ASSESSMENT OF THE PHARMACEUTICAL MANUFACTURING INDUSTRY IN KENYA TO FORECAST LOCAL PRODUCTION SUFFICIENCY

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University or for any other award.

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DEDICATION

This thesis is dedicated to my parents for their impact on the core of my being.

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DEFINITIONS OF TERMS

Active pharmaceutical ingredient
Any substance intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used will confer pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

Bioavailability
The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of action.

Bioequivalence
This term describes pharmaceutical equivalent or alternative products that display comparable bioavailability when studied under similar experimental conditions.

Capacity
The ability of the local pharmaceutical industry to produce the quantity and quality of products required and also withstand market competition. Capacity of the local pharmaceutical industry will encompass the product range manufactured, market share of local products, price competitiveness, production capacities, premises and quality systems.

Installed production capacity
The designed capacity of the machine. This is the maximum output capability, allowing no adjustments for preventive maintenance, unplanned downtime and facility shutdown.

Available production capacity
This is what is practically feasible; the highest level of operation with an acceptable degree of efficiency, taking into consideration unavoidable losses of productive time.

Utilized production capacity
This is the ratio between the actual output of firms to the maximum available capacity that could be produced with existing plant and equipment.

Compulsory licensing
An authorization which is granted by the government without the permission of the patent holder.

Competitive pharmaceutical product
A pharmaceutical product that attracts more sales than similar pharmaceutical equivalents on the market.

Dosage form
The form of a dose of a chemical compound used as a drug or medication intended for administration or consumption. They are classified according to route of administration or physical form.

Economic utilization
A measure of the ratio of actual output to the level of output beyond which the average cost of production begins to rise.

Essential medicines
Medicines that satisfy the priority health care needs of the population and are available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford.

Excipient
An ingredient that is added to a raw material for a specific functional role. It can include antioxidants, microbiological preservatives, diluents, disintegrants, lubricants and others that help to alter/improve the physical characteristics of the raw material.

Generic drug
A pharmaceutical product, usually intended to be interchangeable with an innovator product that is manufactured without a license from the innovator company and marketed after the expiry date of the patent or other exclusive right.

Good Manufacturing Practices
Part of Quality Management which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and required by the marketing authorization, clinical trial authorization or product specification.

Pharmaceutical alternatives
Drug products are considered pharmaceutical alternatives if they contain the same therapeutic moiety, but are different salts, esters, or complexes of that moiety, or are different dosage forms or strengths.

Pharmaceutical equivalents
Drug products in identical dosage forms that contain identical amounts of the active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety and; do not necessarily contain the same inactive ingredients; and meet the identical compendial or other applicable standard of identity, strength, quality, purity and potency.

Pharmaceutical product
A substance or combination of substances used in treating or preventing disease. It may also be used in restoring, correcting, and modifying physiological function or making a medical diagnosis. A pharmaceutical product is also referred to as a medicinal product, a medicine, or a drug.

Prequalification
A United Nations program managed by WHO which facilitates access to medicines that meet unified standards of quality, safety, and efficacy for products that are used in the management of HIV/AIDS, tuberculosis, malaria and reproductive health.

Process reengineering
Developing new processes to produce copies of existing pharmaceutical products.

Product retention fees
The fee that must be paid by a marketing authorization holder periodically for any registered pharmaceutical product being marketed.

Therapeutic equivalence
Drug products that are pharmaceutical equivalents and have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.

Voluntary licensing
Arrangements between a patent holder and another party in a country, or serving the country's market, to afford opportunities for significant cost-containment.

ABBREVIATIONS AND ACRONYMS

AC	Available Capacity
ANVISA	Agência Nacional de Vigilância Sanitária, (National Health Surveillance Agency, Argentina)
API	Active Pharmaceutical Ingredient
APR	Annual Product Reviews
AU	Africa Union
BE	Bioequivalence
CROs	Contract for Research Organizations
COMESA	Common Market for Eastern and Southern Africa
CTD	Common Technical Document
cGMP	Current Good Manufacturing Practices
DARU	Drug Analysis and Research Unit (of the University of Nairobi)
DMF(s)	Drug Master File(s)
DRA(s)	Drug Regulatory Authority(ies)
EAC	East Africa Community
EM	Essential Medicines
EMA	European Medicines Authority
EPZ	Export Processing Zone
FDC	Fixed-Dosage Combination
FEAPM	Federation of East Africa Pharmaceutical Manufacturers
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome
GLPs	Good Laboratory Practice (s)
KGN	Kenya Gazette Notice

HEPA	High Efficiency Particulate Air
HVAC	Heating Ventilation and Air Conditioning
ICH	International Conference on Harmonization
KEML	Kenya Essential Medicines List
KEMSA	Kenya Medical Supplies Authority
KFPM	Kenya Federation of Pharmaceutical Manufacturers
KNPP	Kenya National Pharmaceutical Policy
MDGs	Millennium Development Goals
MEDS	Mission for Essential Drugs and Supplies
LDCs	Least Developed Countries
NQCL	National Quality Control Laboratory
NMITLI	New Millennium Indian Technology Leadership Initiative
NGO	Non-Government Organization
OEE	Overall Equipment Effectiveness
PE(s)	Pharmaceutical Equivalent(s)
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PPB	Pharmacy and Poisons Board
PMPA	Pharmaceutical Manufacturing Plan for Africa
R&D	Research and Development
QAM	Quality Assurance Manager
QbD	Quality by Design
SDGs	Sustainable Development Goals
SSEM	Self-Sufficiency in Essential Medicines
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UNIDO	United Nations International Development Organization

USFDA	United States Food & Drug Administration
VAT	Value Added Tax
WHO	World Health Organization
WTO	World Trade Organization

ABSTRACT

The World Health Organization's global strategy on public health aims to support Member States to improve access to essential medicines. The desire of Kenya Government to implement this is expressed by formulation of Kenya National Pharmaceutical Policy (2010) which encourages local production of essential medicines for self-sufficiency. The pharmaceutical manufacturing industry in Kenya is engaged in production of various types of dosage forms but its capacity and capability to produce essential medicines for Kenyans have not been determined. The aim of this study was to assess the pharmaceutical manufacturing industry in Kenya to forecast local production sufficiency. This was attained by evaluating the manufacturing capability, production capacities and compliance with international marketing authorization standard of the Kenyan pharmaceutical industry. The 24 licensed manufacturers of medicines for human use were assessed. Data was collected on the current drug situation in Kenya by scanning Pharmacy and Poisons Board database to determine range of products that are registered in Kenya. Local pharmaceutical manufacturer's product lists, Kenya Essential Medicines list and pharmaceutical tender lists of three major procurers in Kenya (Kenya Medical Supplies Authority, Kenyatta National Hospital and Mission for Essential Drugs and Supplies) were examined to establish the proportion of products which was manufactured locally. Prices competitiveness and market share of local products were evaluated and subsequently, pharmaceutical equivalents of 150 locally manufactured essential medicines were determined. Data on production capacity for 5 years (2010-2014) and compliance of facilities with good manufacturing practices standard and other prerequisites of marketing authorization was obtained using a structured questionnaire. Results showed that solid dosage forms were majority (54.9 %) of local products and sterile preparations were minority (2.7 %). Locally manufactured products accounted for 14.5 % of registered and 21.5 % of retained products. Local firms manufactured 38.4 % of products listed as essential medicines and 55.6 %, 24.5 % and 21.8 %, respectively, of pharmaceutical products procured by Kenya Medical Supplies Authority, Kenyatta National Hospital and Mission for Essential Drugs and Supplies. The overall percentage of local pharmaceutical equivalents was 32.5 % for registered products. There was no variation between mean prices of local and imported pharmaceutical equivalents. Scatter diagrams demonstrated that imported pharmaceutical products comprised both low and highly priced brands. The overall utilized production capacity (two shifts) was 21.5 %; tablets (24.1 %), capsules (12.8 %), liquids (25.3 %), dry syrups (21.8 %), external preparations (21.3 %) and oral rehydration salts (23.6 %). This study projected the year for self-sufficiency in non-sterile medicines produced in the local industry as 2043. Good manufacturing practices standard was satisfactory at 11 facilities while the rest were striving to achieve compliance. Research and development of new products was limited in most facilities with 1 % of the workforce deployed in this department. It is concluded from this study that Kenya depends heavily on imported drugs for her essential medicines needs. Majority of local products were less competitive than imported products and production capacity was underutilized. Majority of manufacturers adhered to current good manufacturing practice standards but were inadequate in research. This study recommends augmentation of research and development by the local pharmaceutical industry to generate new products. In addition, substantial government support is required to propel the industry to improve product range, product competitiveness and production capacity utilization.

CHAPTER ONE

1. INTRODUCTION

1.1 Background information to the study

Every human being has the right to the highest attainable standard of health including healthcare services (WHO, 2008). Access to essential medicines (EM) is recognized as a part of that right to health (Meier and Yamin, 2011). The United Nations Millennium Declaration (UN, 2000) committed member states to global alliance and Millennium Development Goals (MDGs), amongst them, the alleviation of extreme poverty and disease by 2015. The MDG 8, Target E acknowledges the need to improve the availability of affordable medicines for the world's poor. It addresses the collaboration of governments with pharmaceutical companies to improve access to EM in developing countries (Forman, 2013). Target 3.8 of the post-2015 Sustainable Development Goals (SDGs) aims to achieve universal health coverage including access to quality and affordable EM by 2030 (UN, 2016). To realize the medicine-related MDGs and SDGs, the World Health Organization (WHO) and partners developed a framework that encourages local production for access to medicines (WHO, 2011a). Local production refers to production of pharmaceutical products by firms located in a country, to specifically meet the demands of the market in that country but does not necessarily entail nationality of ownership (WHO, 2011b**)**.

Pursuit of local pharmaceutical production is a global initiative. Three multilateral organizations; WHO, United Nations International Development Organization (UNIDO) and the International Finance Corporation of the World Bank Group provide support for local production. The government of Germany and UNIDO co-

funded a project to strengthen local production in Least Developed and Developing Countries (LDCs/DCs), including Africa (UNIDO, Germany, 2010, UNIDO, Germany, 2012). The envisaged benefits of local production include avoidance of unreliable medicine supply, facilitation of technology transfer, promotion of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities and enhancement of self-sufficiency in EM (African Union, 2007, Nicol and Owoeye, 2013, Sisule, 2005).

African pharmaceutical manufacturers contributes about 30 % of the continent's medicine needs **(**EFPIA, 2013**).** The African Union (AU) assembly in 2005 mandated the AU commission to develop a pharmaceutical manufacturing plan for Africa (PMPA) (African Union, 2005). The core objective of the PMPA is to support local production in order to increase access to affordable quality medicines (Ngozwana *et al.,* 2012). The Federation of East African Pharmaceutical Manufacturers has developed a strategic plan that seeks to assist the East Africa Community (EAC) in harnessing the existing initiatives on local production (EAC, 2012). Consequently, Kenya has established the Kenya National Pharmaceutical Policy (KNPP) that aims to promote self-sufficiency in essential medicines through expansion of local production (Ministry of Health, Kenya, 2012a)

Kenya'**s** pharmaceutical manufacturing industry is the second largest in the Common Market for Eastern and Southern Africa (COMESA) region (Waithaka, 2005). The industry is engaged in secondary and tertiary production. Currently, the pharmaceutical manufacturing companies are mostly owned by indigenous Kenyans, with only one multinational, GlaxoSmithKline (GSK). The pharmaceutical market

share in Kenya from local production was 28 % in 2007 (Frost and Sullivan, 2008) and 25 % in 2014 (Watu and Kungu, 2014). Kenya supplies nearly 50 % of the regions pharmaceutical market share; however, Kenyan pharmaceutical exports contributed less than 0.5 % of all Kenyan exports to COMESA's (Watu and Kungu, 2014; Kinoti, and Njeru, 2013). The local market consists of the government, non-governmental organizations (NGO's) and private institutions. The three major procurers of the pharmaceutical products are the Kenya Medical Supplies Authority (KEMSA), a government procurer; Mission for Essential Drugs and Supplies (MEDS), a faith based non-governmental organization and Kenyatta National Hospital (KNH), the largest public and referral hospital in Kenya. The private sector is served by wholesale dealers who distribute both local and imported products. The private sector handles volumes comparable to the public sector (BroadReach, 2011).

Pharmaceutical manufacturing in Kenya is regulated by the Pharmacy and Poisons Board (PPB), the drug regulatory authority (DRA). The National Quality Control Laboratory (NQCL) which is the technical arm of the PPB carries out quality control testing of pharmaceutical products and post market surveillance. An assessment of current Good Manufacturing Practices (cGMP) standard in the local industry was carried out by UNIDO in 2012 upon which the cGMP roadmap for the industry in Kenya was established (UNIDO, Kenya, 2014). However, there is no explicit link between cGMP improvement and the capacity of the local industry to manufacture and supply EM to the domestic market. The impact of global harmonization of pharmaceutical product market authorization application dossier on local production and the risk on registration approvals is not clearly addressed. The Common Technical Document (CTD) format which has been adopted requires comprehensive

data as evidence that the product is adequately designed (Patel and Shah, 2014). The CTD format was adopted by Kenya in 2010 and requires data on research and development (R&D) and bioequivalence (BE) studies on some products (PPB, 2010). Currently, there is no BE center in Kenya and R&D of new products is limited in most facilities. Furthermore, price competitiveness of locally manufactured products needs careful deliberation since affordability has significant influence on access and product market share (Center for Pharmaceutical Management, 2003).

The implementation mechanisms for the envisaged benefits of local production are not devised by the KNPP (UNIDO, Kenya, 2010). Additionally, the pharmaceutical sector has not been selected as a target sub-sector for development under the Industrial Development master plan since it did not meet the criteria as a sector with potential contribution to industrial transformation (Ministry of Industrialization, Kenya, 2008, Ministry of Planning and National Development, Kenya, 2012). Fundamental factors that determine access to essential medicines include; government policies, assured quality, affordable prices, and an unhindered supply chain (MSH, 2012a). The pharmaceutical industry requires capability and capacity to manufacture the requisite essential medicines. Supportive laboratories should be easily available and affordable. Based on the preceding factors, the prerequisite for achieving self-sufficiency in essential medicines (SSEM) through local production is that the local industry must have the capability and production capacity to manufacture the products. These products must comply with quality standards and be able to withstand market competition. This study assesses the capacity of the Kenya pharmaceutical industry to make and supply essential medicines in order to forecast local production sufficiency.

1.2 Statement of the problem

To achieve self-sufficiency in essential medicines through local production, the pharmaceutical manufacturing industry requires capability and capacity to make and supply sufficient, affordable and quality medicines to meet the nation's demand. Currently, the capability of the local pharmaceutical industry to manufacture essential medicines is unclear. There is no comprehensive data on the contribution of locally manufactured essential medicines to the medicines that are marketed in Kenya. Additionally, there is no data on pharmaceutical equivalents (PE) to locally manufactured essential medicines. Furthermore, capacity of the industry to withstand market competition from imported products is not known.

Review of literature indicates that no comprehensive study has been carried out on production capacities in this industry and there is no quantitative data on installed, available and utilized production capacities in this sector. The first report on production capacities in the local industry by UNIDO in 2010 provided tentative values on capacity utilization based one unit operation for each production line. In view of the unsynchronized unit operations in production for the majority of the companies, and the complexity in capacity determination, a follow up survey is necessary to determine the available capacity. The available capacity of any machinery depends on its down time, efficiency and quality performance (Subramaniam *et al*., 2009). This will entail the analysis of all unit operations on the various production lines at each facility in this sector.

Compliance of the local industry with product market authorization prerequisites in Kenya is uncertain. The DRAs in East and Central Africa region have adopted the

stringent CTD format of dossier preparation for application of product registration (EAC, 2014). The dossier provides proof that a product has been developed and manufactured under the specified cGMP standards that govern pharmaceutical production to ensure product efficacy. The state of the pharmaceutical industry in Kenya and her readiness to provide essential medicines to the domestic market is not known. In this study, the product range manufactured by the local industry, market share of local products, pharmaceutical equivalents, price competitiveness, production capacities and compliance of the industry with standard that governs market authorization will be evaluated.

1.3 Justification

Implementation of the Kenya National Pharmaceutical policy and strategic planning requires analysis of data on capacities in the local industry. Capacity of the industry will depend on range of products that are manufactured locally, product price competitiveness, production capacities, facilities, utilities, quality systems, qualified technical personnel and research and development status. This research endeavours to establish the capability of the industry to make and supply essential medicines. This is the first study that aims to generate comprehensive and quantitative data on capacities in the Kenya pharmaceutical manufacturing industry. The results are essential for identification of new products to develop, projection of utilized production capacity and upgrading of manufacturing practices in the pharmaceutical industry. The findings are fundamental for developing strategic plans for Kenya pharmaceutical policy and demonstrate the linkage between industry and academia in policy making process. This study provides essential elements of quantity and depth to an earlier profile of the local pharmaceutical industry by UNIDO in 2010.

1.4 Research questions

This study aimed at answering the following questions;

i. What is the current situation of local pharmaceutical production in domestic supply of essential medicines in Kenya?

ii. What is the production capacity of the Kenya pharmaceutical industry, factors envisaged by the industry to affect its utilization and the projection for full capacity utilization?

iii. Does the Kenya pharmaceutical industry comply with the prerequisites of marketing authorization of pharmaceutical products?

1.5 Research hypothesis

The pharmaceutical industry in Kenya has the capacity to produce and supply Kenya's essential medicines requirements.

1.6 Objectives

1.6.1 General objective

To determine the capacity of the local pharmaceutical industry to produce and supply Kenya's essential medicines requirements.

1.6.2 Specific objectives

i. To determine the capability of the Kenya pharmaceutical industry to produce and supply essential medicines for the domestic market.

ii. To determine the production capacity of the pharmaceutical industry in Kenya, factors envisaged by the industry to affect its utilization and to forecast full capacity utilization.

iii. To assess the compliance of the Kenya pharmaceutical industry with the prerequisites of market authorization of pharmaceutical products.

1.7 Delimitation

The study comprised all licensed manufacturers of medicines for human use in Kenya.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Pharmaceutical production

Manufacturing of a pharmaceutical product encompasses all operations of purchase of materials, production, quality control, storage, distribution, and the related controls. Production refers to all steps involved in preparation of a pharmaceutical product from receipt of raw materials to completion of the finished product (WHO, 2011a). The three levels of production are; primary (manufacture of active pharmaceutical ingredients and intermediates), secondary (production of finished dosage forms from raw materials) or tertiary (packaging and labeling finished products). Most of the pharmaceutical manufacturers in developing countries are engaged in secondary and tertiary manufacturing operations (Kaplan *et al.*, 2011). Pharmaceutical production requires appropriately designed premises that are fitted with quality impacting utilities, production machinery, quality systems and technical expertise. Contributory institutions such as contract research organizations (CROs) are essential to ensure quality, efficacy and safety of products. Capacity for innovation, government incentives, transport infrastructure, access to a reliable supply of water and electricity are critical for success in production (Kgosana *et al.*, 2014). Pharmaceutical production is governed by legislation and cGMP regulations that ensure that products are safe and fit for the intended use. It is estimated that 38 countries in Africa have pharmaceutical manufacturing entities. Eight countries in Sub-Saharan Africa; Botswana, Bukina Faso, Chad, Congo, Gambia, Mali, Sierra Leone and South Sudan have no pharmaceutical manufacturing industry whereas Cameroon, Lesotho, Malawi, Namibia and Swaziland, have one or two manufacturers (Ngozwana *et al.*, 2012).

2.2 Pharmaceutical production requirements

2.2.1 Pharmaceutical quality standards

The pharmaceutical manufacturing industry is highly regulated to ensure consistent production of quality products (MSH. 2012b). The main regulatory standard for ensuring pharmaceutical quality is the cGMP regulation for human pharmaceuticals. The cGMPs are quality requirements that have been adopted as guidelines by the industry to ensure that products are consistently produced according to quality standards appropriate to their intended use (Haleem *et al.*, 2013). The cGMP guidelines that are widely applied in the pharmaceutical industry are; European Medicines Agency (EMA), United States Food and Drug Administration (USFDA), the WHO and International Conference on Harmonization (ICH) which is a special project that congregates regulatory authorities and experts from the pharmaceutical industry to discuss scientific and technical aspects of product registration. The WHO cGMP guidelines contains 17 quality elements namely; quality assurance, utilities impacting on cGMP, sanitation and hygiene, qualification and validation, complaints, product recalls, contract production and analysis, self-inspection, personnel, training, personal hygiene, premises, equipment, materials, documentation, good practices in production and in quality control (WHO, 2014). Quality covers all aspects of the manufacturing cycle and cannot be determined by end product testing (WHO, 2006a). The USFDA definition of drug quality is that the product consistently delivers clinical performance as per label claim and does not introduce additional risks due to unexpected contaminants (Woodcock, 2004). The ICH guideline on the Technical Requirements for Registration of Pharmaceuticals for Human Use, ICHQ8 defines quality as the suitability of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength, and purity.

The ICHQ6A emphasizes the role of specifications, stating that “specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities” (ICH, 2000). Product specifications usually are derived using test data from one or more batches, often not at production scale. As a result, the complexities of process scale-up, particularly for complex dosage forms are often not recognized. Quality is not created spontaneously. Product design and development significantly influence the quality of a pharmaceutical product. Building quality into the product in the course of development is fundamental.

During product development, appropriate formulations and dosages of the product are established. This includes a combination of *in-vitro* studies, *in-vivo* studies and trials. A study by a consulting firm, Bain & Company reported that the cost for discovering, developing and launching a new drug was nearly $1.7 billion in 2003 **(**Pinkney, 2003). Quality is a complex concept and encompasses three dimension; production process, product performance, and aesthetics (Yacuzzi *et al.*, 2001). Quality from the process viewpoint is the degree of adherence to the design and manufacturing process in order to conform to the predetermined specifications of a product. Conformance is achieved through adequate product development, process validation, equipment qualification and personnel training (Yu, 2008).

2.2.2 Quality assurance

The concept of quality assurance advocates that quality cannot be created at the end of processing, but has to be in-built into a product at every step of manufacturing process. Improvement in quality systems is ensured by internal audits, documentation and validation. The cGMP guidelines are constantly updated to more

stringent standards. The conventional procedure of establishing quality is to test the finished product against the specifications. Most pharmaceutical companies currently rely on resource-intensive quality control systems to prevent defective products getting to the market (Robert *et al.*, 2008). Under this system, product quality and performance are ensured by raw material testing, a fixed drug product manufacturing process, in-process and end product testing. Extensive in-process tests are conducted, such as blend uniformity, tablet hardness, weight uniformity and disintegration to ensure that the finished product complies with quality specifications. The combination of fixed manufacturing steps and extensive testing is what ensures quality. The aim is then to meet quality specifications. During product registration application, companies submit an extensive amount of data on the chemistry, manufacturing and material control part of the dossier, most of which is not directly related to the quality of the product (IBM, 2005). In addition, during the dossier evaluation, all products are treated equally without regard to the risk to the consumer. This has the effect of placing too much review time and effort on low-risk products and significantly takes away needed resources from the review of high-risk products such as modified release products, trans-dermal as well as narrow therapeutic index drugs. Regardless of the available cGMP guidelines, many product formulations and processes are based upon practice and experience and not on knowledge obtained through development studies (Krause, 2007). Developing a process to scale up a bench process to a commercial batch is a challenge for generic manufacturers. What works in the laboratory may not work in process development (Roth, 2007). The main cause of non-conformance is excessive variability in the manufacturing process (Baum, 2008). To reduce non-conformances, frequent inspections, both internal and external are carried out. Dependence on inspection will cease only when the

manufacturing process is understood to the extent that quality can be predicted from upstream activities and measurements. In view of these challenges, the ICH has developed three quality guidelines aiming at developing a harmonized pharmaceutical quality system applicable across the lifecycle of the product and which emphasize an integrated approach to risk management, thus introducing the concept of quality by design (QbD) approach to manufacturing. Emphasis on QbD by USFDA began with the recognition that increased testing does not improve product quality. The Industrial ICH Q8 guidelines on pharmaceutical development introduces the concept of QbD, the objective of which is to design a quality product and manufacturing process to consistently deliver the intended performance of the product (ICH, 2007). Quality by Design requires an understanding of how formulation and process variables influence product quality. It ensures product and process performance characteristics are scientifically designed to meet specific objectives (Patil and Pethe, 2013). The guidelines on Quality Risk Management, ICH Q9 depict science and risk-based approaches for pharmaceutical product and manufacturing process development (ICH, 2005). It describes systematic processes for the identification, assessment, control, communication and review of quality risks. The Pharmaceutical Quality Systems guidelines, ICH Q10, describe systems that facilitate establishment of a state of control for process performance and quality. The QbD scope assumes that problems can be anticipated and their occurrence prevented by reviewing data, analyzing risks associated with operational and quality system processes, by keeping abreast of changes in scientific developments and regulatory requirements. When fully developed and effectively managed, a QbD system leads to consistent, predictable processes that ensure that products are safe and effective (Garcia *et al*., 2008; Somma, 2007; Roy, 2012; Trivedi, 2012). Quality

by design integrates quality systems and risk management approaches into its existing programs with the goal of providing the necessary framework for implementing quality by design, continual improvement and risk management in the production process and also for post development changes and optimization. The USFDA Guidance for Industry aligns process validation activities with existing ICH guidelines for the industry; Q8, Q9 and Q10 (ICH, 2010**)**.

2.2.3 Pharmaceutical production premises and utilities

The WHO guidelines for cGMP (WHO, 2014) provide the standard for premises and auxiliary utilities used in pharmaceutical production. The building in which pharmaceutical products are produced must be designed in such a manner that it provides logical flow for both personnel and production materials. The material of construction of the building is defined and surfaces must be easy to clean. Utilities are designed and constructed such that particulate contamination and product mix ups are avoided. The guidelines provide requirements for the Heating Ventilation and Air Conditioning (HVAC) system for dosage forms. The HVAC system must provide sufficient protection to the product, personnel and environment. Production areas should be effectively ventilated, with air-control facilities (including filtration of air to a sufficient level to prevent contamination and cross-contamination, as well as control of temperature and, where necessary, humidity) appropriate to the products being handled, to the operations undertaken and to the external environment. Water used in the manufacture of pharmaceutical products should be purified and suitable for its intended use. Compliance to quality standards in pharmaceutical production necessitates huge investment and the cGMP requirements for premises and utilities have the greatest financial implication in the

pharmaceutical industry. There is significant disparity in compliance to cGMP standards in the developing countries. By 2015, thirteen companies in 6 African countries were WHO-GMP compliant and had attained WHO prequalification for one or more products as follows; South Africa (five companies; 14 products), Morocco (one company; 3 products), Uganda (one company; 2 products), Zimbabwe (one company; 2 products), four companies in Nigeria and one company in Kenya (Universal Corporation) for the antiretroviral, zidovudine/lamivudine (GIZ, 2012).

2.2.4 Market authorization of pharmaceutical product

2.2.4.1 Marketing authorization dossier

Drug regulatory authorities institute a system which subjects all pharmaceutical products to premarketing evaluation, marketing authorization and post marketing review to ensure that they conform to required standards of quality, safety and efficacy. Application for pharmaceutical product marketing authorization entails submission of a dossier on the product to the DRA (WHO, 1998). The content and format of the dossier must follow rules as defined by the DRAs. The dossier contains data covering the whole product cycle, starting from product design, research and development, process scale up, production process, quality control, stability, BE, clinical studies and more. Until the year 2000, each region had its own format requirements. To avoid compiling different registration dossiers for different regions, the CTD dossier was developed by EMA, USFDA and the Ministry of Health, Labour and Welfare (Japan) and was implemented in 2003 (Jordan, 2014).

2.2.4.2 Common technical document content

The CTD provides a common format for the preparation of technical documentation to support a marketing authorization application that will be acceptable in all the three regions (Europe, Japan and the United States). The CTD is divided into five modules; Module 1 (administrative and prescribing information), Module 2 (overviews and summaries of modules), Module 3 (quality-pharmaceutical documentation), Module 4 (non-clinical reports), Module 5 (clinical study reports). The common format simplifies exchange of regulatory information between regulatory authorities and ensures compliance to a universal international quality standard. Control of pharmaceutical raw materials is a CTD and cGMP requirement. All manufacturers must carry out vendor qualification to ensure material consistency. Raw materials from facilities that are approved by stringent regulatory authorities such as USFDA or materials with drug master files (DMF) are more expensive due to inbuilt quality costs (European Medicines Agency, 2013). Raw material control is essential since their characteristics affect performance of the finished product. Data on raw material characterization, R&D, preformulation, formulation, production process, validation, product stability and BE studies form part of the CTD.

2.2.4.3 Research and development

Research and development is a complex, laborious process that requires technical expertise. The pharmaceutical industry is the most research-intensive industry in the USA. Pharmaceutical Research and Manufacturers of America members allocate about 20 % of their domestic sales to R&D. The average cost of discovering, developing and introducing a drug into the market in the USA was $1.3 billion in 2007 (Petrova, 2014). In developing countries, manufacturers find it difficult to raise

the necessary finance and in 2002, Africa spent just 0.3 % of its gross domestic product on R&D versus the global average of 1.7 % and had only 1.2 % of the world's researchers (Berger *et al.,* 2010). Local pharmaceutical companies are not involved in any original R&D work (Ngozwana *et al.,* 2012).

2.2.4.4 Bioequivalence requirement

Bioequivalence study between generic and innovator product is a requirement for market authorization of pharmaceutical products especially those with active pharmaceutical ingredients (APIs) which have low solubility and permeability (Handoo *et al.,* 2012). Two drug products are considered bioequivalent if they are pharmaceutical equivalents whose rate and extent of absorption do not show a significant difference when administered at the same molar dose of the active moiety under similar experimental conditions, either single dose or multiple dose (WHO, 2006b). Majority of countries in Africa lack BE centres (Venkatesh *et al.,* 2016), consequently companies outsource these services to foreign laboratories. The cost of performing BE studies is prohibitive and ranges from $50,000 to $200,000 which is out of reach for most local pharmaceutical companies (Aregay, 2010). There is only one accredited center for BE studies in Africa; Biopharmaceutics Research Institute (BRI), Rhodes University, South Africa (UBRICA, 2015).

2.3 Production capacity utilization

Production capacity utilization is one way of measuring the performance of an industry, and grows with increase in demand for goods and services (Ray, 2011). Installed production capacity is the maximum output capability, allowing no adjustments for preventive maintenance, unplanned downtime, breakdowns and facility shutdown.

Available capacity is what is practically feasible; the highest level of operation with an acceptable degree of efficiency, taking into consideration unavoidable losses of productive time. Manufacturers invest in automation and high capacity machinery, with fast change procedures to reduce the downtime. Process optimization is carried out to ensure that each operation is running at the maximum validated speed that yields the desired quality attributes (Murray, 2012). Capacity utilization is the ratio between the actual output of firms to the maximum available capacity that could be produced with existing plant and equipment. Thus, it refers to the relationship between actual output produced and potential output that could be produced with installed equipment, if the available capacity was fully utilized (Satik, 2015). However, as output increases and well before the absolute physical limit of production is reached, most firms might experience an increase in the average cost of production because of the need to operate extra shifts or to undertake additional plant maintenance (Ray, 2011). The available capacity can be determined from the Overall Equipment Effectiveness (OEE), which quantifies how well production equipment operates relative to its designed capacity (Capstone Metrics, 2011). The OEE calculation combines the factors of time, speed and quality. The OEE breaks the operation of a manufacturing unit into three separate but measurable components: Availability, Performance, and Quality. Availability is the percentage of scheduled time that the equipment is available, performance is the running speed as a percentage of its designed speed and quality refers to the good units produced as a percentage of the total units stated since in normal production, some units are rejected, used for inprocess quality control checks or reworked. The available capacity (AC) which is dependent on OEE is determined as:

AC = (Equipment Availability) x (Performance) x (Quality) (1)

(Tilkar and Nagaich, 2013; Sisodiya *et al.*, 2014). Some sterile formulation plants operated at OEE levels of 10 %, whereas typical solid oral formulation plants operated with OEEs of about 30 %. Multi-purpose packaging lines also have OEE levels of about 25 to 30 % **(**ISPE, 2007). Table 2.1 illustrates typical ranges of performance at variety of pharmaceutical manufacturing facilities globally. Extensive downtime, lengthy change over time, unscheduled production and non-optimized processes contribute to the low OEE for solid dosage forms. Official estimates of capacity utilization are not released by many countries probably due to variance in results arising from the different methods of computation. India did not have official estimation by 2012 (Mukherjee and Misra, 2012).

Table 2.1: Global production capacity utilization for various dosage forms

	Overall Equipment Effectiveness (%)		
Type of plant	Minimum	Maximum	Average
Sterile production	10	80	45-50
Solid dosage form production	05	30	15
Semisolid form production	20	60	50
Packing	15	80	25

Source: International Society for Pharmaceutical Engineering (2007)

2.4 Local pharmaceutical production in developing countries

Most of the pharmaceutical manufacturers in developing countries are engaged in the production of finished dosage forms, packaging and labeling of finished products or repackaging finished products. The capacity to manufacture sufficient pharmaceutical products for local demand varies among developing countries. Six low or middle income countries: Argentina, China, India, Mexico, Russian and Montenegro had innovative capability whereas Bangladesh, Ethiopia, Ghana Iran, Jordan, Kenya, Nigeria, South Africa, Tanzania, Thailand, Tunisia, Uganda and

Vietnam have substantial capacity (WHO, 2004). It is estimated that 38 countries in Africa have pharmaceutical manufacturing entities. Eight countries in Sub Saharan Africa; Botswana, Bukina Faso, Chad, Congo, Gambia, Mali, Sierra Leone and South Sudan have no pharmaceutical manufacturing industry, whereas Cameroon, Lesotho, Malawi, Namibia and Swaziland have one or two manufacturers (Ngozwana *et al.,* 2012). Some developing countries in the Middle East, Asia and Latin America produce a wide range of pharmaceutical products in quantities that are almost adequate for local sufficiency. Bangladesh, China, Egypt and Turkey supply more than 85 % of their total market for finished products through local production (Kaplan and Laing, 2005; Amara and Aljunid, 2012). Argentina and Brazil locally manufacture more than 50 % of the domestic demand. A survey in 11 African countries indicated that local production contributed less than 30 % of the market demand (Isa, 2010). There is significant disparity in technology and compliance to cGMP standards in the developing countries. A few manufacturers have achieved international cGMP accreditation but majority comply with local standards. Most companies have small R&D departments where reverse engineering of generic products is carried out.

2.5 Essential medicines

2.5.1 Production of essential medicines

Essential medicines satisfy priority health needs of a population and nearly all developing countries have a published national essential medicines list (Wirtz *et al.,* 2017). The WHO has identified products and prepared a model EM list which presents the minimum medicine needs for a basic health-care system. Essential medicines are selected with due regard to disease prevalence, evidence of clinical

efficacy, safety and cost-effectiveness. In many developing countries, access to essential medicines is not adequate and the countries generally do not have the capacities to manufacture their own drugs (Amara and Aljunid, 2012). The WHO framework for 2016–2030 aims to provide a strategic path to help Member States achieve universal access to safe and quality-assured health products. It is estimated that 79 % of all pharmaceutical products in Africa are imported (Dong and Mirza, 2016). Access to EM is influenced by physical availability, quantity available, affordability, quality of products and services**.** However, data on capacities in the local pharmaceutical industry is limited (Kaplan and Laing, 2005).

2.5.2 Challenges of essential medicines production

Challenges facing local pharmaceutical production in developing countries include access to low cost investment funds required for cGMP compliance and inadequate personnel with specialized skills. The synergy of collaboration between government, academia and the pharmaceutical industry does not exist in many developing countries. Additionally, an ineffective regulatory system and poor infrastructure have negative impact on competitiveness of local products (SEATINI and CEHURD, 2013). A study on determinants of manufacturing location of choice for multinational companies cited availability of infrastructure and low cost of production as the key determinants (Gatundu and Wario, 2014). Decline in local production facilities has been reported in several countries such as Tanzania, South Africa and Zambia. The pharmaceutical manufacturing sector in Tanzania which expanded significantly between 1980 and 2009 has since been on the decline. In 2004-2005, seven pharmaceutical manufacturers were in operation, and in 2009, Tanzanian production supplied an estimated 35 % of the local market. By 2013, the number of

pharmaceutical manufacturers had decreased to 5 and the domestic market share shrunk to under 20 %. The decrease was attributed to the stringed cGMP requirements, limited manufacturing technology, international donor prequalification requirements and availability of more competitive pharmaceutical imports (Wangwe, 1995; Mackintosh *et al.*, 2015). Likewise, the number of pharmaceutical manufacturers in South Africa has subsided, 35 pharmaceutical plants had closed down since 1994, the majority being multinational R&D companies. By 2007 only ten out the 16 multinational pharmaceutical companies operating in South Africa still had manufacturing facilities. The decline was attributed to globalization and trade liberalization that occurred in the 1990's opening South Africa to competitive generic imports. The ratio of imported medicines to locally produced medicines was 8:1 in 1998 and by 2006 this ratio had increased to 17:1 (Naudé and Luiz, 2013). The number of pharmaceutical manufacturing facilities in Zambian is also declining due to its inability to compete with imported pharmaceutical products. Liberalization of pharmaceutical trade, lack of government incentives, investment capital, poor infrastructure, limited innovation and technological transfer were cited as the main factors that have a direct impact on the growth of the industry (Kachali *et al.*, 2014).

2.6 Pharmaceutical production in Kenya

2.6.1 Pharmaceutical manufacturing industry

Local pharmaceutical manufacturing in Kenya dates back to the 1940's when multinationals installed subsidiary manufacturing sites in East Africa. Kenya Overseas Company Limited was set up in 1947, Sterling Winthrop Inc. (US) in 1953, Burroughs Wellcome East Africa Ltd. (UK) in 1955 and Aspro-Nicholas (EA) Ltd. (Australia) in 1961 (Wangwe, 1995, Watu *et al.*, 2014). Following independence in

1963, the government pursued a policy of import substitution to attract foreign investors to manufacture for the domestic market. This policy was intensified in 1970, when tariffs were increased to discourage importation of goods (Gertz, 2008, Mumo, 2010). The pharmaceutical manufacturing industry developed steadily with Kenyan pharmaceutical wholesalers venturing into tertiary manufacturing in the 1970's, and eventually to secondary production. The pioneering pharmaceutical manufacturers owned by Kenyan nationals are Laboratory & Allied Ltd., Elys Chemical Industries Ltd., Cosmos Limited, Manher Brothers (K) Ltd., and Didy Pharmaceuticals Ltd. Dawa Limited was established in 1974 as a joint venture between the Kenyan and Yugoslavian (now Slovenia) government. The number of pharmaceutical manufacturers has been previously reported as 40 (Watu and Kungu, 2014; Orwa *et al.*, 2004), 43 (Fortunak *et al.*, 2010), and 45 (Kinoti and Njeru, 2013). The list of licensed pharmaceutical manufacturers in the Kenya government gazette notice No. 15427 of 2012 contains 37 companies including non-main stream manufactures whose products are regulated by PPB. Companies included in this list are Kenya Veterinary Vaccine Production, Reckitt & Colman Ltd., Manhar Brothers, Synerchemie Limited and facilities such as Gesto that are currently not operational. Kenya is currently the hub of the pharmaceutical manufacturing sector in the East African region. According to PPB database, most of the products manufactured are non-sterile and include tablets, capsules, syrups, suspensions, ointments and creams. Three companies; Autosterile EA Ltd., Ivee Aqua EPZ Ltd., and Infusion Kenya Ltd. manufacture sterile products, while Aesthetics Ltd., Coopers (K) Ltd., Nerix Pharma Ltd., Norbrook (K) Ltd., Impact Pharmaceuticals and Ultravets (K) Ltd., are dedicated to the manufacture of veterinary products. Four manufacturers; Biodeal Laboratories Ltd., Cosmos Limited, Dawa Limited and Laboratory & Allied Limited

produce both human and veterinary products. The main therapeutic categories produced are antimalarials, antibacterials, analgesics, antihelmintics, anti-allergies, antifungals, dermatological preparations and gastrointestinal agents. More than 80 % of raw materials used in production in Kenya are imported and production capacity is underutilized (UNIDO, Kenya, 2010).

2.6.2 Regulation of the pharmaceutical manufacturing industry

The Kenya National Drug Policy was introduced in 1994 but was hardly implemented due to lack of an enabling legal and institutional framework. The second edition which forms the basis of Sessional Paper No.4 of 2012 on KNPP is an integral part of Kenya Health Policy 2012-2030. The Health policy endeavors to advance universal access of EM by promoting local production and Vision 2030, the long term development plan for Kenya. The goal for the manufacturing sector is to develop a robust, diversified and competitive industry by strengthening local production (Ministry of Planning and National Development, Kenya, 2012). The PPB which is established under the Pharmacy and Poisons Act, Chapter 244 of the Laws of Kenya is the regulatory body for the pharmaceutical sector. The PPB performs regular inspections of local and foreign pharmaceutical manufacturers to ensure compliance with cGMP standard that govern pharmaceutical production. It also ensures compliance to good manufacturing and distribution practices, authorizes marketing of pharmaceutical products through a product registration process that entails evaluation of product quality and clinical attributes, and approves subsequent annual product retention for which a fee must be paid. The PPB evaluates applications for advertisements of pharmaceutical products and carries out pharmacovigilance and post-market surveillance to ensure that all medicinal products

manufactured in, imported into or exported from the country conform to prescribed standards of quality, safety and efficacy. The PPB endeavors to ensure a regulated market that guarantees quality and affordability of products to the consumer. The pharmaceutical industry is heavily regulated, with some laws which are in duplication (Wanyanga and Weche, 2009). Other legislations that impart on the pharmaceutical industry include the Anti-Counterfeit Act, 2008, which prohibits trade in counterfeit goods, Patent registration Act Cap 508 for patent protection, The factories and other places of work Act, Cap 514 that deals with health and safety at the work place, Public Health Act, Cap 242, for securing and maintaining health; Food and Drugs and Chemical Substances Act, Cap 254, for the prevention of adulteration of food, drugs, and chemical substances, the Environmental Management and Co-ordination Act of 1999 and the Labour Act, Cap 226 of 2012 which defines the fundamental rights of employees (Yano, 2010).

2.6.3 Kenya pharmaceutical manufacturers' affiliation

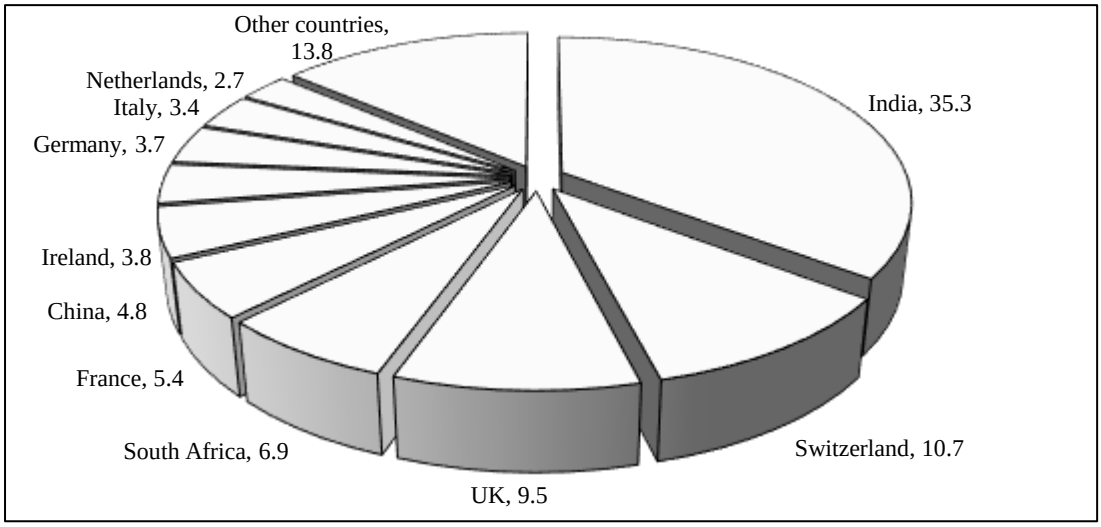
The Federation of Kenya Pharmaceutical Manufacturers (FKPM) is the umbrella body through which local pharmaceutical manufacturers articulate and convey their interests to relevant forums within the country regarding policies, regulations, trade and quality. The FKPM is member of the Federation of East Africa Pharmaceutical Manufacturers (FEAPM), which is an association of pharmaceutical manufacturers within the East African Community Partner States. The mission of FEAPM is to strengthen local production capacity to meet at least 50 % of the EAC's demand for affordable, quality medicines by the year 2020. The FEAPM is a member of Federation of African Pharmaceutical Manufacturers Associations (FAPMA) whose founding members include: Federation of East Africa Pharmaceutical Manufacturers,

the West African Pharmaceutical Manufacturers Association and the Southern African Generic Medicines Association. The FAPMA is a central mouthpiece for advocacy and promotion of local production in Africa (Reinhardt, 2013).

2.6.4 Essential medicines demand and market share

The Kenya Essential Medicines List (KEML) (Ministry of Health, Kenya, 2010a) is based on the 16th WHO model list of EM. The demand for EM in Kenya is a function of disease prevalence, population size and patterns, government procurement and export market opportunity. By the year 2010, infectious diseases were the leading cause of deaths in Kenya. The top ten causes of outpatient morbidity are malaria, diseases of the respiratory system, the skin, diarrhoeal diseases, intestinal worm infestation, accidents, pneumonia, eye infections, rheumatism and urinary tract infections (Ministry of Health, Kenya, 2010b). Between 1994 and 2010, the leading causes of deaths in Kenya were HIV/AIDS, conditions arising during prenatal period, lower respiratory tract infections, tuberculosis, diarrhoeal diseases and malaria (Ministry of Health, Kenya, 2012b). The Kenya Health Policy (2012-2030) anticipates reduction in some conditions such as HIV/AIDS and malaria, and an increase in lifestyle related diseases such as hypertension, diabetes, heart disease and cancers by 2030, hence, increased demand for products used in management of lifestyle diseases. If the Health policy (2012) directions in Kenya are sustained, the overall mortality will reduce by 14 % annually by 2030. The contribution by disease domain will change, with a 48 % reduction in deaths due to communicable diseases, but a 55 % increase due to non-communicable conditions (Ministry of Health, Kenya, 2012b). The estimated domestic market for pharmaceutical products in Kenya was US$ 720 million in 2014 (Espicom Business Intelligence, 2016). A

summary of pharmaceutical imports into Kenya, as a percentage, by country of origin is presented in Figure 2.1 (Wanyanga and Weche, 2009). Trade statistics demonstrate increase in both imports and exports of pharmaceuticals in Kenya as illustrated in Table 2.2 (ITC, 2012). India was the leading competitor to Kenyan manufacturers.



Source: Wanyanga and Weche (2009). The status of the pharmaceutical industry in Kenya

Figure 2.1: Pharmaceutical imports into Kenya by country of origin in 2007

The imports exhibit a consistent increase trend over the period whereas the increase in exports shows fluctuation; the value of exports in 2009 and 2010 were less than that of 2008. The growth in export trade was dismal (ranging from 7.9 to 23.9 %) in comparison to imports. The ratio of exports to the total pharmaceutical trade declined consistently from 2007 to 2011. The government is the major institutional buyer of locally manufactured pharmaceutical products through KEMSA under the Ministry of Health. The KEMSA purchases constitute nearly 30 % of all prescription drugs in the domestic market (UNIDO, Kenya, 2010).

Table 2.2: Pharmaceutical products trade value in Kenya from 2001 to 2011

Year	Imports (US$)	Exports (US$)	Total (imports & exports) (US$)	(Export/ Total)%
2001	88,650	22,086	110,736	19.9
2002	95,267	8,152	103,419	7.9
2003	109,788	29,945	139,733	21.4
2004	127,820	28,151	155,971	18.1
2005	158,019	37,797	195,816	19.3
2006	203,554	43,826	247,380	17.7
2007	222,175	69,722	291,897	23.9
2008	289,295	81,135	370,430	21.9
2009	283,066	70,241	353,297	19.8
2010	332,480	74,950	407,430	18.4
2011	438,232	84,655	522,887	16.2
Total	2,348,336	550,660	2,898,996	19.0

Source: Trade statistics, International Trade Centre, 2012

2.6.5 Competitiveness of pharmaceutical products

Medicines must be affordable in order to ensure access to the world's poor populations. Public sector availability of EM was on average, 34.9 % for 27 developing countries (WHO, 2015) and in Kenya, the availability was 50 % in 2014 (Watu *et al.*, 2014). In most developing countries, price competitiveness of pharmaceutical products is a key determinant in the choice of products to be procured by the government due to a limited health budget. Competitive generic products are associated with lower prices. Kenya does not currently have price control legislation or policy and instead the equilibrium price is determined by pharmaceutical inputs and the dynamics between supply and demand providing sufficient opportunity for competition. An informal pricing structure that allows a 10

% mark-up for the manufacturers over their production costs, a 15 % mark-up for distributors and wholesalers, and finally, a retail mark-up of up to 33 % on the wholesale price is practiced in some cases (Private Sector Innovation Programme for Health, 2014). The cost based pricing model is commonly used to compute the price of pharmaceutical products, whereby the sale price is deduced from all costs accrued during the manufacture and marketing of the product (Osemene, 2003). This involves computing all costs for making the product and adding a certain percentage as a mark-up to arrive at the wholesale selling price. The costs encompass research and development, raw materials, production process, quality control, maintenance, insurance, duty, transportation, labor and marketing of the pharmaceutical product. Kenya does not carry out primary production and most pharmaceutical inputs are imported, mostly from India and China (Ministry of Health, Kenya, 2012a). A few excipients are manufactured locally and these include maize starch, refined sugar and rectified spirit. Crude artemisinin is the only API currently produced in Kenya. Importation of material for pharmaceutical production impacts negatively on cost of production and wholesale price of locally manufactured products in developing countries (Yimer, 2009).

Procurement of pharmaceutical products by public agencies in Kenya is usually awarded to a bidder with the lowest quoted price. The quoted price does not cover hidden costs associated with rush shipments, product failures or unscheduled downtime, which are the risks usually associated with the cheapest price. The amount the customer eventually pays may be higher for a cheaply quoted imported product **(**Skhumbuzo, 2014). A report on the determinants of growth for the pharmaceutical industry in Kenya, with special emphasis on how government

purchases of pharmaceutical products affect the industry found out that despite the dominant government presence, the response of pharmaceutical manufacturers to government purchases of pharmaceuticals has not been clearly established. Besides, the extent and impact of initiatives that offer preferences and reservations to local manufacturers is not known. The study found the coefficient for government purchases to be significant but negative implying that there is negligible participation of local manufacturers in government tenders which indicates that government purchases are not directed towards local manufacturers thus placing local manufacturers in direct competition with imported pharmaceuticals (Hedwig, 2012). Key to sustainability of local production is the degree to which the locally manufactured products can compete with imported PEs. Pharmaceutical equivalents are drug products in identical dosage forms that contain the same active ingredient(s), use the same route of administration, are identical in strength and are formulated to meet the same applicable standards (USFDA, 2015). The government in its endeavor to promote local production has put in place a legislative provision which allows a margin of 15 % in public procurement for goods manufactured in Kenya (Procurement and Disposal Act, Kenya, 2005) and has also given a tax exemption for imported raw materials that are used in pharmaceutical production.

2. 6.6 Production capacity utilization

An average annual capacity utilization of 60 % has been reported for most dosage forms produced in Kenya (Watu and Kungu, 2014). There is limited documented literature on production capacity and capacity utilization in the pharmaceutical industry in Kenya. A survey by UNIDO on pharmaceutical production in Kenya in 2010 showed that capacity utilization ranged between 53 and 67 %. The survey was

based on 12 companies, 8 hour shift and focused on one unit operation for each production line that is; compression of tablets, filling of capsules, liquids and external preparations.

2.7 The cGMP standards and quality of pharmaceutical products in Kenya

2.7.1 The cGMP standards

The primary objective of the PPB is to ensure provision of quality, safe and efficacious pharmaceutical products to Kenyans. The PPB-GMP inspectorate unit carries out regular audits of the local pharmaceutical manufacturers to ensure compliance to cGMP. Despite the cGMP approval by the PPB, Kenyan pharmaceutical manufacturers are at different levels of cGMP status, ranging from a few that have achieved international cGMP accreditation to some that are struggling to comply with quality standards. In 2007, three companies, Cosmos Limited, Regal Pharmaceuticals Ltd., and Universal Corporation Ltd., upgraded their facilities to achieve international cGMP standard and received the European Pharmaceutical Inspection Cooperation Scheme (PIC/S) certification. The Pharmaceutical Sector Profile, Kenya, 2010 classified the local pharmaceutical manufacturing industry in Kenya into four categories based on the cGMP status of the facility as: new startup, least developed (companies with limited infrastructure such as air handling Units, water purification and quality control laboratory), developing **(**companies which have several years manufacturing experience with potential to progress) and developed companies which had international accreditation. This report recommended the upgrading of cGMP status in this sector. An assessment of this sector was carried out by UNIDO in 2012 on the quality elements of cGMP described in the WHO-GMP guidelines for pharmaceutical production. The

assessment report showed that compliance in majority of key quality elements needed improvement or were inadequate. Based on the findings of this assessment, the Kenya GMP Roadmap for the pharmaceutical industry was developed by UNIDO in conjunction with the local pharmaceutical industry, Ministry of Industry and the Ministry of Health. The roadmap which is a stepwise approach for the pharmaceutical industry in Kenya towards attaining WHO-GMP standards was launched in December 2014 (UNIDO, Kenya, 2014). It also provides opportunity for manufacturing facilities to aim for higher international accreditation and prequalification. Prequalification is a United Nations program managed by WHO which aims to facilitate access to medicines that meet unified standards of quality, safety, and efficacy for products that are used in the management of HIV/AIDS, tuberculosis, malaria and reproductive health (WHO, 2011c). Currently, only one company in Kenya, Universal Corporation Ltd. has been accorded WHO prequalification, for the antiretroviral, zidovudine/lamivudine. Prequalification is a comprehensive standardized quality assessment procedure to evaluate the acceptability of pharmaceutical products for purchase by United Nations agencies. At present, pharmaceutical products that are used in the management of HIV/AIDS, tuberculosis and malaria in Kenya are mostly donor funded and the prequalification requirement disqualifies participation of most of the local industry.

2.7.2 Standard for market authorization of pharmaceutical product

The CTD format of dossier preparation adopted by PPB of Kenya in 2010 compels the local industry to impress the QbD approach in production in order to generate the required data. This means that API’s will no longer be sourced from traders but from audited and approved suppliers and this may impact finished product price. The CTD

requirement may also be a hindrance to new registration approvals due to limitations by the local industry to generate the requisite data. Kenya lacks many of the basic essentials for technology development. Apart from training, most institutions in Kenya provide little or no research or technical services to pharmaceutical manufacturing industry making this sector inadequate in technological capabilities (UNCTAD, 2003). Furthermore, the pharmaceutical industry in Kenya manufactures generic products which must demonstrate comparability and equivalence with the innovator product in order to elicit the same pharmacological effect. Currently, there is no center within the East African region accredited by internationally recognized bodies such as the WHO to carry out BE studies which is a requirement for market authorization of some products such as those with narrow therapeutic index, low permeability and low solubility. In principal, products containing Biopharmaceutics Classification System (BCS) class II and IV API's are excluded from the BCS-based bio waiver procedure. There are 63 essential medicines in this category, including products that are used in the management of communicable diseases such as rifampicin, artemether, lumefantrine, most ARV products, azithromycin, trimethoprim, pyrimethmine, griseofulvin and nitrofurantoin (WHO, 2006b). In 2008 the German Agency for Technical Cooperation (GTZ), in collaboration with strategic partners, in their effort to develop local capacities for production of high quality pharmaceutical products in the East African region, proposed the establishment of a BE center in Ethiopia. However, this project has stalled due to operational logistics, as most of the manufacturers are situated in Kenya. For products that require BE study, local manufacturers have to perform the study outside the region at costs that are exorbitant for most of the local manufacturers. The CTD requirement raises the bar for market authorization of

new products and consequently, this may affect access to medicines through local production. Its implementation will therefore requires careful deliberation.

Pre-registration quality control testing of pharmaceutical products is carried out by the NQCL, Drug Analysis Research Unit (DARU) of University of Nairobi and MEDS. Compliance is based on end product quality control testing. Other quality parameters that determine market authorization of a pharmaceutical product and facility accreditation by DRAs such as product development, bioequivalence studies, pharmacological tests, stability studies and quality related risks during manufacturing are assessed during the market authorization technical evaluation process. In addition, quality of local and imported pharmaceutical products in the Kenyan market is monitored through market surveillance. Studies on quality of pharmaceutical products are regularly carried out, mostly the DARU of Kenya, and more than 20 journal publications on product compliance to quality specifications have been produced. Among these publications are studies on the quality of antiretroviral products, intravenous fluids, ampicillin preparations and cotrimoxazole tablets in Kenya (Abuga *et al.,* 2003; Orwa *et al.*, 1995; Kamau *et al.,* 2001; Kibwage *et al.,* 1998; Thoithi *et al.,* 2002; Thoithi *et al.*, 2005). A total of 1,700 local and imported pharmaceutical products were analysed at the DARU during the period, 1981-2007 (Abuga *et al.*, 2013). Local products were majority of the products analysed up to the year 2000 (mean 62 %) but declined thereafter to an average of 30.5 %. The prevalence of imported products after the year 2000 could be attributed to removal of trade barriers due to global trade liberalization which resulted in the influx of imported products into Kenya. The overall failure ranged from 6 to 31 % over the entire period. The average failure rate for local and imported products

during 1981-1986 was 48.5 and 28.5 %, respectively. The overall failure rate dropped to less than 10 % during the years 2001-2007, with no failure for local products in 2006 and 2007. Classification of failure by therapeutic category showed that dermatologicals, electrolytes, antituberculosis products and analgesics had the highest percentage failure ranging from 33-67.7 %, 30.8-45.5 %, 14.9-31.5 % and 9.1-20.0 %, respectively. The NQCL, Kenya reported a failure rate of 42 % out of 229 antimalarial samples analyzed between 2002 and 2005. The sulphur/pyrimethamine based products accounted for 39 % of the failure (Chepkwony *et al.,* 2007). The high failure was among the factors that prompted their removal as first line product in treatment of malaria. The quality control findings signifies the extent of substandard medicines in Kenya. Counterfeits medicines which are products that are deliberately and fraudulently mislabeled with respect to identity and/or source have also been identified during the cause of quality analysis at DARU and NQCL. The counterfeit medicines encountered include antimalarials such as quinine tablets, analgesics, corticosteroid based external preparations and β-lactam antibiotics. In a study carried out to determine the influence of manufacturing practices on the quality of pharmaceutical products manufactured in Kenya, questionnaires were administered to examine how the code of cGMP has been used in the production of each pharmaceutical product by 13 companies. The finding was that inadequacy of appropriate qualified personnel may be a contributing factor to poor compliance to cGMP in the industry. It was observed that industries that engaged in the manufacture of more than 100 drug products and had few pharmacists showed higher failure rates compared to those producing a smaller range of products with more skilled technical personnel (Orwa *et al.,* 2004).

2.8 Case studies on successful and progressive pharmaceutical production

2.8.1 Developed countries

In the 1970's, pharmaceutical production was concentrated in developed countries particularly the United States, Japan and Germany (WHO, 2004). In 2007 high-income countries accounted for more than 80 % of world pharmaceutical production by value (Lybecker, 2011). Factors that have contributed to growth and success in pharmaceutical production in these three countries are herein explored.

United States of America

Pharmaceutical manufacturing in the USA outperforms all other industries in terms of profitability (Field, 2012). In 1935 the USA pharmaceutical market comprised of hundreds of small firms and about fifty large ones. By 1955 less than twenty firms were controlling nearly 80 % of sales and these companies have maintained the top position till the 21st century. The success of these companies is traceable to their partnership with the USA government in the penicillin production program during World War II (Younkin, 2008). Most of the current successful companies such as Squibb & Sons Limited, Eli Lilly and Company, Merck & Co., Inc., and Pfizer Inc. participated in this program. The selection of these firms gave them the opportunity to venture into research oriented pharmaceutical production. Currently, the USA is the world's largest market for pharmaceutical products and leader in drug discovery and development. The USA government's support for research and innovation has immensely propelled the growth and success in this industry (Petrova, 2014). Other conducive factors include; stringent regulatory framework, demand for the pharmaceutical products, satisfactory quality assurance system, government subsidies and support for product patents (Field, 2012).

Germany

The success in the pharmaceutical manufacturing in Germany has been stimulated to a large extend by appropriate government incentives and innovations. Germany is the world's fourth largest pharmaceutical market (after France, Japan and USA) (Kumra *et al*., 2015) and the home for successful pharmaceutical manufacturers such as Roche, Bayer-Schering Pharma and Sanofi-Aventis. Germany has excellent infrastructure, and sufficient manufacturers of pharmaceutical inputs required in production (Germany Pharmaceutical Industry Association, 2013).

Japan

The Japanese pharmaceutical industry thrives on local innovation and is self-sufficient. The Japanese government implemented revitalization policies after World War II (Brückler, 2015), including rigid economic measures such as restrictions on imports and non-tariff barriers designed to promote domestic manufacturing, encouraging the use of generic medicines and investing in local production. Foreign investment was allowed under joint ventures. Global absence of patent protection in the 1970’s made it possible for Japan to produce versions of inventions and later progressed to strengthening research and drug discovery capacity (Robert, 2010).

2.8.2 Developing countries

Many developing countries in Africa, Asia and South America have taken deliberate steps to encourage local production by implementation of common or country specific initiatives. Nigeria, Ghana and Kenya represent cases in Africa with a progressive pharmaceutical industry and local production is promoted. Four countries in Asia; Bangladesh, India, China and Malaysia exemplify successful local

pharmaceutical production. In Latin America, Brazil and Argentina have a developed pharmaceutical industry with high-quality manufacturing capabilities.

Nigeria

The pharmaceutical market in Nigeria was estimated to be worth US$1.05 billion in 2012 (Espicom Limited, UK, 2015). Government policies are designed to encourage local production in accordance with the Nigeria National Drug Policy (NNDP). There are about 120 local drug manufacturers operating in Nigeria. Nigeria has prohibited the importation of 18 essential medicines that are produced locally and in sufficient quantity (Medical Writing Institute, 2010). The pharmaceutical industry in Nigeria has grown at an average annual rate of between 10 and 15 % since 2001 (UNIDO Project, Nigeria, 2011). The drug regulatory authority has supported the Nigerian manufacturers in their effort to upgrade their facilities. Four facilities; Evans Medical Ltd, May & Baker Nigerian Ltd, Chi Pharmaceuticals Limited, and Swiss Pharma Nigeria Limited are WHO-GMP compliant (WHO, Nigeria, 2014).

Ghana

In Ghana, the government developed a health policy in 1989 that would promote local pharmaceutical production and reduce reliance on imports. The key features of the policy were; price preference for locally produced products and tax incentives (Ariane *et al.,* 2011). Raw materials and pharmaceutical equipment were exempted from tax. Importation was prohibited for 44 pharmaceutical products. Finished products permissible for importation were subjected to import duty and value added tax. The impact of the policy is evidenced by a rise of pharmaceutical manufacturers from 9 in 1989 to 55 in 2014 (Frost and Sullivan, 2014), upgrading of the

manufacturing facilities towards international cGMP standards, partnerships with multinational companies and one manufacturer, La Gray is engaged in primary production (Al-Bader *et al.,* 2010).

Bangladesh

The state of Bangladesh was formed in 1971 and has a population of about 150 million (Bangladesh Bureau of Statistics, 2014). Bangladesh is nearly self-sufficient through local production and has sufficient capacity to export (Nazmul *et al*., 2011). The success of the pharmaceutical industry in Bangladesh is significantly attributed to the utilization of the exemption from the obligation to implement the patent protection law that was accorded to LDCs to formulate pharmaceutical products. Additionally, the National Drug Policy promotes local production to ensure availability, affordability and safety of essential drugs (Alam and Habib, 2011). The Drugs Control Ordinance controls the manufacture, import, distribution and sale of drugs in Bangladesh. Foreign brands are not allowed to be manufactured under license if similar products are being manufactured in the country. Multinational companies that do not have a production facility in Bangladesh are not allowed to market their products. The ordinance identified 117 drugs as essential, with controlled price. This resulted in the withdrawal of many foreign companies from the market in which they had a share of about 70 % in 1970. The major impact of this Ordinance was the rapid development of local manufacturing capability (Anesary *et al.,* 2014). There are 224 licensed manufacturers and 97 % of domestic demand of EM is met through local production (Amin and Sonobe, 2013). The national regulatory authority ensures adherence to cGMPs standards (Alam, 2009).

Bangladesh exports to more than 100 countries including the highly regulated markets such USA and Europe (Sultana, 2016).

India

The Indian pharmaceutical industry ranks first amongst India's science-based industries with wide ranging capabilities in drug manufacture and technology (Sateesh, 2015; 2011; Agrawal *et al.*, 2006). The pharmaceutical industry is one of the most profitable industries in India (Kalotra, 2014; Joseph, 2012). Before 1970, the pharmaceutical market share was dominated by foreign companies. The implementation of the Indian Patent, which recognized process patents and disallowed patents for pharmaceutical products contributed greatly to the growth of the local industry making the Indian market undesirable to multinational companies (Damanjeet, 2010; Amara and Aljunid, 2012). India developed reengineering innovation skills and by 2005, nine of the top 10 companies in India were domestically owned, compared with just four in 1994. However, India became a member of the World Trade Organization (WTO) in 1995 and was obligated to comply with TRIPS in 2005 (Tyagi and Nauriyal, 2013). India has the third-largest drug R&D workforce globally after the USA and China (Lawton, 2014). The Pharmaceutical industry in India meets approximately 70% of the country's demand for production raw materials and finished pharmaceutical products. India exports to more than 200 countries, with USA being its biggest market (Shirley, 2010). Factors that have fueled growth in this industry include; the growing population of over a billion, a huge patient base, availability of health insurance schemes and patent expiries (Khurana and Jaipuriar, 2014). Other favorable factors include; low production costs, high production capacities, innovative manpower and national

laboratories (Indian Pharmaceutical Industry, 2010). In addition, appropriate government policies ensure availability of quality and affordable pharmaceutical products, promote export trade, encourage R&D, and advance new technologies and linkages with the pharmaceutical industry (Wessner and Wolff, 2012).

China

The Chinese pharmaceutical market is the second greatest globally after the US (Huang, 2015). From 1999 to 2008, its development went beyond any other industry in China with its annual growth rate of 18.9 % (Liang and Xiaoming, 2011). Along with economic growth, China's pharmaceutical industry switched from imitation to innovation in order to be competitive. China's drug R&D evolution utilized intellectual property provisions in four phases; pure imitation (copy method from innovator), innovative imitation (change mode of delivery), imitative innovation (modifications of the structure), and independent innovation (new entity discovery) (Jingxi *et al.,* 2011). China is currently the world's second-highest investor in R&D (Huang, 2015). In addition, government policies, incentive programs and high talent pool base have impacted growth in this industry (Pricewaterhouse Coopers, 2009).

Malaysia

The Malaysian pharmaceutical manufacturing industry is effectively regulated. This industry is recognized in the Malaysian 2006-2020 industrial development plan. The Ministry of Health has a unit to propel pharmaceutical exports. The industry focuses on compliance to quality standards and innovations. Malaysia is a member of the PIC/S, whose mission is to lead international development, implementation, maintenance and harmonization of cGMP standards and quality systems of

pharmaceutical inspectors (PIC/S, 2016). The local industry produces 80 % of the medicines on the Malaysian EM list and supplies more than 60 % of the public sector pharmaceutical requirements (Piong and Loong, 2014; Babar *et al.*, 2011).

Brazil

The growth of the local industry in Brazil is accredited to: the government's commitment to its health policy, indigenous research and innovation capacity, civil society coalition built around health equity, independent national regulatory authority, utilization of flexibilities within TRIPS agreement and the international harmonization of quality assurance and clinical standards related to pharmaceutical research and development (Arzeno *et al.*, 2004; Guennif and Ramani, 2010). The production capacity utilization was 74 % in 2009. The growth of generic drugs in Brazil is due to the combination of equal quality products with prices around 50 % lower than brand products. The National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária, ANVISA) ensures cGMP compliance and BE is a requirement for market authorization of products (Vera, 2006).

Argentina

Argentina is the fourth-largest pharmaceutical market in Latin America behind Brazil, Mexico and Venezuela (Deloitte, 2015). Both local and multinational manufacturers operate in the country. Success in local production is attributed to tariff protection, high generic prescribing, health insurance cover for significant percentage of population and product reengineering prior to the TRIPS agreement (Javier *et al.*, 2002; Malich and Marion, 2015).

2.8.3 Lessons from the case studies

Establishing a viable pharmaceutical manufacturing industry requires capital investment to ensure cGMP compliance, adequate regulatory environment, available pharmaceutical inputs, skilled personnel, technologies and adequate infrastructure**.** It is evident from the literature review cited on local production that the commonality in the pharmaceutical industry in developing countries which are nearly self-sufficient through local production is that governments have propelled the growth by implementing policies that promote the local industry by providing adequate business incentives and enforcement of regulations. The government has invested in R&D institutions and capacity building in the pharmaceutical sector. Collaborative R&D between the pharmaceutical industry and the government, availability of research grants and non-tariff barriers intervention have contributed to the growth**.** Partnership between governments and the pharmaceutical industry is vital for successful local production. Government's facilitating policies are key determinants of industrialization of nations (UN, 2003). The individual manufacturers have invested in facility upgrading in order to comply with international cGMP standards and to be competitive globally. Additionally, the pharmaceutical manufacturers utilized the opportunity prior to TRIPS implementation in 2005, by engaging in product reengineering and have continued to invest in innovation. The Aspen Pharmacare, SA case study illustrates a company that embraced technology to become a producer of antiretroviral products (UNDP, 2007).

2.9 Production capacity forecasting

Adequate production capacity is a vital requirement for self-sufficiency in EM through local production (Wilson *et al.,* 2012). Historical data on production capacity

utilization and market share of locally manufactured products may be used to forecast the feasibility of SSEM. The principal function of forecasting is to predict future demand using available data (Lindeke, 2005).

2.9.1 Forecasting methods

There are three primary methods of forecasting namely; qualitative, time series methods and causal models (Chase *et al.*, 2016). The first uses qualitative data such as expert opinion and does not necessarily take the past into consideration. This method is used when data is scarce. Human judgment is used to turn qualitative information into quantitative estimates. The reliability of qualitative method is questionable. The second (time series) focuses on patterns, pattern changes and thus relies entirely on historical data. These are statistical techniques used when several years' data for a product sales or demand are available and when relationships and trends are both clear and relatively stable and make accurate forecasts. The causal method is a highly refined sophisticated tool that uses historical data and takes into account specific information and special events and also makes use of the relationship between two or more variables (Makridkis and Wheelwright, 1989). The time series is one of the methods applied in capacity utilization projection (Mukherjee and Misra, 2012).

2.9.2 Time Series forecasting

The time series forecasting system projects future values by extrapolating patterns in the past values of the series or by extrapolating the effect of other variables on the series. The goal is to isolate patterns in past data, model the data and then make a future prediction (Chambers *et al.*, 2015). Different time series models are

considered depending on the shape of the line which best fits the observed data as; stationary, trend, seasonality, cycles or randomness. The methods which can be used for future projection are the moving averages, linear-regressions, and exponential smoothing. They differ by the importance they give to the data and their complexity. Generally, a two-step procedure is used to determine the time series model and method to apply in forecasting. The first step is to plot the observed values against time for identification and selection of the model to use, followed by computation of the forecast using an appropriate software. The model selected will depend on whether it is reasonable to assume a constant, an increasing, a decreasing or a seasonal demand. Trend projection is adopted to predict company sales, exports and production demand, since these forecasts often approximate a straight line. Trend projection requires minimum of five years historical data. The Microsoft Excel® function is commonly used in projections where linear regression analysis is required (Nadler and Kros, 2007). Other applications including SAS® and SPSS® generally require 30 or more data points for accurate projections (Yaffee and McGee, 2000). Forecasting of capacity utilization in the pharmaceutical manufacturing industry is intricate since utilization is influenced by numerous factors which affect demand for medicines such as disease patterns, government policies, political and economic situations, market competition and availability of investment capital by the manufacturers. Uncertainty or variance in these factors may challenge the accuracy in long term forecasting of capacity utilization thus, short term projections of 3-5 years are preferred.

Developing countries that encourage self-sufficiency in EM through local production require the capability to manufacture the medicines, sufficient production

capacity and supportive infrastructure that is necessary for pharmaceutical production. Production practices must comply with international cGMP standards and the manufactured products should be able to withstand market competition. A comprehensive analysis of the capacities of the Kenyan pharmaceutical manufacturing industry will provide a valid basis for strategies that are necessary for achieving self-sufficiency in essential medicine through local production.

CHAPTER THREE

3. MATERIALS AND METHODS

3.1 Research design

In this study, a survey was conducted on capacity of the pharmaceutical manufacturing industry in Kenya to make and supply sufficient essential medicines to the domestic market. Data was collected on range of products manufactured by the local pharmaceutical industry, pharmaceutical products marketed in Kenya, registered pharmaceutical equivalents of these products, competitiveness and domestic market share of local products. Further, information was generated on production capacities, manufacturing premises and quality systems in the local pharmaceutical industry. Data was obtained by scanning official pharmaceutical databases and pharmaceutical product lists. Prices of local and imported pharmaceutical equivalents was obtained from manufacturer price lists. A standard questionnaire was used to collect data on capacities, manufacturing premises and quality systems in the pharmaceutical industry. The questionnaire was administered to quality assurance managers who were the respondents in the pharmaceutical manufacturing companies. Installed production capacities were determined from machine catalogues and available capacity was computed for all machines that were used in production unit operations. Performance indicators based on WHO guidelines on current GMP for pharmaceutical products (WHO, 2014) were used in evaluation of manufacturing premises and quality systems. A survey method was selected due to the high representativeness brought about by this method, the large amount of data that is collected, and the ease to obtain quantifiable results which can be used in forecasting (University of Surrey UK, 2015).

3.2 Location of study

The study was conducted in Nairobi, Kiambu and Machakos counties in Kenya, where the 30 licensed pharmaceutical manufacturing companies are situated. Twenty five of these companies are located in Nairobi, four in Kiambu and one in Machakos. Kiambu and Machakos counties are within a 30 kilometer radius from Nairobi, the capital city of Kenya and the focal commercial city in East Africa. Nairobi has an expansive industrial area, extensive transportation infrastructure consisting of integrated road network, a robust air transport and access to the port of Mombasa, the most important deep-water port in the region. Nairobi also has administrative services which are essential for the manufacturing industry.

3.3 Study population

The study population comprised the licensed pharmaceutical manufacturers in Kenya in the year 2014. Respondents were the quality assurance managers at each of the pharmaceutical manufacturing company.

Inclusion criteria

Manufacturers of medicine for human use who agreed to participate in the study were assessed.

Exclusion criteria

Manufacturers that were dedicated to the production of medicines not intended for human use and those that declined to participate were excluded from the study.

3.4 Sampling techniques and sample size

3.4.1 Number of manufacturers; Evaluation of capacities in the local industry

The local pharmaceutical industry in Kenya consisted of 30 licensed manufacturers at the time of this study**.** Twenty four firms manufactured pharmaceutical products for human use and 6 were dedicated to the manufacture of veterinary products. Due to the small study population, the equation for calculating sample size for finite population was used to determine the sample size (Singh and Masuku, 2014).

$$n = \frac{n_0}{1 + \frac{(n_0 - 1)}{N}} \qquad (2)$$

Where,

n = Sample (corrected) to be taken

n_o = Uncorrected value

$$n_0 = \frac{Z^2 pq}{e^2}$$

e = target level of error (at 0.05 for 95 % confidence interval)

Z = standard normal deviation at the 95 % confidence level.

p = proportion in the target population possessing the variable of interest; p = 0.1 to 0.5. Since the prevalence of the study variable is uncertain, sample size will be computed using two values, p = 0.1 and 0.5, and the value that gives a bigger sample size will be selected and q = 1- p

N = Actual study population size (24 companies)

The computed sample size is 22.6 and all 24 manufacturers of human medicines were assessed and hence the risk of variability was eliminated.

3.4.2 Sampling of manufacturers from which to obtain product price lists

Local pharmaceutical manufacturers that produced a wide range of products and large distributors of imported pharmaceutical products were selected. The purposive sampling method (Black, 1999) was used to select the local and foreign pharmaceutical manufacturers from which to obtain price lists for product price comparison. This sampling method was preferred since it allowed the researcher to hand pick firms that were informative and possessed the required characteristics. Ten firms that manufactured more than 50 of the products on KEML were selected to provide the medicines to evaluate for price comparison with imported pharmaceutical equivalents. Price lists were obtained from the 10 local firms and from 20 wholesale distributors of imported pharmaceutical products listed in the pharmaceutical/ Yellow Pages Ltd., the official online business directory, 2015.

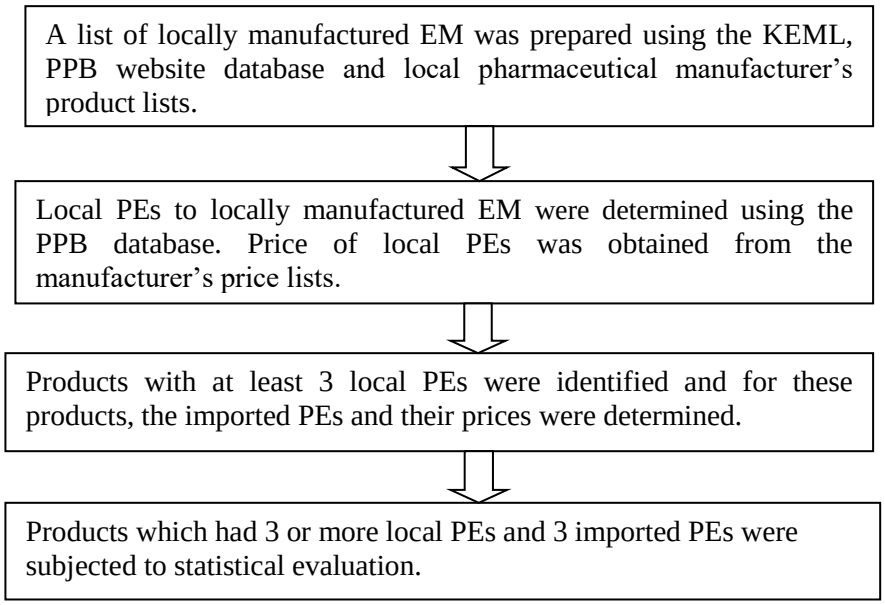
3.4.3 Selection of products for price evaluation

Pharmaceutical products that were manufactured in Kenya and listed as essential medicines were selected for evaluation. The selection criteria and process of products that were used for price evaluation is presented schematically in Figure 3.1. The manufacturer's wholesale price was used in this evaluation.

3.5 Pre-Testing of questionnaire

Pre-testing of the questionnaire was carried out at four companies to detect any problem with the questionnaire design leading to ambiguity, misinterpretation of a question, inability to answer a question and any other feedback on the data collection procedure. The responses were evaluated and it was concluded that the questionnaire

was easy to understand and collected the information that was required to achieve the objectives of the study on production capacity and quality systems.



PE: pharmaceutical equivalents, PPB: Pharmacy and Poisons Board
KEML: Kenya essential medicines list

Figure 3.1: Schematic presentation of products for price evaluation

3.6 Validity of instruments used in the study

The questionnaire used in this study was developed using the WHO cGMP guidelines. The questionnaire was comprehensive and structured to cover all aspects of pharmaceutical production such as facility design and quality systems. The findings on cGMP were validated by a PPB regulatory officer who was familiar with the Kenyan pharmaceutical industry.

3.7 Reliability of instruments used in the study

The data on the questionnaire was filled in by qualified and proficient personnel in pharmaceutical production operations. This insured consistency, repeatability and accuracy of the information supplied.

3.8 Data collection techniques

Data on the pharmaceutical products marketed in Kenya was obtained by examining pharmaceutical product lists, the PPB website and Kenyan Gazette Notices. Data on production capacity and cGMP attributes in the local industry was obtained using a structured questionnaire. All companies were assessed using the same criteria. Rating of compliance of the facility and quality systems were based on the observations made by use of performance indicators based on WHO guidelines on GMP. The data collection process entailed making telephone calls, sending electronic mails and a visit to each facility. The contact person at the facilities was the Quality Assurance Manager (QAM), who is the custodian of quality compliance. The QAM was responsible for liaising with the respective departments at the site for collection of data. As a cGMP practice, a visit was made by the researcher to each facility to validate the information provided on the questionnaire.

3.9 Data Analysis

3.9.1 Capability of the pharmaceutical industry to produce essential medicines

3.9.1.1 Range of essential medicines manufactured and marketed in Kenya

Essential medicines manufactured locally

The range of products manufactured, registered and retained by each facility was determined from the manufacturers' product lists together with the PPB website. Product lists were obtained from each of the 24 local manufacturers of human pharmaceutical products. The products manufactured by the local industry were classified based on dosage form and production lines. The percentage of the various dosage forms produced in this sector was computed. The products manufactured were subsequently categorized into therapeutic classes.

Local and imported pharmaceutical products marketed in Kenya

Data on all pharmaceutical products registered in Kenya was used to compute percentage of registered and retained products that were locally manufactured and those imported, the source of retained products in the market and the respective percentages. The KEML, pharmaceutical stock lists from KEMSA, MEDS and Kenyatta National Hospital were scanned to establish the dosage forms encompassed and the proportion of locally manufactured products.

3.9.1.2 Pharmaceutical equivalents to locally manufactured products

The list of registered and retained pharmaceutical products at the PPB and the KEML were used to determine the essential medicines that were manufactured by the local industry. The number of local and imported pharmaceutical equivalents of all essential medicines that were manufactured in Kenya were computed.

3.9.1.3 Competitiveness of local products

Price comparison between local and imported pharmaceutical equivalents was carried out on essential medicines which were locally manufactured. The price for the selected products was obtained from; manufacturers product lists, the Pharma Finder, and the Drug Index catalogue, East African Pharmaceutical Loci, and these provided a data base for all pharmaceutical equivalents of the products under evaluation. Statistical computation was carried out using Microsoft Excel® software on products that had three or more local and imported brands. The local brands and imported brands were analyzed independently, to determine the mean, range, standard deviation and the variance values for each of the two groups. Mean values for the local brands and the imported brands were compared. Since the sample size

for the available brands was less than 30, the student's t-test (Hughes, 2014) was used as the inferential statistics to establish whether there was variation between the two means. The *t* statistic was calculated as:

$$t = \frac{\overline{X}_1 - \overline{X}_2}{s_{\overline{X}_1 - \overline{X}_2}} \quad (3)$$

Where, $\bar{x}_1$ and $\bar{x}_2$ are the means of the two samples

$$s_{\overline{X}_1 - \overline{X}_2} = \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}.$$

s_1 and s_2 are the standard deviations of the two samples

n_1 and n_2 are the sizes of the two samples

The two-tailed test was adopted and the computation was done at 95 % confidence interval thus 5 % significance level and $\alpha = 0.05$.

Scatter plots of local and imported PEs for the evaluated products were drawn to determine any trend or relationship within and between the price for local and imported products and any other observation not detected by the student's t-test. Data on costing of local products was obtained from the manufacturers through a structured questionnaire. Product cost was derived from pharmaceutical inputs, taxes, handling costs, production costs, and other costs incurred during production process.

3.9.1.4 Market share of local products

Sales turnover for the local pharmaceutical industry for the years 2010-2014 was acquired from manufacturers in this industry using a structured questionnaire (Appendix1). The sales turnover was compared with the domestic market for pharmaceutical products in Kenya to determine the local market share.

3.9.2 Evaluation of production capacity

Manufacturers and dosage forms

Data on production capacity based on two shift operations was obtained from the 24 manufacturers of human pharmaceutical products using a standard structured questionnaire (Appendix 1). Production capacity for six dosage forms namely; tablets, capsules, oral liquids, external preparations, dry powders for reconstitution and oral rehydration salts was evaluated.

Installed, available and utilized production capacity

A questionnaire (Appendix 1) was used to obtain information on installed, available and utilized production capacities for each unit operation in the production process for the dosage forms (tablets, capsules, oral liquids, external preparations, dry powders for reconstitution and oral rehydration salts) that were manufactured at each facility for a period of five years, from 2010 to 2014. Computation of production capacities was based on the overall equipment effectiveness model. The installed production capacity was computed as the designed output capability of the production machine. Available production capacity was determined by making adjustments to installed capacity to cater for changeover time, preventive maintenance, unplanned downtime and facility shut down. Utilized capacity was computed as the ratio between the actual output to potential output that could be produced with installed machine, if capacity was fully utilized (available production capacity). The utilized production capacity was calculated as the ratio between the number of units (batch size x number of batches) of the dosage form that were produced annually to the available production capacity.

Forecasting of capacity utilization in the local pharmaceutical industry

Forecasting of production capacity utilization was evaluated using the time series forecasting method (Chambers *et al.*, 2015). Production capacity utilization/time series plots were drawn for the dosage forms that were assessed for a period of 5 years; 2010 to 2014 to establish any pattern in capacity utilization upon which the forecasting method was based. A trend-based time series model was applied in the forecasting using the linear trend equation (Cengage Learning Inc., 2012),

$$T_t = b_0 + b_1 t \qquad (4)$$

Where,

T_t is capacity forecast at time *t*, b_0 is intercept of the linear trend line and b_1 is slope of the linear trend line.

The Microsoft Excel® function of forecasting was used in the projection of future production capacity utilization since it uses a linear regression to predict *Y* when historical values of *X* and *Y* are known. Market for the projected capacity was available as the current market share of locally manufactured pharmaceutical products was approximated to be 30 % in 2014 (Watu *et al.*, 2014).

3.9.3 Compliance of facilities with cGMP standards

Data was collected using a standard structured questionnaire (Appendix 1). Information was obtained on cGMP accreditation status of facilities (local, regional and international), compliance of manufacturing facilities with key cGMP quality elements namely; premises, utilities that impact cGMP, practices in quality control, R&D and personnel. The quality elements were assessed using the EU and WHO cGMP guidelines. The assessment was based on rating of the observations on cGMP compliance of premises and key parameters of the quality system. Observations were

categorized as critical (potential risk harm to the user), major (major deviation from cGMP) and minor (departure from good practice). The rating assigned was dependent on the risk of the observation (deficiencies) taking into account the nature and extent of the deviations as well as the number of occurrences. The quality parameters were rated on a scale of 1 to 4 as; unsatisfactory (critical observations, unsuitable premises, no quality system), poor (critical and major deficiencies), satisfactory (few major and minor deficiencies), good (minor deficiencies) (UNIDO, 2015; Health Canada, 2012; Bujar *et al.*, 2015). The workforce in various departments in this industry and their qualification were evaluated. An average score of ≤ 2 and > 2 was construed as cGMP noncompliance and compliance, respectively.

3.10 Ethical consideration

Research authorization was sought and granted by the National Commission for Science, Technology and Innovation, the Nairobi County Commissioner and the County Director of Education, Nairobi County. The research met the requirements for industry based study not using human subjects and ethical clearance was therefore not mandatory.

CHAPTER FOUR

4. RESULTS

4.1 Capability of Kenya pharmaceutical industry to produce essential medicines

4.1.1 Range of products manufactured and marketed in Kenya

Figure 4.1 shows the profile of Kenyan pharmaceutical manufacturing industry compiled from lists of licensed manufacturers obtained from Kenya gazette notices during the period;1963 to 2014 and forms an introduction to this section. The local industry exhibited a steady growth in number of manufacturers from the year 1963 until 2012. The Kenyan-owned companies have gradually increased with time; growing by 13 companies from 1975 to1985 and a further increase by 12 between 1985 and 2014. The multinational companies increased from inception up to 1977, then stagnated till 1990 when it began to decline. By 2014, the ownership structure of the local pharmaceutical manufacturing industry in Kenya was predominantly Kenyan, with one company, GlaxoSmithKline, being a multinational.

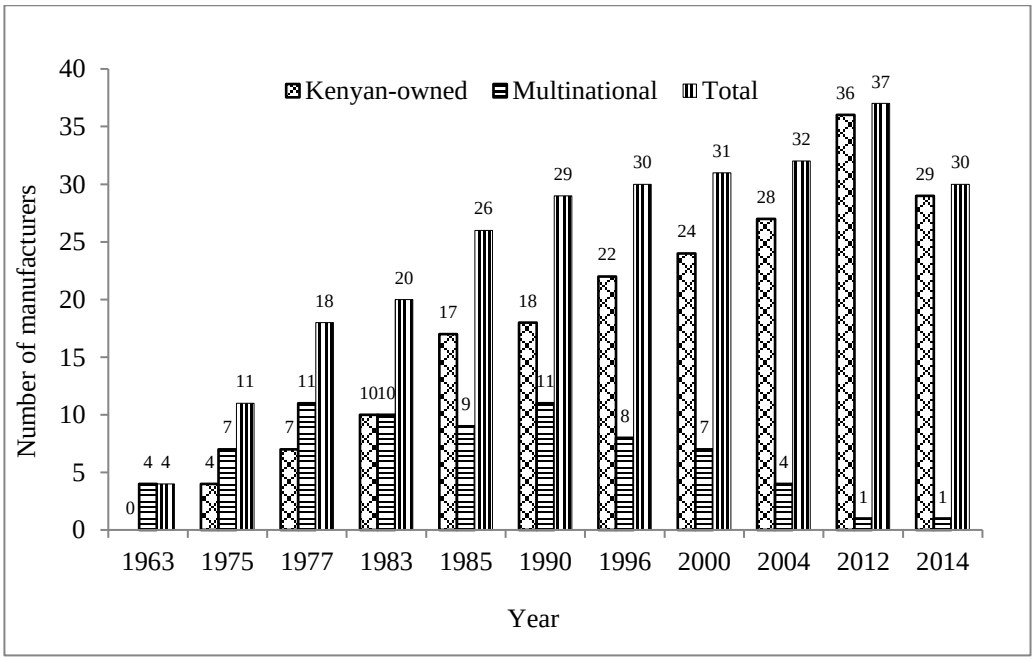


Figure 4.1: Trends in the Kenyan pharmaceutical manufacturing industry

The decline in the number of multinational companies is mainly attributed to mergers, restructuring in view of global markets, unfavorable business conditions in Kenya and the free market policy adopted by Kenya as a prerequisite to the structural adjustment loan with the World Bank in the 1980's (Gertz, 2008).

4.1.1.1 Products manufactured locally

Table 4.1 shows the dosage forms, production lines and the number of products manufactured by the local industry. The Kenyan pharmaceutical manufacturers (Appendix 2) produced similar products, which were mainly non-sterile (97.3 %) comprising solids (54.9 %), semisolids (10.3 %) and liquid preparations (32.1 %). Solid dosage forms were largely non β-lactam products, the majority being tablets.

Table 4.1: Dosage forms and production lines in the local industry in 2014

Dosage Form		Production lines	Manufactured products
Solids	Tablets	Non β-lactam tablets	614 (39.8 %)
		β-lactam tablets	5 (0.3 %)
	Capsules	Non β-lactam capsules	111 (7.2 %)
		β-lactam capsules	44 (2.9 %)
	Dry syrups	Non β-lactam dry syrups	42 (2.7 %)
		β lactam dry syrups	31 (2.0 %)
Semisolids		Creams and ointments	159 (10.3 %)
Liquids		Syrups and suspensions	496 (32.1 %)
Others		Sterile products	42 (2.7 %)

4.1.1.2 Therapeutic categories

The main therapeutic categories manufactured were analgesics, anti-allergies, anti-convulsants, anti-diabetics, antifungals, antihelmintics, antimalarials, antibacterials, antiretrovirals, anti-tuberculosis products, β-lactam products, cardiovascular products, central nervous system acting drugs, dermatological preparations, diuretics and gastrointestinal agents. Most of the products manufactured were listed as essential medicines and were necessary in management of communicable diseases

that are currently prevalent in Kenya. Two companies had ventured into the manufacture of products used in the treatment of lifestyle diseases such as cardiovascular ailments and diabetes. Six antidiabetic and 17 cardiovascular products presented in Table 4.2 were produced locally.

Table 4.2: Locally produced antidiabetic and cardiovascular products

Product (Tablets)	Number of companies
Amlodipine 5 mg	5
Atenolol 50 mg	4
Bendroflumethiazide 2.5 mg	1
Captopril 25 mg	2
Carvedilol 6.25 mg	1
Enalapril 5 mg	1
Furosemide 40 mg	5
Hydralazine25 mg	1
Hydrochlorothiazide 25 mg	1
Lisinopril 5 mg	1
Losartan 50 mg	1
Losartan + amlodipine 50/5 mg	1
Losartan + hydrochlorothiazide 50/12.5 mg	1
Methyldopa 250 mg	5
Nebivolol 5 mg	1
Nifedipine10 mg	1
Propranol 25 mg	2
Chlorpropamide 250 mg	1
Glibenclamide 5 mg	2
Gliclazide 80 mg	1
Metformin + glibenclamide 500/5 mg	1
Metformin 500 mg	4
Pioglitazone 30 mg	1

Table 4.3 shows the number of products from various local facilities which were registered and retained in the market in 2014. There was a huge disparity in the number of products registered from each facility, ranging from 3 to 233 products.

Table 4.3: Products registered and retained in the local industry in 2014

Company	Non - sterile products						Sterile products	Total
	`Registered / Retained	Tablets	Capsules	Dry powders	Semi solids	Liquids		
Aesthetics	Registered			4				4
Autosterile	Registered						4	4
	Retained						13	13
Benmed	Registered	8	1		1	8		18
Beta Healthcare	Registered	10				18		28
	Retained	10				19		29
Biodeal	Registered	54	8	3	26	68		159
	Retained	52	6	4	26	58		146
Biopharma								22
Cooper (K)	Registered			6		2	17	25
	Retained			3		7		10
Cosmos Limited	Registered	140	10	14	7	32		203
	Retained	148	9	16	11	32		216
Dawa limited	Registered	34	14	8	10	25	32	123
	Retained	35	12	18	15	39	5	124
Elys	Registered	61	17	9	11	17		115
	Retained	58	17	9	10	17		111
GSK	Registered							40
	Retained	6	1	2		3		12
Infusion Medicare	Registered						11	11
	Retained						11	11
Ivee Aqua	Registered						27	27
	Retained						4	4
Lab & Allied	Registered	93	23	14	16	51	36	233
	Retained	92	23	14	16	51	36	232
Mac's	Registered	37	13		18	10	2	80
	Retained	11	1	0	4	4	2	22
Medivet	Registered		6	6	5	10	35	62
	Retained		8	7	12	21		48
Nerix Pharma	Registered			6	1	20	5	32
	Retained			6	1	20	5	32
Norbrook	Registered	1			0		91	92
	Retained	7		5	1	10	31	54
Novelty	Registered						7	7
Oss-Chemie	Registered					18		18
	Retained	0	0	0	0	18	0	18
PMC	Registered	48	13	2	26	46		135
Regal	Registered	45	12		19	49	11	136
	Retained	27	9	5	13	43		97
Skylight	Registered					7		7
Sphinx	Registered	1	3		1	25		30
	Retained	1	2	4	4	17		28
Stedman	Registered	1	1			2		4
Synerchem	Registered					3		3
Universal	Registered	87	28	1	13	53	1	183
	Retained	51	7	3	7	11		79

Retrieved from Pharmacy and Poisons Board of Kenya database, 2014

Ten facilities, mainly new start-up companies had registrations of less than 10 products each. Eight facilities had registrations of more than 100 products each, accounting for 72.3 % of the registered local products in the market. A summary of the local industry based on the number of products registered by each facility is presented in Table 4.4

Table 4.4: Products registered at various facilities the local industry in 2014

Number of products registered	Number of companies
Less than 10	10
10-50	9
50-100	3
100-200	6
200-250	2

4.1.1.3 Local and imported pharmaceutical products marketed in Kenya

In 2014, the PPB retained 7466 (60.6 %) of the products that were registered in Kenya as indicated in Table 4.5. Local products accounted for 21.5 % of retained products in the market. Local manufacturers retained 90.2 % of the registered products whereas only 55.6 % of the imported products were retained. Six companies contributed 65.7 % and 65.9 % respectively, of the local products registered and retained in the market. Solid dosage forms and liquid preparations formed majority of local products that were retained in Kenya.

Table 4.5: Pharmaceutical products registered and retained in Kenya in 2014

Source of product	Registered products	Retained products
Locally manufactured	1,779 (14.5 %)	1,604 (21.5 %)
Imported products	10,534 (85.5 %)	5,862 (78.5 %)
Total	12,313 (100.0 %)	7,466 (100.0 %)

Figure 4.2 presents comparison between dosage forms from the local industry that were registered and retained by the PPB in 2014. Non-beta lactam tablets contributed largely to both registered and retained products. The profile of registered and retained products was similar since local manufacturers retained most of the registered products.

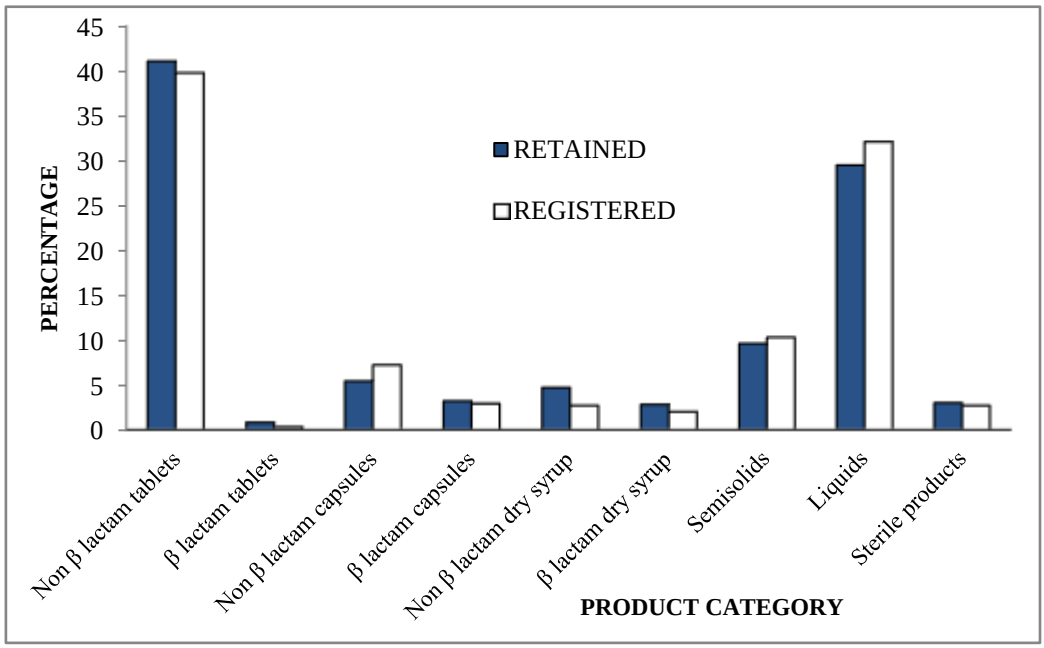


Figure 4.2: Comparison between registered and retained local products

4.1.1.4 Country of origin of pharmaceutical products

In 2014, the retained pharmaceutical products in Kenya were from Africa, Asia, Australia, Europe, N. America and S. America. Fifty four (54) countries had registered and retained their products in Kenya. Figure 4.3 and Appendix 3 show the country of origin of the retained pharmaceutical products. Majority of the products were from Asia (55.8 %), with 44.2 % of the imported products originating from India compared to 21.5 % manufactured locally. Other countries that had a substantial number of products were Bangladesh, Pakistan, and China, with 3.6 %, 3.5 % and 2.4 % of the total retained products, respectively.

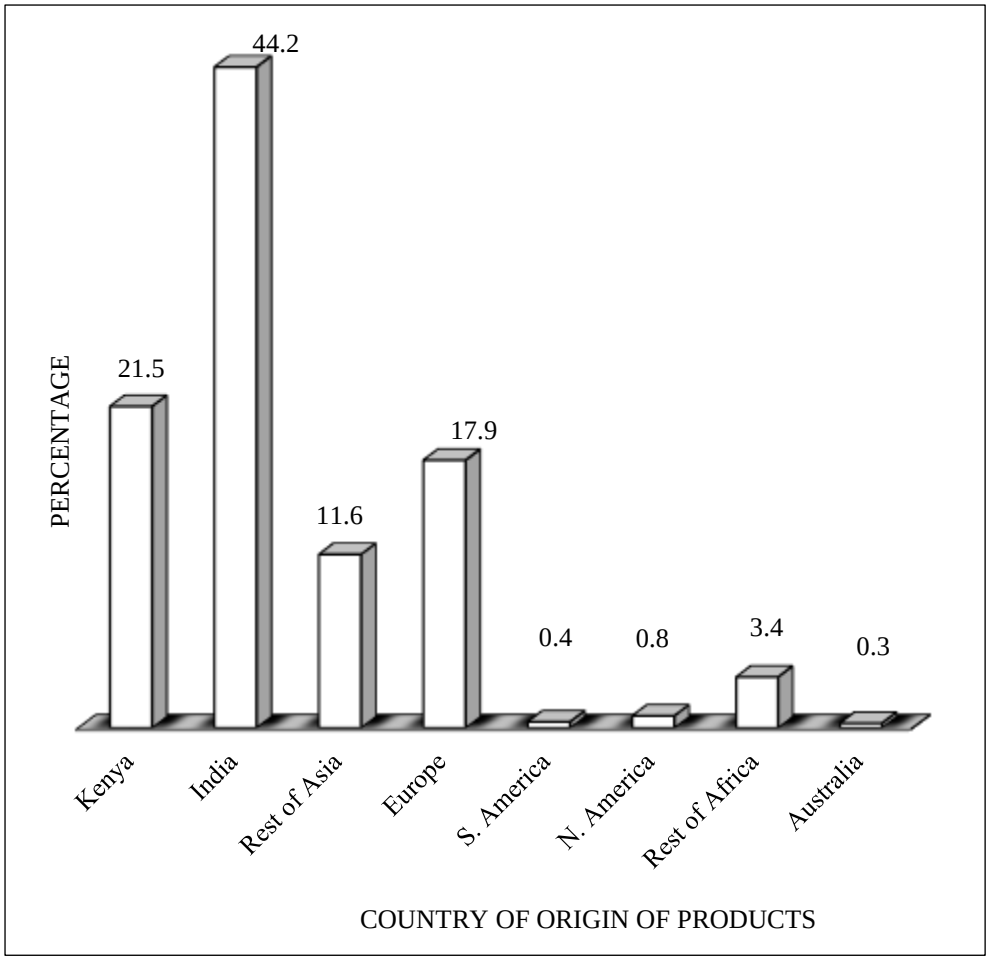


Figure 4.3: Origin by continent of products retained in Kenya in 2014.

4.1.1.5 Proportion of locally manufactured products on pharmaceutical stock lists

The 2010 Kenya essential medicines list consists of 422 products, 168 of which are sterile and 254 non-sterile. In 2014, the local pharmaceutical industry manufactured 162 (38.4 %) of the products on the KEML; 12 were sterile and 150 were non-sterile as presented in Appendix 4. Table 4.6 shows the therapeutic classes of medicines on the KEML, the number of products in each therapeutic class and the ones that are locally produced. Majority of the listed products for management of communicable diseases such as antibacterial products, dermatological products and antiprotozoals were produced locally.

Table 4.6: Essential medicines that is manufactured in Kenya

Therapeutic class	Number of products on KEML	Number of products locally produced
Anesthetics	16	1
Analgesics, antipyretics, NSAIDS	14	6
Anthelminthics	5	4
Anti allergies and anaphylaxis	7	3
Anti convulsants/antiepileptics	12	5
Anti migraine medicines	1	1
Anti parkinsonism medicines	2	1
Antibacterials	62	43
Antidotes	12	0
Antifungals	9	7
Anti-protozoals	23	14
Antiretrovirals	37	10
Blood products and plasma substitutes	11	2
Cardiovascular medicines	20	6
Dermatological products	11	11
Diagnostics	6	0
Disinfectants and antiseptics	5	5
Diuretics	3	1
Ear & oropharyngeal medicines	3	2
Electrolyte and acid-base balance products	12	5
Gastrointestinal medicines	11	8
Hormones/endocrine medicines	19	2
Immunologicals	17	0
Immunosuppressives and cytotoxin products	46	6
Muscle relaxants (peripherally acting)	3	0
Neonatal care	5	0
Opthalmologicals	9	9
Oxytocics and antioxytocics	6	0
Peritoneal dialysis solutions	1	0
Preparations for total parenteral nutrition	3	0
Psychotherapeutics	13	5
Respiratory tract products	8	2
Vitamins and minerals	10	3
Total	422	162

NSAIDS; non-steroidal anti-inflammatory drugs

Anaesthetics, opioid analgesics, antidotes, anticonvulsants/antiepileptics, muscle relaxants, endocrine medicines, diagnostics, cytotoxins, immunosuppressive and palliative care products were hardly produced. All the opthalmological drugs on the KEML were produced at Ivee Aqua EPZ Ltd.

Pharmaceutical products stocked by three major public procurers of the pharmaceutical products in Kenya; KEMSA, KNH and MEDS during the period 2012-2014 are presented in Table 4.7. The number of products stocked by KEMSA, KNH and MEDS were 180, 600 and 356, respectively. The KEMSA stock list had 164 (91.0 %) of its products listed on KEML while the KNH and MEDS lists had 338 (56.3 %) and 163 (45.8 %), respectively.

Table 4.7: Products on pharmaceutical procurers stock lists from 2012 to 2014

Institution	Number of products on stock list			Number of products produced locally	Number of Products on KEML
	Sterile	Non sterile	Total		
KEMSA	60	120	180	100	164
KNH	287	313	600	147	338
MEDS	66	290	356	78	163

The proportion of locally manufactured products on the KEMSA, KNH and MEDS stock lists was 55.6 %, 24.5 % and 21.8 %, respectively. None of the sterile products on the stock lists were manufactured locally. Majority of non-sterile products stocked by KEMSA were manufactured locally. The local industry manufactured 100 (83.3 %), 147 (47.0 %) and 78 (26.9 %) of the non-sterile products on the KEMSA, KNH and MEDS stock lists, respectively.

4.1.2 Pharmaceutical equivalents to locally produced essential medicines

The 150 non-sterile essential medicines that were locally produced had one or more PEs registered or retained by the PPB. The PEs in Kenya originated from 18 local and 138 foreign manufacturers (Appendix 6). Some of the products had both local and imported PEs while others had either one of the two. Table 4.8 presents the proportion of local and imported PEs of various categories of pharmaceutical

products on the KEML. Appendix 5 gives the details of the drugs in each category. The imported PEs dominated the Kenyan market for both registered and retained products. The local industry had a majority of PEs in three classes; anti-TB products, dermatologicals and central nervous system acting drugs. The number of local PEs in each pharmacological class depended on the dosage form, the cGMP requirements and procurement requirements. The prevalence of local and imported pharmaceutical equivalents of essential medicines in Kenya, categorized according to the KEML is detailed hereafter.

Table 4.8: Pharmaceutical equivalents of essential medicines in Kenya in 2014

	% Registered		% Retained	
Pharmacological class	**Imported**	**Local**	**Imported**	**Local**
Analgesics	73.9	26.1	61.5	38.5
Anti-allergies	58.9	41.1	42.3	57.7
Anti-convulsants	66.7	33.3	45.8	54.2
Anti-diabetics	75.5	24.5	55.8	44.2
Antifungals	67.8	32.2	55.1	44.9
Antihelmintics	62.5	37.5	49.2	50.8
Antimalarials	82.6	17.4	74.2	25.8
Antiretrovirals	84.0	16.0	95.0	5.0
Anti-tuberculosis products	47.7	52.3	42.5	57.5
Beta lactams	76.4	23.7	62.8	37.2
Cardiovascular products	76.8	23.2	62.8	37.2
CNS acting drugs	36.5	63.5	54.2	45.8
Dermatological	41.3	58.7	32.7	67.3
Diuretics	76.7	23.3	63.6	36.4
GIT/Antacids	84.6	15.4	47.1	52.9
Other antibacterials	56.8	42.3	44.4	55.6
Other drugs	77.6	22.4	74.2	25.8
Overall (%)	67.5	32.5	56.7	43.3

CNS: central nervous system, GIT:Gastrointestinal tract

4.1.2.1 Analgesic products

Fourteen analgesic products; 4 opioid and 10 non-opioid analgesics were listed on the KEML. The opioid analgesics; codeine tablets 30 mg, morphine tablets 60 mg, morphine oral liquid 10 mg/5 ml and morphine injection 10 mg/ ml were not manufactured locally. Six non-opioid products; aspirin tablets, diclofenac tablets, ibuprofen syrup, ibuprofen tablets, paracetamol syrup and paracetamol tablets were manufactured. Appendix 5.1 presents the PEs of analgesic products in Kenya. Diclofenac, paracetamol, and ibuprofen tablets recorded high numbers of PEs. Diclofenac tablets 50 mg had 57 PEs comprising 51 imported and 6 local PEs, paracetamol tablets 500 mg had 38 imported and 16 local, ibuprofen tablets 200 mg had 35 imported and 8 local while indomethacin capsules 25 mg had 34 imported and 8 local PEs. Three products; aspirin tablets 300 mg, ibuprofen syrup 100 mg/5 ml and paracetamol syrup 120 mg/5 ml had more local PEs than imported ones. Paracetamol tablets 500 mg had the highest number of local PEs in the market. Despite absence of fixed dosage combination (FDC) analgesics products on the KEML, aspirin/caffeine/paracetamol and aspirin/caffeine FDCs were manufactured and marketed by 8 companies. Other analgesics which were not listed on the KEML but prevalent in the market were indomethacin capsules 25 mg and mefenamic capsules 250 mg, with 34 and 20 PEs respectively. One local PE of diclofenac tablets 75 mg was registered. Nine local products in this class had 100 % retention whereas all imported products had less than 50 % retention. The percentage of local PEs for 11 out of the 14 analgesic products was less than 30 %. The overall percentage of analgesics that were locally manufactured was 26.1 % and 38.5 % for the registered and retained products, respectively.

4.1.2.2 Antimalarial products

The KEML has 7 antimalarial products namely; artemether/lumefantrine (A/L) tablets 20/120 mg, artemether injection 80 mg/ ml, dihydroartemisinin/piperaquine tablets 40/320 mg, quinine injection 300 mg/ ml, quinine tablets 300 mg, doxycycline tablets 100 mg and sulphadoxine/pyrimethamine 500/25 mg. The guidelines on malaria in Kenya recommended artemether/lumefantrine as the first line treatment for uncomplicated malaria, quinine is recommended for severe malaria, and sulphadoxine/pyrimethamine (S/P) and doxycycline are used in prophylaxis (Ministry of Health, Kenya, 2006). The local industry had registration approvals for four of the seven antimalarial products; A/L tablets 20/120 mg, quinine tablets 300 mg, doxycycline tablets 100 mg and sulphadoxine/pyrimethamine 500/25 mg. The PPB had registrations for 20 PEs of A/L tablets 20/120 mg, 5 being local. The 15 imported A/L PEs were all retained whereas only 2 (11.8 %) local PEs were retained. Less than 12 % of the retained A/L (PEs) were locally manufactured. The PEs of antimalarial products in Kenya are presented in Appendix 5.2. Twenty-two PEs of quinine tablets 300 mg were registered; 14 local and 8 imported and each had retained 4 PEs. Twenty eight PEs of S/P tablets were registered; 8 local and 20 imported. The local and six imported PEs of S/P tablets were retained in the market. Twenty six PEs of doxycycline capsules 100 mg; nine local and 17 imported were registered. Five imported and all local PEs of doxycycline capsules were retained. The overall percentage of antimalarial products that were locally manufactured was 17.4 % and 25.8 %, for the registered and retained products, respectively.

4.1.2.3 Antiretroviral pharmaceutical equivalents

The KEML contains 37 antiretroviral (ARV) products. Ten ARVs; efavirenz tablets 200 mg, lamivudine tablets 150 mg, nevirapine tablets 200 mg, stavudine tablets 30 mg, stavudine/lamivudine/nevirapine tablets 300/150/200 mg, zidovudine 300 mg tablets, zidovudine/lamivudine tablets 300/150 mg, lopinavir/ritonavir tablets 200/50 mg, tenofovir/emtricitabine/efavirenz tablets 300/200/600 mg and zidovudine/ lamivudine/nevirapine tablets 300/150/200 mg were registered by the local industry by 2014 (Appendix 5.3). Four local manufacturers had registered at least one ARV product. Four ARVs produced locally; lamivudine tablets 150 mg, zidovudine 300 mg tablets, zidovudine/lamivudine tablets 300/150 mg and tenofovir/emtricitabine/efavirenz tablets 300/200/600 mg were retained at the PPB. Two local manufacturers had ventured into formulation of fixed dose combination ARVs. The overall percentage of ARV PEs that was produced in Kenya was 16.0 % and 5.0 %, for the registered and retained products, respectively.

4.1.2.4 Antituberculosis pharmaceutical equivalents

Appendix 5.4 shows the antituberculosis PEs that were registerd in Kenya. The local industry had registration approvals for 11 out of the 19 anti-TB products listed as essential medicines. The 11 products were; rifampicin capsules 150 mg, rifampicin capsules 300 mg, isoniazid tablets 100 mg, isoniazid tablets 300 mg, ethambutol tablets 400 mg, pyrazinamide tablets 500 mg and five FDCs; ethambutol/isoniazid tablets 400/150 mg, rifampicin/isoniazid tablets 150/75 mg, rifampicin/isoniazid tablets 300/150 mg, rifampicin/isoniazid/pyrazinamide tablets 150/75/400 mg and rifampicin/isoniazid/pyrazinamide/ethambutol tablets 150/75/400/275 mg. Three local and 6 imported PEs of rifampicin/isoniazid FDC tablets were in the market.

One PE (imported) of rifampicin/isoniazid/pyrazinamide/ethambutol FDC tablets which is prescribed for intensive phase of anti-TB treatment had been registered. The overall percentage of anti-TB PEs that was produced in Kenya was 52.3 % and 57.5 %, for the registered and retained products, respectively.

4.1.2.5 Beta lactam antibiotics

Nine β-lactam antibiotics, amoxycillin syrup 125 mg/5 ml, amoxycillin capsules 500 mg, amoxycillin capsules 250 mg, ampicillin syrup 125 mg/5 ml, ampicillin capsules 250 mg, ampicillin capsules 500 mg, cefuroxime capsules 250 mg, flucloxacillin capsules 250 mg and flucloxacillin syrup 125 mg/5 ml were locally manufactured (Appendix 5.5). In this category, amoxycillin syrup 125 mg/5 ml had the largest number of PEs, 11 locally manufactured and 60 imported. Flucloxacillin capsules 250 mg and flucloxacillin powder 125 mg/5 ml had the least number of PEs; both products had 3 local and 3 imported PEs. The β-lactam class had products with high number of PEs in the market; amoxicillin dry powder and amoxicillin capsules 250 mg had 71 and 60 PEs, respectively. The number of PEs for amoxicillin capsules 500 mg, ampicillin dry powder 125 mg/ 5 ml and ampicillin capsules 250 mg ranged between 40 and 58. The overall percentage of β-lactam PEs that was produced in Kenya was 23.7 % and 37.2 % for the registered and retained products, respectively.

4.1.2.6 Cardiovascular products

Six out of the 20 cardiovascular products on the KEML; amlodipine tablets 5 mg, atenolol tablets 50 mg, enalapril tablets 5 mg, frusemide tablets 40 mg, hydrochlorothiazide tablets 25 mg and methyldopa tablets 250 mg were manufactured

locally (Appendix 5.6). In this category, the number of local PEs ranged from 1 to 6 while the range for the imports was 21 to 52. Atenolol tablets 50 mg had the highest number of PEs; 4 local and 52 imported. Methyldopa tablets 250 mg had the highest percentage (19.4 %) of local PEs followed by amlodipine tablets 5 mg (19.2 %). The overall percentage of cardiovascular PEs that was locally manufactured was 23.2 % and 37.2 %, for the registered and retained products, respectively.

4.1.2.7 Dermatological pharmaceutical equivalents

The locally manufactured dermatological products in the Kenyan market were; betamethasone cream 0.1 % w/w, betamethasone ointment 0.1 % w/w, clotrimazole cream 1 % w/w, hydrocortisone cream 1% w/w, hydrocortisone ointment 1 % w/w, miconazole cream 2 % w/w, silver sulphadiazine cream 1 % w/w and tetracycline hydrochloride ointment 3 % w/w (Appendix 5.7). Clotrimazole cream 1 % w/w had the largest number of PEs, 9 locally manufactured and 27 were imported. Local registrations were higher for 62.5 % of local products. Apart from hydrocortisone ointment, the local products had 100 % retention. The overall percentage of dermatological PEs that was produced in Kenya was 58.7 % and 67.3 % for the registered and retained products, respectively.

4.1.2.8 Antiallergies pharmaceutical equivalents

Nine antiallergy products were registered and all registered local PEs for 6 products were retained compared to one product for imported PEs (Appendix 5.8). The overall percentage of antiallergies PEs that was produced in Kenya was 41.1% and 57.7 % for the registered and retained products, respectively.

4.1.2.9 Anti-convulsants/anti-epileptics pharmaceutical equivalents

Four anti-convulsants/anti-epileptics products were registered in Kenya (Appendix 5.9). Carbamazepine tablets 100 mg had the highest number of PEs; 25 imported and 5 locally produced. Ten out of 12 PEs of phenytoin tablets 100 mg in the market were imported. The overall percentage of registered anti-convulsants/anti-epileptics PEs that was locally produced in Kenya was 33.3 % .

4.1.2.10 Anti-diabetic pharmaceutical equivalents

Five local manufacturers had registration approvals for at least one of the three oral anti-diabetic products in the market, namely; chlorpropamide tablets 250 mg, glibenclamide tablets 5 mg and metformin tablets 500 mg (Appendix 5.10). Metformin tablets had the highest number of PEs; 28 imported and 5 locally produced. The overall percentage of registered anti-diabetic PEs that was locally produced was 24.5 %.

4.1.2.11 Other pharmacological classes on the essential medicines list

Appendices 5.11 - 5.17 present the PEs of products in other pharmacological classes outlined on the KEML, that is; antifungals, antihelminthics, diuretics, GIT/antacids, other antibacterials, CNS drugs and other drugs. Apart from the CNS products, the local PEs were fewer than the imported. The overall percentage of local PEs in the market was; antifungals (32.2 %), antihelminthics (37.5 %), diuretics (23.3 %), GIT/antacids (15.4 %), other antibacterials (42.3 %) and other drugs (22.4 %). The overall percentage of local PEs in Kenya was 32.5 % for the registered and 43.3 % for the retained products.

4.1.3 Competitiveness of locally manufactured essential medicines

4.1.3.1 Price comparison

The competitive advantage of locally produced essential medicines based on price is fundamental in achieving self-sufficiency through local production. The local industry had registration approvals for 162 (12 sterile and 150 non-sterile) products out of the 422 listed essential medicines in Kenya. Twenty products listed in Table 4.9 were not retained by the PPB and were also not listed on the manufacturer's price lists. These products included ARVs and antituberculosis products which are mostly donor funded and are procured from facilities with WHO prequalification status. A combined price list from Kenyan manufacturer's contained 130 products which were presented in 208 pack sizes. Pharmaceutical equivalents of these products in Kenya were from all local manufacturers of human pharmaceutical products and 138 foreign manufacturers (Appendix 6).

Table 4.9: Registered products that were not retained in 2014

Allopurinol tablets 100 mg	Isoniazid tablets 300 mg
Allopurinol tablets 300 mg	Rifampicin/isoniazid/pyrazinamide tablets 150/75/400 mg
Codeine tablets 30 mg	Rifampicin mg/isoniazid tablets 300/150 mg
Diazepam tablets 5 mg	Rifampicin/ isoniazid/pyrazinamide/ethambutol tablets 150/75/400/275 mg
Ferrous tablets 200 mg	Stavudine /lamivudine/nevirapine tablets 30/150/200 mg
Niclosamide tablets 500 mg	Stavudine /lamivudine tablets 30/300 mg
Phenobarbitone tablets 30 mg	Acetic acid 2 % in alcohol (ear drops)
Phenytoin tablets 100 mg	Stavudine capsules 30 mg
Isoniazid tablets 50 mg	Zidovudine capsules 100 mg
Isoniazid tablets 100 mg	Zidovudine capsules 300 mg

The imported PEs originated from Africa, Asia, Australia, Europe, North America and South America. Products which had less than 3 PEs in either or both local and imported categories were not evaluated since the PEs available were considered to be

inadequate for statistical analysis and accurate interpretation of results. Sixty three products out of the 130 retained products had 3 or more local PEs. Twenty seven products had 3 or more local and 3 or more imported PEs and these were selected for the price comparison evaluation. It was found that some of these 27 products had more than one commercial pack size and in total, they constituted 38 pack sizes. Commercial pack size was used as the unit of measurement. The resultant number of PEs at each step of the selection process is shown in Figure 4.4.

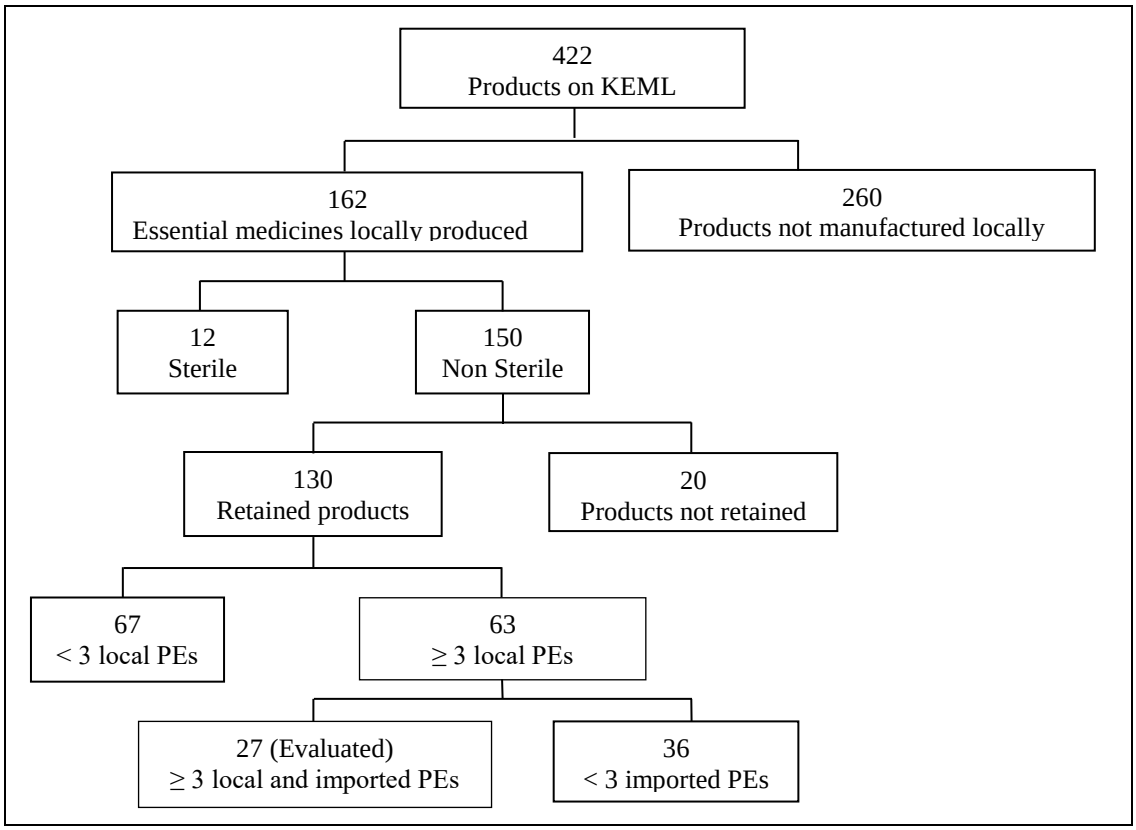


Figure 4.4: Selection of local and imported products for price evaluation

Table 4.10 shows the local and imported PEs of 38 pack sizes of 27 products that were assessed for wholesale price (without discounts) comparison. A local PE was cheapest on 15 (39.5 %) pack sizes, an imported PE was cheapest on 18 (47.4 %) pack sizes and on 5 (13.2 %) pack sizes, the prices of the cheapest local and imported PEs were equal. A PE was cheaper by more than 100 % for 2 local

products; paracetamol syrup 120 mg/5 ml and nystatin oral drops 100,000 I.U. and for 2 imported products; erythromycin tablets 250 mg and clotrimazole vaginal tablets 100 mg, 6's. The cheapest local and imported PE of metformin tablets 500 mg, paracetamol tablets 500 mg 1000's, amoxycillin capsules 500 mg 100's, and doxycycline capsules 100 mg 100's were equally priced. A pack size did not determine whether a local or imported PE would be cheaper for products with more than one pack size. An imported PE was cheaper for both the 100 and 1000 pack sizes of ibuprofen tablets 200 mg; a local PE was cheaper for the 10 pack while the imported PE was cheaper for 100 pack for ciprofloxacin tablets 500 mg tablets and a local PE was cheaper for 1000 pack of amoxycillin capsules 250 mg.

4.1.3.2 Statistical evaluation

Table 4.11 shows the computation of student's t-test for variance between mean price values of local and imported PEs for 27 products (38 pack sizes) which had 3 or more local and imported PEs, calculated at 95 % confidence interval. The t-test showed that there was no variance between mean price values of local and imported PEs for 24 products. The mean price value of ciprofloxacin tablets 500 mg (10 tablets pack), ketoconazole tablets 200 mg (30 tablets pack), and nystatin oral drops 100,000 I.U 30 ml was lower for the local PEs. The standard deviation values for the prices were higher for majority of imported products (63 %).

Table 4.10: Pharmaceutical equivalents assessed for price comparison

	Pack size	Number of local PEs	Number of imported PEs	Local highest price	Import highest price (KSh.*)	Mean local price (KSh.)	Mean Import price (KSh.)	Standard Deviation (local)	Standard Deviation (Import)	Local lowest price (KSh.)	Import lowest price
Tablets											
Amitriptyline 25 mg	1000	3	4	600	720	432.5	456.3	128.485	176.322	375	350
Ciprofloxacin 500 mg	10	7	18	260	1420	107.9	351.4	77.452	344.325	35	60
Ciprofloxacin 500 mg	100	7	14	2000	2600	682.1	657.3	607.357	638.551	300	240
Clotrimazole 200 mg	3	5	5	240	275	81.6	134	90.362	88.275	23	45
Clotrimazole 100 mg	6	6	9	210	410	73.5	103.5	70.809	131.360	25	8
Diclofenac sodium 50 mg	100	6	20	200	550	148	163.4	70.894	148.799	55	50
Erythromycin 250 mg	100	5	7	539	600	454.4	321.1	53.557	161.539	390	177.6
Erythromycin 250 mg	1000	6	5	5286	4255	4537.7	3033	786.076	846.711	3000	2450
Frusemide 40 mg	1000	4	4	450	800	405	555	42.032	172.530	350	420
Frusemide 40 mg	100	4	3	100	120	82	91.7	13.267	27.538	68	65
Hyoscine 10 mg	1000	6	3	3990	3392.5	2648.3	3064.2	705.420	413.343	2000	260
Ibuprofen 200 mg	1000	10	11	1200	850	454.6	401.3	266.532	214.080	280	230
Ibuprofen 200 mg	100	6	6	190	75	104.8	58.4	54.591	14.995	60	40
Ibuprofen 400 mg	500	8	4	450	420	353.5	345	51.997	80.726	300	240
Ibuprofen 400 mg	100	5	6	300	720	160.8	156.8	84.813	102.918	100	71
Ketoconazole 200 mg	30	4	7	240	720	159.3	392.7	55.338	231.390	120	170
Mebendazole 100 mg	1000	7	3	420	400	334.9	340	73.005	52.915	219	300
Mebendazole 100 mg	6	3	8	30	50	20.5	25.6	9.212	11.037	12	14
Metformin 500 mg	100	3	13	300	800	193.3	305.7	94.516	170.773	120	120
Metronidazole 400 mg	1000	6	3	739	510	417.5	430	177.381	121.655	210	290
Metronidazole 200 mg	1000	8	3	456	400	375.1	326.7	61.462	63.509	300	290
Paracetamol 500 mg	1000	10	11	420	560	325.7	279	72.575	103.258	210	210
Paracetamol 500 mg	100	9	5	371	235	134.1	128.6	95.174	83.470	60	60
Tinidazole 500 mg	4	5	9	24	20	12.4	9.2	6.691	4.525	7	6

Table 4.10 continued

	Pack size	Number of local PEs	Number of imported PEs	Local highest price	Import highest price (KSh.*)	Mean local price (KSh.)	Mean Import price (KSh.)	Standard Deviation (local)	Standard Deviation (Import)	Local lowest price (KSh.)	Import lowest price
Capsules											
Amoxycillin 250 mg	1000	10	10	3300	2115	1852.9	1560.3	667.248	354.013	1056	1080
Amoxycillin 250 mg	100	7	9	959	370	307.1	190.5	289.446	74.085	160	125
Amoxycillin 500 mg	500	7	5	3300	1900	1835	1606.7	707.525	205.589	1200	1350
Amoxycillin 500 mg	100	5	7	1843	700	699.6	425.1	653.371	151.094	300	300
Doxycycline 100 mg	100	8	4	200	145	149.3	119.1	32.592	18.892	96	96
Indomethacin 25 mg	1000	7	5	440	400	338.6	277	69.144	80.747	250	200
Mefenamic acid 250 mg	100	4	4	320	350	188.8	166.3	100.530	125.327	75	76
Syrups											
Amoxycillin 125 mg/5 ml	100 ml	11	6	236	249	88.4	94.4	79.534	78.356	36	28
Amoxycillin 125 mg/5 ml	60 ml	8	4	50	120	30.8	67.5	8.932	45	20	30
Cetrizine syrup 5 mg/5 ml	60 ml	4	4	135	144	90	108.3	31.885	26.738	60	80
Nystatin 100000 iu/ ml	30 ml	3	3	120	354	70	249.8	43.589	99.733	40	155.3
Paracetamol 120 mg/5 ml	60 ml	13	4	120	650	33.1	221.1	24.082	287.724	17	43.2
External preparations											
Betamethasone 0.1% w/w	15 g	11	4	190	55	61.2	35.3	46.850	13.301	30	26
Clotrimazole 1% w/w	20 g	8	5	75	150	38.1	87.6	18.357	50.008	22	18

*** (100 KSh ≈1US$)**

Table 4.11: Students t-test values for local and imported products in Kenya

PRODUCT	I t I	α = 0.05 (two tailed)	Hypothesis test
Tablets			
Amitriptyline 25 mg	0.03977968	2.57058183	No variation
Ciprofloxacin 500 mg	2.8223707	2.0686576	**Variation**
Ciprofloxacin 500 mg	0.08696571	2.09302405	No variation
Clotrimazole 200 mg	0.57230477	2.16036865	No variation
Clotrimazole 100 mg	0.92753388	2.30600413	No variation
Diclofenac sodium 50 mg	0.34808008	2.06389855	No variation
Erythromycin 250 mg	2.03266801	2.22813884	No variation
Erythromycin 250 mg	1.73195407	2.26215716	No variation
Frusemide 40 mg	1.68941488	2.44691185	No variation
Frusemide 40 mg	0.56112685	2.57058183	No variation
Hyoscine butyl Br 10 mg	1.11181089	2.36462425	No variation
Ibuprofen 200 mg	0.50146525	2.09302405	No variation
Ibuprofen 200 mg	2.01013177	2.22813884	No variation
Ibuprofen 400 mg	0.19164712	2.22813884	No variation
Ibuprofen 400 mg	0.07007763	2.26215716	No variation
Ketoconazole 200 mg	2.54512988	2.26215716	**Variation**
Mebendazole 100 mg	0.76241894	2.26215716	No variation
Mebendazole 100 mg	0.12319169	2.30600413	No variation
Metformin 500 mg	1.55498651	2.14478668	No variation
Metronidazole 400 mg	1.13693124	2.26215716	No variation
Metronidazole 200 mg	0.12390619	2.36462425	No variation
Paracetamol 500 mg	0.11249703	2.17881283	No variation
Paracetamol 500 mg	1.19329348	2.09302405	No variation
Tinidazole 500 mg	0.95362493	2.17881283	No variation
Capsules			
Amoxycillin 250 mg	1.22499699	2.10092204	No variation
Amoxycillin 250 mg	1.03940841	2.14478668	No variation
Amoxycillin 500 mg	0.80733152	2.22813884	No variation
Amoxycillin 500 mg	0.92196878	2.22813884	No variation
Doxycycline 100 mg	1.1913462	2.36462425	No variation
Indomethacin 25 mg	1.38127783	2.22813884	No variation
Mefenamic acid 250 mg	0.2800863	2.44691185	No variation
Syrups			
Amoxycillin 125 mg/5 ml	0.14929255	2.13144954	No variation
Amoxycillin 125 mg/5 ml	1.61417733	2.22813884	No variation
Cetrizine syrup 5 mg/5 ml	0.87714454	2.44691185	No variation
Nystatin 100000 iu	2.86042826	2.77644511	**Variation**
Paracetamol 120 mg/5 ml	1.30508253	2.13144954	No Variation
Creams			
Betamethasone 0.1% w/w	1.66324689	2.16036865	No variation
Clotrimazole 1% w/w	2.12457908	2.20098516	No variation

4.1.3.3 Scatter diagrams

Scatter correlation between imported and local PEs demonstrated that a higher percentage of imported PEs were less priced than local PEs. Scatter correlation between price of local and imported PEs is presented in Appendix 7. Appendix 7.16 illustrates the impact of an outlier on the mean price of the local or imported products in the market. An outlier was caused by one exorbitantly or cheaply priced PE. A comparison between the price of local and imported PEs of paracetamol tablets 500 mg (Appendix 7.22) shows that despite the tie on the cheapest PE for this product, majority of the imported PEs were less priced. The mean price of locally produced ketoconazole tablets 200 mg was lower compared to that of imported products but the prevalence of cheaper imported PEs was higher in the market. Local PEs were shown to be less priced for 10 products; amoxycillin syrup 125 mg/5 ml 60 ml pack, ciprofloxacin 500 mg (10's) clotrimazole cream 1 % w/w, clotrimazole pessaries 200 mg (3's), frusemide tablets 40 mg (1000's), hyoscine butyl bromide tablets 10 mg (1000's), metronidazole tablets 400 mg (1000's), mebendazole tablets 100 mg (1000's), nystatin oral suspension 100,000 IU 30 ml and paracetamol suspension 120 mg/5 ml. Although a local PE was cheapest for amoxycillin capsules 250 mg (1000's), majority of imported PEs for this product were cheaper. The trend in price for betamethasone cream 0.1 % w/w and mebendazole tablets 100 mg (6's) were similar for both local and imported PEs. The correlation demonstrated that imported PEs for 16 products were less priced compared to local PEs. Examples of less prices imported PEs are; ciprofloxacin tablets 500 mg (100's), clotrimazole tablets 100 mg (6's), erythromycin tablets 250 mg (1000's), ibuprofen tablets 200 mg (1000's) and paracetamol tablets 500 mg (1000's).

4.1.3.4 Costing of pharmaceutical products

The costing of oral tablets, liquids, and external preparations detailing the contribution as a percentage of each constituent to the wholesale price is presented in Table 4.12 and Figure 4.5 illustrate the overall contribution as a percentage, of each constituent to the product price.

Table 4.12: Costs contributing to price of pharmaceutical products

Constituent	Tablets		Oral Liquids	External preparations
	Bulk pack	Unit pack		
Raw materials	52	47	29	31
Packaging materials	5	9	15	17
Insurance+ duty+ transport	9	8	7	3
Direct and indirect labor	7	6	11	12
Utilities and maintenance	4	3	5	6
Quality control and R&D	3	2	4	4
Marketing costs	7	7	5	5
Miscellaneous costs	5	3	6	7
Mark up	8	15	18	15
Total (%)	100	100	100	100

Raw materials and packaging materials contributed about 50 % of the product wholesale price. The highest percentage mark-up was on liquid preparations (18 %) and the lowest was on bulk packs (8 %). The average mark up on these dosage forms in this industry was 14 %. Quality control and R&D costs contributed the least (3 %) to the product price. Almost all materials used in production were imported. The big and established companies sourced materials from overseas whereas the small scale start-up companies bought a high percentage of the material from agents based in Kenya. The established companies imported 94 % APIs and 91.7 % of excipients. Start-up companies imported on average 29 % of the production inputs and purchased the rest from local agents.

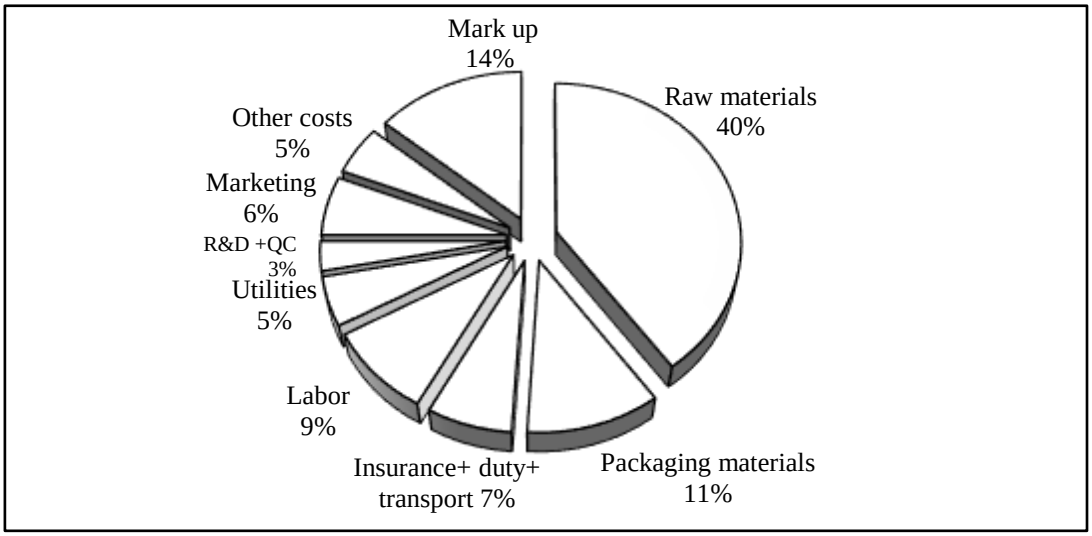


Figure 4.5: Contribution of each constituent to product price

The percentage use of locally produced packaging materials by the pharmaceutical industry in Kenya is shown in Table 4.13. All outer cartons and more than 50 % of plastic bottles were produced in Kenya. The overall percentage of packaging material produced locally was 50.8 % and 81.3 % for the small and big companies (producing more than 50 products), respectively.

Table 4.13: Percentage of packaging materials produced in Kenya

Packaging material	Big companies	Small companies
Glass bottles	19.2	50.0
Plastic bottles	54.5	100.0
Unit boxes/labels	29.5	75.0
Outer cartons	100.0	100.0

4.1.4 Market share of local products

The main clients for the Kenyan pharmaceutical industry were the public procurement agencies; KEMSA, MEDS, Medical Supplies Department (MSD),

Tanzania, Uganda Medical Stores and the large pharmaceutical distributors in Kenya, such as; Transchem Pharmaceuticals Ltd. and Transwide Pharmaceuticals.

The annual turnover for 15 Kenyan pharmaceutical manufacturers, including 6 leading companies (Cosmos Ltd, Lab & Allied, Regal Pharmaceuticals Ltd, Elys Chemical Industries Ltd., Universal Corporation and Dawa Limited) was US$ 109.6 million. The sales to the local market was US$ 81.9 million. The turnover for the 15 companies could represent approximately 60 % of the annual sales of the local industry, implying that the market share for local products was US$ 136.5 million, accounting for 19 % of the estimated domestic market of US$ 720 million in 2014.

Figure 4.6 shows the average export and local sales for 8 local pharmaceutical manufacturers for the years 2010-2014. The export market accounted for 31 %, 25.5 %, 30.7 %, 25.8 % and 28.3 % for the 5 years, respectively. In 2014, the established firms had a substantial portion of the sales from export market (Regal - 47 %, Elys - 58.7 %, Dawa - 71.8 %, Universal - 23.3 % and Lab & Allied - 63.1 %).

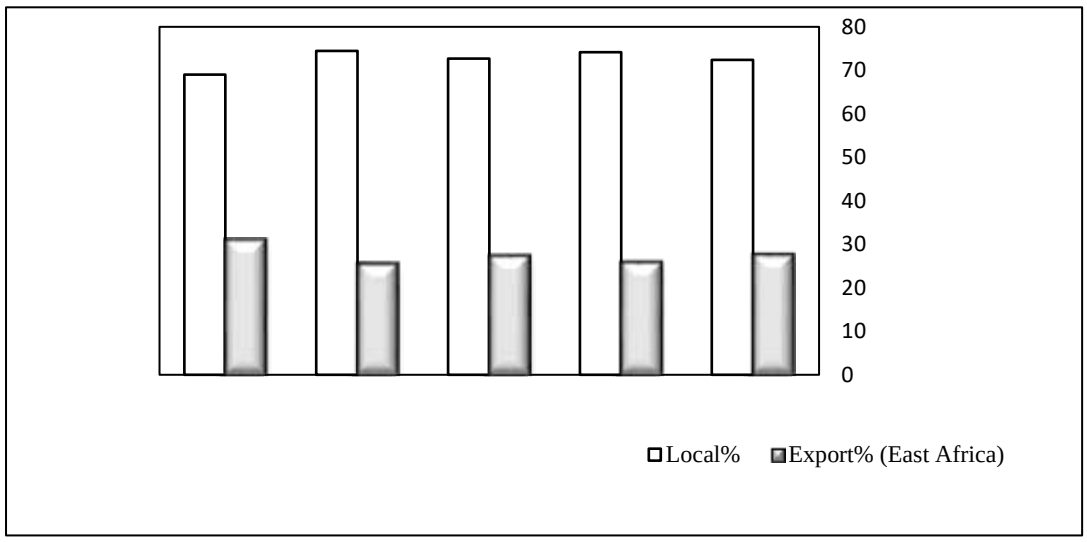


Figure 4.6: Pharmaceutical products export and local sales from 2010 to 2014

4.2 Production capacity of the pharmaceutical manufacturing industry

4.2.1 Installed, available and utilized production capacities

Sixteen (66.7 %) manufacturers out of 24 local manufacturers of human medicines responded to the questionnaire on capacities in the Kenyan pharmaceutical industry. Table 4.14 presents the annual installed and available production capacities of 14 non sterile manufacturers, based on two shift operations for six production lines in the Kenyan pharmaceutical industry in 2014. Data on installed production capacities was available at all facilities. The average available capacity for the industry was 77.3 % for tablets, 81.7 % for capsules, 82.7 % for oral liquids, 80.9 % for external preparations, 77.0 % for dry powders and 80.7 % for oral rehydration salts. The available capacity for the individual companies, ranged from 66.7-80 % for tablets, 80-90.5 % for capsules, 60.5-90.9 % for oral liquids, 77.8-90 % for external preparations, 57.1-85.7 % for dry powders and 80-83.3 % for oral rehydration salts. The local pharmaceutical industry has capacity to manufacture approximately 30 billion tablets and 2 billion capsules. The established companies have invested in mega compression and capsulation machines, large (≥4000L) liquid manufacturing tanks in readiness for public tenders which are usually time bound. Three companies had scanty records on utilized production capacity due to poor record keeping and a manual documentation system. Less than 50 % of the available production capacity was utilized for all dosage forms across the whole pharmaceutical manufacturing industry. The production capacity utilization for individual dosage forms represented in Tables 4.15-4.20 are derived from available production capacities in Table 4.14.

Table 4.14: Installed and available annual production capacity in 2014

Companies	Dosage forms					
	Tablets	**Capsules**	**Oral liquids (bottles)**	**External preparations (tubes)**	**Dry powders for reconstitution (Bottles)**	**Oral rehydration salts (Sachets)**
A.	1,342,500,000	-	30,000,000	-	-	-
B.	2,000,000,000	104,000,000	29,000,000	12,000,000	-	-
C.	-	-	10,000,000	-	-	-
D.	3,000,000,000	170,000,000	30,000,000	9,240,000	-	20,000,000
E.	2,130,000,000	83,600,000	48,000,000	4,840,000	6,600,000	-
F.	2,400,000,000	800,000,000	24,000,000	20,000,000	40,000,000	20,000,000
G.	1,000,000,000	-	-	-	-	-
H.	7,000,000,000	400,000,000	44,000,000	18,000,000	-	30,000,000
I.	1,000,000,000	-	6,600,000	-	-	-
J.	-	-	18,000,000	-	-	-
K.	1,552,500,000	143,750, 000	16,000,000	15,750,000	-	-
L.	2,400,000,000	336,000,000	160,000,000	16,000,000	35,200,000	-
M.	1,500,000,000	60,000,000	20,000,000	10,000,000	10,000,000	-
N.	4,000,000,000	220,000,000	7,680,000	8,800,000	-	20,000,000
Total available capacity	**29,325,000,000**	**2,317,350,000**	**443,280,000**	**114,630,000**	**91,800,000**	**90,000,000**
Total installed capacity	**37,946, 250,000**	**2, 834, 900, 000**	**535, 875, 000**	**141, 650, 000**	**119, 200, 000**	**111, 500, 000**

Dash- signifies that the dosage form was not produced by the manufacturer

The dashes in Table 4.14 denote that the company did not manufacture that particular dosage form, whereas the dashes in Tables 4.15-4.20 signify that the manufacturer was not able to avail data on utilized capacities.

4.2.1.1 Tablets production capacity

The annual installed and available production capacity was 37.9 and 29.3 billion tablets, respectively. The percentage of available production capacity that was utilized for the years, 2010 to 2014 is shown in Table 4.15.

Table 4.15: Utilized production capacity for tablets

	Available	**% Utilized capacity (Year)**				
Company	**capacity (2014)**	**2010**	**2011**	**2012**	**2013**	**2014**
A	1,342,500,000	22.4	21.6	24.6	26.9	29.8
B	2,000,000,000	-	-	-	-	-
D	3,000,000,000	-	-	-	-	-
E	2,130,000,000	30.0	30.0	33.0	33.0	25.0
F	2,400,000,000	40.7	36.0	27.0	24.7	32.1
G	1,000,000,000	25.0	25.0	30.0	30.0	30.0
H	7,000,000,000	14.8	7.0	12.0	16.8	13.5
I	1,000,000,000	-	-	-	15.0	30.0
K	1,552,500,000	18.0	19.3	22.5	25.8	27.1
L	2,400,000,000	-	-	-	-	-
M	1,500,000,000	19.5	19.5	32.5	32.5	35.0
N	4,000,000,000	11.4	12.6	16.3	21.1	21.8
Total available capacity	**29,325,000,000**					
Average utilized capacity (%)		22.8	21.3	24.8	24.9	26.8

Dash - signifies that the data was not provided by manufacturer

Three companies did not provide data on utilized capacity, and one provided data for 2 years, either due to poor record keeping or upgrading of the documentation system. The trend in capacity utilization varied among the manufacturers, and showed either an

increase, decrease or fluctuation. Capacity utilization of 5 companies; A, I, K, M and N increased gradually during this period. Capacity utilization growth for company G was steady, H fluctuated whereas E and F demonstrated a reduction. The average production capacity utilization increased by 4 % during the 5 years, which is interpreted as an increase of 0.8 % per year. Tablets production line was underutilized by over 50 %.

4.2.1.2 Capsules production capacity

The trend of capacity utilization for the capsules filling line is shown in Table 4.16. Companies, B, D and L did not avail capacity utilization data. The installed and available production capacity was 2.8 and 2.3 billion capsules, respectively. Two companies utilized less than 3.5 % of the available capacity during this period. Two manufacturers, E and M depicted an increase in capacity utilization, F showed a decrease. Utilization capacity for H, K and N fluctuated. The capsules filling line was the most underutilized.

Table 4.16: Utilized production capacity for capsule filling

	Available	**% Utilized capacity (Year)**				
Company	**capacity(2014)**	**2010**	**2011**	**2012**	**2013**	**2014**
B	104,000,000	-	-	-	-	-
D	170,000,000	-	-	-	-	-
E	83,600,000	20.0	23.0	25.0	25.0	27.5
F	800,000,000	14.7	14.4	18.7	9.7	6.0
H	400,000,000	1.0	1.1	1.9	2.6	2.1
K	143,750, 000	0.8	1.0	1.0	3.5	1.5
L	336,000,000	-	-	-	-	-
M	60,000,000	19.5	19.5	26.0	26.0	30.0
N	220,000,000	12.3	11.4	21.8	8.2	10.7
Total available capacity	**2,317,350,000**					
Average utilized capacity (%)		11.4	11.7	15.7	12.2	13.0

Dash- signifies that the data was not provided by manufacturer

4.2.1.3 Liquid filling line production capacity

The average utilized capacity for liquids filling line was less than 30 % as shown in Table 4.17. Two facilities utilized less than 7 % of the available capacity during the 5 year period. The utilized capacity on this line varied across the industry with one manufacture utilizing more than 50 % of the available capacity. The utilized capacity fluctuated for manufacturers F and I but the rest demonstrated a gradual increase.

Table 4.17: Utilized production capacity for liquid filling

Company	Available capacity (2014)	% Utilized capacity (Year)				
		2010	2011	2012	2013	2014
A	30,000,000	8.7	8.3	10.0	19.3	20.3
B	29,000,000	-	-	-	-	-
C	10,000,000	-	15.0	20.0	25.0	25.0
D	30,000,000	-	-	-	-	-
E	48,000,000	35.0	38.0	38.0	37.5	40.0
F	24,000,000	14.7	16.8	25.3	29.6	15.2
H	44,000,000	1.2	1.3	2.4	2.9	4.6
I	6,600,000	3.0	4.5	6.8	5.3	2.7
J	18,000,000	-	-	-	-	-
K	16,000,000	10.0	11.3	12.5	15.6	17.5
L	160,000,000	-	-	-	-	-
M	20,000,000	45.5	52.0	45.0	58.5	55.0
N	7,680,000	59.9	58.6	59.9	61.2	75.5
Total available capacity	443,280,000					
Average utilized capacity (%)		22.3	22.9	24.4	28.3	28.4

Dash - signifies that the data was not provided by manufacturer

4.2.1.4 External preparations, dry syrups and oral rehydration salts

The average utilized production capacity for external preparations, dry syrups and ORS in 2014 was 21.0 %, 28.6 % and 46.7 %, respectively. The trend of production capacity utilization for the three categories of products is shown in Tables 4.18-4.20. The utilized capacity for external preparations was steady for manufacturer K, fluctuated for manufacturers F, H and N and increased steadily for two manufacturers; E and M.

Table 4.18: Utilized production capacity for external preparations

Company	Available Capacity (2014)	% Utilized capacity (Year)				
		2010	2011	2012	2013	2014
B	12,000,000	-	-	-	-	-
D	9,240,000	-	-	-	-	-
E	4,840,000	1.0	22.5	30.0	40.0	45.0
F	20,000,000	17.2	22.6	20.7	22.9	17.0
H	18,000,000	7.6	3.6	17.3	7.8	1.6
K	15,750,000	16.5	17.8	18.4	19.1	19.7
L	16,000,000	-	-	-	-	-
M	10,000,000	19.5	19.5	26.0	26.0	30.0
N	8,800,000	23.9	26.1	68.2	37.5	12.5
Total available capacity	**114,630,000**					
Average utilized capacity (%)		14.3	17.9	30.1	25.6	21.0

Dash- signifies that the data was not provided by manufacturer

The production capacity utilization for dry syrups increased for companies E and M during this period. Company F had the largest available production capacity, lowest capacity utilization and this declined from 2012. Oral rehydration salts was produced by 4 manufacturers. Capacity utilization for ORS increased for 2 of the facilities that were evaluated. The capacity utilization for H was less than 5 % during this period.

There was an increase in capacity utilization for all dosage forms assessed. However, the available production capacity for all dosage forms was underutilized during this period. The average utilized production capacity was less than 50 % for the dosage forms that were assessed as presented in Figure 4.7.

Table 4.19: Utilized production capacity for dry syrups

Company	Available capacity (2014)	% Utilized capacity (Year)				
		2010	2011	2012	2013	2014
E	6,600,000	17.1	20.4	19.9	23.0	37.5
F	40,000,000	6.2	8.5	10.3	5.2	3.3
L	35,200,000	-	-	-	-	-
M	10,000,000	13.0	19.5	32.5	58.4	45.0
Total available capacity	91,800,000					
Average utilized capacity (%)		12.1	16.1	20.9	28.9	28.6

Dash-signifies that the data was not provided by manufacturer

Table 4.20: Utilized production capacity for oral rehydration salts

Company	Available capacity (2014)	% Utilized capacity (Year)				
		2010	2011	2012	2013	2014
D	20,000,000	-	-	-	-	-
F	20,000,000	25.8	54.8	16.6	26.9	45.6
H	30,000,000	1.4	2.7	1.5	3.9	2.5
N	20,000,000	-	-	-	28.5	92.0
Total available capacity	**90,000,000**					
Average utilized capacity (%)		13.6	28.8	9.1	19.8	46.7

Dash-signifies that the data was not provided by manufacturer

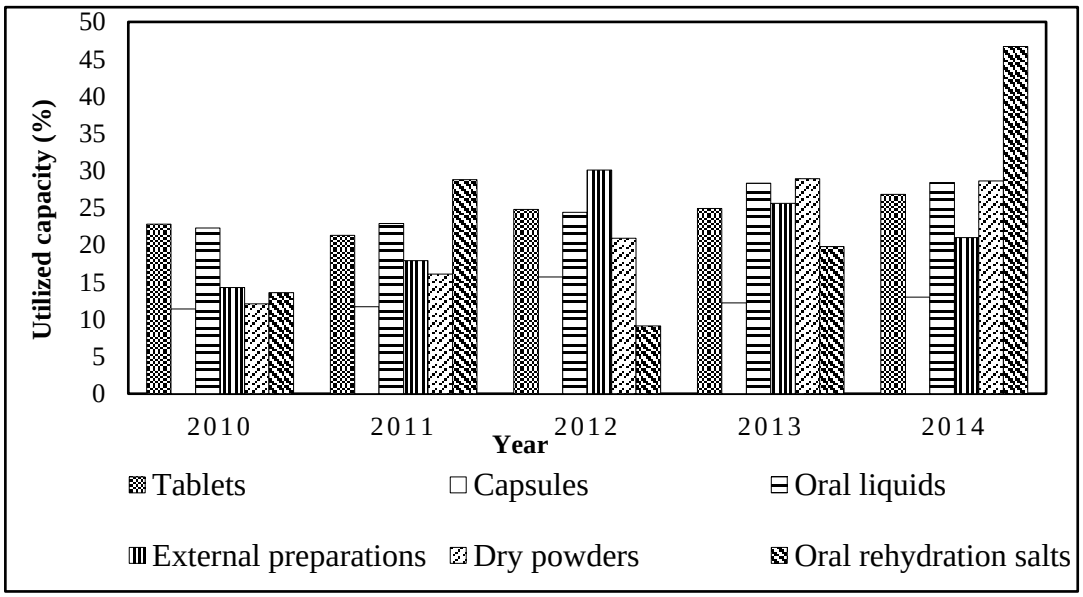


Figure 4.7: Average capacity utilization for various dosage forms, 2010-2014

4.2.2 Projection of self-sufficiency in essential medicines

Figure 4.8 presents the probable year for achieving self-sufficiency through local production from questionnaire responses. Majority (57.1 %) of the predictions ranged from 2030 to 2065 and (42.9 %) reported that the year was not predictable due to the many variables that affect self-sufficiency. The respondents opinion were that favorable government policies and their implementation were key determinants of achieving self-sufficiency through the local pharmaceutical manufacturing industry.

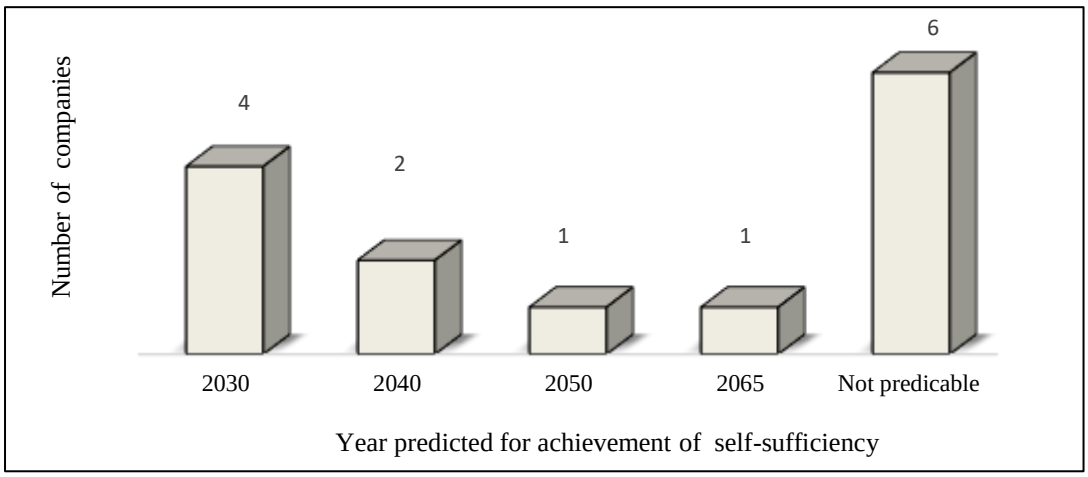


Figure 4.8: Probable year for achieving self-sufficiency in essential medicines

A summary of utilized production capacity for dosage forms that were assessed (tablets, capsules, oral liquids, external preparations and ORS) for a period of 5 years; 2010 to 2014 is presented in Table 4.21. A steady increase was demonstrated for tablets, liquids and dry syrups while utilization capacity for capsules, external preparations and ORS fluctuated. The fluctuation could have been due to the impact of importation of capsules by some manufacturers instead of local production and a huge demand of ORS in 2014 from a facility with international cGMP accreditation. The overall capacity utilization increased by 11.3 % during the 5 years. The overall production capacity utilization/time plot demonstrated linearity as shown in Figure 4.9.

Table 4.21: Utilized production capacities in the local pharmaceutical industry

Year	Percentage utilized capacity (%)						
	Tablets	Capsules	Oral liquids	Externals	Dry powders	ORS	Average (overall)
2010	22.8	11.4	22.3	14.3	12.1	13.6	**16.1**
2011	21.3	11.7	22.9	17.9	16.1	28.8	**19.8**
2012	24.8	15.7	24.4	30.1	20.9	9.1	**20.8**
2013	24.9	12.2	28.3	25.6	28.9	19.8	**23.3**
2014	26.8	13.0	28.4	21.0	28.6	46.7	**27.4**
Average	**24.1**	**12.8**	**25.3**	**21.8**	**21.3**	**23.6**	**21.5**

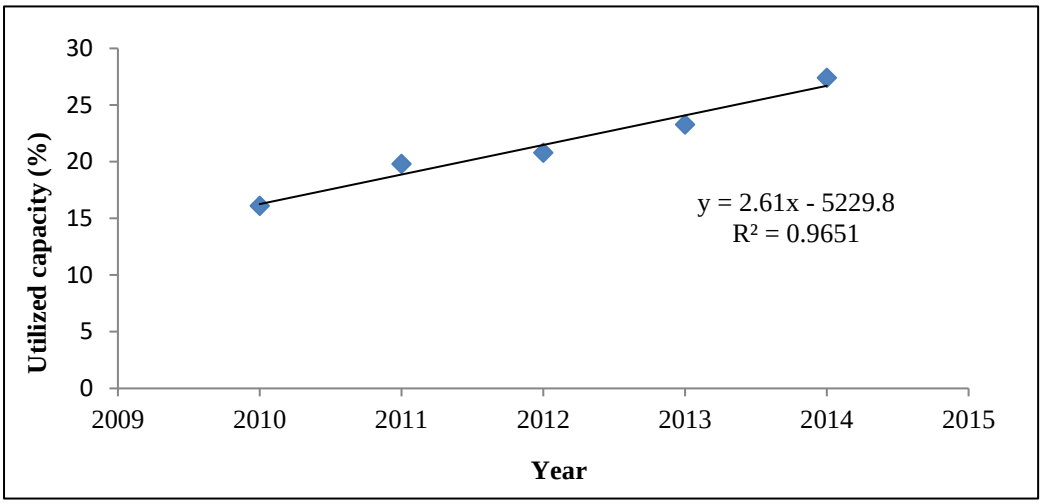


Figure 4:9 Overall average production capacity utilization versus time

The projected utilized production capacity based on trend-time series model of forecasting for the period 2016 to 2050 is presented in Table 4.22. Apart from ORS and dry powders for reconstitution which were projected to have a 100 % capacity utilization by 2030, the other dosage forms will utilize less than 60 % of the available capacity, with tablets (45.0 %), capsules (19.5 %), oral liquids (56.9 %) and external preparations (59.8 %). Table 4.23 presents the projected year for full capacity utilization for the various dosage forms. The Microsoft Excel® function of forecasting by use of linear regression was used to compute the values. On average, the forecasted year for

achieving full capacity utilization is 2043. In view of the local market share of 25 % cited earlier in this study, and an average production capacity utilization of 27.4 % (local and exports), it is postulated that self-sufficiency in these dosage forms will be achieved at full capacity utilization. Assumptions made in the projection were that market for the projected capacity utilization was available in Kenya, the cGMP upgrading program of facilities will run in accordance to the PPB cGMP roadmap and all facilities that will be operational in 2020 will be cGMP compliant.

Table 4.22: Projected capacity utilization (percent) for the years 2016 to 2050

Year	Tablets	Capsules	Oral liquids	Externals	Dry powders	ORS	Average (overall)
2016	28.8	14.3	32.3	30.2	39.6	46.4	31.9
2018	31.1	15.0	35.8	34.4	48.8	57.8	37.1
2020	33.4	15.8	39.3	38.7	58.0	69.3	42.4
2022	35.7	16.5	42.9	42.9	67.1	80.7	47.6
2024	38.0	17.2	46.4	47.1	76.3	92.1	52.8
2026	40.4	18.0	50.0	51.3	85.4	103.5	58.0
2028	42.7	18.7	53.4	55.5	94.6	114.9	63.2
2030	45.0	19.5	56.9	59.8	103.8	126.4	68.5
2035	50.8	21.3	65.7	70.3	126.7	154.9	81.5
2040	56.6	23.2	74.5	80.9	149.6	183.5	94.6
2050	68.2	26.9	92.1	102.0	195.4	240.6	120.7

Table 4.23: Projected year for full production capacity utilization

Dosage Form	Full capacity utilization projection (Year)
Tablets	2078
Capsules	2250
Oral liquids	2055
External preparations	2050
Dry powders	2029
Oral Rehydration Salts	2025

4.3 Compliance of facilities and quality systems with cGMP standards

4.3.1 The cGMP accreditation status of facilities

Compliance with cGMP standards in regard to premises, utilities impacting product quality, personnel, product development and quality control of products for the 16 facilities that responded to the questionnaire on capacities in Kenyan pharmaceutical industry is presented. The degree of conformance to the required WHO cGMP standard that governs the local pharmaceutical manufacturing industry in Kenya varied amongst the manufacturers. All the manufacturers assessed had cGMP approval by the PPB, Kenya and 11 facilities had been approved by various DRAs in the East Africa region. Three manufacturers, Cosmos Limited, Regal Pharmaceuticals Limited and Universal Corporation received the European Pharmaceutical Inspection Cooperation Scheme certification in 2007, and Universal was accorded WHO prequalification for the antiretroviral, zidovudine/lamivudine in 2011. In 2015, Universal Corporation submitted a second dossier for evaluation while Cosmos Limited was in the final stages of prequalification process for an ARV product.

4.3.2 Premises and utilities

Good manufacturing practices require pharmaceutical production premises to be located, designed, constructed, adapted, and maintained to suit the operations to be carried out. Nine of the 16 facilities were appropriately designed to allow logical flow of personnel and production materials, intermediates and finished products. Material of construction of production premises was impervious, floors and walls were smooth to allow good cleaning. Production areas were ventilated through air handling units to prevent contamination and cross-contamination, as well as to control temperature and,

where necessary, humidity. Table 4.24 presents the type of ventilation and water purification system at the respondent facilities. Eleven facilities had installed terminal high efficiency particulate air (HEPA) filters in production areas to prevent cross-contamination. Pressure differential was maintained for areas with different levels of cleanliness. Five facilities utilized high capacity blowers to propel air through F8 filters into production areas. Reverse osmosis and/or deionization were used to purify water. Eight facilities had a loop system for continuous water circulation which provided good control of viable particulate matter. Viable and non-viable particles were monitored. Eight facilities had validated the HVAC and water purification systems to ensure that these systems were operating and performing in accordance with the design specifications.

Table 4.24: Ventilation and water system in the pharmaceutical industry in 2014

Facility	**HVAC System**	**Water Purification**
Beta Healthcare	Air Handling Units. Terminal HEPA	Reverse Osmosis
Biodeal	Forced ventilation (Upgrading was ongoing)	Reverse Osmosis/Deionization plant
Comet	Forced ventilation /Filters	Deionization plant
Cosmos Limited	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant
Dawa Limited	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant
Elys	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant
GSK	Air Handling Units. Terminal HEPA	Reverse Osmosis/UV
Ivee Aqua Ltd	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant
KEMRI	Air Handling Units. Terminal HEPA	Reverse Osmosis + Distillation
Lab &Allied	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant
Macs	Forced ventilation /Filters	Deionization plant
Oss Chemie	Air Handling Units	Deionization plant
PMC	Air Handling Units. Terminal HEPA	Deionization plant/UV
Regal	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant
Sphinx	Air Handling Units	Reverse Osmosis
Universal	Air Handling Units. Terminal HEPA	Reverse Osmosis/Deionization plant

4.3.3 Quality control department

The 16 facilities had a quality control (QC) department that was independent of production. The QC department at these facilities was equipped with an ultraviolet spectrophotometer, infrared spectrophotometer, high performance liquid chromatography and a microbiology section. This department was adequately equipped to perform analysis of raw materials, intermediate products and finished pharmaceutical products. Specifications were available for the materials analysed. Pharmacopeial test procedures were followed and documented. The Head of QC was responsible for approval of both raw materials and finished products. Standard operating procedures for instruments and other laboratory procedures were in place. Most of the quality control analysts were diploma or Bachelor of Science (B.Sc.) graduates. Apart from one firm which had a pharmacist as Head of department, the rest were headed by B.Sc graduates.

4.3.4 Research and development

Majority of local manufacturers did not have facilities for R&D activities. Three facilities, a research institution and two manufacturers had operational R&D departments. Nine facilities were in the processes of setting up this unit, whereas four facilities carried out formulation activities either in quality control or production areas. The research and development activities performed by the local industry focused mainly on product formulation and quality improvement studies.

4.3.5 Personnel

The workforce at the 16 respondent manufacturers was 2,798, consisting of persons of different qualifications, disciplines and skills necessary for the operations carried out in

this industry. Most of the skilled workers had at least diploma qualification, specializing in pharmacy, chemistry (analytical, organic, synthetic, medicinal), biological sciences (biochemistry, microbiology), engineering and management. Among these employees were 2 Ph.D. holders and 33 pharmacists. One Company had engaged 5 pharmacists and this was the highest number at any one facility. Two companies had 4 pharmacists each, two had 3, 4 had 2, 6 had one and one facility had no pharmacist. The qualification for the workforce in this industry is shown in Table 4.25. The workers were deployed in production, quality assurance, quality control, regulatory, R&D and their distribution is as shown in Figure 4.10. Majority of the employees worked in production department, and R&D had the least workforce (1 %).

Table 4.25: Personnel qualification in the pharmaceutical manufacturing industry

Qualifications	Number of personnel
Doctor of Philosophy	2
Master of Science	15
Bachelor of Pharmacy	33
Bachelor of Science	140
Diploma	131
Others	2477
Total	2798

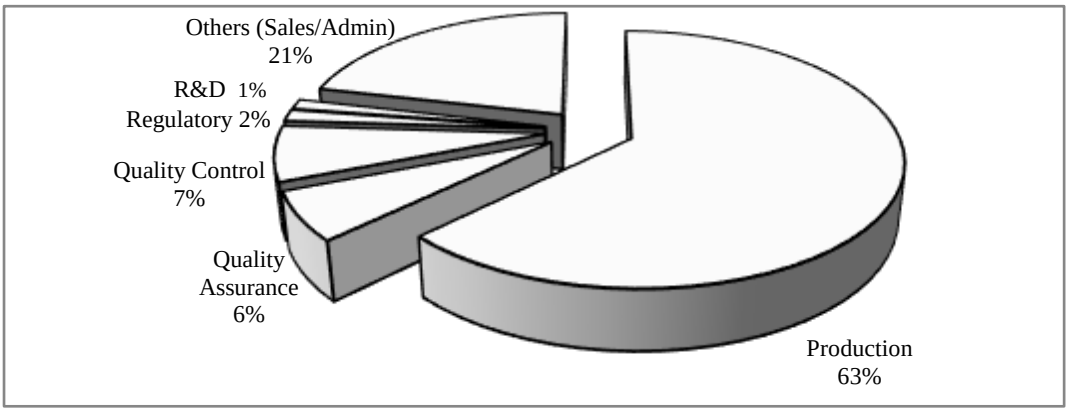


Figure 4.10: Deployment of workers in the local pharmaceutical industry

4.3.6 Overall cGMP compliance rating of facilities and quality systems

Table 4.26 presents the overall cGMP compliance rating of the companies that were assessed.in the study. Compliance to cGMP standards varied among the facilities. Conformance of premises, utilities and quality elements to the cGMP standard requirement was rated on a scale of 1 to 4 as: unsatisfactory, poor, satisfactory and good. Premises and air handling units were satisfactory at 9 and 11 facilities, respectively. Eight facilities had qualified their air handling units and water purification systems. The overall rating of 7 facilities was poor. Nine facilities had an overall rating of 3 and above and this was construed as satisfactory. Quality elements with a rating of less than 3 will require correction of and preventive actions of the non-conformances observed in order to comply with the acceptable cGMP standard.

Table 4:26: Summary of compliance of the pharmaceutical manufacturing industry with quality impacting parameters.

Quality Parameter	Number of compliant facilities
Manufacturing Premises	9 (56.25 %)
Air Handling Units	11 (68.75 %)
Water for pharmaceutical use	16 (100 %)
Quality Control unit	14 (87.5 %)
Personnel	6 (37.5 %)
Research and Development unit	2 (12.5 %)
Overall compliance	**9 (56.25 %)**

CHAPTER FIVE

5. DISCUSSIONS, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

Data on capacities in the local pharmaceutical industry in many countries is limited (Kaplan and Laing, 2005). This study is the first comprehensive and quantitative research on capacities in the Kenya pharmaceutical manufacturing industry that influence local production and supply of essential medicines. All 24 manufacturers that were engaged in production of medicines for human use during the period of this study were assessed. Results of this study add essential elements of depth to an earlier qualitative profile of the pharmaceutical industry by UNIDO in 2010. The findings comprise capability of Kenya pharmaceutical industry to produce essential medicines, production capacity in the Kenyan pharmaceutical industry and compliance of facilities with cGMP standards that govern pharmaceutical production. These findings present the state of the local pharmaceutical industry and the level of readiness of Kenya to achieve self-sufficiency in essential medicines through local production as envisaged by the Kenya National Pharmaceutical Policy. The research indicates that minority of the essential medicine that are marketed in Kenya are made by the local industry. The production capacity in this industry is underutilized and majority of the facilities comply with the cGMP standard that governs pharmaceutical production.

5.1.1 Capability of the local pharmaceutical industry to produce essential medicines

5.1.1.1 Range of essential medicines manufactured and marketed in Kenya

Range of products manufactured by the local pharmaceutical industry

The pharmaceutical industry manufactured solid, semi-solid and liquid dosage forms, most of which were non-sterile and of various pharmacological categories. Prevalence of the different dosage forms and therapeutic categories varied and depended on pharmaceutical advantage associated with the dosage form, the need for the product and the ease of production. The study established that majority of local products were in tablet form followed by liquid preparations (Table 4.1). This is probably due to the pharmaceutical advantages associated with solid forms such as stability and ease of administration that make tablets the most popular pharmaceutical products. Many pharmaceutical products are therefore designed as tablets (Nyamweya and Tirop, 2012). Liquid dosage forms were produced by all manufacturers unlike solid dosage forms since formulations such as cough syrups which require simple technology were made.

The β-lactam products were produced by a few (6) companies that were able to comply with the cGMP requirement of containment of β-lactam products during the manufacturing process. The β-lactam ring is associated with hypersensitivity reactions, hence production of these products must be under a segregated air handling unit to avoid cross contamination (Bhattacharya, 2010).

A few sterile products were manufactured locally, signifying that Kenya depended heavily on imports for her sterile product's needs. Sterile production process demands compliance to very stringent cGMP standard due to the high risk associated with the use of these products. Viable and non-viable particulate contamination of products is strictly controlled. This requirement necessitates appropriately constructed premises and adequate quality systems to ensure minimum risk to the product. Facility design, air

handling units specifications, water purification systems, other quality impacting utilities, manufacturing zone classification, preventive maintenance practices are stipulated in guidelines for sterile production. Sterile production requires vast technical and financial input with a large market to recuperate the cost of production which is not guaranteed for the local industry. Production of sterile products was therefore considered to be a non-viable venture by most manufacturers. One top-class sterile manufacturing facility which is located in the Export Processing Zone (EPZ) produces pharmaceutical products for export only. Four local manufacturers had obtained market authorization by the PPB to sale sterile products manufactured by overseas firms in order to participate in government and NGO's bids for these products.

Majority (72.3 %) of local products that were registered by the PPB were produced by 8 established companies with more than 15 years manufacturing experience. This could be attributed to their manufacturing goals, technical capability and access to investment capital. The therapeutic classes which were used in the management of diseases that are common in Kenya were manufactured across the industry. Anti-infectives and dermatological products which are used in management of communicable diseases were prevalent. Two established manufacturers, Cosmos Limited and Universal Corporation Ltd. had product registrations for a substantial number of cardiovascular and diabetic products in readiness for reversal of the dominant diseases in Kenya as predicted in the Kenya Health Policy 2012-2020. The two manufacturers had also registered ARV and antimalarial products that are currently donor funded, in readiness for this market since donor priorities are prone to change. Pharmaceutical products that are used in the management of HIV/AIDS, tuberculosis and malaria in Kenya are mostly donor funded

and the prequalification requirement disqualifies participation of most of the local industry (Abbott, 2014). Prequalification is a stringent standardized quality assessment procedure to evaluate the acceptability of pharmaceutical products for purchase by United Nations agencies (WHO, 2011c). Currently, only one company in Kenya, Universal Corporation Ltd. has been accorded WHO prequalification, for the antiretroviral, zidovudine/lamivudine. High risk products such as potent molecules which are administered in low doses and controlled release products were hardly produced due to limited technology.

Range of pharmaceutical products marketed in Kenya

The local industry did not manufacture a significant number of pharmaceutical products on the KEML and this may have contributed to dominance of registered imported pharmaceutical products in Kenya. The local industry had limited R&D capacity and technology that are required to develope products associated with high risk such as those used in management of non-communicable diseases. Products originating from India were majority in Kenya and this dominance has been characteristic of the Kenyan pharmaceutical market in the past (Private Sector Innovation Programme for Health (PSP4H), 2014). India has more than 20,000 registered pharmaceutical manufacturers and intense domestic competition has prompted the government to implement policies that encourage exports. Additionally, cost effective products and increased R&D have impacted positively on exports and global expansion of the Indian pharmaceutical industry (Shilpi *et al.*, 2014). Kenya is Africa's third largest importer of Indian pharmaceutical products after South Africa and Nigeria (Bridges, 2009).

Proportion of locally manufactured products on pharmaceutical lists

The percentage of locally manufactured products on major pharmaceutical lists in Kenya; the PPB list of registered and retained pharmaceutical products, the KEML, and KEMSA, KNH and MEDS pharmaceutical product stock lists were used as indicators of prevalence of local products. The proportion of locally manufactured products on the KEMSA, KNH and MEDS stock lists was 55.6 %, 24.5 % and 21.8 %, respectively. The dominance of imported pharmaceutical products on the stock lists was the outcome of production of common products by the local industry, low production of sterile products and a limited scope of locally manufactured essential medicines. The local industry manufactured 162 (38.4 %) of the products on the KEML, 12 sterile and 150 non-sterile. However, this study revealed that the local industry is capable of producing 84 % of the non-sterile products stocked by KEMSA; implying that the demand for non-sterile products can be met through the local industry.

5.1.1.2 Pharmaceutical equivalents to locally produced essential medicines

Foreign manufacturers had market authorization by PPB to sell identical dosage forms (pharmaceutical equivalents) of essential medicines that were produced in Kenya. The large number of foreign manufacturers contributed to the prevalence of imported pharmaceutical equivalents to locally produced essential medicines. The products were categorized based on the KEML pharmacological classification for ease of interpretation. The overall percentage (32.5 %) of local PEs in Kenya obtained from comprehensive analysis of products in each pharmacological class was comparable to the findings of a survey carried out on the pharmaceutical sector in 2008 and a report on the local pharmaceutical industry in 2014 (Frost and Sullivan, 2008, Watu and

Kungu, 2014). The report showed that the market share of the local pharmaceutical industry based on sales was 28 % and 25 %, respectively. The high percentage of imported pharmaceutical equivalents in Kenya and the limited capacity of the local industry to manufacture a significant number of essential medicines may have contributed to the high market share of imported pharmaceutical products. Pharmaceutical products such as anti-infectives, analgesics and dermatologicals which are used in the management of communicable diseases had a large number of local PEs. This included beta - lactam products which are broad spectrum antibiotics, widely used to treat infectious diseases (Clement, *et al.,* 2014) and are in high demand due to the prevalence of communicable diseases in Kenya.

5.1.1.3 Competitiveness of locally manufactured essential medicines

In 2014, the PPB retained on the market 130 of the 150 non-sterile products that were registered, and these were assessed for price competitiveness with imported pharmaceutical equivalents. Statistical evaluation using t-test at 95% confidence interval for comparison of means established that there was no difference between the mean values of prices of local and imported pharmaceutical equivalents for most products since all products on the market were analysed, including the innovator brands which were highly priced. This is illustrated by clotrimazole cream 1 % w/w; the price of 8 imported PEs ranged from KSh. 18 to 150, while that of 5 local PEs ranged from KSh. 22 to 75. Scatter correlation between imported and local PEs demonstrated that a higher percentage of imported PEs were less priced than local PEs. Due to low availability of medicines in the public sector, patients are often obligated to purchase medicines in the private sector and high medicine prices hinders access to essential medicines. In

economies where procurement is based on the lowest bidder, with a large public sector market and patients without a health insurance cover, the mean price of PEs on the market as an indicator for product competitiveness is superseded by the less priced outlier PEs. The possibility of an imported product being selected in a bid was higher than for the local products as demonstrated by the scatter diagrams. This could imply that despite the capability of the local industry to manufacture significant portion of the listed essential medicines, local products may not be competitive since the tendering process is often based on product price. This concurs with a study on the determinants of growth for the pharmaceutical industry in Kenya, which stated that despite the dominant government presence, the extent and impact of initiatives that offer preferences and reservations to local manufacturers is not known. The study found that there was negligible participation of local manufacturers in government tenders which indicates that government purchases are not directed towards local manufacturers thus placing local manufacturers in direct competition with imported pharmaceuticals (Hedwig, 2012). A report titled 'Why manufacturers exit Kenya' stated that the high cost of manufacturing locally and bureaucracy were among the causative factors for relocation of multinationals. Companies with global supply chains identified markets where they could optimize operation costs and be competitive (Kwama, 2007).

Costing of pharmaceutical products

The price of dosage forms was computed from the sum of all costs accrued during the manufacture and marketing of the product. Local pharmaceutical production was disadvantaged due to importation of most pharmaceutical inputs and the small production capacity. Large companies benefit from their economies of scale in research,

manufacturing, and marketing. The established companies in Kenya imported 94 % of the APIs and 91.7 % of excipients. Start-up companies imported on average, 29 % of the production inputs and purchased the rest from local agents. The overall percentage of packaging material imported was 35 % and 59.4 % for the small and established companies, respectively. Importation of pharmaceutical production materials contributed to high cost of production leading to the non-competitiveness of local products. High price of locally produced pharmaceutical products has been reported in many African countries. Uganda and Tanzania are examples (Center for Health, Human Rights and Development, 2013). A policy brief on the state of pharmaceutical manufacturing industry in Tanzania stated that due to increased imports competition, local firms had moved out of production because they were no longer profitable, and import prices had fallen below local production costs, or even below full materials costs (Wangwe *et al.*, 2014). The negative impact of dominance of imported products on local production has led some countries such as Ghana and Nigeria to prohibit importation of 44 and 18 essential medicines, respectively, (Ariane *et al.*, 2011; UNIDO Project, Nigeria, 2011) in order to promote self-sufficiency in essential medicines through local production. Ethiopian Government incentives to local production include; duty exemption on importation of production materials and machinery, 25 % price preference to local manufacturers on tender awards, advance payment of up to 30 % of the value of orders, tax-free loans of up to 70 % for new investments and 60 % for upgrading of projects, exemption from income tax for companies exporting 50 % of their products and fast tracking of product registration process for local manufacturers to an average of one month **(**HIME and WHO, 2015; Dong and Mirza, 2016**).** The Pharmaceutical Manufacturing Plan for Africa has acknowledged the challenge of

producing pharmaceutical products that comply with international quality standards and ensuring that such production is economically viable and advocates for government support through favorable policies and financial commitment in order to achieve a competitive local industry (AU, 2015).

5.1.1.4 Local market share

In 2014, the annual turnover for 15 pharmaceutical manufacturers, including 6 leading companies (Cosmos Ltd, Lab & Allied, Regal Pharmaceuticals Ltd, Elys Chemical Industries Ltd, Universal Corporation and Dawa Limited) was US$ 109.6 million). The 15 companies were estimated to represent 60 % of the annual sales of the local industry, implying that the market share for local products was US$ 136.5 million which is 19 % of the estimated domestic market of US$ 720 million in 2014. This finding is at variance with the estimated value of 28 % reported by Frost & Sullivan in 2008, but both signify that Kenya relies heavily on imported pharmaceutical products for essential medicines needs. The Kenya's export share of domestic production was found to be 28.3 %, and this differed from the value obtained by Watu in 2014 (15 to 20 %). The export market varied with individual manufacturers, ranging from zero for startup companies to 77 % for a manufacturer located in EPZ. The export market for three leading companies was more than 50 % of the annual sales in 2014. The Eastern Africa region (Tanzania and Uganda) and COMESA were the major market for the pharmaceutical products.

5.1.2 Production capacity of the Kenyan pharmaceutical manufacturing industry

Sixteen out of 24 local manufacturers of human medicines responded to the questionnaire on the Kenyan pharmaceutical industry and this included one

manufacturer of sterile products, one facility that produced rapid diagnostic kits and 14 manufacturers of non-sterile products. Evaluation of production capacity was performed for the non-sterile manufacturers and was based on two shift operations. Six dosage forms namely; tablets, capsules, oral liquids, external preparations, dry powders for reconstitution and oral rehydration salts were manufactured at the facilities. The available production capacity was in billions (B); tablets (29.3B), capsules (2.3B), oral liquids (0.4B bottles), external preparations (0.1B bottles), dry powders for reconstitution (0.1B bottles) and oral rehydration salts (0.1B sachets). The six established manufacturers had upgraded their installed capacities to increase batch size in order to improve the manufacturing efficiency by reducing the number of batches and minimizing on the frequency of change-over time and quality control analyses and also in anticipation for purchase orders from local and regional government tenders and emergency supplies where the available production capacity is usually among the prequalification criteria. The production capacity in the Kenyan pharmaceutical industry was underutilized. The average capacity utilization during the period 2010 to 2014 was; tablets (24.1 %), capsules (12.8 %), oral liquids (25.3 %), external preparations (21.8 %), dry powders for reconstitution (21.3 %) and oral rehydration salts (23.6 %). Production of identical products by the local industry may have contributed to the capacity underutilization since all the companies were not engaged in new product development and were therefore competing for the same products. Non-participation of the Kenyan industry in donor funded international tenders for ARVs and some anti-malarial products due to the prequalification prerequisite impacts negatively on capacity utilization. The annual consumption of artemether/lumefantrine tablets, the first line treatment regimen for malaria in Kenya, which is donor funded was estimated as 17

million doses, at 45:10:20:25 ratio for 24's, 18's, 12's and 6's tablets respectively, which translates to 300 million tablets (Amin *et al.,* 2007). This is about 1 % of the available production capacity for tablets in Kenya (29.4 billion) implying that Kenya has sufficient capacity to manufacture and export this product. Respondents attributed capacity underutilization to the presence of competitive imports in the Kenyan market without sufficient incentives from the government to support local production. Additionally, the high cost of electricity, financial constraints, high interest rates, lack of incentives to motivation of personnel by the employers, inadequate technology to produce newer molecules affected capacity utilization. The Tanzanian pharmaceutical industry is also faced with capacity underutilization which is attributed to prevalence of competitive imports. Shelly's Pharmaceutical Limited, a leading manufacturer utilized, in 2005, only 36 % of capacity in tablets and 30 % in capsules. Likewise, production capacity for Keko Pharmaceutical Industries Limited and Tanzansino United Pharmaceuticals Limited were underutilized. The manufacturers attributed underutilization of capacities mainly to robust import competition (Chaudhuri *et al,* 2010). Similar factors; demand deficit, transport infrastructure, failure in power supply, mechanical/maintenance breakdown, workers industrial strikes were stated as major causes responsible for underutilization of production capacity in India (Ray, 2011**)**. Production capacity in the local pharmaceutical industry is underutilized in many African countries. In Nigeria, capacity utilization in the production of liquid preparations was between 33 and 55 %, while the corresponding value for the tablets was 36 to 50 % (Ogaji *et al.,* 2014). The pharmaceutical industry in Uganda operated at an average capacity utilization of between 30 and 55 % **(**UNIDO, Uganda, 2010). The production capacity utilization in Ghana, South Africa and Zimbabwe was 55 %, 35 %,

and 20 %, respectively (Pharmaceutical Manufacturers Association of Ghana, 2012; Nsingo, 2015; Lemarchand and Schneegans, 2014). Capacity utilization is mostly driven by demand (Ray, 2011**)** which is significantly influenced by government policies and the manufacturers marketing strategies (Ogaji *et al.*, 2014). It is imperative for the Kenyan pharmaceutical industry in partnership with the government to design strategies that will consistently create demand in the midst of competition from imported pharmaceutical equivalents in order to utilize the available production capacity.

5.1.3 Compliance of facilities and quality systems with manufacturing standards

5.1.3.1 Quality elements

The pharmaceutical manufacturing industry is governed by regulations to ensure consistent production of safe, efficacious and quality products. The main regulatory standard for ensuring pharmaceutical quality is the current Good Manufacturing Practices regulation for human pharmaceuticals. The WHO cGMP guidelines which is commonly used, contains 17 quality elements namely; quality assurance, utilities impacting on cGMP, sanitation and hygiene, qualification and validation, complaints, product recalls, contract production and analysis, self-inspection, personnel, training, personal hygiene, premises, equipment, materials, documentation, good practices in production and in quality control (WHO, 2014). The cGMP requires that premises must be located, designed, constructed, adapted, and maintained to suit the operations to be carried out. The compliance with cGMP in regard to premises and quality systems was varied among the manufacturing facilities in the Kenyan pharmaceutical industry. The level of compliance of the manufacturer greatly depended on the market targeted. Firms that were engaged in export business to regional markets such as Uganda and Tanzania

had upgraded their facilities to comply with the requirements of the respective DRAs. These firms had adequate air handling units and water purification systems. Three companies had achieved Pharmaceutical Inspection Cooperation Scheme (PICs) certification, one of these facilities had received WHO prequalification for zidovudine/lamivudine and a second company has submitted an ARV product dossier for evaluation and was in the final stage of the prequalification process in 2015. Prequalification is a comprehensive standardized quality assessment procedure of WHO to evaluate the acceptability of pharmaceutical products for purchase by United Nations agencies. A five year stepwise plan to strengthen and upgrade pharmaceutical manufacturers to WHO cGMP standards has been developed by PPB in collaboration with local stakeholders which implies that by 2020 facilities that will be operational in Kenya are those that will be compliant with the cGMP international standards. This is a grand plan for the local industry and some facilities may be forced out of manufacturing due to the financial requirements of facility upgrading. This happened in India when Schedule M of Drugs and Cosmetics act, 1940, which prescribes the GMP for the pharmaceutical Industry in India was implemented in 2005. Seventy small and medium companies closed down in 2006, and no new manufacturers came up during the three year period ending in 2009 (Joseph, 2016). However, the resilient and visionary manufacturers pursued the upgrading and innovation and now dominate the export market including the highly regulated countries. India has the second highest number of USFDA approved pharmaceutical manufacturers (Shilpi *et al.*, 2014) after the USA.

This study showed that upgrading of a facility resulted in reduced local sales and regional exports but improved sales through international tenders and the overall sales. Upgrading of a facility and quality systems to ensure compliance with cGMP and its

maintenance entails heavy financial investment and also results in higher running costs. Increasing product price is one way of recuperation of these expenses. Products manufactured in an upgraded facility are bound to be uncompetitive against other local and imported pharmaceutical equivalents. A case study on the sales profile of Universal Corporation, a WHO prequalified facility showed a significant decrease in local and regional sales after achievement of the prequalification. However, sales through international tenders increased by more than 5 times within 3 years. In 2014, this manufacturer sold 35 % to local market, 15 % to regional export market and 50 % through international tenders. Sales to KEMSA were significantly reduced. It can therefore be postulated that facility upgrading and cGMP compliance to international standards is principally an avenue to international markets and therefore the local market will continue to be deluged with imported products so long as procurement of pharmaceutical products by the government are price driven. Quality Chemicals Limited (QCL), Uganda, which obtained WHO prequalification in 2010 has remained in business mainly due to the government intervention (Taylor *et al.*, 2009; QCL, 2012). In 2005, the government of Uganda negotiated with Cipla Ltd., India, to partner with QCL in the production of antiretroviral and anti-malarial drugs in order to decrease dependence on foreign suppliers and committed to buy all ARVs and ACTs. In April 2012, the commitment was extended for a further 7 years. The success of QCL is greatly dependent on the protection by the government. The implementation of the cGMP Roadmap for the Kenyan pharmaceutical manufacturing industry implies that Kenyan pharmaceutical manufacturers will be required to comply with international cGMP standards by the year 2020. The preceding scenario, regarding the impact of WHO prequalification should be of interest to the Kenyan pharmaceutical

manufacturers and policy makers as it seems to indicate that facility upgrading to international standards may have an immediate negative effect on self-sufficiency through local production. However, facility upgrading is a worthwhile enterprise since it eventually provides opportunity to compete beyond the domestic market and enables manufacturers to access the lucrative international market and donor funded pharmaceutical procurements.

5.1.3.2 Quality control

Quality control in pharmaceutical manufacturing ensures that the necessary and relevant tests are carried out and that materials are not released for use, nor products released for sale until their quality has been judged to be satisfactory. The quality control departments were adequately equipped to perform analysis of raw materials, intermediate products and finished products. Seven percent of the workforce was deployed in quality control. Quality control was rated as inadequate by UNIDO assessment in 2012 and this was mainly from observations raised on the quality management system which does not require intensive capital investment and corrective actions are currently in progress.

5.1.3.3 Research and development

Research and product development is fundamental to success in pharmaceutical industry, but is an expensive, complex, laborious endeavor and requires technical expertise (Petrova, 2014). The Kenyan pharmaceutical industry had not ventured into innovation, product development, or formulation of products that require high technology. This study showed that R&D department had the least percentage of

workers (1 %) and this department was non-existent in a majority of the companies. Developed countries such as Germany and the USA and developing countries such as India and Brazil have succeeded consistently in pharmaceutical manufacturing mostly due to investment in R&D which is steered by government through significant incentives and research collaboration. These countries spent 10 to 15 % of their revenue on R&D. An analysis of the top 12 drug manufacturers in America showed that the median percentage of revenue dedicated to R&D was 12.4 % (Gray and Matsebula, 2010). In 2009, the pharmaceutical industry in Germany invested 13.7 % of its revenue in R&D. India has the third-largest drug R&D workforce globally, and one company, Aurobindo Pharma Ltd., with over 550 R&D scientists, spent 14 % of its total revenues on R&D in 2014 (Aurobindo Pharma, 2014). The R&D data forms part of the pharmaceutical product registration application dossier as the evidence that the product was appropriately designed and developed to elicit the expected quality attributes. The dossier contains data covering the whole product cycle, starting from product design, research and development, process scale up, production process, quality control, stability, BE, clinical studies and more. To avoid compiling of different registration dossiers for different regions, a common format (CTD) was developed and the East African DRAs, including the PPB of Kenya, have adopted the CTD format of dossier submission, and this was to be fully implemented from 2015 but has been delayed due to the impact on access to essential medicines. In view of the immense financial and technical requirements in R&D enterprises, two manufacturers in Kenya; Cosmos Limited and Universal Corporation signed technology transfer agreements with a multinational company for production of saquinavir in 2006 but the manufacture did not commence due to prequalification requirement since procurement of this product was

donor funded. At present, pharmaceutical products that are used in the management of HIV/AIDS, tuberculosis and malaria in Kenya are donor funded and the prequalification requirement disqualifies participation of most of the local industry.

5.1.3.4 Personnel

Pharmaceutical production is a highly technical operation and requires personnel with specific qualifications and skills to work in the various departments including research scientists, chemists, engineers, pharmacists and microbiologists. The workforce at the 16 respondent manufacturers was 2,798; which is a portion of the workforce in the pharmaceutical manufacturing sector. Among these employees were 2 Ph.D., 15 M.Sc. and 140 B.Sc. holders and 33 pharmacists. The industry did not have sufficient technical personnel to work in specialized areas such as pharmaceutical and validation engineers, R&D scientists, and personnel with sufficient knowledge in cGMP which is reviewed frequently. Most local pharmacists are not interested in industrial pharmacy since they are ill-equipped and in addition, this sector is considered to be non-lucrative. The UNIDO report, 2012 on cGMP self-assessment in Kenya, stated that most pharmacists do not have adequate industrial exposure and thus have limited skills and knowledge required in the industry, since the pharmacy courses offered in the local universities lack the relevant curriculum of industrial pharmacy. The University of Nairobi, recognized the need to build human capacity in the pharmaceutical manufacturing sector and launched a master's degree program in Industrial pharmacy in the year 2012, to equip the industrial pharmacist with technical, specialized requirements in this industry. However, at the time of this study, most graduates of this program had opted for the academia and none was employed in the local industry.

5.1.3.5 Achieving self-sufficiency in essential medicines through local production

The post MDGs agenda; The Sustainable Development Goal 3:8 aims to achieve universal health coverage, including access to safe, effective, quality and affordable essential medicines by 2030. Numerous fundamental factors interplay to determine the degree of access to essential medicines. These factors include; government policies that guarantee access to the needed medicines, assured quality, affordable prices, and an unhindered supply chain (Bate 2008). The pharmaceutical industry should possess capability and capacity to manufacture and be engaged in R&D to ensure availability of the essential medicines. Supportive laboratories that perform BE studies and clinical trials should be easily available and affordable. Based on the preceding factors, the prerequisite for achieving SSEM through local production is that the local industry must have the capability and production capacity to manufacture the products. These products must comply with quality standards and be able to withstand market competition. Good manufacturing practices were satisfactory at 11 facilities while the rest were striving to achieve compliance. However, the local industry produced only 38.4 % of the listed essential medicines in Kenya, with technology and personnel limitation in developing of new products and also lacked the supportive laboratories that perform BE studies to ensure quality of pharmaceutical products. This study showed that the local industry has adequate production capacity since an average capacity utilization in 2014 was 27.4 % (both local and exports). Apart from ORS and dry powders for reconstitution which were projected to have a 100 % capacity utilization by 2030, projection for the other dosage forms were; tablets (45.0 %), capsules (19.5 %), oral liquids (56.9 %) and external preparations (59.8 %) by 2030. The projection for sterile products was not evaluated in this study since only 7.1 % of the sterile products on the KEML were locally manufactured, hence Kenya will

be dependent on imported products for most of her sterile products need. On average, the forecasted year for achieving 100 % capacity utilization for non-sterile products assessed is 2043. Under the current situation, it is not feasible for Kenya to attain self-sufficiency in all the listed essential pharmaceutical products. It is almost impossible for any country to achieve self-sufficiency in a liberalized economy. The local pharmaceutical industry in India, despite its capability, capacity and success, meets approximately 70% of the country's demand for raw materials, drug intermediates, and finished pharmaceutical products (Sateesh, 2015). A more pragmatic approach for Kenya is for the pharmaceutical industry and the government to collaborate and identify medicines which are locally produced in adequate quantity, and restrict importation of their pharmaceutical equivalents for a defined period in which to implement sustainable incentives aimed at strengthening local production.

5.2 Conclusions

From the results of this study and the subsequent discussion, the following conclusions can be made on the pharmaceutical manufacturing industry in Kenya;

i. Majority of pharmaceutical products listed as essential medicines in Kenya are not locally produced. This is illustrated by the proportion of local products on the list of registered products in Kenya, the Kenya essential medicines list and stock lists at the major pharmaceutical procurement agencies and as well as the prevalence of imported pharmaceutical equivalence to local products.

ii. The local pharmaceutical industry manufactures majority of non-sterile products stocked by KEMSA, the major government pharmaceutical procurement agency.

iii. Locally manufactured pharmaceutical products are non-competitive in public sector procurement and other agencies where the lowest bidder is contracted.

iv. The market share for local products was US$ 136.5 million, accounting for 19 % of the estimated domestic market of US$ 720 million in 2014.

v. The available production capacity in the Kenyan pharmaceutical manufacturing industry is underutilized.

vi. Capacity utilization projections indicated that sufficiency in non-sterile products that are locally produced is feasible beyond the year 2043

vii. Compliance with cGMP standards varied among the facilities that were assessed; some having achieved international accreditation and others struggling to comply with national cGMP requirements.

viii. The Kenyan pharmaceutical industry had insufficient technical personnel with specialized skills and was limited in development of new products with less than 3 % of their revenue and 1 % of workers dedicated to R&D activities.

5.3 Recommendations

The recommendations below are aimed at sustaining the Kenyan pharmaceutical industry in order to promote self-sufficiency in essential medicines and support the development of a viable local industry that is competitive, reliable, innovative, productive and strategic as envisaged in Kenya Vision 2030.

i. The pharmaceutical industry should prepare a time-bound blueprint that will ensure improvement of product range and price competitiveness of locally produced essential medicines and engage the government to play its catalytic role of ensuring its implementation.

ii. The government may consider import restriction of products with adequate local production capacity, review the prescribed margin of preference in public procurement for locally manufactured goods from the current 15 % and designate some public tenders to locally manufactured products.

iii. The pharmaceutical industry should consider production cost reduction measures such as pooled procurement of raw materials, reference standards, and cGMP audits of raw material vendors.

iv. The cGMP non-compliance observed at the various facilities should be addressed by the PPB of Kenya.

v. The government should build human capacity to work in local industry, provide significant incentives such as research grants, tax rebate for companies engaged in research.

vi. The local pharmaceutical industry should invest substantially in R&D and pursue collaborations for development of essential medicines

5.4 Further research

Successful pharmaceutical production is research and capital intensive and targets both domestic and global markets. Further research could be carried out to determine:

i. Other factors apart from incentives that may propel growth in the Kenyan pharmaceutical manufacturing sector and production capacity utilization.

ii. The impact of facility upgrading on sales to domestic market and self-sufficiency in medicines in Kenya.

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APPENDICES

Appendix 1: Capacity of the local pharmaceutical industry in Kenya

Introduction

This questionnaire is intended to generate comprehensive data on the capacity of the local pharmaceutical industry to forecast self-sufficiency in essential medicines through Local Production. This is in pursuant of partial fulfillment of degree requirement at Kenyatta University. The information provided in this questionnaire will be handled confidentially, and any reference to it will be coded to conceal identity. Kindly complete the questions to the best of your ability.

I: General information

1. Name of company ……
   Physical address ……
   Postal address ……
   Telephone …….
   Email address……
2. Date of incorporation……
3. State the number of products manufactured in your establishment……
4. Kindly provide the products list……

II: Representative clients

1. List your three main customers……
2. What percentage of your sales is for export market? .....
3. Describe the trend of Local sales in your company for the last 5 years in the table below

Year		**2010**	**2011**	**2012**	**2013**	**2014**
Total sales	**Local**					
	Export					

III: Employees and qualification

Total personnel: ……: … Production personnel…….
Quality Assurance……Research and development……..
Quality Control……Regulatory Affairs…… Other……

Qualification of employees (current)

Unit/Department		Qualification				
		Diploma	BSc	MSc	Ph.D.	Other
Management	General Manager					
	Economist					
	Pharmacist					
	Other					
	Sales					
Quality Control	Pharmacist					
	Chemist					
	Other					
Production	Chemical Engineer					
	Chemist					
	Pharmacist					
	Other					

Appendix 1 (continued)

Qualification of employees cont.						
Research & Development	Pharmacist					
	Chemist					
	Other					
Quality Assurance	Pharmacist					
	Chemist					
	Other					
Maintenance/Engineering	Pharmaceutical Engineer					
	Chemist					
	Mechanical .Engineer					
	Other					

Employees and qualification

1. In which of the listed departments is there staff shortage, and what are the probable reasons for this shortage? …….. .
2. How would you rate job satisfaction for a pharmacist working in the manufacturing industry versus those in other sectors? Kindly choose the number which best describes your opinion and explain;

   1 = manufacturing offers minimum job satisfaction

1	2	3	4	5

   Reason……
3. How would you describe personnel turnover rate at your work place? Kindly choose the number which best describes your opinion and explain; 1= Very low,

1	2	3	4	5

   Reason……

IV: Premises and utilities

1. Briefly describe the ventilation system at your facility, including the parameters that are controlled and monitored ……
2. Briefly describe the water purification system at your facility ……
3. Are the production areas constructed using non shredding materials with coved, easy to clean edges? Describe the type of material that are used in the construction. …….....
4. Is the raw material entry different from finished goods exit? ……....
5. Briefly describe the product development unit at your facility…….....

V: Facility upgrading

1. Many local manufacturers are currently upgrading their facilities. In your opinion, what has triggered this? …….
2. Is your facility manufacturing sterile products? If your answer is no, give the reasons.....
3. List the regulatory authorities of other organizations who have audited and approved your facility for supply of medicines ……..

Appendix 1 (continued)

VI: Production capacity for 1 shift (8hr)

Fill in the table below; Annual installed (IC), Available (AC) and utilized capacity (UC) of products manufactured

1. **TABLETS**

NON BETA LACTAMS	**Machine**	**Installed Capacity**	***Available Capacity**	**Utilized capacity**				
				2010	2011	2012	2013	2014
OPERATION								
GRANULATION	1							
Granulators	2							
DRYING	1							
Driers	2							
MILLING	1							
Millers	2							
BLENDING	1							
Blenders	2							
COMPRESSION	1							
Compression Machines	2							
COATING	1							
Coating machines	2							
BLISTERING	1							
Blistering Machines	2							
STRIPPING	1							
COUNTING/	1							
BULK	2							

AC= (Equipment Availability) x (Equipment Efficiency Performance) x (Equipment Quality Performance)

Availability is the percentage of scheduled time that the equipment is available.

Efficiency is the running speed as a percentage of its designed speed.

Quality represents the good units as a percentage of the Total Units Stated.

BETA LACTAMS

TABLETS	Machine	Installed Capacity	*Available Capacity	**Utilized capacity**				
				2010	2011	2012	2013	2014
OPERATION								
GRANULATION	1							
Granulators	2							
DRYING	1							
Driers	2							
MILLING	1							
Millers	2							
BLENDING	1							
Blenders	2							
COMPRESSION	1							
Compression	2							
Machines	3							
COATING	1							
Coating machines	2							
BLISTERING	1							
Blistering Machines	2							
STRIPPING	1							
COUNTING/	1							
BULK	2							

Appendix 1 (continued)

2. CAPSULES PRODUCTION CAPACITY

NON BETA LACTAM PRODUCTS

OPERATION	Machine	Installed Capacity	*Available Capacity	**Utilized capacity**				
				2010	2011	2012	2013	2014
BLENDING	1							
	2							
FILLING	1							
	2							
BLISTERING Blistering Machines	1							
	2							
STRIPPING	1							
	2							
COUNTING / BULK PACKING	1							
	2							

BETA LACTAMS

OPERATION	Machine	Installed Capacity	*Available Capacity	**Utilized capacity**				
				2010	2011	2012	2013	2014
BLENDING	1							
	2							
CAPSULE FILLING	1							
	2							
BLISTERING Blistering Machines	1							
	2							
STRIPPING	1							
	2							
COUNTING/ BULK PACKING	1							
	2							

3. LIQUIDS PRODUCTION CAPACITY

LIQUIDS	Installed capacity	*available capacity	**Utilized capacity**				
			2010	2011	2012	2013	2014
Manufacturing Tanks	1						
	2						
Filling Lines i. Automated	1						
	2						
ii. Semi Automated	1						
	2						
Labelling/ Packing i. Automatic	1						
	2						
ii. Semi-Automatic	1						
	2						

Appendix 1 (continued)

4. SEMI - SOLIDS PRODUCTION CAPACITY

TUBE FILLING				**Utilized capacity**				
	Machine	Installed Capacity	Available capacity	2010	2011	2012	2013	2014
Mixing Tanks	1							
FILLING & SEALING i. Automated	1							
	2							
	3							
ii. Semi Automated	1							
	2							
CARTONING	1							
	2							

5. DRY SYRUP

OPERATION	Machine	Installed Capacity	Available capacity	**Utilized capacity**				
				2010	2011	2012	2013	2014
BLENDING	1							
FILLING Automatic	1							
	2							

6. SPECIFIC PRODUCT CAPACITIES

Anti –retroviral products							
	Product name	Installed capacity	**Utilized capacity**				
			2010	2011	2012	2013	2014
1							
2							
3							
4							
5							
Antimalarial products							
1							
2							
3							
4							
5							
Anti-tuberculosis products							
1							
2							
3							
4							

VII. Capacity improvement

1. Is the current capacity utilization satisfactory? Yes/No. Explain.
   ……
2. What is your projected capacity utilization in 2015?.....
   What are the factors that hinder capacity improvement, and how can they be alleviated? You may add extra sheets. ……..
3. When do you project that Kenya will achieve self-sufficiency in pharmaceutical products through local production? …….....

Appendix 1 (continued)

VIII. Costing of pharmaceutical finished products

1. The table below contains the ingredients used to determine the price of a finished pharmaceutical product. On a scale of 1-100% indicate the percentage of each ingredient to the total price of the finished product.

	Particulars/ Ingredients	Tablets		Semi Solids 15g /20g	Liquids Syr/Susp 100ml/ 60ml	Antimal arial Products (**ACT**) oral	**ARV** Products
		Bulk Pack (1000's, 500's)	Unit Pack (Blister/ Strip) (10's)				
1.1	Normal Batch Size						
1.2	Raw materials cost						
	Packaging materials cost						
	Insurance + duty + Transportation cost						
	Direct and Indirect labor cost						
	Utilities; Repairs, Qualifications, and maintenance cost						
1.3	Quality Control, R&D cost						
1.4	Marketing; advertisement; free samples etc cost						
1.5	Other costs						
1.6	% Mark up						
	Total cost	100 %	100 %	100 %	100 %	100 %	100 %

2.0 In your opinion, what percentage of the raw materials and packaging materials used in pharmaceutical production as listed below is sourced locally?

Item	Active Pharmaceutical Ingredients	Excipients	Pack aging Materials				
			Glass bottles	Plastic bottles	Unit boxes/label	Outer cartons	Blisters/ Strips
Percentage							

3.0 What compliance standards do the packaging material suppliers adhere to?

	Glass bottles	Plastic bottles	Boxes/labels, Cartons	Blisters/strips
Standard; for example, ISO, Company Standard etc.				

Appendix 2: List of licensed pharmaceutical manufacturers in Kenya in 2014

Name of manufacturer	Dosage form	Human/Veterinary/ Other	Location (County)
Aesthetics Ltd.	Non sterile	Veterinary	Nairobi
Autosterile EA. Ltd.	Sterile	Human	Nairobi
Benmed Ltd.	Non sterile	Human	Kiambu
Beta Healthcare International Ltd.	Non sterile	Human	Nairobi
Biodeal Laboratories Ltd.	Non sterile	Human/ Veterinary	Nairobi
Comet Healthcare Ltd.	Non sterile	Human	Nairobi
Concept Africa Ltd	Non sterile	Human	Nairobi
Cooper (K) Brand Ltd.	Non sterile	Veterinary	Nairobi
Cosmos Limited	Non sterile	Human/ Veterinary	Nairobi
Dawa Limited	Non sterile	Human/ Veterinary	Nairobi
Elys Chemical Industries Ltd.	Non sterile	Human	Nairobi
GlaxoSmithKline Ltd (GsK)	Non sterile	Human	Nairobi
Impact Ltd.	Non sterile	Veterinary	Nairobi
Infusion Medicare (K) Ltd.	Sterile	Human	Nairobi
Ivee Aqua EPZ Ltd.	Sterile	Human	Machakos
Kenya Medical Research Institute (KEMRI)	Non sterile	Diagnostic kits	Nairobi
Laboratory and Allied Ltd.	Non sterile	Human	Nairobi
Mac's Pharmaceuticals	Non sterile	Human/ Veterinary	Nairobi
Medivet Products Ltd.	Non sterile	Human	Kiambu
Nerix Pharma Ltd.	Non sterile	Veterinary	Nairobi
Norbrook Kenya Ltd.	Non sterile	Veterinary	Kiambu
Oss-Chemie (K)Ltd.	Non sterile	Human	Nairobi
Pharmaceutical Manufacturing Co. (K) Ltd.	Non sterile	Human	Nairobi
PZ Cussons East Africa Ltd.	Non sterile	Human	Nairobi
Regal Pharmaceuticals Ltd.	Non sterile	Human	Nairobi
Skylight Chemicals Limited	Non sterile	Human/ Veterinary	Nairobi
Sphinx Pharmaceuticals Ltd.	Non sterile	Human	Nairobi
Stedman Pharm. Manufacturing Ltd.	Non sterile	Human	Nairobi
Ultravet (K) Ltd.	Non sterile	Veterinary	Nairobi
Universal Corporation Ltd.	Non sterile	Human/ Veterinary	Kiambu

Appendix 3: Country of origin of imported products retained in Kenya in 2014

COUNTRY	No. of Products retained	%
Argentina	17	0.29
Australia	21	0.36
Austria	34	0.58
Bahamas	1	0.02
Bangladesh	270	4.61
Belgium	81	1.38
Brazil	4	0.07
Bulgaria	1	0.02
Canada	13	0.22
China	175	2.99
Cyprus	75	1.28
Denmark	24	0.41
Egypt	71	1.21
France	213	3.63
Germany	203	3.46
Greece	24	0.41
Hungary	19	0.32
Iceland	2	0.03
India	3303	56.35
Indonesia	14	0.24
Iran	1	0.02
Iraq	1	0.02
Ireland	27	0.46
Israel	4	0.07
Italy	99	1.69
Japan	6	0.10
Jordan	12	0.20
Kyrgyzstan	1	0.02
Malaysia	29	0.49
Mexico	5	0.09
Morocco	4	0.07
Netherlands	42	0.72
New Zealand	4	0.07
Norway	1	0.02
Pakistan	258	4.40
Poland	9	0.15
Portugal	1	0.02
Saint Helena	1	0.02
Saudi Arabia	3	0.05
Singapore	3	0.05
South Africa	156	2.66
South Korea	20	0.34
Spain	68	1.16
Sri Lanka	1	0.02
Sweden	51	0.87
Switzerland	181	3.09
Tanzania	9	0.15
Thailand	20	0.34
Turkey	16	0.27
Uganda	11	0.19
United Arab Emirates	44	0.75
United Kingdom	163	2.78
United States of America	45	0.77
Uzbekistan	1	0.02
Total Imports Retained	**5862**	
Total Local Retained	**1604**	
Total Retained	**7466**	

Appendix 4: Locally manufactured essential medicines in 2014

Tablets

Acyclovir 200 mg	Haloperidol 5 mg
Albendazole 400 mg	Hydralazine 25 mg
Allopurinol 100 mg	Hydrochlorthiazide 25 mg
Allopurinol 300 mg	Hyoscine butylbromide10 mg
Aluminium hydroxide, magnesium trisilicate 120/250 mg	Ibuprofen 200 mg
Amitriptylline 10 mg	Isoniazid 100 mg
Amitriptylline 25 mg	Isoniazid 300 mg
Amlodipine 5 mg	Isoniazid 50 mg
Amoxycillin+clavulanic 625 mg	Lamivudine 150 mg; Zidovudine 300 mg; Nevirapine 200 mg
Artemether 20 mg; lumefantrine 120 mg	Lamivudine 150 mg
Aspirin 300 mg	Lamivudine 150 mg, zidovudine 300 mg
Aspirin 75 mg	Levamisole hydrochloride 40 mg
Atenolol 50mg	Lumefantrine 120 mg; artemether 20 mg
Azithromycin 250 mg	Magnesium trisilicate 250 mg, aluminium hydroxide gel 120 mg
Azithromycin 500 mg	Metformin hydrochloride 500 mg
Benzhexol hydrochloride 5 mg	Methyldopa 250 mg
Bisacodyl 5 mg	Metoclopramide 10 mg
Bromocriptine 2.5 mg	Metronidazole 200 mg
Calcium carbonate 400 mg	Metronidazole 400 mg
Carbamazepine 100 mg	Nevirapine 200 mg
Carbamazepine 200 mg	Nicotinamide (Vit B_3) 50 mg
Cefuroxime axetil 250 mg	Niclosamide 500 mg
Chlorpheniramine maleate 4 mg	Nitrofurantoin 100 mg
Chlorpromazine hydrochloride 100 mg	Nitrofurazone 25 mg
Ciprofloxacin hydrochloride 250 mg	Ofloxacin 200 mg
Clarithromycin 500 mg	Ofloxacin 400 mg
Clotrimazole 200 mg	Paracetamol 500 mg
Codeine phosphate 30 mg	Phenobarbitone 30 mg
Dapsone 100 mg	Praziquantel 600 mg
Dexamethasone 2 mg	Prednisolone 5 mg
Diazepam 5 mg tablets	Propranolol 40 mg
Diclofenac sodium 100 mg	Pyrazinamide 500 mg
Diclofenac sodium 25 mg	Pyridoxine hydrochloride 50 mg
Digoxin 250 µg	Pyrimethamine 25 mg
Enalapril maleate 5 mg	Quinine 300 mg
Erythromycin stearate 250 mg	Ranitidine hydrochloride 150 mg
Ethambutol 400 mg, isoniazid 150 mg	Rifampicin 100 mg
Ethambutol 400 mg.	Rifampicin 150 mg, isoniazid 75 mg
Ferrous sulphate 200 mg	Rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg
Folic Acid 5 mg	Rifampicin 300 mg, Isoniazid 150 mg
Frusemide 40 mg	Rifampicin 150 mg, isoniazid 75 mg pyrazinamide 400 mg ethambutol 275 mg
Glibenclamide 5 mg	Salbutamol sulphate 4 mg
Griseofulvin 125 mg	Spironolactone 25 mg

Appendix 4 (Continued)

Stavudine 300 mg, lamivudine 150 mg, nevirapine 200 mg	Tinidazole 500 mg
Stavudine 300 mg, lamivudine 300 mg	Vitamin B_6 100 mg
Sulphadiazine 500 mg	Warfarin sodium 5 mg
Sulphadoxine 500 mg, pyrimethamine 25 mg	Zidovudine 300 mg
Sulphamethoxazole/ trimethoprim 400/80 mg	Zinc sulphate 20 mg
Capsules	
Amoxycillin 250 mg	Nifedipine 10 mg
Chloramphenicol 250 mg	Omeprazole 20 mg
Didanosine 125 mg	Phenytoin sodium 100 mg
Doxycycline hydrochloride 100 mg	Rifampicin 300 mg
Efavirenz 200 mg	Rifampicin 150 mg
Flucloxacillin 250 mg	Stavudine 30 mg
Fluconazole 200 mg	Tetracycline hydrochloride 250 mg
Fluconazole 50 mg	Vitamin A 200,000 I.U
Fluoxetine hydrochloride 20 mg	Vitamin A 50,000 IU
Loperamide hydrochloride 2 mg	Zidovudine 100 mg
Oral Liquids	
Amoxicillin 125 mg/5 ml	Lamivudine 50 mg/ 5 ml
Amoxicillin + cavulanic 250/62.5 mg /5 ml	Metronidazole 200 mg/5 ml
Azithromycin 200 mg/ 5 ml	Nystatin 100 000 I.U
Chloramphenicol 125 mg/5 ml	Oral rehydration salts
Chlorpheniramine maleate 2 mg/5 ml	Paracetamol 120 mg/5 ml
Clarithromycin 125 mg/5 ml	Promethazine hydrochloride 5 mg/5 ml
Erythromycin ethyl succinate 125mg/5 ml	Salbutamol 2 mg/5 ml
Ferrous fumarate 140 mg/5 ml	Sulphamethoxazole 200 mg, trimethoprim 40 mg/5ml
Flucloxacillin sodium 125 mg/5 ml	zidovudine 50 mg /5 ml
Ibuprofen 100 mg/5 ml	
External Preparations	
Acetic acid 2% w/v in alcohol (ear drops)	Hydrocortisone acetate 1% w/w
Benzyl benzoate 25% w/v	Povidone Iodine 1% w/w
Betamethasone 0.1% w/w	Salicylic acid 5% w/w
Ciprofloxacin 0.3% w/v (ear drops)	Silver sulphadiazine 1% w/w
Calamine 15% w/v	Sodium hypochlorite 4-6% w/w
Chlorhexidine gluconate 5% w/v	Tetracycline hydrochloride 1% w/w
Ethanol oral solution 40% w/v	zinc Oxide 5% w/w
Glutaraldehyde 2% w/v	
Sterile preparations	
Anhydrous glucose 50% w/v	Mannitol 20 % w/v
Ephedrine hydrochloride 0.5% w/v	Metronidazole 0.5% w/v
Gentamicin sulphate 0.3% w/v	Pilocarpine nitrate 2% w/v
Glucose injection 10% w/v	Prednisolone acetate 1% w/v
Glucose injection 10% w/v	Timolol maleate 0.25% w/v
Glucose injection 10% w/v	Timolol maleate 0.5% w/v

Appendix 5: Therapeutic classification of pharmaceutical equivalents in Kenya

Appendix 5.1: Analgesics pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Aspirin tablets 300 mg	6	7 (53.8%)	1	7 (87.5%)	17.0	100.0
Diclofenac tablets 100 mg	23	4 (14.8%)	16	4(20.0%)	70.0	100.0
Diclofenac tablets 25 mg	26	3 (10.3%)	1	0(0%)	4.0	0
Diclofenac tablets 50 mg	51	6 (10.5%)	40	4 (9.1%)	78.0	100.0
Diclofenac tablets 75 mg	6	1 (14.3%)	4	1 (20.0%)	67.0	100.0
Ibuprofen syrup 100 mg/5ml	9	14 (60.9%)	4	6 (60.0%)	44.0	43.0
Ibuprofen tablets 200 mg	35	8 (18.6%)	13	8 (38.1%)	37.0	100.0
Ibuprofen tablets 400 mg	34	6 (15.0%)	19	6 (24.0%)	56.0	100.0
Indomethacin capsules 25 mg	34	8 (19.0%)	4	4 (50.0%)	12.0	50.0
Mefenamic capsules 250 mg	20	5 (20.0%)	3	3 (50.0%)	15.0	60.0
Mefenamic tablets 500 mg	9	1 (10.0%)	4	1 (25.0%)	44.0	100.0
Paracetamol tablets 500 mg	38	16 (29.6%)	27	16 (37.2%)	71.0	100.0
Paracetamol syrup 120 mg/5 ml	9	15 (62.5%)	4	15 (79.0%)	44.0	100.0
Overall (%)		**26.1 %**		**38.5 %**		

Appendix 5.2: Antimalarial pharmaceutical equivalents

	Registered products		Retained products		% Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Artemether injection 300 mg/ ampoule	20	0 (0%)	14	0 (0%)	70.0	0
Artemether/lumefantrine tablets 20/120	15	5(25.0%)	15	2(11.8%)	100.0	40.0
Dihydroartemisinin + piperaquine 40/320	8	0(0%)	6	0(0%)	75.0	0
Doxycycline tablets 100 mg	17	8(32.0%)	5	8(61.5%)	29.4	100.0
Quinine injection 300 mg/ ml	14	0 (0%)	8	0(0%)	57.1	0
Quinine tablets 300 mg	14	8(36.4%)	4	4(50.0%)	28.6	36.4
Sulfadoxine /pyrimethamine 500/25	20	8(28.6%)	6	8(57.1%)	30.0	100
Overall (%)		**17.4%**		**25.8%**		

Appendix 5.3: Antiretroviral pharmaceutical equivalents

	Registered products		Retained products		% Retained Registered	
Product (Tablets)	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Abacavir 300 mg	3	0 (0%)	2	0 (0%)	67.0	0
Didanosine 50 mg	9	0 (0%)	3	0(0%)	33.0	0
Efavirenz 200 mg	16	1 (5.9%)	15	0 (0%)	94.0	0
Lamivudine 150 mg	9	4 (30.8%)	7	1 (12.5%)	78.0	25.0
Lopinavir/Ritonavir 200/50 mg	5	0 (0%)	4	0 (0%)	80.0	0
Nevirapine 200 mg	10	1(9.1%)	10	0 (0%)	100.0	0
Stavudine 30 mg	16	7 (30.4%)	1	0 (0%)	6.0	0
Stavudine/Lamivudine 300/300 mg	14	3 (17.7%)	3	0 (0%)	21.0	0
Stavudine/Lamivudine/ Nevirapine 300 /150/ 200 mg	17	2 (10.5%)	4	0 (0%)	24.0	0
Tenofovir/Emtricitabine/ Efavirenz 300/200 /600 mg	2	1 (33.3%)	2	1 (33.3%)	100.0	100.0
Zidovudine 300 mg	11	6 (35.3%)	8	1 (11.1%)	73.0	17.0
Zidovudine/Lamivudine 300 /150 mg	10	3 (23.1%)	10	1 (9.1%)	100.0	33.0
Zidovudine/Lamivudine/Nevirapine 300/150/200 mg	7	1 (12.5%)	7	0 (0%)	100.0	0.
Overall (%)		**16.0%**		**5.0%**		

Appendix 5.4: Antituberculosis products pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Ethambutol tablets 400 mg	2	3(60.0%)	1	0 (0%)	50.0	0
Ethambutol /isoniazid tablets	0	2(100.0%)	0	2(100.0%)	0	100.0
Isoniazid tablets 100 mg	1	4(80.0%)	1	2 (66.7 %)	100.0	60.0
Isoniazid tablets 50 mg	1	0(0%)	1	0 (0%)	100.0	0
Isoniazid tablets 300 mg	0	1(100%)	0	1(100.0%)	0	100
Pyrazinamide tablets 500 mg	3	2 (40.0%)	1	1 (50.0%)	33.0	50.0
Rifampicin capsules 150 mg	12	4(25.0%)	0	3(100.0%)	0	100.0
Rifampicin capsules 300 mg	10	3 (23.1%)	0	3(100.0%)	0	100.0
Rifampicin/ Isoniazid 150/75 mg	4	2 (33.3%)	4	1 (20.0%	100.0	25.0
Rifampicin/ Isoniazid 300/150 mg	2	1 (33.3%)	2	1 (33.3%)	0	100.0
Rifampicin/Isoniazid/Pyrazinamide 150/75/400 mg	4	2(33.3 %)	4	1 (20.0%)	100.0	50.0
Rifampicin/Isoniazid/Pyrazinamide Ethambutol 150/75/400/275 mg	0	1(100.0%)	0	1(100%)	100.0	100.0
Overall (%)		**52.3%**		**57.5%**		

Appendix 5. 5: Beta lactam pharmaceutical equivalents

	Registered products		Retained products		% Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Amoxycillin syrup 125 mg/5 ml	60	11 (15.5%)	13	5 (27.8%)	22.0	45.0
Amoxycillin capsules 500 mg	31	11 (26.2%)	16	6 (27.3%)	52.0	55.0
Amoxycillin capsules 250 mg	49	11 (18.3%)	39	6 (13.3%)	80.0	55.0
Ampicillin syrup 125 mg/5 ml	32	9 (21.9%)	2	6 (75.0%)	6.0	67.0
Ampicillin capsules 250 mg	48	10 (17.2%)	9	6 (40.0%)	19.0	60.0
Ampicillin capsules 500 mg	31	7 (18.4%)	5	4 (44.4%)	16.0	57.0
Cefuroxime capsules 250 mg	18	1 (5.3%)	14	1 (6.7%)	78.0	100.0
Flucloxacillin capsules 250 mg	3	3 (50.0%)	2	3 (60.0%)	67.0	100.0
Flucloxacillin syrup 125 mg/5ml	3	2 (40.0%)	3	2 (40.0%)	100.0	100.0
Overall (%)		**23.7%**		**37.2 %**		

Appendix 5.6: Cardiovascular pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Amlodipine tablets 5 mg	21	5 (19.2%)	21	5 (19.2%)	100.0	100.0
Atenolol tablets 50 mg	52	4 (7.1%)	28	4 (12.5%)	53.8	100.0
Frusemide tablets 40 mg	12	6(33.3%)	6	5(45.5%)	50.0	83.0
Hydrochlorothiazide tabs 25 mg	1	1(50.0%)	0	1(100%)	0	100.0
Methyldopa tablets 250 mg	25	6 (19.4%)	7	5 (41.7%)	28.0	83.3
Nifedipine tablets 10 mg	35	4 (10.3%)	22	1 (4.4%)	62.9	25.0
Overall (%)		**23.2%**		**37.2%**		

Appendix 5.7: Dermatological pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Betamethasone cream 0.1% w/w	7	10(58.8%)	4	10(71.4%)	57.0	100.0
Betamethasone ointment. 0.1% w/w	3	8 (72.7%)	3	8(72.7%)	100.0	100.0
Clotrimazole cream 1% w/w	27	9 (25.0%)	15	9(37.5%)	56.0	100.0
Hydrocortisone cream 1% w/w	3	7 (70.0%)	0	7(100.0%)	0	100.0
Hydrocortisone ointment1% w/w	5	10 (66.6%)	2	8(80.0%0	40.0	80.0
Miconazole cream 2% w/w	8	7 (46.6%)	8	7(46.7%)	100.0	100.0
Silver sulphadiazine cream1% w/w	1	4 (80.0%)	1	4(80.0%)	100.0	100.0
Tetracycline ointment 3% w/w	2	2 (50.0%)	2	2(50.0%)	100.0	100.0
Overall (%)		**58.7%**		**67.3%**		

Appendix 5.8: Anti-allergies/ Anti-asthmatics pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Chlorpheniramine 2 mg/5 ml	5	10(66.7%)	2	10(83.3%)	40.0	100.0
Chlorpheniramine tablets 4 mg	12	8(40.0%)	3	5(62.5%)	25.0	63.0
Loratidine Syrup 5 mg/5 ml	2	1(33.3%)	1	1(50.0%)	50.0	100.0
Loratidine tablets 10 mg	7	2(22.2%)	6	2(25.0%)	86.0	100.0
Prednisolone tablets 5 mg	12	6(33.3%)	2	6(75.0%)	17.0	100.0
Promethazine tablets 25 mg	5	6(54.6%)	0	6(100.0%)	0	100.0
Salbutamol 2 mg/5 ml	7	13(60.5%)	7	11(61.1%)	100.0	85.0
Salbutamol tablets 2 mg	9	4(30.8%)	0	0(0%)	0	0
Salbutamol tablets 4 mg	16	5(23.8%)	3	5(62.5	19.0	100.0
Overall (%)		**41.1%**		**57.7%**		

Appendix 5.9: Anti-convulsants/Anti-epileptics pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Carbamazepine tablets 100 mg	25	5(16.7%)	1	5(83.3%)	4.0	100.0
Phenobarbitone tablets 30 mg	0	6(100.0%)	0	4(100%)	0	67.0
Phenytoin tablets 100 mg	10	2(16.7%)	4	2(33.3%)	40.0	100.0
Valproic acid tablets 500 mg	2	0(0%)	0	0(0%)	0	0
Overall (%)		**33.3 %**		**54.2 %**		

Appendix 5.10: Anti-diabetic pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Chlorpropamide tablets 250 mg	4	2(33.3%)	0	1(100.0%)	0	50.0
Glibenclamide tablets 5 mg	9	3(25.0%)	9	2(18.2%)	100.0	67.0
Metformin 500 tablets mg	28	5(15.2%)	24	4(14.3%)	86.0	80.0
Overall (%)		**24.5%**		**44.2%**		

Appendix 5.11: Antifungal products pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Clotrimazole tablets 200 mg	11	3(21.4%)	10	3(23.1%)	91.0	100.0
Fluconazole capsules 50 mg	14	2(12.5%)	10	1(9.1%)	71.0	50.0
Fluconazole capsules 200 mg	17	3(15.0%)	11	3(21.4%)	65.0	100.0
Griseofulvin tablets 125 mg	6	3(33.3%)	3	3(50.0%)	50.0	100.0
Griseofulvin tablets 250 mg	2	4(66.7%)	0	4(100.0%)	0	100.0
Griseofulvin tablets 500 mg	8	6(42.9%)	3	4(57.1%)	38.0	67.0
Ketoconazole tablets 200 mg	14	7(33.3%)	6	7(53.9%)	43.0	100.0
Average (%)		**32.2%**		**44.9%**		

Appendix 5.12: Antihelmintics pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Albendazole liquids	33	27(45%)	12	27(69.2%)	36.0	100.0
Albendazole tablets	29	17(40.0%)	24	14(36.9%)	83.0	82.0
Mebendazole tablets 100 mg	20	6(23.1%)	4	6(60.0%)	20.0	100.0
Mebendazole 100 mg/5 ml	9	9(50.0%)	1	8(88.9%)	11.0	89.0
Mebendazole tablets 1000 mg	2	0(0%)	0	0(0%)	0	0
Mebendazole tablets 500 mg	1	2(66.7%)	1	1(50.0%)	100.0	50.0
Overall (%)		**37.5%**		**50.8%**		

Appendix 5.13: Diuretics pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Frusemide tablets 40 mg	12	6 (33.3%)	6	5(45.5%)	50%	83.3%
Spironolactone tablets 25 mg	9	1(10.0%)	9	0(0%)	100%	0%
Amiloride tablets 5 mg	1	0(0)	1	0(0%)	100%	0%
Hydrochlorothiazide tablets 25 mg	1	1(50.0%)	0	1(100.0%)	0%	100%
Overall (%)		**23.3%**		**36.4%**		

Appendix 5.14: Gastro-intestinal/antacids pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Cimetidine tablets 200 mg	24	9(27.3%)	3	3(50.0%)	13.0	33.0
Omeprazole tablets 20 mg	42	4(8.7%)	42	4(8.7%)	100.0	100.0
Ranitidine tablets 150 mg	52	6(10.3%	0	3(100.0%)	0	50.0
Overall (%)		**15.4%**		**52.9%**		

Appendix 5.15: Other anti-bacterial pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Azithromycin tablets 500 mg	26	1(3.7%)	26	1(3.7%)	100.0	100.0
Azithromycin syrup 200 mg/5 ml	10	1(9.1%)	10	1(9.1%)	100.0	100.0
Azithromycin capsules 250 mg	7	1(12.5%)	7	0(0%)	100.0	0
Chloramphenicol syrup125 mg/5 ml	0	5(100%)	0	5(100%)	0	100.0
Chloramphenicol capsules 250 mg	0	3(100%)	0	3(100%)	0	100.0
Ciprofloxacin tablets 250 mg	3	3(50%)	3	3(50%)	100.0	100.0
Ciprofloxacin tablets 500 mg	18	7(25%)	10	6 (37.5%)	90.1	85.7
Clarithromycin tablets 500 mg	11	0 (0%)	11	1(9.1%)	100.0	0
Clarithromycin syrup125 mg/5 ml	2	0 (0%)	2	1(33.3%)	100.0	0
Dapsone tablets 100 mg	1	2(66.7%)	0	1(100%)	0	50.0
Doxycycline capsules100 mg	17	9(34.6%)	4	9(69.3%)	24.0	100.0
Erythromycin syrup 125 mg/5 ml	0	2 (100%)	0	2(100%)	0	100.0
Erythromycin tablets 250 mg	5	3 (37.5%)	5	2(28.6%)	100.0	67.0
Metronidazole tablets 200 mg	31	9(22.5%)	5	9(64.3%)	16.0	100.0
Metronidazole tablets 400 mg	6	8(57.1%)	1	7(87.5%)	17.0	88.0
Nitrofurantoin tablets100 mg	1	4(80%)	0	2(100%)	0	50.0
Ofloxacin tablets 200 mg	6	3(33.3%)	6	3(33.3%)	100.0	100.0
Tetracycline capsules250 mg	30	12(28.6%)	1	3(75%)	30.0	25.0
Overall (%)		**42.3%**		**55.6%**		

Appendix 5.16: Other CNS acting drugs pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Amitriptyline tablets 25 mg	0	2(100.0%)	0	2(100.0%)	0	100.0
Amitriptyline tablets 10 mg	0	2(100.0%)	0	0(0%)	0	0
Benzhexol tablets 5 mg	0	2(100.0%)	0	2(100.0%)	0	100.0
Chlorpromazine tablets 100 mg	1	3(75.0%)	1	3(75.0%)	100.0	100.0
Fluoxetine tablets 20 mg	3	1(25.0%)	3	1(25.0%)	100.0	100.0
Haloperidol tablets 5mg	5	2(28.6%)	3	0(0%)	60.0	0
Loperamide tablets 2 mg	7	1(12.5%)	4	0(0%)	57.0	0
Metoclopramide tablets 10 mg	1	2(66.7%)	1	2(66.7%)	100.0	100.0
Overall (%)		**63.5%**		**45.8%**		

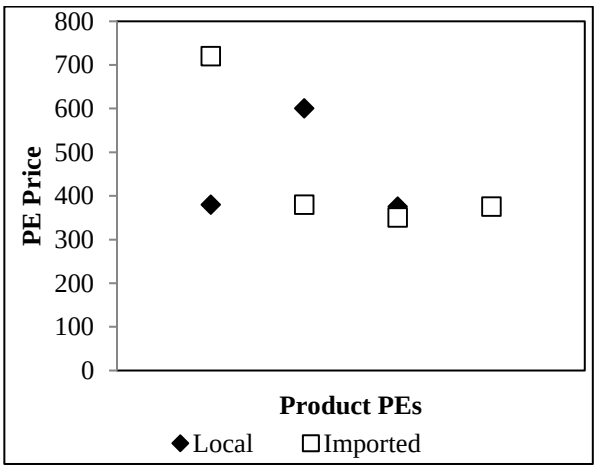
Appendix 5.17: Other drugs-pharmaceutical equivalents

	Registered products		Retained products		%Retained Registered	
Product	**Imported**	**Local**	**Imported**	**Local**	**Imported**	**Local**
Allopurinol tablets 300 mg	4	1(20.0%)	2	0(0 %)	50.0	0
Allopurinol tablets 100 mg	2	0(0%)	2	0(0%)	100.0	0
Bisacodyl tablets 5 mg	5	1(16.7%)	4	1(20.0%)	80.0	100.0
Bromocriptine tablets 2.5 mg	1	0(0%)	0	0(0%)	0	0
Folic acid tablets 5 mg	4	3(42.9%)	1	3(75.0%)	25.0	100.0
Hyoscine tablets 10 mg	5	6(54.6%)	4	6(60.0%)	80.0	100.0
Overall (%)		**22.4%**		**25.8%**		

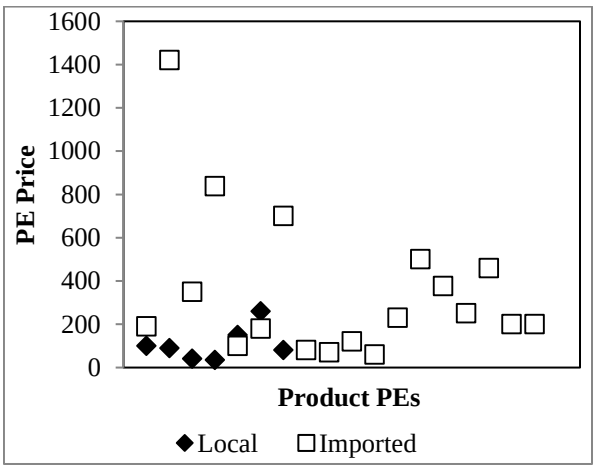
Appendix 6: Foreign manufacturers assessed for price competitiveness

Abacus Pharma Ltd., Uganda	Flamingo Impex Pvt, India	Pharco Pharma, Egypt
Acme Labs, Bangladesh	Fourrts Pvt, India	Pharmaco, New Zealand
Adcork Ungram, SA	General Pharma Ltd., India	Pharma drug, Germany
Advanced Pharma, USA	Getz Pharma Ltd., Pakistan	Pharmaniaga, Malaysia
Aegis Ltd., Cyprus	Global Merchants, India	Pharmathen, Greece
Agio Pharma, India	Gracure, India	Plethico Pharma, India
Aglowmed Ltd., India	Gufic, India	Prism Life Sciences, India
Aim International Pharm, India	Halewood, UK	Questa Care Inc., India
Ajanta Pharma Ltd., India	Harleys Ltd., Local Distributor	Ranbaxy Labs, India
Alembic, India	Hikma Pharma, UK	Ray Pharma, Pakistan
Almirall Prodes, SA	Hilton Pharma, Pakistan	Recon Ltd., India
Ampus Life Sciences, India	Household, India	Remedica Ltd., Cyprus
Amriya Pharma, Egypt	Hovid, Malaysia	Riva Pharma, Egypt
Aristo Pharma, Bangladesh	Ind Swift, India	Rivopharma, UK
Atco Labs, Pakistan	Indoco Remedies, India	Rup Pharmacy Ltd. (K) Distributor
Aurobindo Pharma, India	Intas Exports, India	Sai Pharma, India
Balpharma Ltd., India	Ipca, India	Salama Pharma, Tanzania
BDH, India	Jayson Pharma, Bangladesh	Sarabhai, India
Beijing Holley Cotec, China	Julphar Gulf Pharma, United Amirates	Sarabhai, India
Bells, Sons Co., UK	Kopran, India	Shanghai Pharma, China
Benmed Pharmaceuticals Ltd.	Korlyns, UK	Sharon Bio, India
Bentley & Remington, India	Leben Labs, India	Sol Pharm, India
Beximco Pharma, Bangladesh	Li Taka Pharma, India	Square Pharmaceuticals, Bangladesh
Bio-Generics, Phillipines	Lifepharma, Sri Lanka	Stallion Labs, India
Bombay Tab, India	Lincoln, India	Sun Pharma, India
Bristol-Myers, UK	Lupin Labs, India	Surgilinks Ltd. (K) Distributor
Cadila Pharma, India	M J Biopharm, India	Teva, Israel
Cipla Ltd., India	Macleods Pharma, India	Torrent Ltd., India
Comed Chemicals Ltd., India	Macter Int., Pakistan	Troikaa Pharma, India
Coral laboratories Ltd., India	Marksans Pharma, India	Tushar, India
Cosme Pharma, India	Medico Remedies, India	Twokay Chemicals (K) Distributor
Cox Pharma, UK.	Medley Pharma, India	UCB Pharm, SA
Dannes Pharmacy (K) Distributor	Medreich Sterilab, India	Unicure Remedies, India
Demo, Greece	Mega Life Sciences, India	Unison Labs, Thailand
Denk Pharma, Germany	Mepha Basel, Switzerland	USV Ltd., India
Deva, Turkey	Metro Pharma, Phillipnes	USV Ltd., India
Efroze Chemical, Pakistan	Micro Exports, India	Vishal Pharma, India
Eipico, Egypt	Milan Lab, India	West-Coast Int., India
Emcure Pharmaceuticals, India	Mission Pharma, Denmark	Win-Medicare, India
Emil Pharma, India	Nem Labs, India	Wockhardt, India
Epla Labs, Pakistan	Neopharma, United Amirates	Xepa-Soul, Malaysia
Erica Pharma Pvt, India	Nic Pharma, China	Zest Pharma, India
Eskayef Bangladesh, India	Nicholas Piramal, India	Zydus Cadila H/Care, India
Essential Pharma, USA	Ochoa Las, India	Zyg Pharma Pvt, India
Esseti Pharma, Italy	Orbis Pharma, UK	
Essex (Schering-Plough), USA	Panacea Biotica, India	
Europa Healthcare(K) Distributor	PDH Pharma, Pakistan	

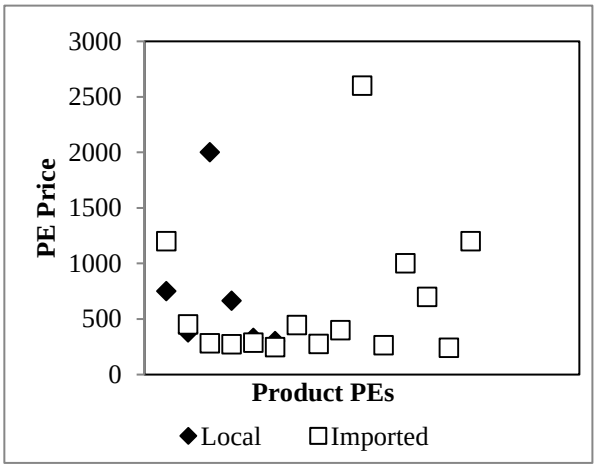
Appendix 7: Scatter diagram comparison of price (Kenyan shillings) of local and imported pharmaceutical equivalents (100 KSh ≈1US$)



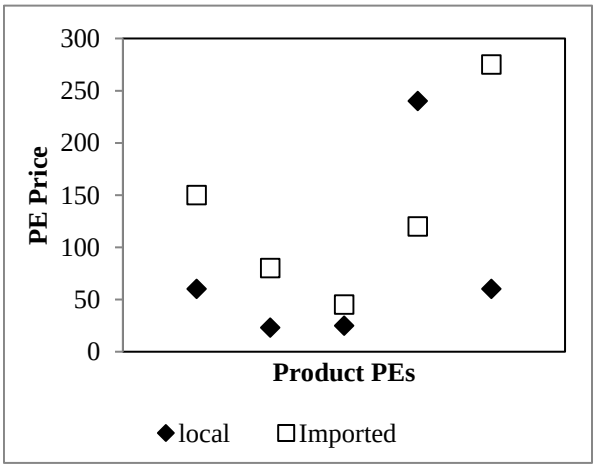
7.1: Amitriptyline tablets 25 mg 1000's



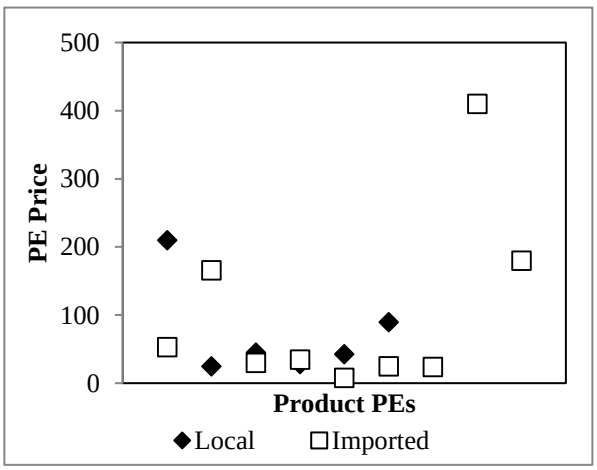
7.2: Ciprofloxacin tablets 500 mg 10's



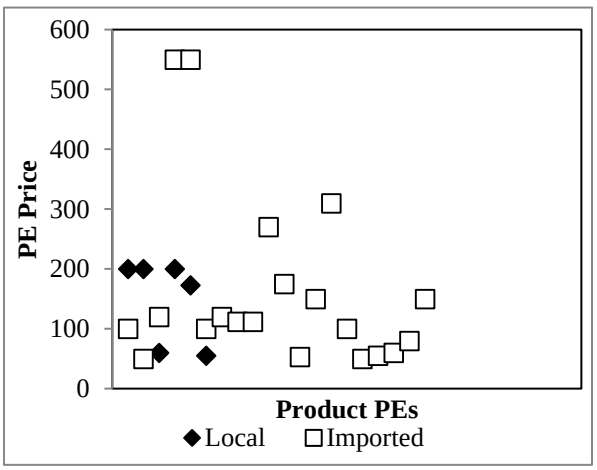
7.3: Ciprofloxacin tablets 500 mg 100's



7.4: Clotrimazole pessaries 200 mg 3's

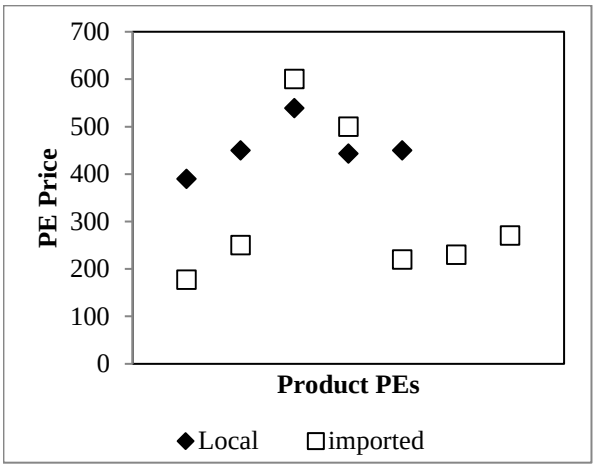


7.5: Clotrimazole pessaries 100 mg 6's

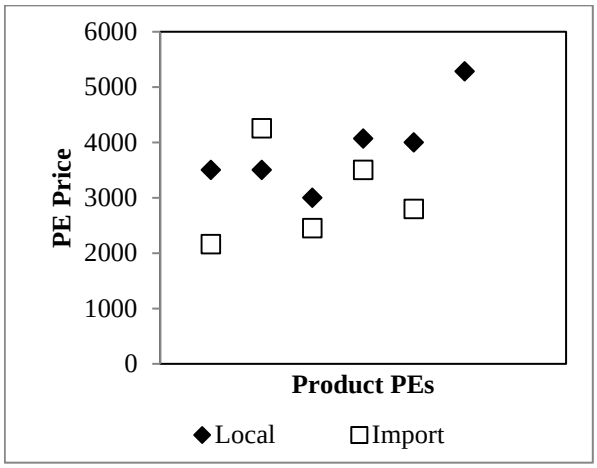


7.6: Diclofenac sodium tablets 50 mg 100's

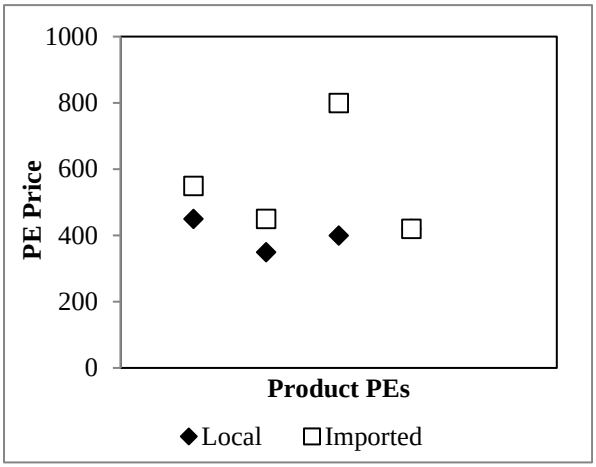
Appendix 7 (Continued)



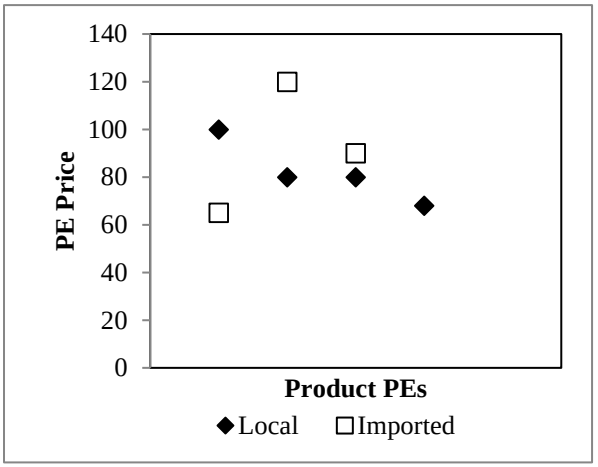
7.7: Erythromycin tablets 250 mg 100's



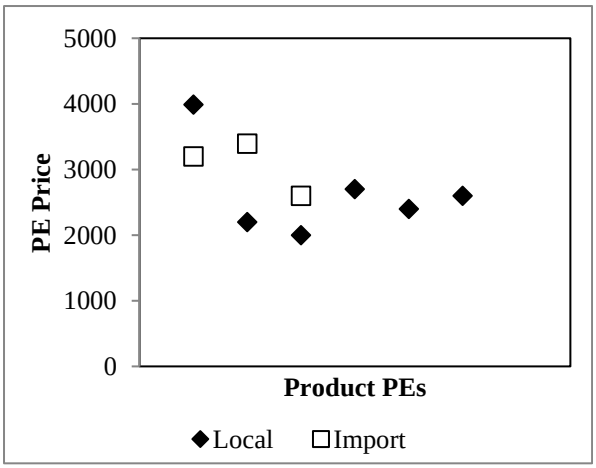
7.8: Erythromycin tablets 250 mg 1000's



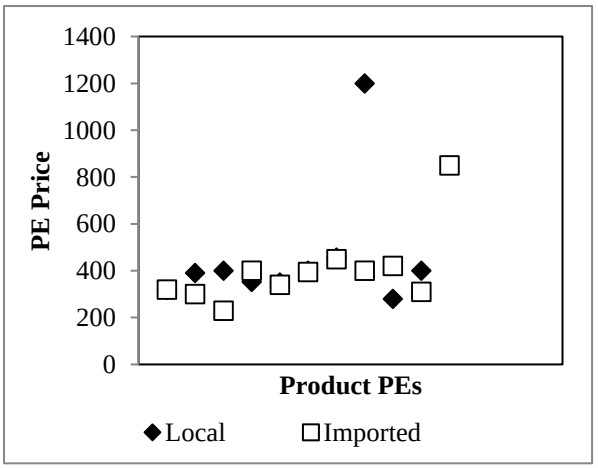
7.9: Frusemide tablets 40 mg 100's



7.10: Frusemide tablets 40 mg 1000's

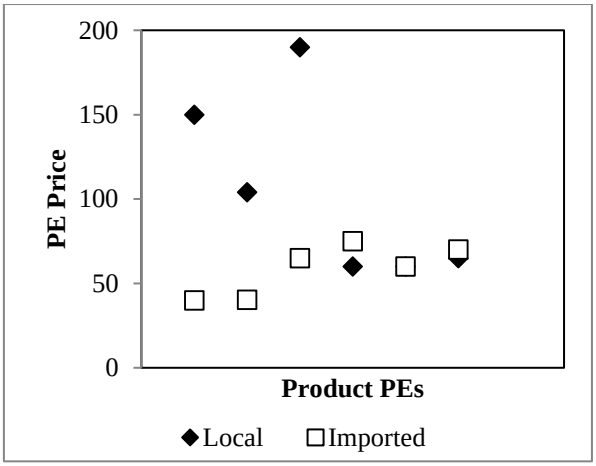


7.11: Hyoscine butyl bromide tablets 10 mg

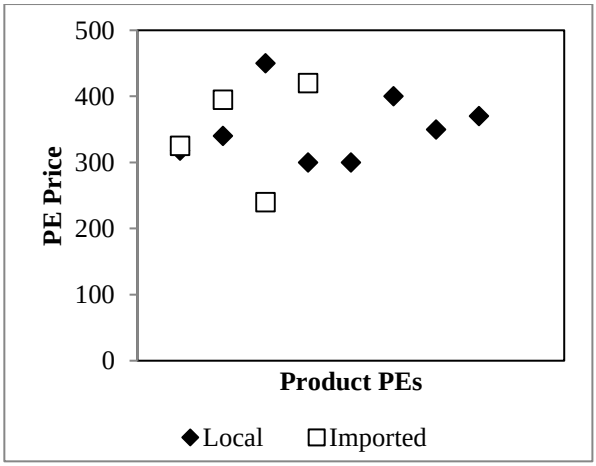


7.12: Ibuprofen tablets 200 mg 1000's

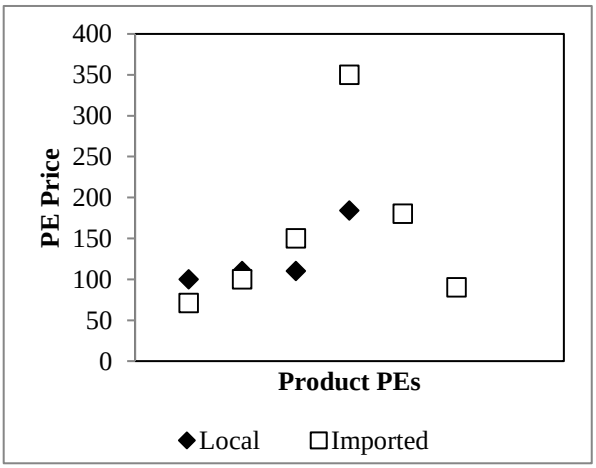
Appendix 7 (Continued)



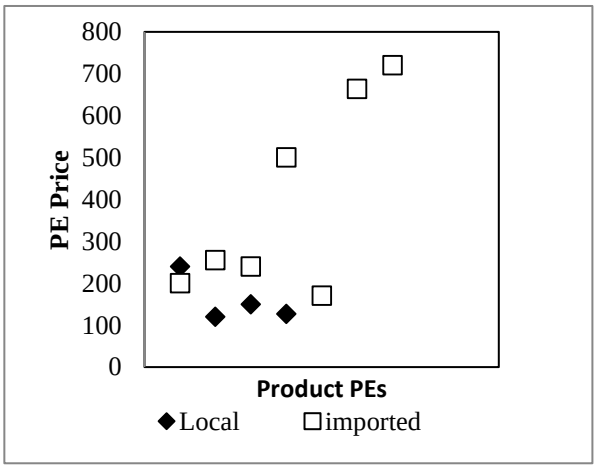
7.13: Ibuprofen tablets 200 mg 100's



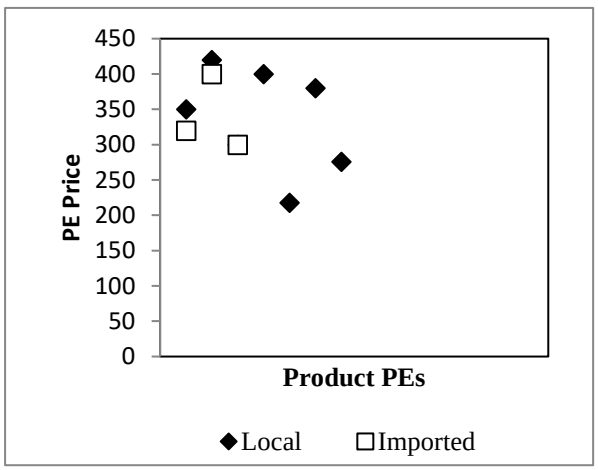
7.14: Ibuprofen tablets 400 mg 500's



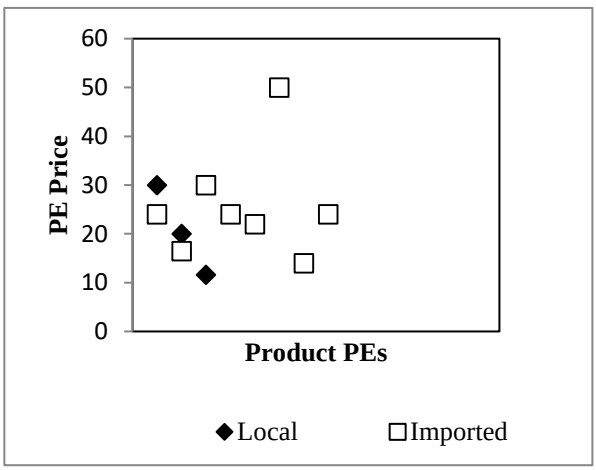
7.15: Ibuprofen tablets 400 mg 100's



6.16: Ketoconazole tablets 200 mg 30's

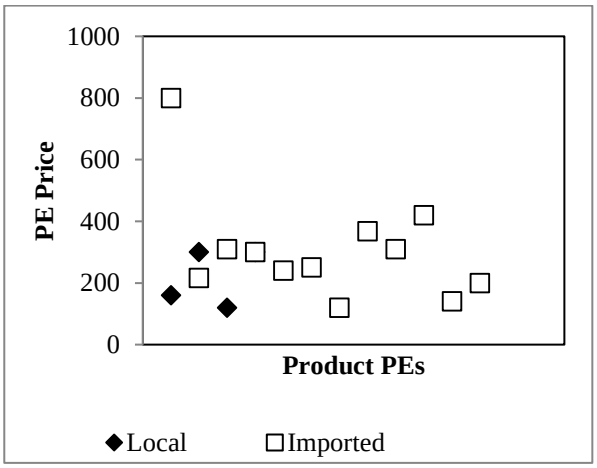


7.17: Mebendazole tablets 100 mg 1000's

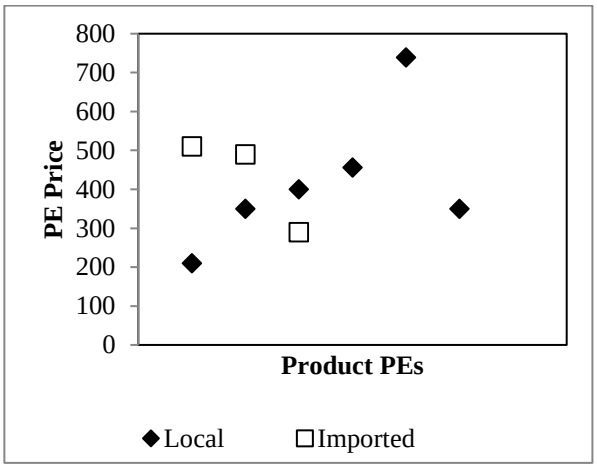


7.18: Mebendazole tablets 100 mg 6's

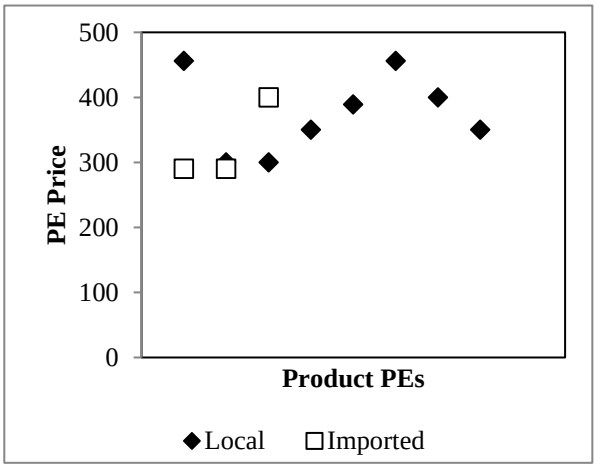
Appendix 7 (Continued)



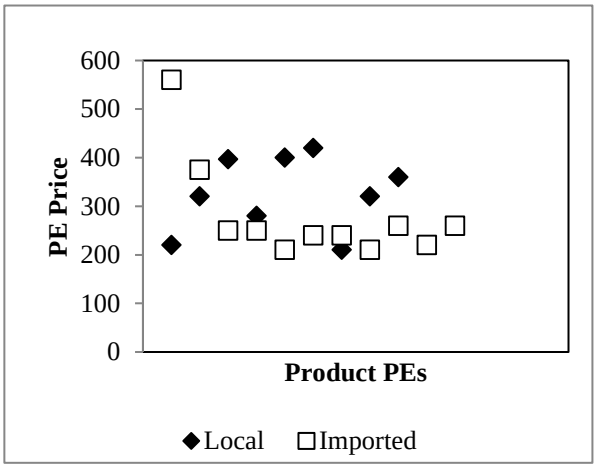
7.19: Metformin tablets 500 mg 100's



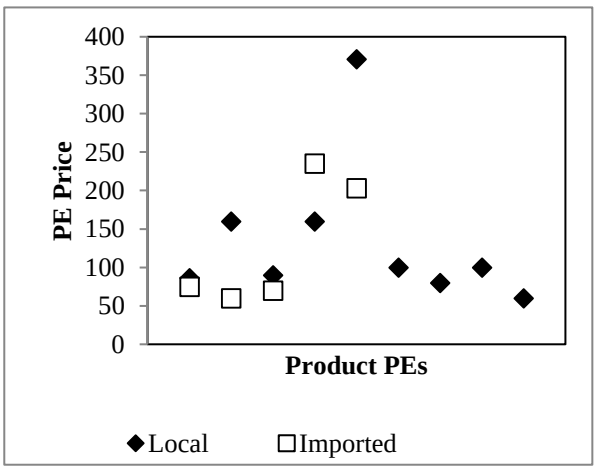
7.20: Metronidazole tablets 400 mg 1000's



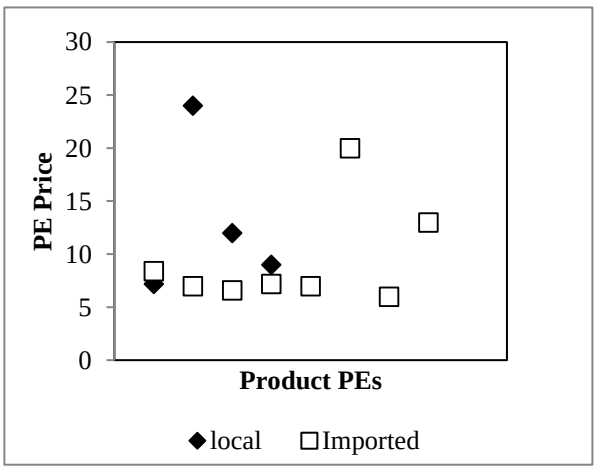
7.21: Metronidazole tablets 200 mg 1000's



7.22: Paracetamol tablets 500 mg 1000's

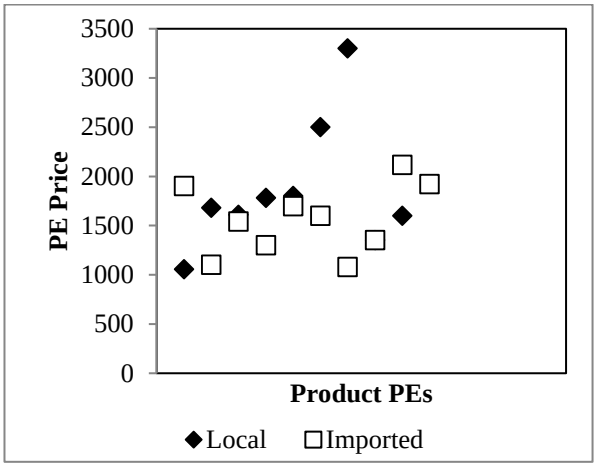


7.23: Paracetamol tablets 500 mg 100's

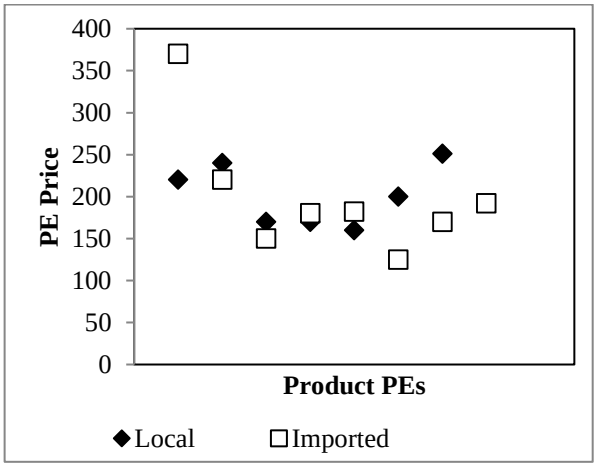


724: Tinidazole tablets 500 mg 4's

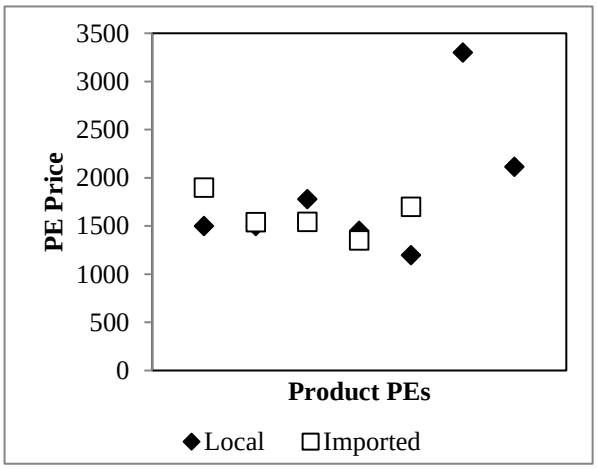
Appendix 7 (Continued)



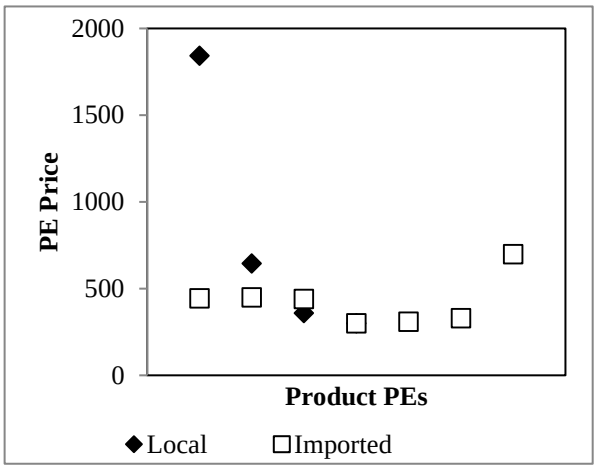
7.25: Amoxycillin capsules 250 mg 1000's



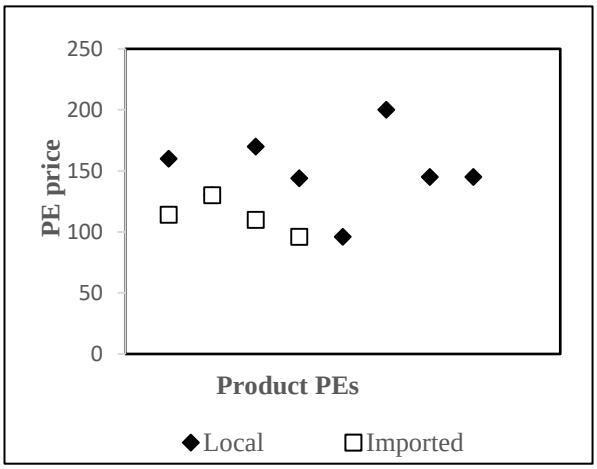
7.26: Amoxycillin capsules 250 mg 100's



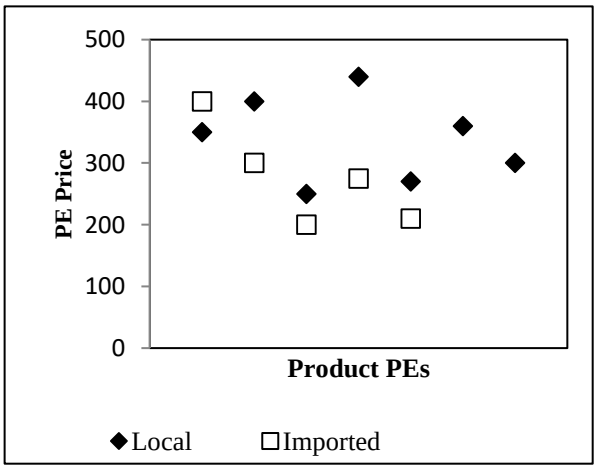
7.27: Amoxycillin capsules 500 mg 500's



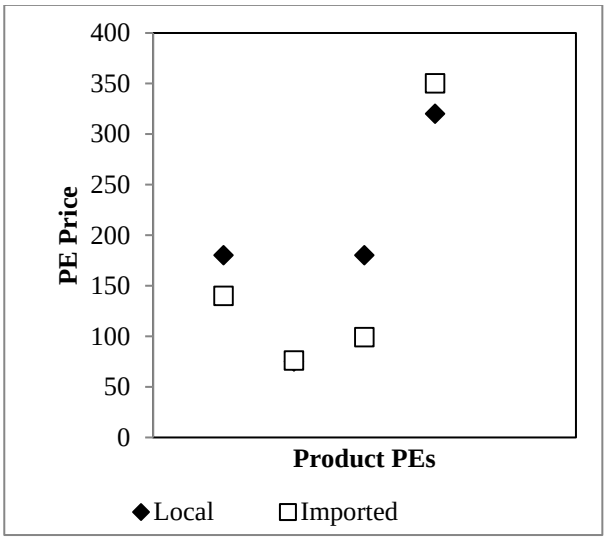
7.28: Amoxycillin capsules 500 mg 100's



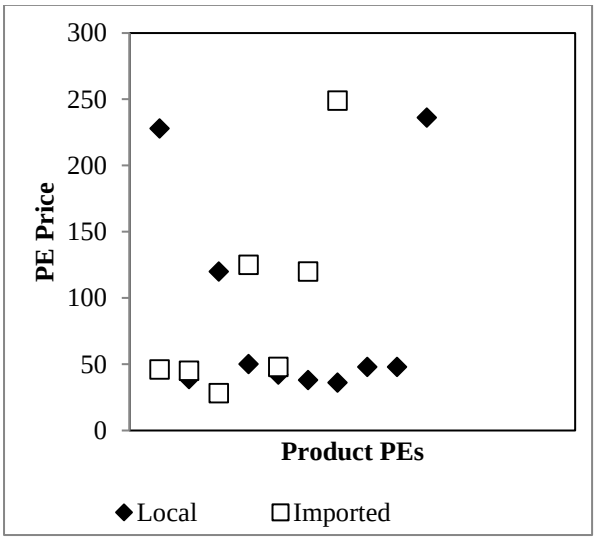
7.29: Doxycycline capsules 100 mg 100's



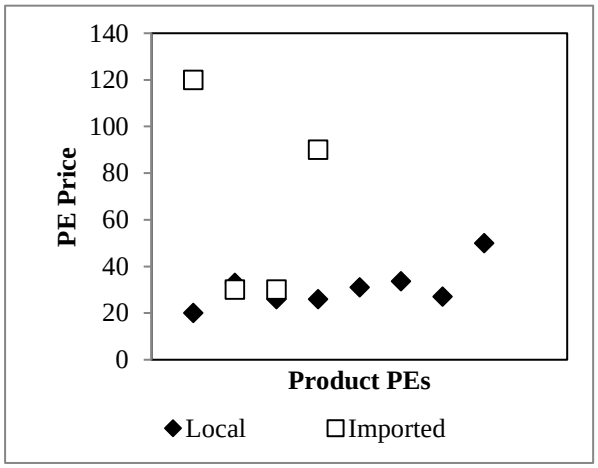
7.30: Indomethacin capsules 25 mg 1000's



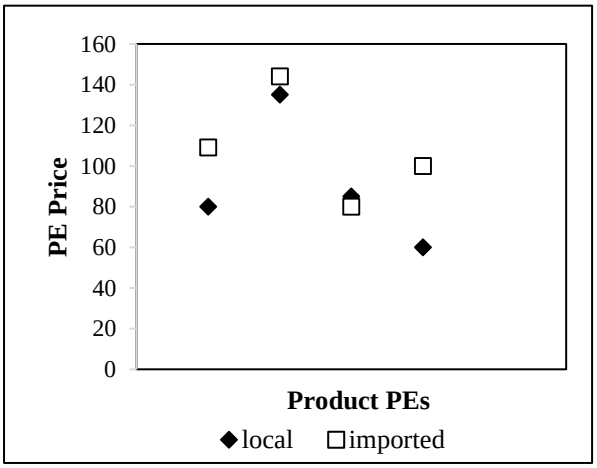
7.31: Mefenamic acid capsules 250 mg 100's



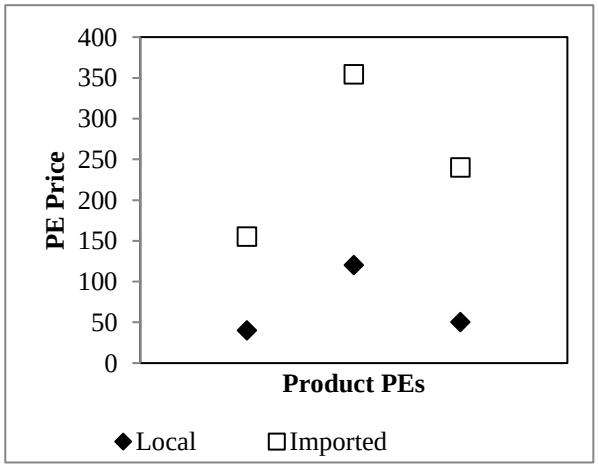
7.32: Amoxycillin 125 mg/5 ml 100 ml



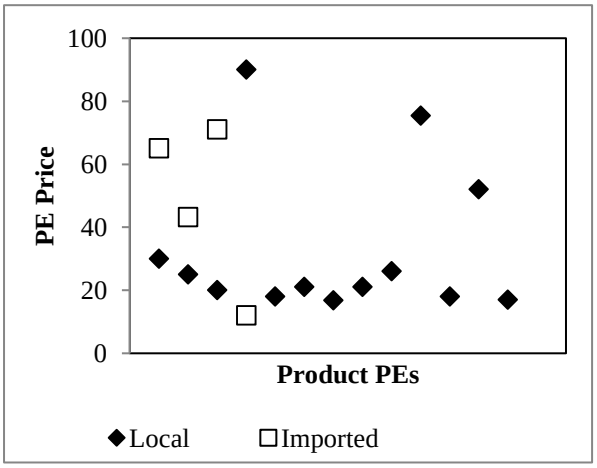
7.33: Amoxycillin 125 mg/5 ml 60 ml



7.34: Cetrizine 5 mg/5 ml 60 ml

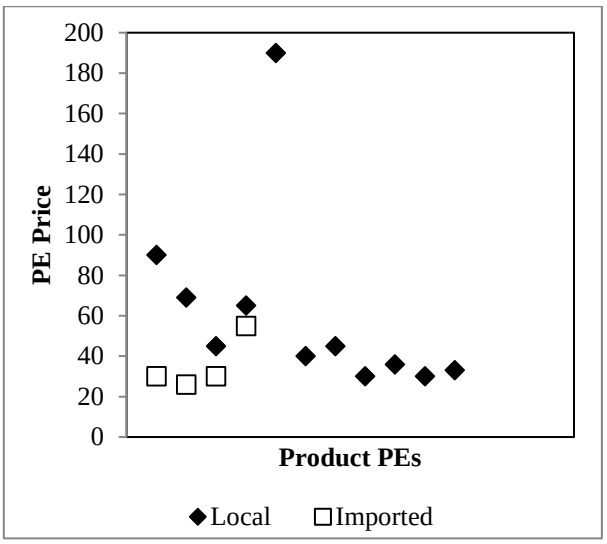


7.35: Nystatin 100000 I.U 30 ml

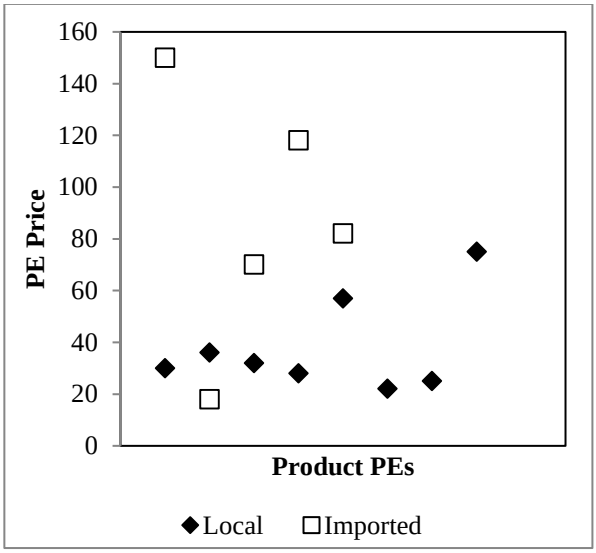


7.36: Paracetamol 120 mg/5 ml 60 ml

Appendix 7 (Continued)



7.37: Betamethasone 0.1%w/w 15 g



7.38: Clotrimazole 1%w/w 20 g

Appendix 8 : National Commission for Science, Technology Approvals

NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY AND INNOVATION

Telephone: +254-20-2213471,
2241349, 310571, 2219420
Fax: +254-20-318245, 318249
Email: secretary@nacosti.go.ke
Website: www.nacosti.go.ke
When replying please quote

9th Floor, Utalii House
Uhuru Highway
P.O. Box 30623-00100
NAIROBI-KENYA

Ref: No.

Date:

21st August, 2014

NACOSTI/P/14/5511/3000

Sarah Kadesa Vugigi
Kenyatta University
P.O. Box 43844-00100
NAIROBI.

RE: RESEARCH AUTHORIZATION

Following your application for authority to carry out research on *"Assessment of the pharmaceutical manufacturing industry in Kenya to forecast local production sufficiency,"* I am pleased to inform you that you have been authorized to undertake research in **Nairobi County** for a period ending 1st **September, 2015.**

You are advised to report to **the County Commissioner and the County Director of Education, Nairobi County** before embarking on the research project.

On completion of the research, you are expected to submit **two hard copies and one soft copy in pdf** of the research report/thesis to our office.

COUNTY DIRECTOR OF EDUCATION
26 AUG 2014
MINISTRY OF EDUCATION
P. O. Box 74629, NAIROBI

SAID HUSSEIN
FOR: SECRETARY/CEO

COUNTY COMMISSIONER
NAIROBI COUNTY
P. O. Box 30124-00100, NBI
TEL: 341666

Copy to:

The County Commissioner
The County Director of Education
Nairobi County.

NATIONAL COMMISSION FORSCIENCE, TECHNOLOGY ANDINNOVATION

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2241349,3310571,2219420
Fax: +254-20-318245,318249
Email: dg@nacosti.go.ke
Website: www.nacosti.go.ke
When replying please quote

9th Floor, Utalii House
Uhuru Highway
P.O. Box 30623-00100
NAIROBI-KENYA

Ref: No. **NACOSTI/ADM/120**

Date: **18th July, 2017**

TO WHOM IT MAY CONCERN

RE: SARAH VUGIGI - PHD PROPOSAL RESEARCH CLEARANCE

This is to confirm that Ms. Sarah Vugigi PhD research titled **"Assessment of the pharmaceutical manufacturing industry in Kenya to forecast local production sufficiency"** was granted a Research License as per the Science, Technology and Innovation Act, 2013 on 20th August, 2014.

The Protocol met the requirements for industry based study not using human participants. Ethical Clearance would have been mandatory if the study involved human subjects.

Do not hesitate to seek further clarification if necessary from the undersigned.

GODFREY P. KALERWA MSc., MBA, MKIM
FOR: DIRECTOR-GENERAL/CEO

CONDITIONS

1. You must report to the County Commissioner and the County Education Officer of the area before embarking on your research. Failure to do that may lead to the cancellation of your permit
2. Government Officers will not be interviewed without prior appointment.
3. No questionnaire will be used unless it has been approved.
4. Excavation, filming and collection of biological specimens are subject to further permission from the relevant Government Ministries.
5. You are required to submit at least two(2) hard copies and one(1) soft copy of your final report.
6. The Government of Kenya reserves the right to modify the conditions of this permit including its cancellation without notice

REPUBLIC OF KENYA

NACOSTI

National Commission for Science, Technology and Innovation

RESEARCH CLEARANCE PERMIT

Serial No. A 2945

CONDITIONS: see back page

THIS IS TO CERTIFY THAT:
MS. SARAH KADESA VUGIGI
of KENYATTA UNIVERSITY, 0-200
NAIROBI,has been permitted to conduct research in *Nairobi County*

on the topic: *ASSESSMENT OF THE PHARMACEUTICAL MANUFACTURING INDUSTRY IN KENYA TO FORECAST LOCAL PRODUCTION SUFFICIENCY*

for the period ending:
1st September,2015

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Applicant's Signature

Permit No : NACOSTI/P/14/5511/3000
Date Of Issue : 21st August,2014
Fee Recieved :Ksh 2,000

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Secretary
National Commission for Science, Technology & Innovation