drug Administration. Pharmacy Compounding. 2006 Limited FDA Survey of CompoundedDrugProducts.2012.http://www.fda.gov/Drugs/GuidanceComplianceRegulatory

Vernon, J.A. and Golec, J.H., 2011. Correctly measuring drug development risk: A public policy imperative. Expert review of pharmacoeconomics& outcomes research, 11(1), pp.1-3.

World Health Organization, 2004. The world medicines situation (No. WHO/EDM/PAR/2004.5). World Health Organization.

World Health Organization. Global strategy and plan of action on public health (2008), innovation and intellectual property. Sixty-first world health assembly 2008: agenda item 11.6;Geneva,Switzerland.Availableat: http://apps.who.int/gb/ ebwha/pdf_files/A61/A61_R21-en.pdf.

World Trade Organization (WTO).Declaration on the TIPS agreement and public health. World Trade Organization Ministerial Conference Fourth Session, Doha, 9 - 14 November 2001.Availableat:http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.pdf.

World Trade Organization (WTO) (2001), Declaration on the TIPS agreement and public health. World Trade Organization Ministerial Conference Fourth Session, Doha. Available at: http://www.wto.org/english/thewto_e/minist_e/min01_e/ mindecl_trips_e.pdf.

# 12. Annexes

## 12.1. Annex IChecklist to assess regulatory compliance of small scale local pharmaceutical manufacturing companies in Addis Ababa, Ethiopia

Addis Ababa University

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Purpose: This checklist is adopted from EFMHACA directive 2014 minimum requirement forsmall scale pharmaceutical manufacturing establishment. Your response is very important and valuable to the successful completion of the study. The data collection will solely be used for research purposes and could be an input for capacity building of local pharmaceutical manufacturing companies. As such the survey is confidential, anonymous, and data will be analyzed in aggregates.

Small scale Pharmaceutical manufacturing company code number_____

Product type (Reagent, antiseptics, medical supply)_____

| Regulatory compliance element | | F I | P I | NI |
|---|---|---|---|---|
| 10.1. Personnel Requirement | | | | |
| 1.1. | Qualified and adequate personnel available? | | | |
| 1.2. | Organization chart available? | | | |
| 1.3. | Job description available? | | | |
| 1.4. | Responsibilities clearly defined? | | | |

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|---|---|---|---|---|
| 1.5. | Quality control/assurance head/production head<br>are they independent from each other? | | | |
| 1.6. | Quality control/assurance head/ production head<br>are the key personnel working full time? | | | |
| 1.7. | Is there continuous training program for all staff? | | | |
| 1.8. | Are there detailed written hygiene programs for clothing,glovingandshowering? | | | |
| 1.9. | Medical examination<br>□On recruitment? | | | |
| | □Regular examination? | | | |
| 1.10. | Absence of food and drinks (chewing gum) in the working area | | | |
| 1.11. | Toilet and refreshment rooms adequately separated fromproduction areas? | | | |
| | 2. Premises Related | | | |
| | 2.1.warehouse | | | |
| 2.1.1. | Suitable for intended purpose? | | | |
| 2.1.2. | Adequate size? | | | |
| 2.1.3. | Located and designed to exclude external contamination? | | | |

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|---|---|---|---|---|
| 2.1.4. | Appropriate lighting and air conditioning? | | | |
| 2.1.5. | Controlled access for authorized person only? | | | |
| 2.1.6. | Protection against entry of insects or other animals? | | | |
| 2.1.7. | Provision for different storage condition and mapping (T,RH)? | | | |
| 2.1.8. | Quarantine area sufficiently segregated with controlled access? | | | |
| 2.1.9. | Separate, protected area for sampling? | | | |
| 2.1.10 | Separate and safe storage area for<br>Rejected material?<br>Returned goods?<br>Recalled goods? | | | |
| 2.1.11 | Safe storage of printed packaging materials? | | | |
| 2.1.12 | Security measurement against theft? | | | |
| 2.1.13 | Fire extinguishing system? | | | |
| | 3. Manufacturing Room:Rooms/cubicle, general | | | |
| 3.1.1. | Suitable for the intended purpose?<br>Adequate size?<br>Clean? | | | |
| 3.1.2. | Appropriate lighting and ventilation? | | | |
| 3.1.3. | Recording of temperature and humidity? | | | |

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|---|---|---|---|---|
| 3.1.4. | Protection against entry of insects or other animals? | | | |
| 3.1.5. | Controlled access for authorized personnel only? | | | |
| 4. Procedure and activity | | | | |
| 4.1. | Reception, Sampling and labeling written procedure available? | | | |
| 4.2. | Sampling procedure available? | | | |
| 4.3. | Cleaning of incoming containers? | | | |
| 4.4. | Investigation and corrective action for damaged container? | | | |
| 4.5. | FIFO/FEFO procedure? | | | |
| 4.6. | Incoming goods conformity with approved supplier list? | | | |
| 4.7. | Labeling of incoming containers with<br>□Internal name and code?<br>□Allocated batch number?<br>□Status labeling (quarantine, approved etc)<br>□Expiry date or re-test date? | | | |
| | 5. Equipment | | | |
| 5.1. | Suitable for the intended use? | | | |
| 5.2. | Well maintained? | | | |
| 5.3. | Written cleaning procedures? | | | |
| 5.4. | Maintenance without contamination risk? | | | |
| 5.5. | Calibration procedure? | | | |
| 5.6. | Calibration records? | | | |
| 5.7. | Contents and flow direction marked on pipes? | | | |
| 5.8. | Pipes for distilled and demineralised water regularly monitored | | | |
| 5.9. | Status labeling of not functioning equipment? | | | |
| 5.10. | Equipment cleanliness status? | | | |

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|---|---|---|---|---|
| | 6. QUALITY CONTROL | | | |
| 6.1.1. | Independent QC department available | | | |
| 6.1.2. | Suitable for the intended use? | | | |
| 6.1.3. | Laboratories of adequate size? | | | |
| 6.1.4. | Appropriate level of maintenance? | | | |
| 6.1.5. | Adequate separation from production area? | | | |
| 7. Documentation related question | | | | |
| 7.1.Documentation related to Manufacturing | | | | |
| 7.1.1. | The availability of SOPs for all manufacturing processes | | | |
| 7.1.2. | The availability of Batch manufacturing record | | | |
| 7.1.3. | The availability of Batch packing record | | | |
| 7.1.4. | Logbooks for major equipment which state product name, calibration status, maintenance status, cleaning status including date and name of persons who performed? | | | |
| | 7.2.Documentation related to QA | | | |
| 7.2.1. | BMR and analytical records being reviewed by QA | | | |
| 7.2.2. | Availability of SOPs for designing, revising, handling and controlled documents in QA unit | | | |
| 7.2.3. | Internal quality/GMP compliance audits | | | |
| 7.2.4. | Rejection , reuse and recall of products | | | |
| 7.2.5. | Complaints handling | | | |

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|---|---|---|---|---|
| 7.2.6. | Storage of reference/retention samples | | | |

## 12.2. Annex II: Self-Administered Questionnaires

Annex: Administered questionnaire for data collection for assessment of key challenges for local pharmaceutical manufacturing industry in Addis Ababa, Ethiopia in the implementation of regulatory requirement element.

School of pharmacy, department of pharmaceutics and social pharmacy

Purpose: This questionnaire is designed to assess major challenges in the implementation of regulatory requirement element by local pharmaceutical

manufacturing industry in Addis Ababa,Ethiopia.Your response is very important and valuable to the successful completion of the study. The data collection will solely be used for research purposes and could be an input for capacity building of local pharmaceutical company. I would greatly appreciate your help in responding to this survey.

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For comments/questions please contact wenduketele (0913891278, wketele@yahoo.com) principal assessor for the study.It will take you maximum of 25 minutes to complete the questionnaire.

Section 1. Personal information

1. You are:

   Male ☐ Female ☐

2. Age in years_____
3. Total number of years of experience_____
4. Years of experience at current pharmaceutical company_____
5. Your primary responsibility at the current post_____
6. Your highest academic qualification_____

Section 2. Major challenges of local pharmaceutical manufacturers

1. Market related challenges-Competition, are local drug manufacture faces strong competitions from similar imported finished products fromother manufacturers?

   1. Yes 2. No

2. Are local drug manufacture faces high cost of drugs production?

   1. Yes 2. No

3. If yes to Q# 2,what challenge your manufacturing facility faced ? [more than one answer is possible]

a) Locally manufactured drugs tend to be more expensive due to high cost of imported input materials.
b) All pharmaceutical ingredients (API) required for the production of the drugs, including API were imported from abroad.

c) The transportation infrastructure from Djibouti port to Addis Ababa is also a challenge, it takes many days to transport raw materials into the country which is too expensive in terms of time.
d) Ethiopia being a landlocked country makes importation very expensive.
e) Unsustainable API supply and variation of price of API also factors making locally produced drugs high costs.
f) Others [please specify]_____

4. Inovation and technology transfer; Are there challenges for local pharmaceutical manufacturer to implement GMP qualification and quality assurance system?

1. Yes 2. No

5. If yes to Q# 4,what challenges your manufacturing facility faced ? [more than one answer is possible]

a) Limited local expertise and capabilities
b) insignificant technology transfer practice and experience
c) Suffering economic hardship
d) Poor personnel qualification and skill
e) Old equipements and inapprioprate premises
f) Lack of management and staff commitment
g) Inadequate enforcement by regulatory body
h) Others [please specify]_____

6. Are local productions of pharmaceuticals faces Limited investment in research and development?

1. Yes 2. No

7. If yes to Q# 6,what challenge local pharmaceutical manfacturer faced ? [more than one answer is possible]

a) The growth of the pharmaceutical industry has been inhibited by low levels of R&D.
b) low levels of R&D which has restricted local producers to use TRIPS flexibilities agreement opportunities,
c) Low levels of R&D has restricted local producers to production of invention of new drugs, production of off-patent, and generic medicines.
d) Others specific

8. Are there Lack of overall co-ordination among drugs manufacturers and other stakeholders

1. Yes 2. No

If yes to Q# 11 ,what challenge local pharmaceutical manufacturer faced ? [more than one answer is possible]

a) Poor coordination between factories, government agencies, and development partners (Business Corporation).
b) Poor University-Industry Linkage i.e no sound company -acadamic relationship
c) Lack of collaborative linkages
d) Lack of policy coordination between various relevant ministries, departments and institutions, especially between those for trade, science, technology and innovation on the one hand and health on the other hand.
e) Others [please specify]_____

9. Are Local productions of pharmaceuticals faces inadequate skilled human resources?

1. Yes 2. No

10. If yes to Q# 9,what challenge local pharmaceuticalr manufacturer faced ? [more than one answer is possible]

a) High turnover of the few available skilled personnel
b) Skilled technical personnel with sufficient know-how of the highly sensitive pharmaceutical producing technology and to undertake R&D is in short supply in Ethiopia.
c) There are gaps of Academic institutions to produce human resources the local pharmaceutical industry needs.
d) There were gaps on pharmaceutical industry education curriculum.
e) Lack of Organizing and training programs for local pharmaceutical manfacturers staff.
f) difficult to get technicians locally for equipments and utilities maintenance
g) Lack of Providing consultancy service
h) Others [please specify]_____

11. Are Local productions of pharmaceuticals faces inadequate infrastructure and manufacturing equipments?

1. Yes 2. No

12. If yes to Q# 11,what challenge local pharmaceutical manufacturer faced? [more than one answer is possible]

a) The manufacturing equipments and premises are very old.
b) Utilities and Equipment maintenance problems
c) Poor transport infrastructure
d) Drugs manufacturers in Ethiopia face problems that Kenya, Ghana and other countries with easy access to large ports.
e) Electric power interruptions are one of challenges and the cost of running Generators is high.
f) Others [please specify]_____

13. Is Ethiopian drugs reguratory authority is not stringent due to deprived capacity?

1. Yes 2. No

14. If yes to Q# 13, what do you anticipate from local pharmaceutical manufacturing companies regulatory authority? [more than one answer is possible]

a) Establishing a strong drug regulatory system is perhaps the most essential to enforce execution of GMP requirements and drugs quality assurance system.
b) Timely correct specific deficiencies
c) Training of personnel on GMP
d) provide competent and skilled auditors because there were gaps regarding effective functioning of national drug regulatory authorities
e) Independent pharmaceutical regulatory authority is mandatory which enforce relevant and well formulated laws.
f) Others[please specify]__

15. Are local productions of pharmaceuticals faces inadequate government incentives and access to finance?

1. Yes 2. No

16. If yes to Q# 15 ,what challenge local pharmaceutical manufacturer faced ? [more than one answer is possible]

a) There were no Ethiopian government law forbids import of about drugs, which are sufficiently locally manufactured
b) There was a financial constraint on most of local manufacturers.

c) There were gaps to understand and banks are not interested in providing lines of credit or loans at reasonable interest rates for the special needs of local pharmaceutical manufacturer.
d) Poor access to foreign exchange,purchases on foreign markets is transacted in US dollars. However, manufacturers often complain of difficulties accessing dollars.
e) Inadequate technical and financial support from the government.
f) There are Bureaucratic hustle in every government offices and lack of good governance.
g) Others[please specify]__

## 12.3. Annex III: Ethical clearance from EFMHACA and school of pharmacy