

PHARMACEUTICAL PARTNERSHIPS FOR INCREASED ACCESS TO QUALITY ESSENTIAL MEDICINES - EA REGION

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Pharmaceutical Partnerships for Increased Access to Quality Essential Medicines in the East Africa Region

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Abstract

Pharmaceutical manufacturing industry is research-based, technology-intensive and highly controlled. Many African countries lack capacity to manufacture essential medicines and partnerships may be necessary for leverage of knowledge and technology which are the basis for innovation. This study aimed to establish the innovation capacity of the Eastern Africa pharmaceutical manufacturing industry, identify barriers to Public/Private Partnerships and establish a framework for an impactful pharmaceutical cross-sector partnership system which is pivotal in competitiveness of the industry.

A survey was conducted in the pharmaceutical manufacturing industry, academia and research institutions. The data collection method encompassed comprehensive review, analysis of relevant literature, face-to-face interviews and filling in of structured questionnaires by respondents.

There are about 60 pharmaceutical manufacturers in the region; 35 in Kenya, 11 in Uganda 12 in Tanzania and 9 in Ethiopia. They produce mostly non-sterile medicines comprising tablets, capsules, syrups, suspensions, ointments and creams. Only 28% of the products in the national essential medicines are currently being produced, majority being for management of communicable diseases. Average production capacity utilization was 43% for Kenya. Research and Development scientists and personnel with special skills are few. Respondents stated that policies impacting local industry were incoherent, insufficient and lacked consultation during formulation. Furthermore, there is no linkage between academia, research institutes and pharmaceutical industry. An industry-research institution partnership for product innovation in line with public health priorities articulated by the government is necessary.

Key words

Essential medicines, Local Pharmaceutical Producers (LPPs), Industry, local, manufacturers, partnerships, pharmaceutical.

Introduction

Essential medicines are priority for the well-being of a nation and as such access to safe, effective and quality medicines for all is imperative as envisaged in the Sustainable Development Goal No. 3 of the United Nations.¹ However, access to quality-assured essential medicines remains a challenge, with more than two billion people worldwide, majority being in developing countries lacking regular access to these products. According to the World Health Organization (WHO) World medicines situation, two-thirds of the value of medicines produced globally is accounted for by firms with headquarters located in just five countries - the USA, Japan, Germany, France and the UK.² The pharmaceutical industry in most countries in Africa has inadequate research and development (R&D) capacity. Majority of the manufacturers produce non-sophisticated products with limited specialized formulations to tackle the new emerging trends. In view of this, the WHO, United Nations Conference on Trade and Development (UNCTAD), United Nations Industrial Development Organization (UNIDO) and other partners are advancing activities that enhance medicines access in developing countries. These include promoting investment in domestic industry to upgrade production and human capacity, developing coherent policy frameworks, utilization of Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities, and supporting national intellectual property (IP) legislation reforms. The goal of these initiatives is to enable developing countries to achieve national reliance in essential medicines through local production.

The drug development is an expensive and laborious process that requires technological know-how, skilled researchers, political will and a regulatory framework that protects and rewards innovation. The R&D is also a high-risk undertaking, marked with high failure rates and the cost to identify innovative compounds may exceed USD 2 billion.^{3,4,5} To this end, collaborative/partnerships strategies such as mergers and acquisitions are increasingly seen as a means to expand business, capacity and to

¹ Sustainable Development Goals; SDG 3: Division for Sustainable Development, Department of Economic and Social Affairs, United Nations, and New York. Retrieved from: <https://sustainabledevelopment.un.org/sdg3>.

² World Health Organization (WHO). (2004). The World Medicines situation <https://apps.who.int/medicinedocs/en/d/Js6160e/3.html>, [accessed 14 June 2019]

³ M.S. Raghavendra, John R. Raj, A. Seetharaman (2012). A study of decrease in R&D spending in the pharmaceutical industry during post-recession. *International Journal of Academic Research Part B*; 2012; 4(5), 29-47.

⁴ International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). (2014). The pharmaceutical industry and global health facts and figures 2014.

⁵ International federation of pharmaceutical manufacturers & Associations (IFPMA). (2017). *Pharmaceutical Innovation and Public Health. Facts & Figures 2017*.

improve profitability.⁶ Most of the leading pharmaceutical manufacturers are born out of one or more mergers, for example, GlaxoSmithKline's originators include Glaxo, Wellcome, Smith Kline and Beecham. Partnerships leverage on collaborators' complementary expertise, resources and share risks in order to improve capacities and expand market networks.^{7,8} Private pharmaceutical companies partner with publicly funded research organizations (e.g. universities or research institutes) to develop new products. Public-private partnerships (PPPs) is a strategy by which manufacturers exploit synergies in application and utilization of knowledge and resources, by establishing R&D priorities and optimize the use of available resources. Data analysis shows that the transformation of US leading pharmaceutical firms from basic production to research intensive institutions between the 1920s and 1940s was accomplished through research collaboration with contract research organizations (CROs) and university faculty.^{9,10}

Notably some of these interventions are taking place in the East Africa Community (EAC) region. The interest in the local pharma business by international investors has seen acquisition of some companies, e.g. Universal Corporation Limited/Strides-Shasun merger (Kenya) and CIPLA/Quality Chemical Industries Limited (Uganda). This demonstrates that the pharmaceutical manufacturing industry is starting to embrace technological advancements that will significantly improve access to essential medicines. Nonetheless, majority of pharmaceutical firms in EAC region continue to manufacture common products. A fraction of the listed essential medicines is produced mainly due to lack of infrastructure needed to develop new medicines. In a WHO background paper Report BP8.1,¹¹ PPPs were identified as a promising solution for addressing challenges in pharmaceutical innovation.

⁶ Yasin Çilhoroz, Cuma Songur , Mehmet Gözlü , and Murat Konca. (2016). Mergers and acquisitions in pharmaceutical industry as a growth strategy: an investigation upon practice international journal of business and management vol. iv, no. 3 / 2016. doi: 10.20472/iac.2016.024.024

⁷ Hilde Stevens and Isabelle Huys (2017). Innovative Approaches to Increase Access to Medicines in Developing Countries. *Front Med (Lausanne)*. 2017; 4: 218. Published online 2017 Dec 7. doi: 10.3389/fmed.2017.00218.

⁸ Public-Private Partnerships for Improving Access to Pharmaceuticals (2002). Lessons from Field Implementation in Selected Countries, Initiative on Public-Private Partnerships for Health, Global Forum for Health Research. Published by The Initiative on Public-Private Partnerships for Health, Global Forum for Health Research, 2002.

⁹ Jeffrey L. Furman and Megan MacGarvie (2009). Academic collaboration and organizational innovation: the development of research capabilities in the US pharmaceutical industry, 1927–1946* Article in *Industrial and Corporate Change* · September 2009 DOI: 10.1093/icc/dtp035.

¹⁰ Michelle Palmera and Rathnam Chagaturub (2017). Academia–pharma partnerships for novel drug discovery: essential or nice to have? Expert opinion on drug discovery, 2017 VOL. 12, NO. 6, 537–540 <https://doi.org/10.1080/17460441.2017.1318124>.

¹¹ WHO background paper Report BP8.1: Public Private Partnerships. Elizabeth Ziemba, 2004.

The aim of this study was to establish the innovation capacity of the pharmaceutical manufacturing industry in the EAC region, identify the barriers to PPPs and establish a framework for an impactful pharmaceutical cross-sector partnership system. The specific objectives of this research were to, i) determine the level of production competence of the pharmaceutical industry in EAC region in regard to manufacture of national essential medicines, ii) identify policies and regulations that impact innovation and development of pharmaceutical products, iii) establish mitigation strategies to reduce the product gap between the national essential medicines lists and medicines that are locally produced and iv) to explore how collaborations, financing, research links, and technology transfer can be harnessed to boost production and access to quality and affordable medicines in the EAC region. The study was commissioned by Science Granting Councils Initiative (SGCI) in Sub-Saharan Africa and implemented by the African Centre for Technology Studies (ACTS) consortium.

Methodology

A mixed methods research incorporating both elements of qualitative and quantitative approaches was used. Extensive literature review was performed followed by data collection using comprehensive structured questionnaires and formal semi-structured face to face (F2F) interviews. Three distinct questionnaires based on the objectives of this study were developed. The questionnaires were reviewed and pre-tested as per the work-plan to ensure that they were clear, concise and that they generate useful information. The respondents were pharmaceutical manufacturing industry, academia/research institutions and policy makers. Both close- and open-ended questions were adopted for the study. The questionnaire for the manufacturing industry comprised general questions on production competence, production capacity, good manufacturing practice certification, personnel, factors impacting local production, policies that impact product innovation and research collaborations with academia and research institutions. The other two questionnaires covered aspects of pharmaceutical public-private partnerships and policies. These later two were used to generate data from academia/research institutions and policy makers in the Ministry of Health, Trade & Industry. This study covered the EAC region and Ethiopia.

Prior to data collection, the consultants met with Federation of Kenya Pharmaceutical manufacturers (FKPM), which is the umbrella body of pharmaceutical manufacturers in Kenya, to sensitize members on the data collection exercise and its importance. The questionnaire targeted to the industry was pretested with four Local Pharmaceutical Producers (LPPs) and the feedback used to refine the tool. The questionnaires were then administered to respondents by electronic mail and actively followed-up with phone calls. The questionnaire was distributed to all pharmaceutical manufacturers of

medicines for humans in Kenya and the rest of EAC region. The questionnaire aiming at academia/research institutions was distributed to 4 academic institutions in Kenya (University of Nairobi, Kenyatta University, United States International (USIU) University and Mount Kenya University), Kenya Medical Research Institute (KEMRI) and 2 schools of pharmacy in Tanzania (Muhimbili University of Health and Allied Sciences (MUHAS) and *Kilimanjaro of pharmacy*). Interviews were conducted with the chairperson of FKPM, chief executive officers of five pharmaceutical manufactures in Kenya, government officials in the ministries of Health and Trade & Industry, the Kenya Investment Authority, Pharmacy and Poisons Board of Kenya) All data and feedback were collated and analyzed in line with the objectives of the study.

Data Analysis

The Kenya essential medicines list (EML) was analyzed by abstracting medicine entries using International Nonproprietary Names (INNs) and therapeutic classes in order to identify common medicines produced in Kenya and by extension the region considering that Kenya hosts the largest number of LPPs in the EAC region. A comparison of Kenya (EML with the registered products by LPPs was performed to identify the number of products listed on the EML produced in the region. The same dataset was also used to analysis the main therapeutic classes produced by manufactures in Kenya. Similarly, the human resource capacity and gaps in the pharma sector in different departments, including Research and Development (R&D) was evaluated by analyzing the number of personnel, qualification and experience in all departments at each of the manufacturing facilities. Production capacity utilization in the pharmaceutical industry was also determined. Comprehensive literature review and analysis of existing collaborations (academia, research institution, government and private sector) and case studies on successful and unsuccessful partnerships was performed. All data and feedback from interviews were examined in line with the objectives of the study and the findings are presented in the results section.

Results.

The level of production competence of the pharmaceutical industry in EAC region

There are about 60 pharmaceutical manufacturers in EAC; 35 in Kenya, 11 in Uganda, and 12 in Tanzania. Ethiopia has 9 registered pharmaceutical manufacturers. In Kenya, 16 firms (60% of the 25 contacted) responded to the questionnaire. There was only one response from Tanzania (Zenufa

Laboratories) and one from Uganda (Abacus Pharma Limited). The low response from Uganda, Tanzania and Ethiopia is attributed to confidentiality and policy requirements on data sharing at both cooperate and government levels. As a counter measure, secondary data and public reference materials were used for these countries. The government of Kenya, academic and research institutions in Tanzania (3), and Kenya (5) also participated in the study. Likewise, feedback was received from Key Interview Informants (KIIs) from Kenya, Uganda, Tanzania and Ethiopia.

Majority of manufacturers in the region produced non-sterile products – both beta and non-beta lactams. The major focus is on solids (capsules/tablets) and mostly the non-complicated formulations. One factory in Ethiopia and one in Uganda produce large-volume parenterals. About 56% of the products manufactured were solid dosage forms, mostly tablets (Figure 1.0). Most of the solids are presented as strip/blister/bulk packs.

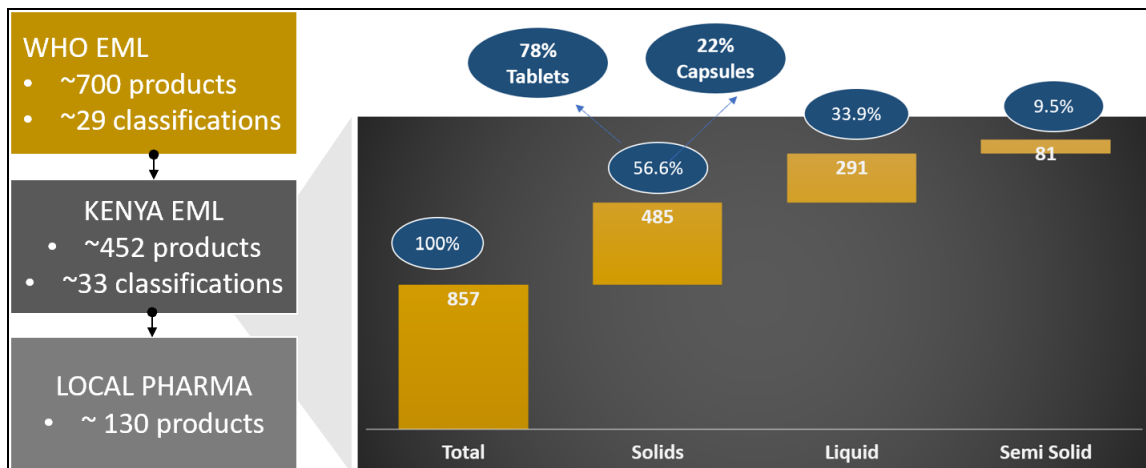


Figure 1.0. Production capacities of LPPs in Kenya (n = 16)

The pharmaceutical industry in Kenya produce about 130 products (~28%) out of 452 listed in the Kenya Essential Medicines List (EML). The same inference could be made about Ethiopia LLPs who produce only 90 of the listed 380 EML products. Notably, manufactures in Kenya continue to focus on a few therapeutic areas at the expense of the bigger need as per the disease burden profile of the EAC region and country. From the essential medicines analysis, anti-infectives, non-opioids & Non-steroidal anti-inflammatory medicines (NSAIMs) and respiratory conditions products are the most manufactured products in the region (Figure 2.0). Only 6% of the products manufactured were antivirals. There are attempts to manufacture products for the control of NCDs with a major focus on cardiovascular related products hence. There were 74 products registered by this industry for management of hypertension, diabetes and osteoporosis. About 65% of the product registered in the

period 2018/2019 were for non-communicable diseases and the balance for mostly communicable diseases. The product registration pipeline in Kenya had approximately 172 products from 16 companies in various stages of dossier evaluation for product registration approval. About 40 products were under development while another 84 were under consideration and a further 23 fully registered in 2019 at the time of the study. Access to new product registrations for Uganda, Tanzania and Ethiopia was not possible but a scan through the product lists of LPPs in these countries suggests that their focus is also on communicable diseases.

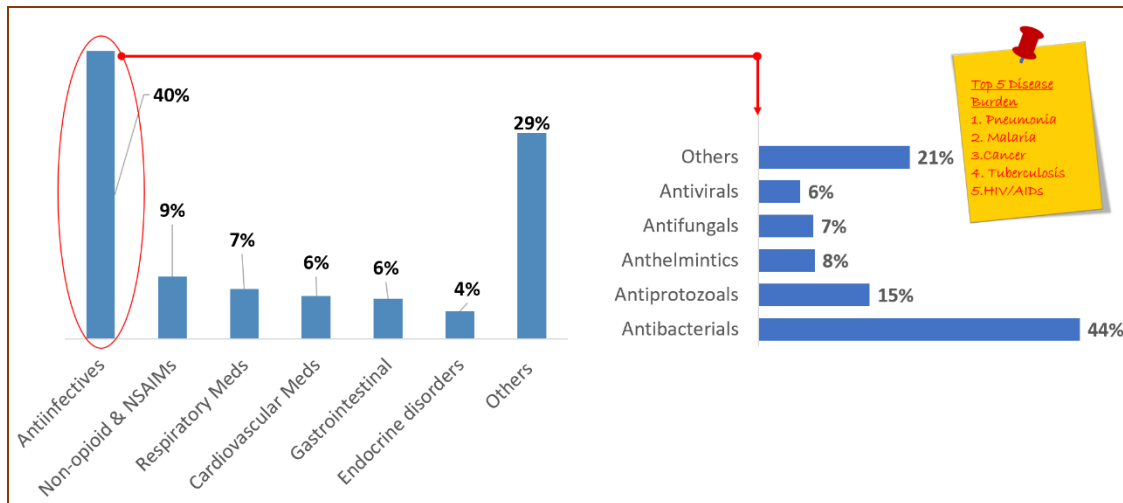


Figure 2.0. EML produced in Kenya against the disease burden

From the results, the production capacity utilization in the region was underutilized. The utilized capacity of Kenya pharmaceutical industry was 43% for non-beta lactam products (tablets, 48%, capsules, 28% and liquids, 52%). The respondents stated that there was no direct linkage between government and the industry that articulates prioritization of essential medicines requirements.

Skills Set for Pharmaceutical Sector

The workforce at the 16 Kenyan firms that participated in this study was 3551. Nearly 20% held diploma or university level qualification and the rest were certificate graduates or had on- the- job training. The supervisory and managerial tasks for quality control (QC)/quality assurance (QA), and production departments are run by graduates with BSc, BPharm, MSc or PhD. Other skills available include craft certificates and O-level qualifications for various skills in plumbing, computer packages, electrical engineering, boiler operation, procurement and administration. The same picture likely occurs across the EAC region. Data collated on Ethiopia and Uganda showed that the number of employees in the sector was approximately 2000 (2010) and 1800 (2014) for Ethiopia and Uganda respectively. Majority have qualification in chemistry, pharmacy, biochemistry etc. There was deficiency of R&D and special skills such as pharmaceutical engineers, validation experts and

formulation experts, process engineers, HVAC¹² and IT specialists. In this study, LPPs placed more emphasis on the need of R&D, formulation, process optimization, validations and technology transfer skills. Most firms felt that they had adequate production, quality management skills.

Policies and Regulations Impacting Innovation and Development of New Products in the Local

Feedback received from CEOs of 5 leading companies indicate that there is lack of clear government policy to support the local industry and this has led to the manufacturers to be apprehensive when it comes to investing in their factories. The industry's view was that there is no adequate incentives to catalyze investing in facility upgrading and quality improvement programs, especially in the production of donor funded products such as antiretrovirals and antimalarials. The executives felt that the return on investment (ROI)¹³ from such effort is negligible. Most LPPs indicated that policies and regulations are necessary for the growth of the industry and there are also policies which are directly related to the pharmaceutical manufacturing industry such as the price preference for procurement of local commodities and zero tariffs on most pharmaceutical inputs where manufacturers invest and claim tax rebates thereafter. However, this rebate process is bureaucratic and takes time to be effected disrupting the cash flow. Additionally, imported finished products are zero rated, and speedily available in the market once they are landed whereas manufacturing process takes time thus increasing the cost of locally produced medicines. This is further worsened by public tenders that are awarded based on the least bidder without regard to other considerations. In Kenya, distributors registered locally enjoy a 10% while a fully-fledged manufacturing firm has a 15% preference. Most of the CEOs interviewed felt strongly that the 5% differential between the two entities is insignificant considering the intensity of activities involved in pharmaceutical production. They were of the view that there is inadequate consultation with pharmaceutical manufacturing experts when formulating policies and that policies and regulations that impact local manufacturing industry are incoherent and inadequate. It is noteworthy that Ethiopia is more supportive to local production where these manufacturers are permitted a preference of up to 25% and awards 30% of the cost upfront and a surety of the remainder.

The manufacture of pharmaceuticals in Kenya is regulated by Pharmacy and Poisons Board (PPB), which is the National Medicines Regulatory Authority (NMRA). All manufacturers were aware that all pharmaceutical products must be registered by the national medicines regulatory authorities

¹² HVAC: Heating, ventilation, and air conditioning system are used to control the conditions within a manufacturing site. This is a basic requirement for any pharmaceutical facility as part of GMP.

¹³ ROI: Return on Investment.

(NMRAs) and compliance with GMP is mandatory for registration approval. Kenyan Pharmaceutical manufacturers have product registrations by NMRAs in several countries such as Uganda, Kenya, Tanzania, Malawi, Zambia and Mozambique. There are on-going activities on EAC harmonization of product registration and GMP inspections to ensure one standard quality of pharmaceutical products within the region. The EAC region has adopted the international and rigorous Common Technical Document (CTD) format of dossier submission which seemed to have slowed down of the registration process in Kenya. It was observed that in the period 2015/16 there was a 61% reduction in product registrations in Kenya with 20 new registrations in 2016 compared to 51 in 2015.

Pharmaceutical Sector Challenges; Gaps and Mitigation in Production of Essential Medicines

Most of the respondents were of the opinion that the industry does not have the requisite know-how and capability to manufacture all formulations. This is true for all manufacturers in the EAC region. There is inadequate investments in facility improvements and new technology in this industry. Attaining international GMP compliance remains a challenge in the region. In addition, the policies to support the local industry are inadequate, fragmented and incoherent. Collaborations/Partnerships across LPPs, government and academic/research institutions are weak. In general, most companies believe that government policies, training, GMP compliance, manufacturing and financing/markets are important factors to ensure successful production of essential medicines. It was also observed that majority of the manufacturers prioritize market-demand products such as Over-The-Counter products than medicines on the EML. It was noted that most executives believe that skills is not a major factor for production of EML, with 50% of the respondents stating that there was no need to invest in skills.

Compliance to Good Manufacturing Practices as a regulatory prerequisite for market authorization of pharmaceutical products contributes immensely to the gap, especially with products that require stringent operations such as parenteral preparations. Majority of respondents were of the opinion that lack of stringent regulations to enforce GMP standards across the board allows for many entrants into the market without clear regulatory guideline for them to follow. Hence, companies that have heavily invested to be GMP compliant as per regulatory requirements felt that there is no level-playing field due to cost of compliance that makes them less competitive. For this reason, some companies tend to avoid investing heavily in product development because of the regulatory gap. This concern has previously been raised with regulators by the stakeholders.¹⁴ Overall majority of the

¹⁴ Discussions with CEOs from the pharma companies

manufacturers view partnerships/collaborations and financing as major factors to consider in order to improve pharma manufacturing standards and product range.

Collaborations & Partnerships to Support Local Pharmaceutical Sector

The finding of this study was that Kenya manufactures only 28% of the medicines on the national essential medicine list. Kenya does not have adequate technical, financial and human capacity to produce all medicines on the essential medicines list. The LPPs were hesitant to engage in development of products that have high potential safety risks, narrow therapeutic indices and high product development costs. When asked about collaborations with other parties, 46% indicated that they had partnerships, but these were operational collaborations. They also were cognizant of the fact that collaborations require financial capital.

There are efforts by some manufacturers to utilize TRIPS flexibilities to manufacture ARVs. For instance, in 2004 Cosmos Limited, Kenya, negotiated with two companies, namely GlaxoSmithKline and Boehringer Ingelheim for voluntary license to produce ARVs in Kenya for the EAC region. This endeavor failed to supply on tender, partly due to the ever-changing ARV treatment regimen and the WHO Pre-qualification prerequisite for the manufacturing site since procurement of ARVs is donor funded. Other initiatives that are being harnessed to improve access to essential medicines include technology transfer and joint ventures. Examples of successful technology transfer enterprises in the EAC region are Universal Corporation Limited/Strides-Shasun merger (Kenya) and CIPLA/Quality Chemical Industries Limited (Uganda). Ethiopia has realized successful joint ventures which have contributed to growth of the pharmaceutical industry and also effectively transferred skill and technology. *Pharmaceutical Joint venture in Ethiopia include Julphar Pharmaceuticals, Cadila Pharmaceuticals Ethiopia PLC, Sino-Ethiop Associate (Africa) PLC, Pharmacure PLC, East African Pharmaceuticals PLC (EAP) and Ethiopian Pharmaceutical Manufacturing (EPHARM).* There exists limited collaboration between the Pharmaceutical industry and Academia. In Tanzania, Muhimbili University, through the support of international partners have built a strong traditional medicines research portfolio with several potential molecules for management of conditions such as asthma, cholesterol and peptic ulcers. The university also has a research laboratory that is linked to the local pharmaceutical sector backed by memorandum of understanding. However, the uptake of their research services has been low.

This study reveals that there is potential for growth in pharmaceutical research in the EAC region. There are efforts to promote R&D work at Muhimbili School of Pharmacy in Dar- es- Salaam, the

Kilimanjaro School of Pharmacy supported by German development agency and the Kenya Medical Research Institute (KEMRI) but this is at nascent stages. Furthermore, the region has many universities with schools offering courses in biological and other sciences and more than 10 schools of pharmacy which can partner with the pharmaceutical industry and explore collaborations for achieving national research agenda. From the information gathered in this project, it was evident that the universities in the region and research institutions have made little effort to create linkages with the pharmaceutical industry. Most of the research that is performed in these institutions is for academic publishing and has not resulted in innovation that is useful for the pharma industry. There is a clear disconnect between academia, research institutes, the pharmaceutical industry and the government leading to a state of mistrust and misconception among these entities. Most companies indicated that their product development portfolio was based on market demand and not necessarily on the need to address government priorities. The academia strongly felt that the industry's main agenda was tailored towards profit and it is necessary to re-engineer management of the pharmaceutical industry and promote skills by transforming ownership from family to corporate governance. Absence of information sharing platforms for the Industry, academia and research institutions was identified as the key hinderance to collaborations and partnerships in EAC region. Most interviewees stated that the government should drive the pharmaceutical research agenda in the country.

Disciusion

The finding of this study is that only 28% of the listed essential medicines are produced locally. Various factors contribute to the inadequate capacity by the local industry in the EAC region to manufacture the required medicines. Tablets and liquid forms were majority most probably because the technology for production of these formulations are well established and readily accessible. It is also important to mention that tablets have demonstrable advantages transferable to the users such as the ease to administer and also provide relatively better stability. In the case of liquids, this provides an easy entry to new players because it entails simple manufacturing processes. Owing to the special regulatory requirements for production of beta-lactam products, i.e. separate and dedicated production units, only four companies in Kenya are producing these products. Though they have mastered production of these products overtime because they do not necessarily require sophisticated technology, the low coverage of the KEML products suggests narrow focus driven by market dynamics that are largely public oriented.

There is little evidence that LPPs have invested in new technology to allow them to introduce new products and formulations in the EML which offers a great potential for growth considering needs

occasioned by new disease burdens. For example, cancer is now among the top-10 killer disease in Kenya according to Kenya National Bureau of Statistics¹⁵, but there are no programs to encourage investments in the development of anticancer products locally. Such investments could include PPPs, JVs and technology transfers. The focus on products for management of communicable diseases is not surprising considering that the market demand exists due to the high infectious disease burden. For example, in Kenya the leading cause of morbidity are diseases of the respiratory system which accounted for 39.3% of the total disease incidences in 2018.¹⁶ The focus on a narrow set of products suggests that there is no link between the disease management and pharma manufacturing sector in terms of key priorities to address national disease burden. This arises from the fact that priorities are not adequately articulated, and the government is not driving the industry towards producing medicines according the disease burden data. Notably the local industry continue to focus on a few therapeutic areas at the expense of the bigger needs as per the disease burden profile of the region and country. The average production capacity utilization of 43% for non -beta lactam products is an improvement from the last assessment of 2014^{Error! Bookmark not defined.} where it was at 28% (for all dosage forms including semisolids, dry powders and beta lactam products). This is a 15% increase in line with the projection in 2014 (37%) by Vugigi et al.^{Error! Bookmark not defined.} That notwithstanding, these manufacturers compete for the same market (largely public) and product range suggesting uptake of small portions on their products. This contributes to the underutilization of the available production capacity. Most manufacturers do not produce ARVs. This is because most ARVs and antimalarials are currently donor-funded and have a WHO PQ requirement. Unfortunately, LPPs who are GMP competent and compliant to supply these products are disadvantaged due to PQ requirements which is quite limiting as such, manufacturers may not be keen to invest in the technology to develop new products for such diseases. For example, antiretrovirals and antimalarials fixed dosage form (FDC) formulations require additional changes of parts on existing machines or new sophisticated technology for development that necessitates a clear view of the return on investment. Additionally, unpredictable treatment regimens (e.g. discontinuation of amodiaquine, lamivudine, zidovudine & lamivudine) further complicates the decision to invest in the development of such products. The LPPs are hesitant to engage in new molecule development that have high potential safety risks and/or narrow therapeutic indices and high product development costs. For instance, new product development would require technology, skilled personnel, and Bioequivalence (BE) studies in order to build confidence in the quality, efficacy and safety of the products. Furthermore, prescriber's requirement for interchangeability evidence is another risk that may lead to poor market penetration

¹⁵ Economic Survey 2018 Highlights, KNBS 2018.

¹⁶ Economic Survey report, KNBS 2019.

of the new products. All these contribute to suppressed attempt at investing more resources for product development by local industry.

Another important factor is on lack of exploitation and working patents which bear commercial risk and cost of litigation unless compulsory licensing has been acquired as per the TRIPS flexibilities and Doha agreement. The Local industry takes a precautionary measure to wait till patent expiry unless the government declares a national disaster of a disease whose product is under patent regime. The Kenyan manufacturer (Cosmos) justified the application for voluntary/ compulsory licensing (TRIPS Flexibility) arising from public demand and declaration of HIV as a national disaster.

The Insufficient and fragmented policies in support of innovation have contributed to meager investment in product development. In addition, there are lost opportunities when policy and implementations are not coherent. For example; in the 1990s, Kenya had several manufacturers producing anti-Malarial products. Due to massive resistance to chloroquine and later Sulphadoxine – Pyrimethamine in early 2010s, there was a deliberate change in therapy to the artemisinin-based combination therapy (ACT). However, the local production of antimalarial products decreased substantially as a result of this change¹⁷. The main reason being that *Artemether/ Lumefantrine (AL)* procurement by the government is donor funded for which most local manufacturers are not eligible due to international prerequisites that participation is open only to manufacturers with WHO prequalification (PQ) status. Malaria at that time was the leading cause of morbidity. There were no initiatives for local sources for AL or other recommended therapies for malaria. Meri Koivusalo and Maureen Mackintosh cite malaria as one of the failure vertical programs¹⁸ for lack of integration with other strategies. It is important to recognize that changes in policy at international fora may be detrimental to an unprepared local industry. There is need to review and improve existing pharmaceutical industry relevant policies and harmonize regional interventions to ensure steady growth of LPPs and access to quality and affordable medicines. This may require development of a tangible framework for investment in the pharmaceutical sector and additional incentives in order catalyse growth and expansion of the industry's scope to address disease burden and improve product portfolio.

¹⁷ Sarah Vugigi Thesis

¹⁸ *Global public action in health and pharmaceutical policies: politics and policy priorities* IKD Working Paper No. 45 February 2009 Meri Koivusalo and Maureen Mackintosh

In spite of the adequate skills-mix for the *current* level of production of essential medicines, there remains a challenge for the industry in view of the need to move into robust product development work. As such, the training institutions (both public and private) need to re-look at their curriculum to address industry needs. Additionally, the current technological advancements leading to automation, production of targeted dosage forms and process efficiencies require skilled persons for operation and maintenance. Acquisition of these skills will lead to a new era of modernization in pharmaceutical production. Thus, there is need for institutions to establish curricula that is tailored towards providing training that meets the requirements for the industry. Furthermore, collaboration with the academic and training institutions is essential to ensure that the curriculum addresses these needs. Some of the specialized and practical skills may be imparted through short courses

To encourage investment in GMP compliance and GMP enforcement, a pragmatic industry accepted approach is necessary. The categorization plan developed by UNIDO in the Kenya GMP roadmap (categorization into A; B; C - Figure 3) could be adopted to ensure compliance with GMP while at the same time support companies to make incremental GMP improvements. This will provide a way of determining the risk inherent in consistently manufacturing quality products such that a site with sufficient infrastructure and quality systems is rated as low risk and most likely to produce quality products and vice versa. In addition, this categorization facilitates, the GMP inspector/regulator can make priorities for follow-up inspections, licensing of premises and choice of products.

RISK LEVEL	RISK CATEGORY	QUALITY STATUS	BENEFIT/ OPTION/PREFERENCE	
Low Risk		GMP compliant	Any products/formulations	
Medium			All/New products/Formulations	
			New technologies	
		R&D / Clinical Trial products		
High Risk			Conditional GMP	Partnerships/Collaborations
				High preferential procurement
				Any product/Formulation by choice
			Conditional License	new products/Formulation
				Partnerships/Collaborations
			Selected Low risk products/Formulations	
			GMP Improvement plan/licensure	
Note: <ul style="list-style-type: none"> • WHO GMP – basic quality requirement • WHO PQ – optional & based on Expression of Interest & product • Other Accreditation – Optional – specific arrangements by international players for programs or projects • Category C and B upward GMP Improvement plan 				

Figure 3. Categorization model for gradual industry growth and production of -quality medicines.

Source: Author

Through the stepwise approach to GMP improvements, structured incentives can be introduced for different levels of categorization to drive compliance. In such a scheme, category A and B producers may be awarded to produce some critical EML products subject to capacity and GMP requirements, while those in category C are supported to produce low risk products subject to the same requirements as for A & B. As the companies invests in GMP, and capacity, they can apply to be considered for the higher category production. Establishment of a framework for attainment of stringent regulator status of the NMRA in the various countries in the region will be essential for implementation of the categorization process.

The current disconnect between the national priorities and the local pharmaceutical industry arises from the fact that government is not driving the industry towards manufacturing products according the public sector needs. This situation is aggravated by lack of linkage between the industry and academia/research institutions. The weaknesses stated herein may be mitigated through stablishment of industry-research institution partnership for product innovation and research in line with the public health needs, especially essential medicines. The government should derive the R&D agenda for the pharmaceutical industry. There is need to establish a structured process to collect,

synthesize and disperse data that is vital to guide industry and academic/research institutions on national priority R&D needs. This necessitates a symbiotic linkage between universities/research institutions and the pharma industry on collaborative arrangements and sharing of knowledge in health and pharmaceutical research priorities for development. **There is need to ensure that each player/stakeholder is benefiting from the partnership and this way it will be sustainable.** However, it is the responsibility of pharmaceutical industry to proactively develop a blue print for development of industry from all spheres including infrastructure, machinery & equipment, and GMP standards.

Conclusion

The local pharmaceutical industry in the EAC region has limited capacity to produce sufficient essential medicines for domestic market. Establishment of a symbiotic linkage between universities, research institutions and industry on collaborative arrangements in pharmaceutical research is necessary for improving the product range. The government should derive the research agenda in line with national priorities.

Study Limitation

Pharmaceutical manufacturers and KIIIs in Uganda, Tanzania and Ethiopia were informed of the same study. Unfortunately, not much was achieved owing non-responsiveness presumably due to confidentiality concerns, internal policies and/or phobia. Notably, data sharing culture is sub-optimal in the region. As a counter measure, the team used the secondary data/literature and public reference materials for these countries. Similarly, some companies in Kenya did not share their product list or even HR information because of confidentiality concerns.

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