PHARMACEUTICAL PARTNERSHIPS FOR INCREASED ACCESS TO QUALITY ESSENTIAL MEDICINES IN THE EAST AFRICA REGION

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

[Final Report]

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List of Acronyms & Abbreviations

ACTS	African Centre for Technology Studies
API	Active Pharmaceutical Ingredients (APIs)
AU	African Union
ARVs	Antiretrovirals
BE	Bioequivalence
CAPAs	Corrective Actions and Preventive Actions
CROs	Contract Research Organizations
CVD	Cardiovascular Disease
EAC	East Africa Community
EAC-RMPOA	East Africa Community Regional Manufacturing Plan of Action
EM	Essential Medicines
GMP	Good Manufacturing Practice
SPA-PHI	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HVAC	Heating Ventilation and Air Conditioning
JV	Joint Venture
KIIs	Key Informants Interviews
KNBS	Kenya National Bureau of Statistics
LMICs	Low-Middle Income Countries
LPPs	Local Pharmaceutical Producers
NCDs	Non-Communicable Diseases
PMPA	Pharmaceutical Manufacturing Plan of Action
PPB	Pharmacy and Poisons Board
SGCI	Science Granting Councils Initiative
TRIPS	Trade-Related Aspects of Intellectual Property Rights
WHO	World Health Organization
UNCTAD	United Nations Conference on Trade and Development
UNIDO	United Nations International Development Organization
WTO	World Trade Organization

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Executive Summary

The PharmaQ team of consultants was commissioned by Science Granting Councils Initiative (SGCI) in Sub-Saharan Africa through African Centre for Technology Studies (ACTS) consortium to conduct a study to establish the importance of pharmaceutical partnerships in increasing access to Quality Essential Medicines in the East Africa Community (EAC) region (Kenya, Tanzania, Uganda and Ethiopia). The SGCI objective is to enhance knowledge exchange between academia and industry and stimulate private sector investments into research and innovation. Among the key challenges that the SGCI sought to address is the lack of interest from academia and private sector actors for research and innovation collaboration despite successful technology transfer and new products emerging from university laboratories. This necessitates an in-depth inquiry on institutional and organizational arrangements, policies, intellectual property right regimes and other factors that have shaped the emergence of successful public-private partnerships (PPPs) focusing on pharmaceutical manufacturing. In pursuance of this, the PharmaQ team of consultants was commissioned to carry out a study on pharmaceutical manufacturing in East Africa region with the overall objective of establishing the innovation capacity of the East Africa pharmaceutical manufacturing industry, identify the barriers to Public/Private partnerships and to establish a framework for an impactful pharmaceutical cross-sector partnership system which is pivotal in competitiveness of the industry. The aims of the study were:

1. To determine the level of production competence of the pharmaceutical industry in East Africa region regarding manufacture of national essential medicines.
2. To identify policies and regulations that impact innovation and development of new products in the local pharmaceutical industry.
3. To establish mitigation strategies to reduce the product gap between the national essential medicines lists and medicines that are manufactured.
4. To explore how collaborations, financing, research links, and technology transfer can be harnessed to not only boost local production of quality essential medicines in the EAC region, but also increase access to affordable medicines.

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.

The EAC pharmaceutical manufacturing industry comprises about 50 manufacturers of human and veterinary medicine, majority (35) of which are based in Kenya, producing a fraction of the listed national essential medicines. Additionally, a small portion of products for management of non-

communicable/lifestyle diseases (NCDs) are produced in the region yet the prevalence of these diseases is on the rise. Similarly, some of the products used in the treatment of communicable diseases such as HIV/AIDS and malaria are also not produced locally. Furthermore, majority of sterile products are imported. Insufficient local production may be attributed to inadequate human capacity development, slow technology uptake, low financing, minimal Research and Development (R&D) activities, non-conducive regulatory environment for product innovation and minimum partnerships.

The team sought to identify ways of strengthening PPPs for enhancing knowledge exchange to stimulate research and innovation in the pharmaceutical manufacturing industry in the EAC region and suggestions for policy reforms. The aim of the study was not only to assess the capability/capacity of the local manufacturers to produce essential medicines, but to also explore how partnerships can be leveraged to expand the range of essential medicines that are manufactured in the region in order to improve access to quality medicines access through local production. To this end, the ability of the pharmaceutical industry to produce essential medicines and its innovation capacity were assessed. Furthermore, the existing public-private sector relations focusing on research, technology and innovation in this industry were evaluated to identify linkages, and successful partnerships that have worked, but also barriers to PPPs and possible mitigations that pharma industry may have employed thus far.

A survey was conducted in the pharmaceutical manufacturing industry, academia and research institutions in the EAC region. The data collection method encompassed comprehensive review and analysis of relevant literature, face-to-face interviews and filling in of structured questionnaires by respondents from local pharmaceutical producers (LPPs) of medicines for human use, academia and research institutions. About 60% of the 25 LPPs contacted in Kenya responded. There was only one response from Tanzania and another from Uganda. The low response from Uganda, Tanzania and Ethiopia is attributed to confidentiality concerns and policy requirements on data sharing at both cooperate and government levels. As a counter measure, secondary data/literature and public reference materials were used for these countries. The data and feedback were analyzed in line with the objectives of the study. We received feedback from Key Interview Informants (KIIs) from Kenya, Uganda, Tanzania and Ethiopia. There was also feedback from government (Kenya), academic and research institutions in Tanzania (3), and Kenya (5). Their feedback helped identify gaps and shape recommendations.

Key Findings from the Study

Range of Products Manufactured by the Local Industry

The local industry does not manufacture all the products listed as essential medicines. Non-sterile products were the majority and encompassed solids (tablets, capsules), liquids (syrups, suspensions) and semisolids (ointments, creams). Only 28% of the listed essential medicines are produced and about 56 % of these products are solids. The industry focuses mainly on common products and few therapeutic classes, mainly for use in management of communicable diseases. However, the trend is changing as 63% of product registration applications during 2018/2019 period were for non-communicable diseases. At the time of the study, there were about three manufacturers of sterile products at various levels of development.

The production capacity in this industry is underutilized. The average production capacity utilization of LPPs in Kenya (2-Shift basis) is ~43% (tablets, 48%, capsules, 28% and liquids, 52%). It was also noted that there was substantial decrease in new product registration approvals for Kenyan pharmaceutical manufacturers in the period of 2014 to2018. This was due to implementation of a rigorous Common Technical Document (CTD) dossier requirement by the regulatory authority.

Many manufacturers are upgrading their facilities to comply with local and international GMP standards and the requisite quality improvements are capital-intensive. LPPs with such investments are disadvantaged as they compete the same local market with companies that have minimal GMP investment input even though licenced to manufacture. Despite the GMP related investments by LPPs, access to markets remains a challenge. Therefore, a framework to incentivize LPPs to continue to invest in GMP upgrades should be enhanced by key stakeholders, especially government and regulators.

There is adequate skills-mix for the *current* levels of essential medicines production. Majority of technical workforce have qualifications in chemistry, pharmacy, biochemistry and other biological sciences. Notably, there is deficiency of R&D and special skills such as pharmaceutical engineers, validation experts and formulation scientists.

Policies and Regulations Impacting Innovation and Development of New Products

Lack of clear and pragmatic government policy to support LPPs has led to apprehension towards investing in their factories. The current incentives on pharmaceutical inputs and the 15% local preference in public procurement are inadequate to promote access of medicine. There is minimal incentives to encourage investing in facility upgrades and quality improvement programs, especially in

the production of donor-funded products such as antiretrovirals, antimalarials and products for management of NCDs. There is also no framework to encourage R&D of new products. Such a program/framework could easily address the negative effects of donor commodity support withdrawal during the transition periods, issues of sustainability and government funding. There is need for institutional framework that underscores sustainability.[1,2]

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

Lack of strategy for product development in the industry has resulted in most companies developing products that do not address government priority needs. These challenges can be addressed through policy, regulations and enforcement, as well as investments in facility, quality systems/GMP and technology. In addition, technology transfer and collaborations/partnerships are necessary to improve the range of products.

There is also disparity between government priorities and medicines manufactured by LPPs. Most companies indicated that their product portfolio was based on market demand. Furthermore, current training curricula and research priorities by local universities and research institutions are not necessarily aligned to the technical needs of the dynamic industry, e.g. technological advancements.

Collaborations and Partnerships in Pharmaceutical Manufacturing

Most companies stated that partnership is very important to make progress in GMP compliance, market penetration and improvement of product portfolio. Some of the examples of partnerships in the region include Universal Corporation/Strides Shasun and Quality Chemicals/Cipla Quality mergers. At the time of writing this report, there was also an intended PPP between Dawa Group, Merck and the Government of Kenya geared towards vaccine production. These partnerships involve technical transfers.

However, one of the major concerns hampering collaborations and partnerships in EAC is the disconnect between pharma industry and academic/research institutions and lack of information sharing platforms. Partnerships can be harnessed to boost local production of quality essential

[1] The Impact of the Global Fund's Withdrawal on Harm Reduction Programs: A Case Study from Serbia, Eurasian Harm Reduction Network. August 2015

[2] Lost in Transition: Three Case Studies of Global Fund Withdrawal in South Eastern Europe. Open Society Foundations Public Health Program. December 2017

medicines (EM) in EAC through creation of information sharing platforms and agreements with the government as the driver of the agenda for development of EM.

Recommendations

Policy

There is need to review, operationalise and improve exisitng pharmaceutical industry relevant policies and harmonize regional interventions to ensure steady growth of LPPs and access to quality and affordable medicines. The highlights of policy relevant recommendations are listed below.

- Develop a tangible framework for investiment in the pharmaceutical sector and auxilliary industry.
- Develop additional incentives and harmonise the incentive regime in order catalyse growth and expansion of LPPs' scope to address SDG 3 and disease burden. For example, the need to consider tax rebates for LPPs that invest in quality improvements and R&D.
- Establish a high level government advisory panel on pharmaceuticals development that collects and collates data necessary to attract investiment in the sector and provide a forum to bring government, industry and academic/research institutions to discuss national priority needs where LPPs will participate.

Pharmaceutical Industry

The pharmaceutical industry needs to proactively develop a blue print for growing their industry from all spheres including infrustructure development, machinery & equipment and GMP standards. This blue print should also guide the industry's research and clinical trials efforts, new product development and Active Pharmaceutical Ingredients (APIs) manufcaturing. The blue print can also enhance engagement processes between LPPs and government to discuss, pro-industry legislation and regulations and priorities.

Human Resource Development

The pharmaceutical sector requires multi-skilled labour that builds on the basic foundation of pharmacy courses. There is need to review curriculum for pharmacy courses in order to adapt and/or incorporate mordern skills into all courses, i.e. in diploma, graduate and post graduate such as pharmaceutical engineering, biotechnology, fomulation and preformulation.

Collaborations & Partneships

Respective institutions and national governments should encourage, motivate and wherever possible facilitate agreements, guarantees, especially those ralated to LPPs and disease burden. The region should harness the potential of their research institutions capabilities to develop new products through structured collaborations & partnerships that can be public-funded to address region's priorities in line with the national disease burden. This structured approach should ensure that the positive outcomes of these research/development work benefits the citizenry.

Establishment of a symbiotic linkage between universities and industry on colloberative arrangements and sharing of knowledge in health and pharmaceutical research priorities is necessary.

1.0 Introduction

This report presents the findings of a study that sought to identify ways of strengthening pharmaceutical partnerships for improvement of medicines access in the EAC region through local production. The ability of the local pharmaceutical industry to produce essential medicines and its innovation capacity were assessed. In addition, the existing public-private sector relations in the areas of research, technology and innovation in this industry were evaluated to identify linkages, successful partnerships, barriers and constrains to partnerships and possible mitigations. The study was commissioned by (SGCI) in sub-Saharan Africa and implemented by ACTS consortium.

1.1 Context: Access to Essential Medicines in EAC and Africa

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.[3] Access to medicines encompasses the consistent availability of appropriate, adequate, quality and affordable essential medicines at health facilities. However, access to quality-assured essential medicines remains a challenge, particularly in developing countries. More than two billion people worldwide, majority being in developing countries including Africa do not have regular access to the medicines they need. In view of this, there are initiatives to change this scenario by organizations such as the World Health Organization (WHO), United Nations Conference on Trade and Development (UNCTAD), United Nations Industrial Development Organization (UNIDO) and other partners participating in various activities that promote medicines access through local production. This includes 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 work on national intellectual property (IP) legislation reforms. The goal is to enable developing countries to achieve national reliance in essential medicines through local production.

[3] 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.

The African Union Commission for Pharmaceutical Manufacturing Plan for Africa (AUC PMPA) Business plan and the regional initiatives in East and West Africa[4,5,6,7] are key development initiatives meant to ensure that local pharma manufacturing grows because this will support the health agenda of Africa, i.e. provision of services and commodities. Other programs in support of local production include the 'Good Manufacturing Practices (GMP) Roadmap', a stepwise approach for the sector to attain WHO-GMP standard which was first implemented in Kenya in 2015 and has extended to other countries in the East African Community (EAC) region.[8] Individual countries are also showing considerable interest in strengthening local pharmaceutical production through incentives and favorable legislation in the manufacturing sector.

However, EAC still lags in production of essential medicines with approximately 30% of the pharma finished products produced locally and the rest imported - predominantly from India and China. This production output accounts for only a fraction of the locally listed essential medicines. This situation is attributable to quality, technology, skills and policy/regulatory issues. It is also clear that there are challenges related to lack of appreciation or encouragement of research and partnerships in the pharmaceutical manufacturing sector.

Partnerships and collaborations are necessary platforms for leveraging on knowledge and technology transfer to improve the range of products. Currently, there is hardly any collaboration or partnership between the pharmaceutical industry and academic/research institutions in EAC, yet their activities are complimentary. In fact, insufficient R&D collaborations has also been attributed to weak policy advocacy environment - both in public and private sector which are essential in promoting linkages of these two sectors. The cause of this gap has not been thoroughly examined and/or articulated.

[4] Pharmaceutical Manufacturing Plan for Africa Business Pharmaceutical Plan, Addis Ababa. African Union Commission and the United Nations Industrial Development Organization. Ngozwana, S., West, A., Olajide, A. and Byaruhanga, J., 2012.

[5] East African Community Regional Pharmaceutical Manufacturing Plan of Action: 2012-2016. Arusha, Tanzania: EAC secretariat. East African Community (EAC), 2012.

[6] United Nations Industrial Development Organization (UNIDO), Kenya. Kenya Pharmaceutical Sector Development Strategy. Vienna, Austria, 2012.

[7] United Nations Industrial Development Organization (UNIDO), Kenya. [2014]. Kenya GMP Roadmap. A stepwise approach for the pharmaceutical industry to attain WHO GMP Standards. Vienna, Austria.

[8] Kenya GMP Roadmap. A stepwise approach for the pharmaceutical industry to attain WHO GMP Standards. Vienna, Austria. United Nations Industrial Development Organization (UNIDO), 2014.

In view of the above, this study was developed to determine the innovation capacity of the East Africa pharmaceutical manufacturing industry, identify the barriers to public private partnerships and establish a framework for an impactful pharmaceutical cross-sector partnership system. This study covered EAC region (Kenya, Tanzania and Uganda and Ethiopia) with an in-depth analysis of pharmaceutical companies in Kenya in relation to the objectives.

1.1 Objectives of the Study

The aims of the study were:

1. To determine the level of production competence of the pharmaceutical industry in East Africa region regarding manufacture of national essential medicines.
2. To identify policies and regulations that impact innovation and development of new products in the local pharmaceutical industry.
3. To establish mitigation strategies to reduce the product gap between the national essential medicines lists and medicines that are manufactured.
4. To explore how collaborations, financing, research links, and technology transfer can be harnessed to not only boost local production of quality essential medicines in the EAC region, but also increase access to affordable medicines.

2.0 Situation Analysis

2.1 Competence of Local Pharmaceutical Production

2.1.1 Infrastructure improvements

The pharmaceutical manufacturing industry in EAC region comprises about 50 manufacturers, majority (35) of which are based in Kenya. The industry is engaged mainly in secondary production (production of finished pharmaceutical products from raw materials and excipients) of generic medicines for human and veterinary use. Over time many of these manufacturers have embarked on infrastructure improvements necessitated by the GMP assessments to have their facilities attain WHO GMP standards. Additionally, there is also a quest by the LPPs to increase their market share beyond their traditional markets. In 2015, all LPPs in Kenya were assessed against international GMP standard by Pharmacy and Poisons Board (PPB) with support from UNIDO. There were two key points that emerged; i) site related GMP and ii) Quality Management System (QMS) related GMP issues. From the assessments, the LLP developed Corrective Actions and Preventive Actions (CAPAs)[9] to address the site and QMS deficiencies raised. Most LPPs have since embarked on the implementing site related GMP aspects, which include either renovations of the existing facility and/or establishment of new/green facilities. For example, about 10 LPPs are actively working on renovations with about three setting up new units all together. It is also important to note that the facility improvements described above have generally raised the GMP standards in the region making the new entrants and/or mergers to comply and operate at the same level which inherently guarantees quality products. For example, there are four new entrants in Kenya

The quality improvement efforts follow the AU- PMPA business plan endorsed by heads of state in 2005 (Figure 1.0) as a master plan for pharmaceutical sector in Africa. From this plan, an EAC- First Regional Pharmaceutical Manufacturing Plan of Action (2012-2016, revised in 2017) was developed. Kenya has now developed a country specific Pharmaceutical Sector Development Strategy (KPSDS, 2012) and implementing one key strategic component of the KPSDS – Kenya GMP Roadmap. Other countries in the region are in the process of developing the same.

[9] CAPA: Corrective and Preventive Actions are set of actions taken by a pharma company to correct any issues highlighted during inspections, and actions taken to mitigate such occurrence or ensure they do not happen repetitively.

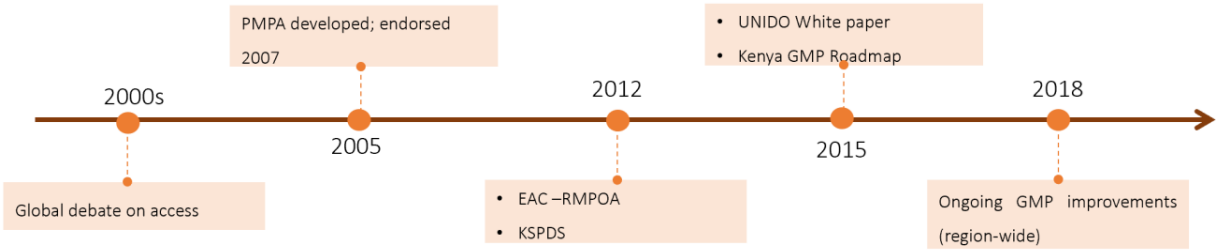

Figure 1.0. East Africa local pharmaceutical manufacturing development timeline

2.1.2 Regulatory Harmonization

Regulatory bodies in the EAC region are engaged in improvement programs in tandem with GMP standards that are steadily advancing globally. One such effort is the harmonization of regulatory approaches in EAC region in order to ensure that there is compliance across the board which synergizes with the GMP improvements.

In order to leverage on TRIPS flexibilities and Doha declaration to access antiretrovirals and antimalarials markets, LPPs worked towards improving GMP standard. As a result, three manufacturers in the EAC region have attained WHO Pre-Qualification (WHO PQ) accreditation. Three companies, i.e. Quality Chemical Industries Ltd (Uganda), Universal Corporation Ltd (Kenya) and Questa Pharmaceuticals (Kenya) have ventured into collaboration with international companies/investors, CIPLA (India), Strides (India) and Mylan (India) respectively; not only for technological advancements and quality improvements, but also as a gateway to expand their markets. This has also increased investor interests in the EAC pharma sector as they also look for value creation (and growth). Be that as it may, there are still several companies in the region that require GMP improvements and it is upon the industry to work with the regulator with support from partners to make this a reality. Furthermore, there are four quality control laboratories that have attained WHO PQ status for quality control of pharmaceutical products (Kenya, 2; Uganda, 1; and Tanzania, 1). These facilities will further enhance the quality status of LPPs in the region.

WTO/TRIPS/Doha agreements are international bona fide instruments that enhance facilitation of LPPs to improve access and be competitive in international markets.[10] However, this needs to be preceded by good manufacturing practices (GMP). A good case is in Bangladesh where between 1982 and the 2000s there

[10] Equitable access to essential medicines: A Framework for Collective Action: WHO Policy Perspectives on Medicines, March 2004 (https://apps.who.int/medicinedocs/pdf/s4962e/s4962e.pdf)

was increased local production to meet >90% of essential medicines needs of the country at reduced costs. This was achieved by leveraging on their exemptions from obligations governing patents and data protection for pharmaceutical products until 2033. As such this has spurred the growth of local industry with several LPPs attaining GMP standards with certification from various stringent regulatory bodies such as US-FDA and UK-MHRA.[11]

2.1.3 Making Access to Essential Medicines Sustainable

About 30% of medicines are produced in the region[12] while 70% are imported. Furthermore, most of the key commodities are funded by donors and this may not be sustainable in the long run. Hence, African Union (AU) developed a pharmaceutical blueprint - the Pharmaceutical Manufacturing Plan of Action (PMPA, 2005) - to ensure development of the pharma industry in Africa for access to quality affordable medicines and reduce dominance on imports.

Despite factories continuing to upgrade their facilities and purchasing new equipment as per their facility improvement plans discussed above, the production capacity utilization remains low (the average utilization was reported as 28% in 2014).[13] The production capacities are underutilized largely due to low access to markets for LPPs and quality considerations. This has direct impact on sales, volumes and investments to improve quality. UNIDO, in partnership with governments in Africa, have supported efforts to help LPPs attain quality standards, a prerequisite for market authorization. This is turn would help LPPs gain more market share and invariably invite them to invest more in quality standards.

2.1.4. Pharmaceutical Skills Sets

The pharma manufacturing is a research-based and technology-intensive industry that requires mixed skills owing to the various functions namely; formulation, production, quality control/assurance, engineering and other support functions such as finance and human resources (HR).[14] Pharmaceutical industry is dynamic with multiplicity of technology and risks associated with the processes therein requiring ongoing capacity

[11] A Review on Revolution of Pharmaceutical Sector in Bangladesh after Liberation War and Future Prospects and Challenges. Sakib Mosharraf et al. Int. J. Pharm. Investigation, 9, 2019,:89.
[12] Second EACRPMPOA 2017-2027.
[13] Production Capacity of Pharmaceutical Manufacturing Industry in Kenya. Sarah Vugigi et al. East Cent. Afr. J. Pharm. Sci. 20, 2017, 3.
[14] Pharmaceutical Manufacturing Plan of Action Business Plan (PMPA).

building, expertise & trainings to ensure safety and compliance. This is very important considering that the sector is linked to the healthcare of the nation.

Pharmaceutical production being an applied science requires continuous development of applicable skills. Currently the academic institutions' curriculum in the region is inadequate for the skills required for the sector. For example, there is a need for specialized skills such as product formulation, pharmaceutical engineering, process optimization and production scale-up to name few. Suffice it to say, other industry relevant trainings supported by donors and other international agencies have helped bridge the gap. Unfortunately, in most cases these are one-offs and/or offered on a need-basis; hence not sustainable.

2.2. Policies and Regulations Supporting Local Pharmaceutical Industry

2.2.1 International Support

More than two billion people worldwide, majority being in developing countries including Africa do not have regular access to the medicines they need. Generally, 30% of the world's population and 50% of those in developing countries lack access to medicines.[10] It is, however, noted that barriers to access to medicines are multiple and can be at multiple levels of any given health system.

The support for LPPs has been an agenda item since the early 2000s necessitated by high mortalities in the least developed countries (LDCs) due to HIV/AIDs; hence a milliard of activities and initiatives came into play to support the least and developing countries establish or support existing LPPs. The analogy goes further to include access to essential medicines as per Doha declaration[15] as a recognition that TRIPS '*accorded the right to protect public health and nothing prevented member countries from taking measures to protect public health*'. Beyond the Doha declaration, the impact of TRIPS flexibilities has continued to shape the policy on access to essential medicines.[16,17] Donor funds have been used to purchase generics of the fixed dose combinations in antiretroviral (ARVs) and anti-malarials, which has led to significant drop in treatment cost and substantial increase in the number of people on treatment. In Sub Saharan Africa, a

[15] Implications of the DOHA Declaration on the TRIPs Agreement and Public Health. Carlos M. Correa University of Buenos Aires June 2002.
[16] Doha+10 TRIPS Flexibilities and Access to Antiretroviral Therapy, UNAIDS Report.
[17] The Doha Declaration Ten Years on and its Impact on Access to Medicines and the Right to Health 20 December 2011, UNDP.

substantial 13-fold increase was noted since 2002 (from 300,000 out of 11 million adults to 5 million from 10.4 million eligible for ARV treatment).

WHO continue to advocate for access to safe, effective and quality medicines and vaccines for all[18] and is one of the targets of the Sustainable Development Goals (SDGs) and a key factor in achieving Universal Healthcare (UHC). In line with this goal, UNIDO has contributed to the improvement of the operational environment and technical capacities through a pragmatic approach of supporting low- and middle-income countries (LMICs) in attaining SDG target 3.8 on *medicines access* in partnership with the manufacturers.

A recent report by UNIDO indicates that many deaths could be prevented if safe and efficacious medicines were readily available to treat patients in Africa who not only lack adequate access of these commodities, but also that the situation is made worse by existence of substandard products and counterfeits in the market. [19] As such, there is strong justification for LPPs because: a) they can be a source of quality medicines and supplicant to substandard and counterfeits; b) easily stop discontinued supplies or prevent stock outs; c) promote local value chain; d) create jobs and technology transfer; e) and could contribute to access of commodities for NCDs and provide a sustainable source beyond donor programs.[20] Considering that medicines are critical for quality healthcare delivery, the availability of these commodities and their quality require great attention[21] and if not addressed, it could lead to poor service delivery, reverse the gains already made and lead to increased out of pocket spending that may exacerbate poverty.

It is imperative that government develop policies that improve access to medicines and to promote access to medicines and other health technologies. It is also important to strengthen implementation of such policies by being intentional through linking these efforts to national priority developmental goals. Such decisions on access on whether to import or manufacture locally are complex and involve a balancing of health and the industrial development policies. Since quality is a point of emphasis, policy formulation must input aspects of sustainability on the basis that the vision for the PMPA is '*to develop a competitive*

[18] WHO Director General Report: Addressing the Global Shortage of, and Access to, Medicines and Vaccines. January 2018.

[20] Source UNIDO Pharmaceutical Production in Developing Countries.

[21] Kaplan (Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines; An Overview of Key Concepts, Issues and Opportunities for Future Research; Warren Kaplan and Richard Laing).

and enduring integrated manufacturing pharmaceutical industry in Africa, able to respond to the continents need for a secure and reliable supply of quality, affordable, accessible safe and efficacious medicines'

2.2.2 UNIDO White Paper on GMP Roadmap Concept

UNIDO white paper and GMP roadmap[22,23] details the design concept of a stepwise approach for the pharmaceutical industry in LMICs to comply with WHO GMP requirements. The approach demystifies WHO GMP as achievable through a phased approach and articulates the fact that quality standards and the risks thereof are specific to facilities. As such, GMP assessments and the gaps identified allows for corrective measures towards attaining WHO GMP that are facility specific depending on their levels of GMP. Compliance with GMP[24] is essential for consistent quality assurance of medicinal products and helps to ensure their quality. It should be notable that quality is inherent in both the facility and product. There are several factors that bring variations in the facility and quality management systems. They include financial, technical, infrastructure, HR and other capacities. The capacity of the national medicines regulatory authority (NMRA) equally influences or impacts and sustains compliance of GMP. Furthermore, the market forces also impact on quality depending on the requirements of NMRA in the export market. These two policy-relevant concepts have provided avenues to further strengthen LPP position and can help shape more policy relevant interventions for the industry.

2.2.3 Africa Medicines Regulatory Harmonization (AMRH)

There are different levels of capacities of NMRA on regulation of the pharmaceutical value chain processes that include licensing of manufacturers and distributors. The AMRH initiative, initiated in 2009[25,26], seeks to strengthen regulatory capacity and encourage harmonization of regulatory requirements with a view of expanding access to quality medicines. It was also meant to provide a platform for sharing experiences, technical know-how and general capacity building (e.g. trainings on regulations and quality). The East African AMRH commenced in 2012 by West African States/West African Economic and Monetary Union

[22] White Paper on UNIDO's GMP Roadmap Concept: Design of a Stepwise Approach for the Pharmaceutical Industry in Developing Countries to Comply with WHO GMP Global UNIDO Project: Strengthening the local production of essential medicines in developing countries through advisory and capacity building support 2015.
[23] Kenya GMP Roadmap, a stepwise approach to achieve WHO GMP.
[24] Technical Series 986 Annex 2 WHO good manufacturing practices for pharmaceutical products: main principles.
[25] WHO Drug Information Vol. 28 No. 1, 2014.
[26] AMRH Newsletter 1Q 2019.

(ECOWAS/UEMOA) and the Southern Africa Development Community (SADC) that launched their regional AMRH projects in 2015.[27] Thus, implementation of the regional AMRH is a concerted effort towards the formation of Africa Medicines Authority (AMA) whose treaty was adopted by the AU Heads of State and Governments during their 32nd Ordinary Session of the Assembly on 11 February 2019 in Addis Ababa, Ethiopia. The progress in EAC MRH has been successful on harmonized technical approaches in joint evaluations of dossiers and GMP inspections. It has also addressed pharmacovigilance activities which may identify nonconforming products or adverse effects, counterfeits amongst others and share information which led to WHO Alert 9/2019[28,29] on falsified products Augmentin tablets and Quinine Sulphate Tablets respectively in the region.

One key deliverable under AMRH is the African Union (AU) Model Law on medical products regulation[30,31] which was endorsed in January 2016. The making of the model law recognized that harmonization of policies, legislation and legal frameworks was a key factor in a diverse regulatory environment. Other forward-looking gains are collaboration and information work-sharing which have improved technical capacities in benchmarking activities in EAC in addition to joint evaluations and GMP Inspections. More products have also been jointly reviewed with over 100 in the Zazibona scheme of SADC as at 2016. Furthermore, a continental regulatory oversight body has been conceptualized at AU by African Heads of States and Governments with support from WHO Regional Committee for Africa for the establishment of the African Medicines Agency (AMA) in response to the enormous health challenges and lack of access to affordable, quality essential medicines[32].

2.2.4 Regulatory Environment

One of the limitations to the development of the pharmaceutical sector is the regulatory climate that has the responsibility of protecting quality of pharmaceutical products on the market. This is attributed to the weak regulatory capacity that allows for licensing of facilities with low GMP and infrastructure status,

[27] AMRH Strategic plan 2016-2020.
[28] Medical Product Alert N° 9/2019 (English version) Falsified Augmentin found in Uganda and Kenya.
[29] Pharmacy & Poisons Board press release on Falsified Augmentin.
[30] African Union Model Law On Medical Products Regulation.
[31] 5th Meeting of the Technical Working Group on Medicines Policy and Regulatory Reforms (TWG-MPRR) Theme: Promoting Domestication of the AU Model Law on Medical Products Regulation
Report October 22- 24 2018, Midrand, South Africa.
[32] African Medicines Agency Business Plan 2016

inadequate manpower to prevent unlicensed practices in the distribution channel (including wholesale and retail) and improper customer perceptions on quality. Indeed, there is insufficient capacity for testing and surveillance capability to monitor local and imported products across the distribution channels. There are insufficient remedial and punitive consequences for firms selling unsafe medicines as most companies assessed represent high risk for product safety. This undermines the genuine quality and by extension manufacturers who have invested in quality improvement.

The interventions suggested to tackle the above-described situation is two pronged – policy reforms and industrial interventions. For policy reforms, there are efforts to ensure there is level playing field where licensing/approvals are linked to the quality requirements as well as promoting regional harmonization of regulatory processes. On the other hand, there is also a need to support LPPs to upgrade their facilities to international standards, streamline distribution and retail networks and capacity building, e.g. trainings for skilled labour. Some of continental, regional and national strategies developed to support local production of pharmaceuticals to promote increased access to life-saving commodities are highlighted in Table 1.

Table 1.0 Comparison of Strategic Approaches [1]

PMPA – continental	EAC (2017)- regional
HR Development	Promotion of competitive and efficient regional pharmaceutical production
Access to product & Technology	Facilitation of increased investment in pharmaceutical production in the region
Access to affordable Finance & Time limited incentives	Strengthening of pharmaceutical regulatory capacity in the region
Regulatory Systems Strengthening & Enforcement	Development of appropriate skills and knowledge for pharmaceutical production in the region
Partnerships, Collaborations & Fostering Business Linkages	Utilization of WTO TRIPS flexibilities to improve local production of Pharmaceuticals in East Africa
Enhancing Market Data Collection & Facilitating Market Access	Innovation, Research and Development within the region's pharmaceutical industry

Source: Extracts by author

Whereas the EAC regional roadmap is geared towards having efficient and effective regional pharmaceutical industry that can supply national, regional and international markets with efficacious and quality medicines, it is true that this process will vary from country to country. For instance, facilities in Kenya, Uganda and Tanzania have been assessed using the UNIDO GMP Roadmap model but at different times (Kenya, 2015; Uganda, 2016; Tanzania, 2018; and Ethiopia, 2016). Consequently in 2019, the member

states launched the 2nd EAC Regional Pharmaceutical Manufacturing Plan of Action for the period 2017-2027 in order to sustain the gains made thus far.

2.3 Gaps between the National Essential Medicines Lists and Medicines that are Manufactured by LPPs

2.3.1. Essential Medicines Lists

WHO has a model Essential Medicines List (EML) that serves as a guide for countries to generate their own EMLs that is frequently updated. It has about 700 entries. In EAC region most countries have their local EML and are used by the national medicine's procurement agencies to stock commodities for public use. It is noted that LLPs produce a fraction of the products in the EML list and mostly 'me too'[33] products. About three companies in Kenya are engaged in sterile production with the majority producing non-sterile products consisting of solids, semi-solids and liquids dosage forms. This is the case across the region.

While there are policies that support local production in the region such as industrial policy, pharmaceutical policies, procurement policies, they are not uniform and present a challenge to LPPs accessing those markets. For instance, Ethiopia has a price preference of 25% for local producers while Kenya is at 15% yet they serve the same regional market. In the spirit of regional block aspiration, it may be prudent to ensure that procurement authorities synchronize their efforts in order to have synergized approach to supporting LPPs. This could include having forums to exchange learnings.

2.3.2 Development of Essential Medicines

Pharmaceutical manufacturing is a science-based industry for which innovation is the primary source of competitiveness. Drug discovery and development as illustrated in Figure 2.0[34] is a complex process comprising four phases namely, drug discovery (laboratory screening of host of compounds), pre-clinical research (laboratory and animal testing), clinical research (testing of drug on humans) and drug regulatory

[33] Me too products; products commonly produced by every player in the sector.

[34] Source: Michael Rosenblatt [2012]. How Academia and the Pharmaceutical Industry Can Work Together. Annual Meeting of the American Thoracic Society, San Francisco, California Michael Rosenblatt1 1Merck, Whitehouse Station, New Jersey.

authority review and approval of the product for sale.[35] Drug discovery begins after years of basic science research that leads to the identification of potential target for drug invention. The process of drug development is intricate and laborious and could last up to 15 years or more. It requires skilled researchers, capital investment, political will and a regulatory framework that protects and rewards innovation. It is a high-risk undertaking, marked with high failure rates as many products fail in the later part of development or are withdrawn soon after introduction into the market due to unanticipated side effects. Escalating R&D costs to identify innovative compounds which may exceed USD 2 billion accompanied by more stringent regulatory approval requirements have caused a decline in new medicine approvals.[36,37,38] Furthermore, expiration of patents on some drugs has meant that the large pharmaceutical R&D manufacturers, which had relied on sales of these drugs for their profitability, re-examine their business models and reinvent accordingly. To this end, mergers and acquisitions are increasingly seen as better collaborative/partnerships strategies to expand business and capacity and to improve profitability.[39] LPPs should therefore be encouraged to embrace this pathway to help them improve their factories and grow their businesses.

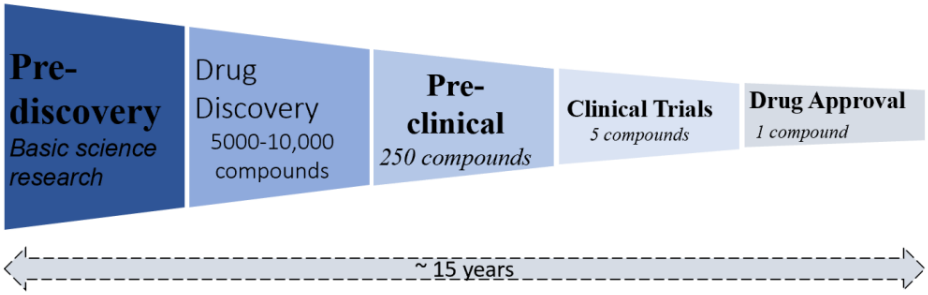

Figure 2.0 Drug Discovery and Development process

[35] Michael Rosenblatt. (2012). How Academia and the Pharmaceutical Industry Can Work Together. Annual Meeting of the American Thoracic Society, San Francisco, California Michael Rosenblatt1 1Merck, Whitehouse Station, New Jersey.

[36] 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.

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

[38] International federation of pharmaceutical manufacturers & Associations (IFPMA). (2017). Pharmaceutical Innovation and Public Health. Facts & Figures 2017.

[39] Yasin Çilhoroz, Cuma Sonğur , 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

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 while Aventis is the consolidation of Hoechst, Rhône-Poulenc, Rorer, Marion, Merrill and Dow. Pfizer is the merging of Pfizer, Warner-Lambert and Pharmacia, which included Upjohn.[40] While these mergers have created big pharma business and pioneered new product developments, several studies have shown that they did not necessarily result in improvement of R&D productivity and new product development.[41] Thus, the pharmaceutical industry, especially in EAC and Africa needs to develop improved merger/collaborative strategies in this area and to mobilize resources from a wide variety of stakeholders in order to remain competitive and develop products for the developing world. In the end, partnerships should leverage on collaborators' complementary expertise, resources and share risks in order to improve capacities and expand market networks.[42,43]

2.4 Collaborations & Partnerships in Pharmaceutical Manufacturing

2.4.1. Research and Technology as an Enabler to Improve Pharma Portfolio

The pharmaceutical manufacturing industry is research-based and technology-intensive. Viability of this industry depends largely on availability of investment capital, technical expertise, reliable quality systems and appropriate legal frameworks. Research & Development is an essential phase in the development of a fully functioning pharmaceutical value chain. The industry players in Africa have not fully embraced research as an important bridge to product innovation and formulation of off-patent molecules. Majority of the manufacturers continue to produce non-sophisticated products with limited specialized formulations to tackle the new emerging trends. Nonetheless, a host of opportunities exist in the region for establishing partnerships arrangements by engaging universities, government agencies, research-based pharmaceutical industries and laboratories to expand their product portfolio. These partnerships are diverse, ranging from

[40] B. Rajesh Kumar (2012). Mega Mergers and Acquisitions.
[41] Remco L. A. de Vrueh1 & Daan J. A. Crommelin (2017). Reflections on the Future of Pharmaceutical Public-Private Partnerships: From Input to Impact Pharm Res (2017) 34:1985–1999.
[42] 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.
[43] 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.

scientific investigations, through to establishing new technologies, to discovery, development and commercialization of a pharmaceutical product.[44] In a WHO background paper Report BP8.1, public-private partnerships were identified as a promising solution for addressing challenges in pharmaceutical innovation where investment in research by the private sector is deemed insufficient. The aim of partnerships is to leverage knowledge, technology transfer and pool-resources in pursuit of a shared research responsibility in new product development with a framework for its execution.

2.4.2 The Role of Partnerships in Improving Medicines Access

2.4.2.1 Global Inequality in Medicine Access

The world's pharmaceutical production is unevenly dispersed, with majority of the manufacturing being concentrated in a limited number of sites located in developed countries. According to the 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.[45] A provision of the Millennium Development Goals encouraged collaborative approaches with pharmaceutical manufacturers to improve medicines access in developing countries. The subsequent post-2015 SDGs, Target 3 specifies the need to develop medicines for diseases that primarily affect developing countries in order to address the disparity in medicines access.[46] Many African countries lack the technical, financial and human capacity to manufacture essential medicines. Initiatives supporting pharmaceutical production in developing countries through Technology Transfer[47] are being implemented by WHO and its partners, with the support of the European Commission. The WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI), the European Union (EU) and United Nations agencies recognize the potential contribution of local production of pharmaceuticals in developing countries and promote local production in these countries through acquisition of technologies and capacity

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

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

[46] United Nations (UN). (2016). Sustainable Development Goals; SDG 3: Division for Sustainable Development, Department of Economic and Social Affairs, UN- New York.

[47] According to WHO, Transfer of technology is defined as "a logical procedure that controls the transfer of any process together with its documentation and expertise between development and manufacture with the intent of enabling technological or manufacturing capacity of the recipient firm.

improvement.[48,49] Technology transfer can be achieved through partnerships and these have been identified as likely solution for addressing challenges in pharmaceutical innovation in developing countries.[50] Developing countries are also encouraged to develop policies consistent with international law governing intellectual property rights, to implement the Agreement on TRIPS and to utilize legal safeguards in the agreement to improve access to medicines.[51] Furthermore, Key research-based pharmaceutical manufacturers have issued voluntary licenses to developing countries for the local production of antiretroviral, malaria and tuberculosis drugs, thus increasing medicines access.[52] This collaborative concept can be engaged to unlock more opportunities for LPPs to produce more products and increase access to life-saving commodities. Collaborations and partnerships can take many forms and shape as briefly highlighted below.

2.4.2.2 Public-Private Partnerships

Public-private partnership (PPP) is a collaborative 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. Sharing the inherent risks of R&D is beneficial to both parties and enables projects to become of interest to potential collaborators. This collaboration fosters operational excellence and a competitive private sector that promotes economic growth and help achieve healthcare objective for the public good.[53] The PPPs may be socially driven or commercially oriented where the developed drug can be sold by the pharmaceutical firm at a profit.

[48] Investment in pharmaceutical production in the least developed countries. (2011). A Guide for Policy Makers and Investment Promotion Agencies- United Nations Conference on Trade and Development 2011.
[49] World Health Organization (WHO). (2011b). Trends in Local Production of Medicines and Related Technology Transfer. World Health Organization, Department of Public Health, Innovation and Intellectual Property. Geneva.
[50] World Health Organization (WHO). 8.1 Public-Private Partnerships and Innovation. Background Paper 8.1 (BP8_1PPPs.pdf).
[51] World Health Organization (WHO). (2016) Advancing the right to health: the vital role of law; Chapter 15; Access to essential medicines, TRIPS and the patent system.
[52] Jeremiah Norris Carol Adelman Yulya Spantchak Kacie Marano. (2013) The Pharmaceutical Industry's Contributions to The UN Millennium Development Goals, economic policy / briefing paper, Hudson Institute, Center for Science in Public Policy.
[53] A. Matter (2014). Public-Private Partnerships in the Pharmaceutical Industry Asia-Pacific Biotech News Vol. 18, No. 08, pp. 21-37 (2014).

Socially driven (Product development) Partnerships, emerged in the 1990's to tackle the global burden of access to medicines in developing nations including those used in management of neglected diseases.[54] The PDPs are non-profit partnerships by the public, philanthropists, academics, private sector and private foundations to drive development of new products in developing countries.[55] For instance, several research-based pharmaceutical companies have responded to WHO's call to develop products for the identified 17 neglected tropical diseases (NTDs).[56]

On the other hand, commercially oriented Public-Private Partnerships in R&D are largely driven by the need to have new business models and competitive strategies to comply with medicine demands by streamlining their R&D processes in order to raise efficiency and productivity. Here, private pharmaceutical and/or biotech companies' partner with publicly funded research organizations (e.g. universities or research institutes) to develop new drugs that can be sold at a profit. The companies may establish small drug discovery units at the manufacturing site and the bulk of drug discovery and development activities through partnerships with specialized Contract Research Organizations (CROs), biotech firms and academia.[57] Working with research partners enable the companies to access unique technologies, tap into public research networks and relevant outside expertise that may increase the project's chance of success.

2.4.2.3 Academia – Pharmaceutical Industry Partnerships

A long history of productive collaboration exists between scientists in academia and the pharmaceutical industry as alluded to in section 2.4.2.2. Data analysis reveals that the transformation of US leading pharmaceutical firms from basic manufacturing to research intensive institutions between the 1920s and 1940s was accomplished through engagement of university-trained scientific and technical staff and by

[54] Pratt B, Loff B. (2013). Linking research to global health equity: the contribution of product development partnerships to access to medicines and research capacity building. Am J Public Health (2013) 103:1968–78.10.2105/AJPH.2013.301341.

[55] Public-Private Partnerships in the Pharmaceutical Industry Asia-Pacific Biotech News Vol. 18, No. 08, pp. 21-37 (2014).

[56] Hopkins AD. (2007). Onchocerciasis control: impressive achievements not to be wasted. Can J Ophthalmol (2007) 42:13–5.10.3129/can%20j% 20 ophthalmol.06-105.

[57] Stevens H, Van Overwalle G, Van Looy B, Huys I. (2013). Perspectives and opportunities for precompetitive public–private partnerships in the biomedical sector. Biotechnol Law Rep (2013) 32:131–9.10.1089/blr.2013.9929.

collaboration and contract research with university faculty.[58,59] Considering the pharma industry research limitations and their focus on market needs, partnering with academic institutions provides a crucial platform for basic research to identify novel molecular targets that can be further evaluated for efficacy and safety. For instance, the innovation and development of anti-malarial and anti-HIV medicines are a demonstration of a successful collaborative effort between academia and the pharmaceutical industry. Despite the need for collaboration between academia and industry, there are some challenges that include inconsistent policies for effective partnerships, irreproducibility/complexity of some data from academia, prolonged approvals and bureaucracy among others.[60] However, the challenges may be mitigated by engaging in R&D that is focused, with common goals, strategy and evolving joint steering committees of experts from both partners to make critical decisions in the process.

In Africa the Academia/researchers – pharma industry collaboration is still low, especially for pharmaceuticals. Most of the partnerships entail grants availed for collaborations between multinationals and Africa institutions, especially for communicable diseases such HIV/AIDs, Malaria, TB and NTDs. While this is laudable, most often, African research institutions serve as test and validation sites for new products in these programs. For instance, Janssen & Janssen are in partnership with Makerere University for Ebola vaccine research work or the GIBEX[61] consortium work focusing on general biotechnology research. Others include the NTDs research work under the Drugs for Neglected Diseases (DND) consortium that involved over 350 collaborations in 43 countries, Africa included.[62] In other cases, the focus has been partnerships for pharmaceuticals capacity building as exemplified by the MERCK pharmaceuticals-University of Nairobi (Kenya) partnership meant to build the capacity of pharmacy/pharmaceutical cadre. This is also a good endeavor as some of graduates may end up in pharmaceutical manufacturing.

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[58] 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.

[59] Michelle Palmera and Rathnam Chaguturub (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.

[60] East African Community (EAC) Secretariat. [2018]. 2nd EAC Regional Pharmaceutical Manufacturing Plan of Action 2017–2027.

[61] Global Institute for Bio-Exploration: An institute that promotes ethical, natural product-based pharmacological bio-exploration to benefit human health and the environment while fostering increased economic and educational activities in developing countries.

[62] An Innovative Approach to R&D for neglected patients: ten years of experience & lessons earned by DNDi

That said, there are few examples of industry- academia engagements that are focused on pharmaceutical products. They range from local to local engagements to Africa-International engagements. This includes malaria research work at the University of Zimbabwe, Medicinal Research work at Muhimbili University (Tanzania) and the Drug discovery work at the University of Cape Town (South Africa). See the summaries below (Exhibit 1 – 3):

Exhibit 1. Bio-assay Directed Evaluation of Traditional Medicinal Plants (Zimbabwe)

In 2001, University of Zimbabwe embarked on a project aimed at commercializing a pure compound from isolated one of the medicinal plants for management of infections in HIV/AIDs and cancer patients. This work was funded by the UNESCO University-Industry Science Partnership (UNISPAR) Programme in Africa that was geared towards promoting university-industry cooperation. The idea of this grant was to encourage active partnership between industry and universities in order to further enhance local drug discovery, development and commercialization.

While the science development process was efficient, the commercialization process was not smooth because of IP related challenges. Even though an international IP for the product was obtained, the negotiations between the University and local pharmaceutical companies was somewhat cumbersome suggesting that there may still be gaps in understanding how drug discovery work and royalties are shared. Be that as it may, this is one of the early bird projects that demonstrate that university-industry engagements are necessary.

Source: University-Industry Partnership for Cooperative Technology Development in Africa, UNESCO 2001

Exhibit 2. Traditional Medicines Research at Muhimbili University (Tanzania)

Tanzania is a host to many joint research projects spanning different subjects. In the case of pharmaceuticals, Muhimbili University, which has a strong expertise in traditional medicine, clinical trials and even diagnostics has demonstrated how research partnerships can work. This goes back to the 90s when they partnered with Beckton Dickinson to develop a rapid diagnostic kit that was later commercialized. Like many others, their successful partnerships have been with more with multinational companies (MNCs) than local players, especially on general research grants.

Through their Institute of Traditional Medicines, the University is leveraging on their inventory of >3000 medicinal plants to develop new efficacious compounds for various applications. It has a pilot plant that has produced several molecules for management of conditions such as asthma, cholesterol and peptic ulcers. While this laboratory is linked to the local pharmaceutical sector backed by MoUs, the uptake of their research services has been low.

Source: Author industry scan

Exhibit 3. Drug Discovery & Development Centre (H3D) at University of Cape Town (UCT) (South Africa)

H3D has proven again that Africa has the capability and capacity to carry out drug research and development for commercialization. The H3D Centre is a fully integrated modern drug discovery & development facility and started in 2010. Their research work entails identification of new molecules for management of various ailments, mainly malaria. The centre has produced stellar results that include a recently patented anti-malarial molecule that attracted funds from Norvatis and Janssen & Janssen (J&J) pharmaceutical companies.

The H3D benefits a great deal from such partnerships with industry. For instance, knowledge exchange between the parties that is critical for research work, support for any drug development process from the onset to clinical stage. For the industry, they will leverage H3D's understanding of the key regional and disease factors that will ensure development of relevant products amongst others.

Source: UCT and H3D.

Overall, the above three case studies illustrate that industry-partnerships exist in EAC and Africa and their maturity are at different levels. There is room to learn from these lessons and work towards strengthening such partnerships.

2.4.2.4 Pharma-to-Pharma Partnership in Africa

There are ongoing global health initiatives with the pharmaceutical industry in Africa aimed at promoting health through access, capacity building and R&D programs. These initiatives focus on priority disease areas in Africa namely; HIV/AIDS, malaria, tuberculosis, tropical diseases and chronic diseases. Technology transfer is one of initiatives being used to improve medicines access for these infectious diseases (Table 2.0).[63] Technology transfer is also being achieved through the sprouting mergers of local companies with

[63] African Union (2010). Strengthening Pharmaceutical Innovation in Africa Designing strategies for national pharmaceutical innovation: choices for decision makers and countries.

research oriented international pharmaceutical manufacturers, e.g. Universal Corporation Limited/Strides-Shasun merger (Kenya) and CIPLA/Quality Chemical Industries Limited (Uganda) and Boehringer-Ingelheim and Aspen Pharmacare (South Africa) to name a few.[63]

Table 2.0. Technology Transfer and ARV licensing in Africa

Technology donor	Technology recipient	Comments
Boehringer-Ingelheim	Aspen Pharmacare South Africa	A non-assert declaration for production of nevirapine
Bristol-Myers Squibb	Aspen Pharmacare South Africa	Transfer of intellectual property and technical know-how. related to manufacturing of Atazanavir
GlaxoSmithKline	South African generic companies: Aspen Pharmacare, Thembalami Pharmaceuticals (Pty) Limited, Feza Pharmaceuticals, Biotech Pharmaceuticals, Cipla Medpro	Manufacture and distribution of generic versions of lamivudine and zidovudine Kenyan generic companies: Cosmos Pharmaceuticals, Universal Corporation received voluntary licensing for ARVs
Roche AIDS Technology Transfer Initiative	Aspen Pharmacare (South Africa), Addis Pharmaceutical Factory (Ethiopia) Varichem Pharmaceuticals Zimbabwe), CAPS Pharmaceuticals Ltd (Zimbabwe), Shelys Pharmaceuticals (Tanzania), Zenufa Laboratories (Tanzania).	Voluntary license for manufacture of generic versions of saquinavir. Since 2008, pan-African training seminars are held for local manufacturers

Source: African Union. 2010. Strengthening Pharmaceutical Innovation in Africa Designing strategies for national pharmaceutical innovation: choices for decision makers and countries.

2.4.2.5 Selected Successful Partnerships Cases in EAC region

There are successful pharma-to-pharma partnerships in the region that are predominantly Joint-Venture (JV) cum technology transfer as illustrated in the three case studies below.

2.4.2.5.1 Uganda: Case study Cipla-Quality Chemical Limited Partnership

- ***Founded:*** 1997 - Quality Chemical Limited (QCL) (Uganda) –was initially incorporated as a distribution company. In 2005, Cipla-Quality Chemical Industries Limited (CiplaQCL) was founded
- **Ownership:** Initially, a JV between Uganda government and Cipla India
- ***Products (by range):*** *S*ix antiretroviral drugs (Lamivudine, zidovudine, nevirapine, efavirenz, tenofovir and fumarate); two hepatitis B drugs (texavir and zentair); and one artemisinin-based combination therapy, Arthemeter and Lumefantrine.
- ***Infrastructure & GMP growth (improvements):***
  - The investment (Cipla and Uganda Government): The government provided free land; set-up of the entire infrastructure and government procurement plan for ARVs worth US$ 30 million per year for 7 years.
  - Growth: Employees increased from 50 in 1974 to currently over 600
  - Value: Increase after-tax: USh6.786 billion (US$1.853 million) (2019)
  - Total assets: USh287.561 billion (US$78.516 million) (March 2019)

Market Authorizations: NDA Uganda; International Committee for Red Cross (ICRC); Kenya Pharmacy and Poisons Board (KPPB); Tanzania Food and Drugs Administration (TFDA); and Rwanda, Namibia, Ivory Coast, Zambia, Zimbabwe, Malawi, Mozambique, Ghana, Ethiopia, Angola and South Sudan. Awaiting South Africa, DR Congo, Ethiopia, Cameroon, Sudan, Senegal, Niger, Benin, Mali.

- **Milestones:**
  - 2005 - WHO GMP and WHO PQ
  - Transfer of technology from Cipla India
  - Implementation of TRIPS flexibilities and Doha Declaration
  - Access to affordable essential medicines
  - May 2017: MoU with Government of Zambia for supply of ARVs, ACTs, hepatitis and other medications valued at ~ USD 10 M per annum for the next 20 years.

- ***Partnerships/Collaborations Type:*** Collaborative agreements on transfer of know-how (technology transfer) of relevance to local research capacity.

- ***Reasons for Partnership:***
  - About 60% of HIV/AIDS and 80% of malaria cases were reported in Sub-Saharan Africa, yet the region could only produce about 1% of the required medicine.
  - Threat to the availability of life-saving medications for developing countries like Uganda.
  - Exploitation of WTO/TRIPS flexibilities.
    The TRIPS agreement flexibilities. Quality Chemical Limited capitalised on this provision and formed a partnership with Cipla (CiplaQCIL) which is WHO approved, to produce antiretrovirals, antimalarials and hepatitis medicines.

Future Plans: The company aims to increase product range and also to venture into primary pharmaceutical production. See annexure for references to the above-mentioned information.

2.4.2.5.2 Kenya: Case Study of Dawa Limited Partnerships

- **Founded:** 1974 -Joint Venture between Government of Kenya and then Yugoslavian government, Slovenia with Kirk pharmaceuticals. In2004: Medisel acquired Dawa Ltd and now operates as Dawa Group.

- **Ownership:** Private by shareholding

- **Products (by range):** Human (Dawa) & Veterinary products (Medisel). Formulations include tablets, capsules, syrups, dry powders and suspensions. The manufacturing Units are separated into an independent Beta lactam and non- Beta Lactam buildings and a different site for veterinary products.

- **Infrastructure & GMP growth (improvements):**
  - Employees increased from 50 in 1974 to currently over 600
  - Tremendous growth since its inception in 1974. However, a steady upward growth was achieved after inception of Dawa Group in 2004. The company has spent over USD 40 million in its upgrading and expansion programs
  - Value: Over US$ 23.7 million (KES 2.4 billion) (2018)

- **Market Authorizations**: Kenya, Uganda, Rwanda, Burundi, Zambia, Malawi, Ivory Coast, Democratic Republic of Congo and South Sudan. Other export ventures include Senegal, Benin, Togo, Guinea, Angola, Madagascar, Tanzania and Ethiopia.

- **Milestones:**
  - 1974 – Dawa Limited founded
  - 1977 – to date supplier to the Kenyan Government through Medical Stores Coordinating unit forerunner to Kenya Medical Supply Authority, KEMSA
  - Since 1980s -Regional and international expansion in distribution network
  - 2004-Dawa limited was acquired by Medisel Kenya Ltd under DAWA group
  - 2013 – Construction of a new Non-Beta Lactam manufacturing plant began
  - 2015- The facilities at Dawa Limited were renovated with new technologies
  - 2015- Acquisition of Kel Chemical limited
  - 2017- Dawa Limited was voted Super brands East Africa's Choice 2017–2018.
- **Partnerships and Collaborations:**
  - 1977 Initial contract for the UK's Beecham Pharmaceuticals which is now known as GSK [1,5].
  - Venturing in a partnership project on vaccine production at the facility

Future Plans: partnership for Vaccine production. See annexure for references to the above-mentioned information about Dawa.

3.0 Methodology & Analysis

3.1 Approach

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 it was 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 and secondary sources. The questionnaire for manufacturing industry comprised of 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/Ministry of Trade & Industry. This study covered the EAC and Ethiopia.

Prior to data collection, the consultants met with Kenya Federation of Pharmaceutical manufacturers, FKPM, which is the umbrella body of pharmaceutical manufacturers in Kenya, to sensitize members on the exercise and its importance. The relevant industry questionnaire was pretested with four LLPs 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. All 25 manufacturers of medicines for humans in Kenya were assessed. A total of five interviews with pharma manufacturing industry CEOs were conducted. Interviews were held with government officials in the ministries of Health and Trade & Industry. More interviews were held with the Kenya Investment Authority and Pharmacy and Poisons Board, Schools of Pharmacy in 3 academic institutions (University of Nairobi, Kenyatta University, United States International University) as well as research institutes (KEMRI) and questionnaires from Research institutions, Training school in Moshi Tanzania (to confirm). All the data and feedback were collated and analyzed in line with the objectives of the study. The results are presented in the discussion section. All the tools and KII interviews are attached in the annexure for reference.

3.2 Data analysis

The Kenya essential medicines list was analyzed by abstracting medicine entries using International Nonproprietary Names (INNs) and 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 shared by companies was performed to identify how many of the products listed on the EML are produced in the region and the main therapeutic classes of interest the major classes of drugs produced by LPP in Kenya. The data and feedback that were collected through the questionnaires and interviews were analyzed in line with the objectives of the study and the findings are presented in the results and discussion section. All the tools and KII interviews are attached in the annexure for reference

3.3 Study Limitation

Identified manufacturers and KIIs in Uganda, Tanzania and Ethiopia were informed of the same study. Unfortunately, not much was achieved owing non-responsiveness presumably due to confidentially 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 (see annexure for pharmaceutical profiles of Ethiopia, Uganda and Tanzania with regards to the objectives of the study). Similarly, some companies in Kenya did not share their product list or even HR information because of confidentiality concerns.

4.0 Results and Discussion

4.1 Production Competence of Local Pharmaceutical Manufacturers

4.1.1 Local Pharmaceutical Production

There are about 60 LPPs in EAC, 35 in Kenya, 11 in Uganda, and 12 in Tanzania according this study. Ethiopia has 9 registered LPPs too. Majority of these LPPs produce non-sterile products – both beta and non-beta lactams; thus, demonstrating their level of competence in production of medicines. The major focus is on solids (capsules/tablets) and mostly the non-complicated formulations commonly known as 'me too' products. Most products manufactured across the EAC region and Ethiopia include antibiotics, gastrointestinal drugs, central nervous system drugs, cardiovascular drugs, anti-diabetic agents, antihistamines, anthelmintics, analgesics and antipyretics, antiprotozoals, respiratory drugs, dermatological preparations, minerals and vitamins. One factory in Ethiopia and Uganda produce large-volume parenterals as well.

In Kenya, 16 companies (60%) of the 25 contacted, gave feedback on their production levels/capacities. From the results, about 56% of the products manufactured are non-sterile solids. Additionally, liquid products constitute ~34% of the products produced (Figure 3.0). This may be because the technology for production of these two formulations is well established and readily accessible. It is also important to mention that LPP focus on tablets because they have demonstrable advantages transferable to the users such as, easy to administer and provides 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. Most of the solids are presented as strip/blister/bulk packs.

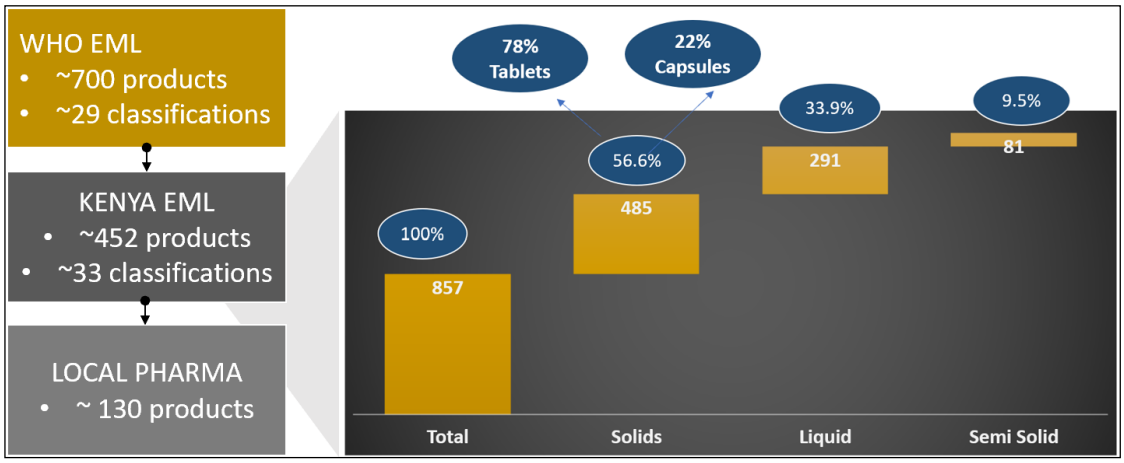

Figure 3.0. Production capacities of LPPs in Kenya (n = 16)

It was also observed that LPP in Kenya produce about 130 products (~28%) out of 452 listed in the local EML, Kenya Essential Medicines (KEML). Though they have mastered production of these products overtime because they do not necessarily require sophisticated technology, the low coverage of the KEML products by LPP (28%) suggests narrow focus driven by market dynamics that are largely public oriented. The same inference could be made about Ethiopia LLPs who produce only 90 of the listed 380 EML products. There is little evidence that LPP 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 profiles/burdens/lifestyle. For example, cancer is now among the top-10 killer disease in Kenya according to KNBS[64], but there are no programs to encourage investments in the development of anticancer products locally yet requirements for facilities are technologically advanced, high level of regulatory requirements. Such investments could include PPPs, JVs and tech transfers. From the essential medicines analysis, anti-infectives, non-opiods & Non-steroidal anti-inflammatory medicines (NSAIMs) and respiratory conditions products are the most manufactured products in the region (Figure 4.0). This 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.[65] The LPPs' focus on a narrow set of products suggests that there is a disconnect between the disease management and pharma manufacturing sector in

[64] Economic Survey 2018 Highlights, KNBS 2018.
[65] Economic Survey report, KNBS 2019.

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.

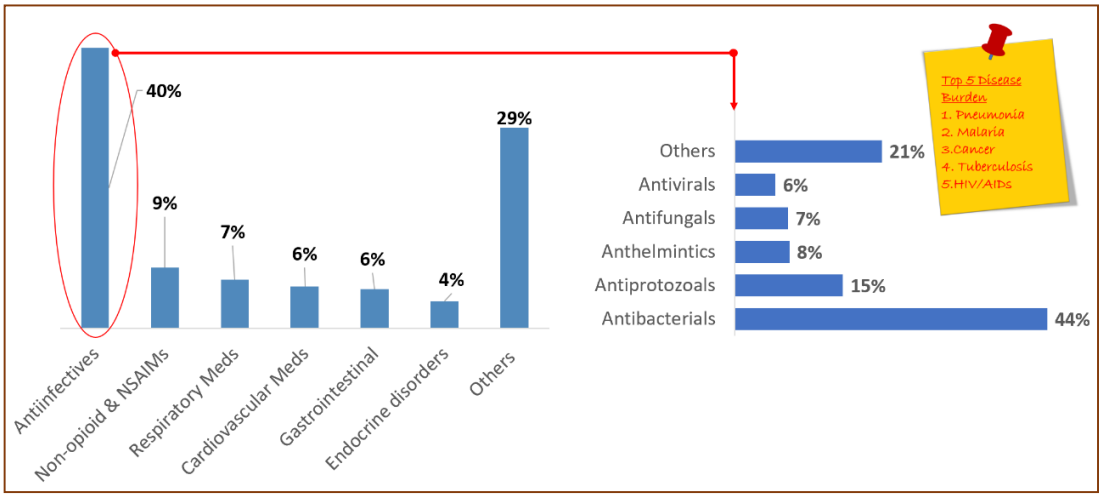

Figure 4.0. EML produced in Kenya against the disease burden

Notably LPPs 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. From the results, the average production capacity utilization of Kenya LPP is 43% for non -beta lactam products (tablets, 48%, capsules, 28% and liquids, 52%). This is an improvement from the last assessment of 2014[13] 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.[13] That notwithstanding, LPPs are competing 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.

4.1.2 Production of Non-Communicable Disease Products

It was also noted that there are attempts by the LPPs to produce NCDs with a major focus on cardiovascular related products. For instance, there are ~74 products registered by LPPs for management of hypertension, diabetes and osteoporosis. This is encouraging considering that LPPs are now producing some NCDs which is a potential for increasing their product profile on the EML and contribute to access to these products. It is also important to note that the product registration pipeline in Kenya has ~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. About 65% of the product registered in the period 2018/2019 were for non-communicable diseases and the balance for mostly communicable diseases (Figure 5.0). As mentioned before, there is no direct linkage between government and pharma sector that enables prioritization of essential needs and maximize on industry capacity to supply EML products. Though access to new product registrations for Uganda, Tanzania and Ethiopia proved difficult during this study, a scan through the product lists of LPPs in these countries suggests that their focus is also on the communicable diseases space.

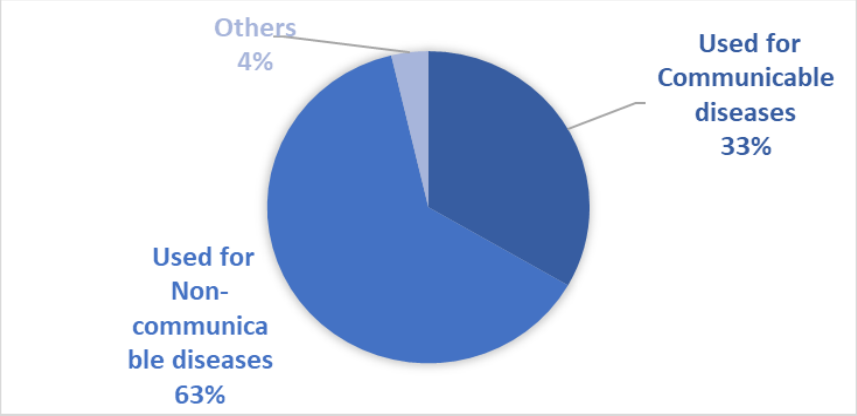

Figure 5.0. New product development categories, 2018/19

4.1.3 Production of Antiretrovirals and Antimalarials

Despite demonstration of production know how of LPP in EAC region, in the case of Kenya, only 6% and 15% of the products manufactured were antivirals and antiprotozoals respectively. 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 requirement which is quite limiting (See Cosmos Case Study below, Exhibit 4). As such, LPPs 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 & lamuvidine) further complicates LPPs' 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, 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 of the new products and inclusion on EML. All these contribute to suppressed attempt at investing more resources for product development by LPPs.

Exhibit 4. Case Study of Cosmos Limited

- **Founded & Ownership:** Cosmos was founded in 1978 for manufacture of quality medicines. It is private family business with more than 500 employees.

- **Products (by range):** Cosmos Pharma has over 300 formulation. They produce both human and veterinary products. Human therapeutic range include products for Infectious Diseases, Gastrointestinal Disorders, Cardiovascular Disorders, Respiratory Diseases, Anti-Diabetics, Dermatological, Anti-Allergy, as well as Central Nervous Disorder. They do not have a Beta lactam facility.

- **Infrastructure & GMP growth (improvements):**
  Cosmos has invested heavily in physical and quality improvements over the years from the 2000s where they successfully participated in the PPP Project (2000) christened '*Improvement of Drug Quality Standards in East Africa*' supported by the Federal Governments of Germany, Kenya and the Private sector. Cosmos achieved compliance and has maintain it.

- **Market Authorizations**: Kenya, Uganda, Rwanda, Burundi, Democratic Republic of Congo, Botswana, South Sudan, Tanzania and Ethiopia. Awaiting Ivory Coast, Zambia, Zimbabwe. Mozambique and Malawi

- **Milestones:**
  - 1979 – Cosmos Limited founded
  - 1979 – to date: supplier to the Kenyan Government through Medical Stores Coordinating unit, a forerunner to Kenya Medical Supply Authority (KEMSA) and also supplies Government of Kenya component of Global Fund products i.e. ARVs; Anti-TB (predominant) ORS-Zinc and other opportunistic infection medicines.

- **Partnerships and Collaborations:**

  2004 – Voluntary licensing for ARVs, the first in East Africa region from GSK and Boehringer. There was no arrangement for technology transfer the process for tabletting was common knowledge.

- **Public procurement**:
  Though compliant with WHO GMP, Cosmos has not been successful in using their capacity to bid for large global tenders due to PQ challenges. However, Cosmos has intermittently supplied quality products during supply shortfalls by foreign manufacturers of ARVs and TB products. For example, between Feb 2010 and April 2013 it supplied ARVs worth over USD 7.3million and between Feb 2010 and Nov 2018 supplied TB products worth is over USD 9.1 million.

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 LPPs take 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.

4.1.4 Skills Set for Pharmaceutical Sector

In addition to having GMP compliant production facilities, there is need for a mix of qualified and skilled personnel to run the facilities. To this end, skills set and talent for pharma sector is critical. In this study, there were a total of ~3551 personnel from 16 companies in various departments (Figure 6.0). Less than 20% have diploma and above (degrees) with the rest being on-the-job training. The supervisory and managerial tasks for quality control (QC)/quality assurance (QA), and production departments are led by graduates with BSc, BPharm, MSc or PhD. Other skills include craft certificates and O-level qualifications for various skills in plumbing, computer packages, electrical engineering, boiler operation, procurement and administration. The same picture is likely to be the same across the EAC region as data collated on Ethiopia and Uganda showed that the number of employees in the sector is ~2000 (2010) and ~1800 (2014) for Ethiopia and Uganda respectively (See Country Profiles Information in the Annexure). Based on Kenya's analysis, it is likely that other EAC countries will have the same skills profile.

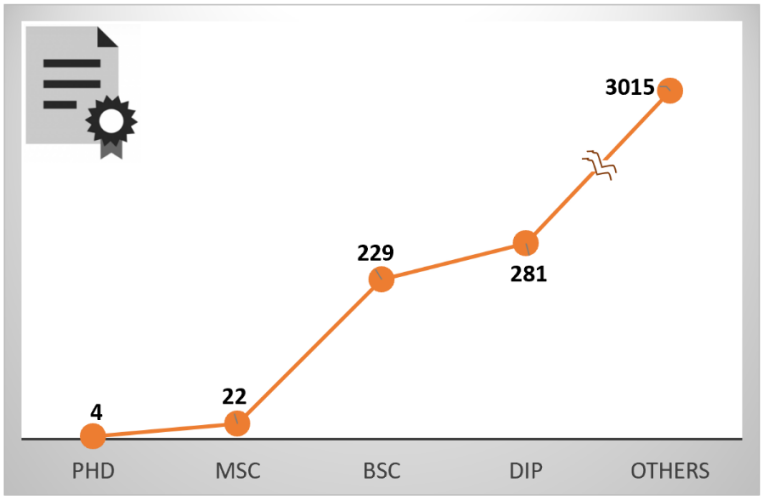

Figure 6.0. Qualification profile in Kenya's Pharmaceutical Sector (n=16 companies)

Based on this data (Figure 6.0), there is adequate skills-mix for the *current* levels of production of essential medicines – which is largely 'me too' production. Majority of the qualification are in chemistry, pharmacy, biochemistry etc. There is deficiency of R&D and special skills such as pharma engineers, validation experts and formulation experts, process engineers, HVAC[66] and IT specialists. This remains a challenge for the industry, especially where there is need to expand scope and move into robust product development work, which require more specialists (Figure 7.0). As such, industry's growth has indicated that 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. In this study, LPP placed more emphasis on the need of R&D, process formulation and optimization, validations and technology transfer skills suggesting that these are the priority areas that require attention. They felt comfortable with production, QMS and documentation skills. In view of the above, there is need for institutions to establish curricula that is tailored towards providing training that meets the requirements for the industry. In addition, collaboration with the academic/training institutions (locally and abroad) is essential to ensure that the curriculum addresses these needs.

[66] 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.

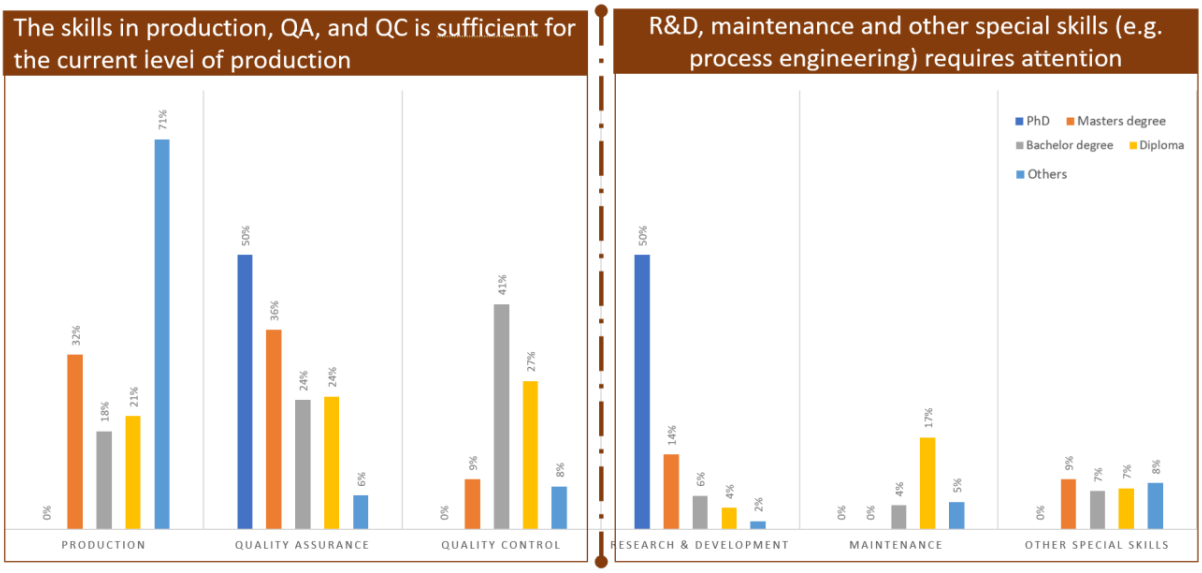

Figure 7.0. Skills matrix analysis: skills needs by industry

4.2. Policies and Regulations Impacting Innovation and Development of New Products in the Local Pharmaceutical Industry

4.2.1 Industry Sentiments

The drivers for investment are not necessarily the market alone, but also the policy environment. In order to improve product development scenario, there is need for supportive policies and regulations for the industry. Feedback received from CEOs of some leading companies indicate that the lack of clear government policy to support LPPs has led to LPPs to be apprehensive when it comes to investing in their factories, considering that the prevailing technologies & machines are working. While the drivers for investment include a) policy/overall policy on export, b) market access, c) personnel for industry, and d) business environment, the industry's view is that there is no adequate incentive to invest in facility upgrading and quality improvement programs, especially in the production of donor funded products such as antiretrovirals, antimalarials and NCDs commodities. The executives feel that the ROI[67] from such effort is somewhat negligible.

[67] ROI: Return on Investment.

Byte: Most CEOs indicated that there is no clarity on ROI in the pharma sector because the market is not readily accessible. Furthermore, LPP find the regulatory environment somewhat discouraging as it offers little protection from counterfeits and unscrupulous business entities. As such, they opine that the risk underlying quality improvement versus business is a key factor behind ROI considerations

Most LPPs indicated that policies and regulations are necessary for the growth of the industry. The LPPs agree that there are policies directly related to the pharmaceutical manufacturing industry, e.g. the price preference for procurement of local commodities, and zero tariffs on most pharmaceutical inputs. In the latter case, the process provides for LPPs to invest and claim tax rebates thereafter. Unfortunately, this rebate process is bureaucratic and takes time to conclude ostensibly holding LPPs finances/cash flow that can be reinvested. Additionally, imported finished products are zero rated, enjoy export compensation in their countries of origin and readily available in the market once it is landed whereas LPPs' receive pharmaceutical inputs and embark on a long manufacturing process which takes time thus increasing their costs. This is further exacerbated by the public tenders that are awarded based on the least bidder without due regard to other considerations. In the case of Kenya, there is also an inconsistency with price preference where distributors registered locally enjoy a 10% while a fully-fledged manufacturing firm has a 15% preference. The 5% differential between the two entities is insignificant considering the intensity of activities involved in pharmaceutical production. It is not surprising that most of the CEOs interviewed felt strongly that there is inadequate consultation with pharmaceutical/manufacturing experts when formulating policies and that policies/regulations that impact local manufacturing industry are incoherent (Figure 8.0).

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.

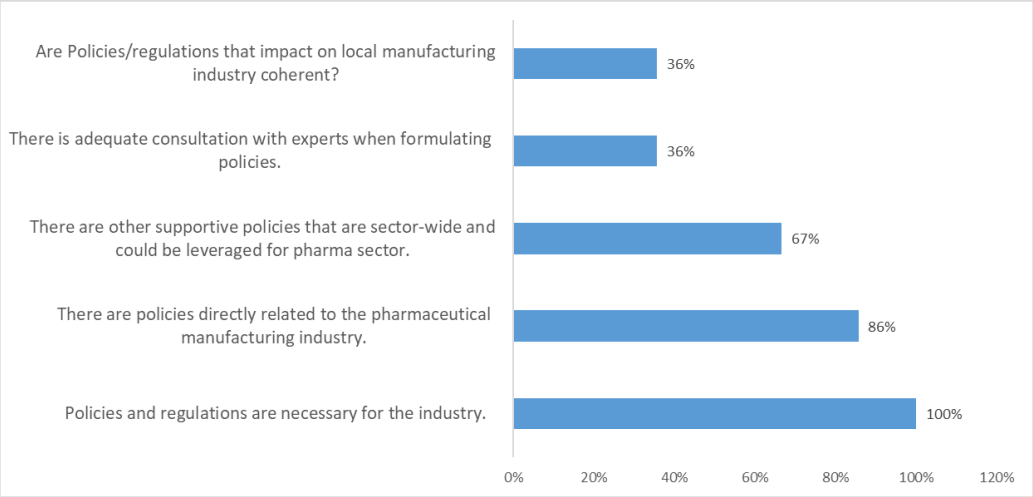

Figure 8.0. Impact of policy decision in the pharma production

4.2.2 Policies and Regulations in Relation to Product Registrations

Kenya local pharmaceutical companies have products registered by NMRAs in several countries namely; Uganda, Kenya, Tanzania, Malawi, Ivory Coast, Zambia etc. It is also noted that about four LPPs have received EAC joint inspection approval, GF, UNICEF, PICS, PFSCM, UNIDO and WHO. Be that as it may, it was observed that in the period 2015/16 there was a 61% reduction in product registrations in Kenya (Figure 9.0). This may be due to change in medicines registration application dossier format from the old system to the stringent Common Technical Document (CTD) format and hence slowing down of the registration process. Fortunately, there are on-going activities on EAC harmonization of product registration and GMP inspections. As such, there is opportunity to develop framework and roadmaps to manage the transition process in order to avoid fluctuation in products availability in the market due to registration constraints that are not necessarily quality related, but more documentation related. This may inadvertently jeopardize access to life-saving commodities to address the disease burden priorities. Further, development of a prudent scheme for joint GMP inspections to prequalify regional manufacturers and their products in order to prioritize registration and market authorizations of the same, in member states, will serve to hasten the process and infer confidence in the harmonization process.

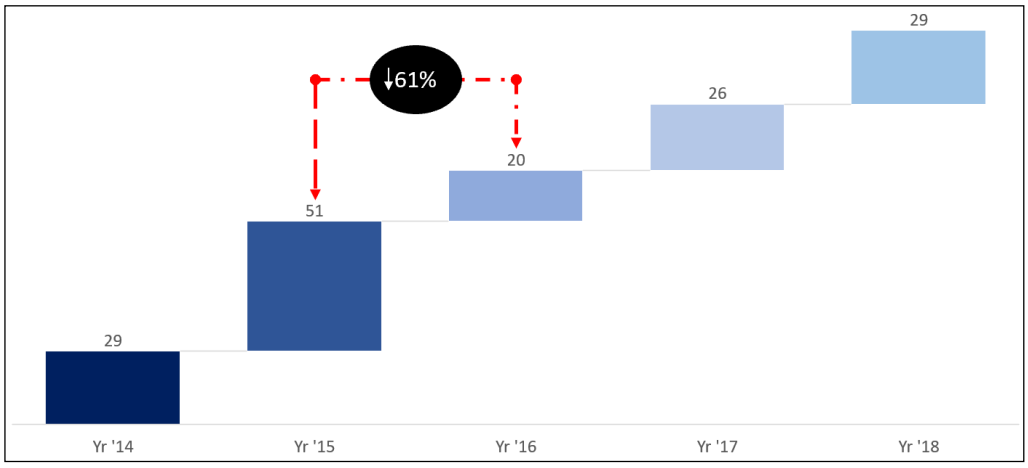

Figure 9.0. No of products registered by your National Medicines Authority in the last 5 years

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

The LPPs do not have the requisite know-how and capability to manufacture all formulations. This is true for all manufcaturers in the EAC region. However, constant skills development and investment in new pharmaceutical technologies can lead to increase in production of quality medicines, including sophisticated ones.

4.3.1 Perceptions about Pharmaceutical Industry Gaps

Identification of the most pressing isssues contributing to the observed gaps between locally manufactured products and those listed in the local EML list was performed by gauging the perception of the LPPs players on what they thought was critical. In general, most companies believe that HR /training, GMP compliance, manufcatruing and financing/markets are important factors to ensure succesfull production of essential medicines (Figure 10). Surprisingly, partnership was rated the least in their perceptions. Presumably due to the fact that partnership is not well understood and the fear of loosing propriatry. It was also observed that majority of the LPPs prioritizes on-demand products such as OTCs than medicines in the EML because of the need to recoup investments quickly.

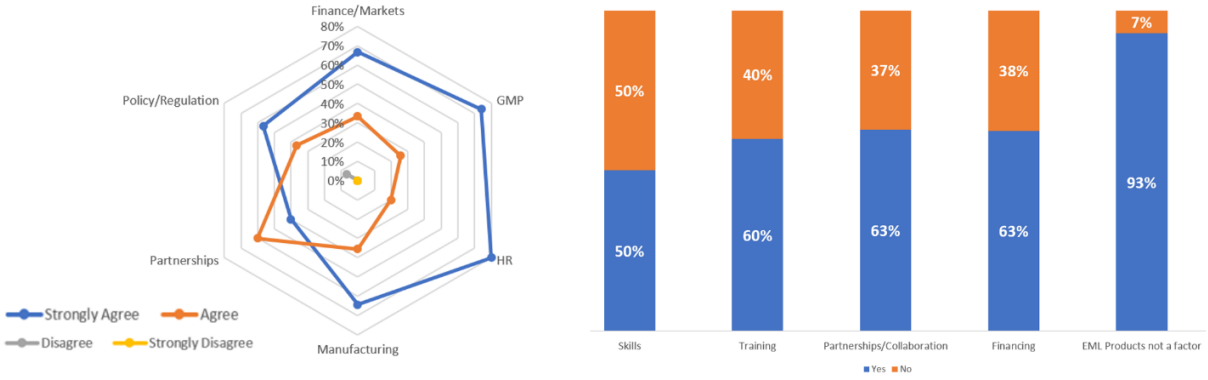

Figure 10. Perception on factors affecting pharma manufacturing vs industry needs

Surprisingly, it was noted that most executives believe that skills is not a major factor for production of EML with 50% of the respondents saying they saw no need to invest in skills. When asked the same question differently, 60% agreed that training was important. The disconnect between the link of skills and success to produce essential drugs may explain why the industry employs few highly qualified workers as depicted in the qualification profile analysis (Figure 6.0). Overall majority believe that partnerships/collaborations and financing are major factors to consider in order to imporve pharma manufcaturing.

4.3.2 Non-compliance to GMP Suppresses Industry Growth

It is clear that GMP still contributes immensely to the gap, especially with products that require stringent operations such as parenteral preparations. Currently the lack of strigent regulations to enforce GMP standards across the board allows for many entrants into th market without clear regulatory process for them to follow. Hence, companies that have heavily invested to be GMP compliant as per regulatory requirements feel that the is no level-playing field due to cost of compliance that makes them less competitive than non-compliant companies. For this reason, companies tend to avoid investing heavily in product development because of the regulatory gap. This concern has been raised with regulators by the stakeholders before.[68] To address this issue, there is need for a pragmatic industry accepted approach. The categorization plan developed by UNIDO in the Kenya GMP roadmap could be a good starting point to ensure that GMP is adhered to while at the same time support companies to make incremental GMP improvents. This provides a way of determining the risk inherent in consistently manufacturing quality

[68] Discussions with CEOs from the pharma companies

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. The GMP roadmap categorization into A; B; C (Figure 11) has also the other advantage of determining the root cause of inferior quality, and the CAPA to fix the problems. In addition, this categorization of facilitates, the GMP inspector/regulator can make priorities for follow-up inspections, licensing of premises and choice of products. Categorization processes follows GMP roadmap implementation already ongoing in EAC. However, it needs to be considered strongly as a policy to stimulate the improvements and enforcement of GMP (see Policy Brief No 1 in the annexure).

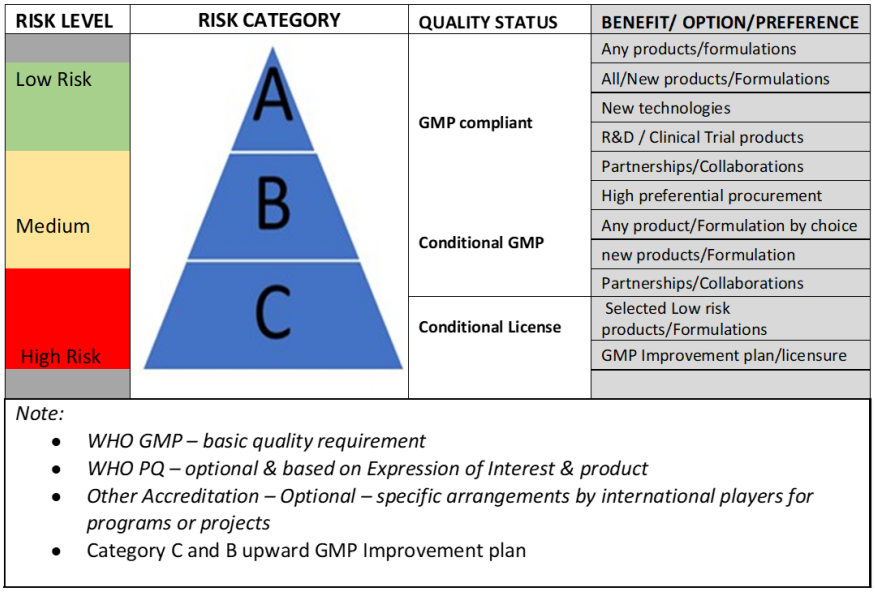

Figure 11. Categorization model for enhancing gradual industry growth and production of high-quality medicines. Source: Author

The categorization approach provides a robust evidence based, scientifically sound way to manage pharmaceutical manufacturers to ensure they attain WHO GMP in their facilities (Figure 11). This risk categorization is a suitable tool for benchmarking GMP compliance of companies and can also be used to monitor companies' development towards full WHO GMP compliance[8] Suffice it to state that enforcement agencies can use their mandate to drive upgrades in domestic facilities by agreeing on the CAPAs and follow-ups on implementation. This way, the national medicines regulatory authorities can help drive industrial growth while ensuring international standards are met. 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 (Figure 11).

4.3.3 LPPs Strategies for Developing New Products and Financing - Market Focused

In a bid to understand LPPs' new product introduction to the market and how this contributes to the gap between products produced in-country versus the EML products, we asked the companies to shade light on their strategies for product development. Most companies indicated that their product portfolio was based on market demand and not necessarily on the need to develop new products to address government priorities. For this reason, their product development pathway is somewhat sub-optimal (Figure 12)

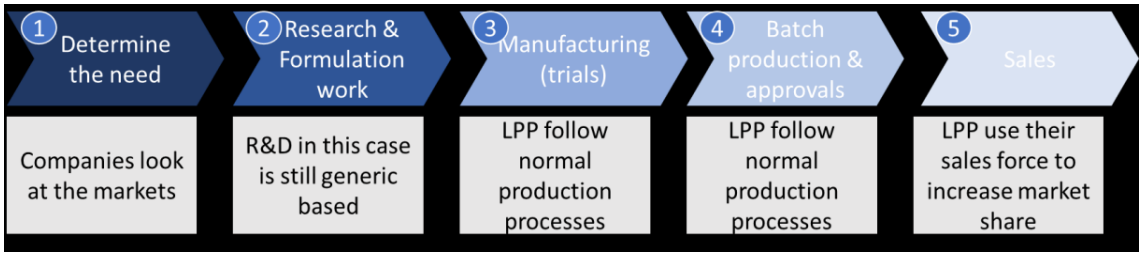

Figure 12. LPPs' product development pathway

Pharmaceutical research and development (R&D) capacity is considered the next phase of growth for the local pharma players. There are some regional efforts to promote this such as the R&D work at Muhimbili School of Pharmacy and the Kilimanjaro School of Pharmacy in Tanzania supported by GIZ and the Kenya Medical Research Institute (KEMRI) but are at nascent stages.

Pharma industry being one of the most stringent manufacturing sectors owing to its links to healthcare, investments in this sector are considered complex by many including the banking sector that is a source of finances. Finance Institutions such as banks indicate that pharma manufacturing sector is risky; hence, they do not often agree to extend credit to the sector for investment and this has suppressed the sector further. As such, access to low interest financing remains a challenge to be addressed.

4.3.4 Mitigations to Reduce the Product Gap between the National Essential Medicines Lists and Medicines Manufactured by LPP

In general, the factors discussed in section 4.3.3 contribute to suppressed production of essential medicines in EAC. However, LPPs have substantial know-how and capability to manufacture pharmaceutical products

and can be encouraged to venture into new spheres of growth, if proper measures are put in place. Taking into consideration data gathered, industry feedback and other key informants, the following key proposal to support LPPs function in the bigger context of health and economic development have been proposed for consideration. The information is summarized in Table 3.

Table 3. Gaps versus Mitigation strategies to enhance LPP participation

Gap	Proposed Mitigation Approaches
1. There is little Investments in facility improvements and new technology	• Clear incentives should be set up to encourage re-investments and quality improvements on licensed existing facilities and attraction for Direct Foreign investment. For example, consider tax rebates when LPPs invests in GMP. This will require clear policy guidelines and roadmaps for implementation.
2. Know-how and skill-mix is inadequate to respond to LPPs industry needs	• LPP industry skills needs are beyond the scope of pharmacy training. Hence, there is need for integration of skills/training in order to respond to these needs. For example, there are challenges in the installation of utilities such as HVAC and water purification system that require adherence to special installation requirements. Therefore, there is need for specialized trainings in order to build capacity in the region for such skills. This requires a cross-collaboration between schools and that includes pharmacy and engineering. This applies to other quality management system requirements.
3. Attaining international GMP compliance remains a challenge in the region	• There is already established investments at various levels of GMP in the region. A framework for stepwise quality improvement for lowering the risk is also in place. However, the regulator remains challenged. There is need to enhance the capacity of the regulators and have a defined inspectorate framework for enforcement and categorization (see annexure), especially for the LPPs. There is need for regular GMP forum to be convened by the regulator for providing updates and tracking of GMP improvements that leads to compliance levels and categorization evaluation.
4. The policies to support LPPs are fragmented and incoherent	• The harmonization program in the region does not clearly articulate the industry needs and regional regulatory requirements. There is need to re-engage the industry to develop a new framework and timelines to support harmonization processes such as pool product registration and joint inspection of facilities. There is need to strengthen the regional regulators' forum to allow sharing of information and development of strategies to ensure growth. • Medicines have a business-health interface that invokes socio-politico and economic considerations. Furthermore, the advisory services for pharmacy policy formulation and implementation is weak in the region. There is need to establish a pharmaceutical services advisory panel, at high level in government, to monitor the market, institute price referencing and monitoring, recommend incentives and update local EML. The panel will also advise the LPPs on government priorities in relation to disease burden and medicines security. An establishment for a Pharmaceutical directorate is needed to support this function. This advisory team will enhance the interface between universities, research and industry to encourage collaboration and ensure tracking of trends in technology, know-how and assist governments with policy making.
5. Collaborations/Partnerships across LPPs, government and academic/research institutions are weak	• There is need for creation of an industry-research institution partnership for product innovation and research in line with the public health needs, especially essential medicines. This includes exploring traditional medicines as a source of medicines. This partnership will run on the strength of not only product development, but also on intellectual property agreements and assurance. A percentage of the royalties could be ploughed back to more research in order to make this sustainable. A data base to capture the level of performance of the industry is necessary as this will be useful for potential investors looking for partnerships. The same information will be critical for policy makers and governments.

4.4 Collaborations & Partnerships to Support Local Pharmaceutical Sector

In this study, it was established that Kenya LPPs manufactures only 28% of the medicines on the national essential medicine list. Like many other African countries, Kenya does not have enough technical, financial and human capacity to produce all medicines on this list. Pharmaceutical partnerships and collaborations serve as conduits for improving access through initiatives such as R&D partnerships, technology transfer, JVs, acquisitions and quality improvement programs. UNIDO has partnered with many developing countries including the EAC region with the aim of capacity improvement to increase access in essential medicines in these countries. There have been efforts by two manufacturers, Universal Corporation Limited and Cosmos Limited 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 PQ requirement since procurement of ARVs is donor funded. 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. They also have a research lab that is linked to the local pharmaceutical sector backed by MoUs. However, the uptake of their research services has been low.

Most companies believe that partnership is very important to make progress in GMP compliance and market penetration; more so partnership with stringent regulatory authority (SRA) approved partners (Figure 13). They also are congnizant of the fact that collaborations require investments for them to work. When asked about collaborations with other parties, 46% indicated that they had partnerships, but these are operational collaborations (Figure 13). Some companies have joint ventures e.g. Autosterialile, a sterile manufacturer, Dawa Limited and UCL. However, one of the major concerns hampering collaborations and partnerships in EAC region is the absence of information sharing platforms, especially with the academic/research institutions (Figure 13).

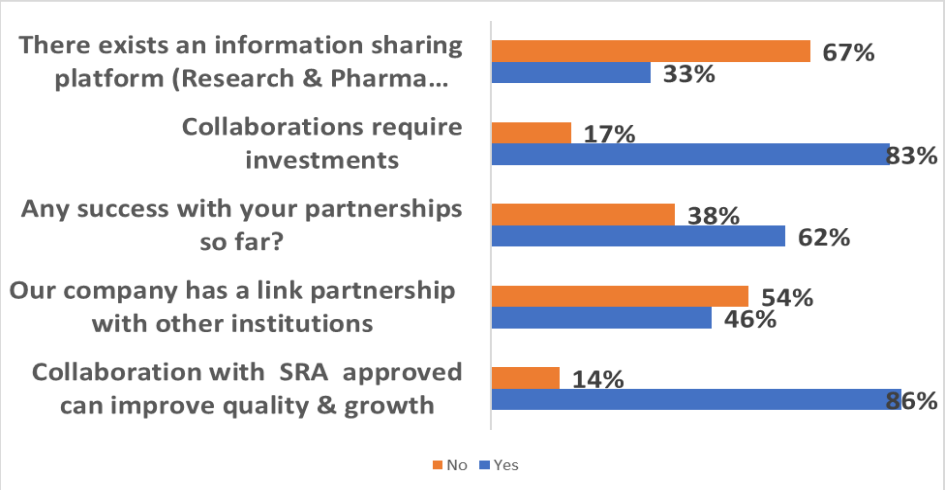

Figure 13. Importance of collaborations and research links in local production of essential medicines

Excerpts of responses from academia, industry and government touching on partnerships are given below

Exhibit 5. Interview excerpts

Institutions	o There is glaring disconnect between university and industry with no robust platform for engagement o The industry is dominated by investors merely for profit and not for holistic development of pharma sector o Formulation and research are strange to LPP and Industry has confidentiality concerns with the universities. There is also need for Industry ownership must move from family to corporate governance to promote industry skills
Industry	o Universities have not made efforts to connect with industry. There is no robust platform for engagement o Agreements, protocols and criteria for industry/university collaboration are weak o R&D at the moment appears to be an academic exercise rather than having impact on society o No incentives to promote new molecules and new product research
Governments	o Most interviewees indicated that MOH should set the R&D agenda and develop complementary centres of excellence and research priorities that will leverage on industry capabilities in terms of product formulations, treatment regimes, operational efficiencies amongst others.

5.0 Conclusion and Recommendations

This Study was aimed at establishing the innovative capacity of the East Africa pharmaceutical manufacturing industry, identifying barriers to public private partnerships and establishing a framework for an impactful pharmaceutical cross-sector partnership system for increased access to essential medicines. From the findings of this study, it is evident that the EAC region produces fraction of the listed essential medicines and the production capacity is underutilized. This study identifies cross cutting weaknesses and gaps that contribute to the slow growth of the industry that are cross-cutting from policy, skills to quality standards. When addressed satisfactorily, will speed up growth and ensure a sustainable source of safe, effective quality medicines as a positive response to SDG #3 and AUC/PMPA business plan and the regional pharmaceutical plan of action. This study highlights different scenario and from literature, fact findings and discussions, establish the need to enhance collaborations and partnerships across the board so as to create a government-industry-research institutions troika for discussing health priority needs that the pharmaceutical industry can support government to achieve, i.e. access to medicines. More importantly, is that government should take a central role to facilitate such partnerships, ensure effectiveness and synergy of the same. Results from this study have allowed for development of recommendations that will potentially address the gaps in the industry, consolidate and streamline efforts being undertaken to catapult growth of LPP in improving access to essential medicines. The recommendations are presented below as high-level summaries of the mitigations for the gaps identified. More work will be required to pilot and test these recommendations.

Recommendations

This study acknowledges several upward improvement examples in pharmaceutical manufacturing industry in the EAC region. However, it has identified areas of mutual concern that would stimulate the LPP growth and contributive effectively to the healthcare system plus economic growth as an objective enshrined in the AUC/PMPA. There are inadequacies, gaps, disconnects, incoherencies and weaknesses which are stated in this report. The following actions, which are not exhaustive but within the context of the study, may be required for enhancement of medicines access through pharmaceutical partnerships in the region.

1. Policy

There is need to review and improve exisitng pharmaceutical industry relevant policies and harmonize regional interventions to ensure steady growth of LPPs and access to quality and affordable medicines. The highlights of policy relevant recommendations are listed below.

- Develop a tangible framework for investiment in the pharmaceutical sector and auxilliary industry
- Develop additional incentives and harmonise the incentive regime in order catalyse growth and expansion of LPPs' scope to address SDG 3 and disease burden. For example, the need to consider tax rebates for LPPs that invest in quality improvements and R&D.
- Establish a high level government advisory panel on pharmaceuticals development that collects and collates data necessary to attract investiment in the sector and provide a forum to bring government, industry and academic/research institutions to discuss national priority needs relevant to the industry for LPPs to participate in them. (see Policy brief No 2 in the annexure).
- Establish a framework for attainment of stringent regulator status of the NMRA for international recognition and benchmarking GMP compliance of companies. (see Policy brief No 1 in the annexure).

2. Pharmaceutical Industry

The pharmaceutical industry, needs to proactively develop a blue print for growing their industry from all spheres including infrustructure development, machinery & equipment, and GMP standards. This blue print should also guide the industry's research and clinical trials efforts, new product development and Active Pharmaceutical Ingredients (APIs) manufcaturing. The blue print can also enhance engagement processes between LPP and government to discuss, pro-industry legislation and regulations and priorities. This will provide guidance to the government to formulate supportive policies and the respective implementation programs.

3. Human Resource Development

The pharmacuetical sector require multi-skilled labour that builds on the basic foundation of pharmacy cources. There is need to review curriculum for pharmacy courses in order to adapt and/or incorporate mordern and applied skills such as quality management systems principals, pharmaceutical engineering, machinery qualification, process optimization and scale-up operations into all courses at graduate and post graduate levels. Some of the specialized and practical skills may be imparted through short courses.

4. Collaborations & Partneships (see Policy brief No 2 in the annexure)

- Establish industry-research institution partnership for product innovation and research in line with the public health needs, especially essential medicines. This should include exploring traditional medicines as a source of medicines. This partnership shall run on the strength of product development, intellectual property agreements and assurance. Respective institutions and national governments should encourage, motivate and wherever possible facilitate the agreements, guarantees, especially those ralated to LPP and disease burden.
- The region should harness the potential of their research institutions capabilities to develop new products through structured collaborations & partnerships that can be public funded to address the priorities in line with the national disease burden. This structured approach should ensure that the positive outcomes of these research/devlopment work benefits the citizenry.

- 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 necesitates a symbiotic linkage between universities/research institutions and the pharma industry on colloberative arrangements and sharing of knowledge in health and pharmaceutical research priorities for development.

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6.0 Annexure

6.1 Country Pharmaceutical Profiles

6.1.1 Pharmaceutical Manufacturing in Ethiopia

Item	Information
Annual pharmaceutical market in Ethiopia (2015, growing at 25% per annum)	$684Million in 2018
Market share of Local manufacturers	15%-20%
Number of importers	200
The number of active manufacturers. (Please note: no API production in Ethiopia)	9 firms
	One firm manufactures empty gelatin capsules, and 5 are engaged in producing medical supplies such as syringes, absorbent cottons, gauzes, bandages and sanitary products.
Oldest plant inception	1964
Product range	• Only 90 of the more than 380 products on the national EML • Antibiotics, gastrointestinal drugs, central nervous system drugs, cardiovascular drugs, anti-diabetic agents, antihistamines, anthelmintics, analgesics and antipyretics, antiprotozoals, respiratory drugs, dermatological preparations, minerals and vitamins, large-volume parenterals. Dosage forms; Tablets, Capsules, syrups, externals • Manufactures sterile products.
Total output supplied to the private sector (From LP)	Around 35–40%
Ethiopian industry pharmaceutical exports in 2014	US$ 2 million
Company ownership	The ownership of the companies is diverse and ranges from two large companies to smaller entities that are joint ventures between Ethiopian entrepreneurs and foreign investors from China, India, Jordan, Saudi Arabia, Sudan and the United Arab Emirates.
Production capacity utilization	improvement during the 2005–14 period, increasing from 29.3% in 2008 to 79.0% in 2013
Number of employees	Approximately 2000 in 2010

National pharmaceutical strategy and plan

In 2015, the country launched an ambitious 10-year national strategy and plan of action to develop local pharmaceutical manufacturing capacity in order to increase access to locally manufactured, quality-assured medicines. The strategy sets out the details of how to transform the pharmaceutical sector in Ethiopia with the goal to become a pharmaceutical manufacturing hub in Africa by 2025

The strategic objectives of plan are to;

- Improve access to medicines through quality local production through Implementation of the GMP Roadmap
- Strengthen the national medicine regulatory system
- Create incentives designed to move along the value chain
- Develop HR through relevant education and establishing Centers of Excellence
- Develop pharmaceutical hubs through Industrial Parks
- Develop APIs, Inputs and Other supportive industries
- Create R&D platform
- Attract FDI in the pharmaceutical sector
- Exploit the LDC status to locally produce patented products
- To encourage exports

Policies

Coherence and complementarity of policies between sectors

1. Human capital development policy (Ministry of Education)
2. Science, technology and innovation policy (Ministry of Science and Technology)
3. Industrial policy (Ministry of Industry)
4. Intellectual property policy (Ministry of Industry)
5. Health policy (Ministry of Health)

GMP

- No pharmaceutical manufacturer in Ethiopia has achieved WHO prequalification status.
- Two companies, assisted by the German Corporation for International Development (GIZ), have achieved GMP certification by the Pharmaceutical Inspection Co-operation Scheme (PIC/S).
- Ethiopia adopted the five-year GMP Roadmap (2013–2018) with the aim of improving public access to sustainable, affordable, safe, efficacious and good-quality medicines produced in Ethiopia.
- An assessment of eight companies was conducted, which grouped the companies in three categories based on level of compliance to GMP as;
    - ❖ Level I: manufacturers with up to 50% GMP compliance.
    - ❖ Level II: manufacturers with 60–80% GMP compliance.
    - ❖ Level III: manufacturers with more than 80% GMP compliance.
    - ❖ Level III and II had one company each and the rest were in level I. The roadmap adopted a three-phased approach for ensuring all companies comply with WHO GMP standards by 2018.

Human Capacity

- Steps taken to improve capacity:

Addis Ababa University is starting an MSc degree programme in regulatory affairs, increasing enrolment of students in science and technology, and improving the capacity of science and technology institutions to produce qualified technicians, engineers and scientists; and providing managers and professionals with short-term training programmes in business management, leadership, GMP and entrepreneurship. The Ministry of Science and Technology has recently issued directives for the establishment of university–industry partnerships for promoting technology innovation, transfer and diffusion in line with its Science, Technology and Innovation Policy (2012).

- The strategic plan aims to address the shortage of skills including product innovation and drug development; quality control and quality assurance; drug approval, supply chain management and regulation; good agriculture practice; GMP; good wholesaling practice; good distribution practice; good laboratory practice; good clinical practice; drug manufacturing; and pharmaceutical management. The plan also provides an indicative list of potential partners and providers of training and technical assistance.

Government Incentives

- Tax-free loans of up to 70% for new investments and up to 60% for upgrading projects during the first five years, 100% custom duty exemption on the import of all granted capital goods,
- Spare parts at up to 15% of the total value of imported investment capital goods are exempted from customs duty.
- Zero tax on exports. Companies exporting 50% of their products or services or supplying 75% of their products or services as production or services input to an exporter, are exempted from income tax for five years. Companies exporting less than 50% of their products or services or supplying only to the domestic market are exempted from income tax for two years.
- Local manufacturers are granted a 25% price preference and also 30% pre-payment of the tender value on awarding the contract; the 70% balance can be accessed through the Development Bank of Ethiopia if the local company requires additional capital and is willing to cede the tender to the bank.
- Fast-track medicine registration for local manufacturers
- Specialized industrial parks for pharma, with all necessary infrastructure and Incentives including Tax exemptions.
- Corporate income tax exemptions–APIs: up to 14 years–Formulations/final medicines: up to 12 years–Pharmaceutical packaging: up to 8 year
- Personal income tax exemptions–5-10 years for expat employees (and long-term visas

Partnerships

Investor friendly policies and attractive manufacturing incentives in Ethiopia have prompted investment in local pharmaceutical production. Ethiopia has realized successful Joint ventures and these have not only contributed to the pharmaceutical industry; they also effectively transferred skill and technology.

Pharmaceutical Joint ventures –success story

Ethiopian Pharmaceutical Manufacturing (EPHARM)

The first pharmaceutical factory in the country is Ethiopian Pharmaceutical Manufacturing (EPHARM), which was established in 1964 as a public company by the Ethiopian government and investors from England. The firm is in Addis Ababa. The company has eight production lines with fully equipped laboratories, producing both sterile and non- sterile dosage forms.

East African Pharmaceuticals PLC (EAP)

East African Pharmaceuticals PLC (EAP) is one of the first privately owned joint venture direct foreign investment Pharmaceutical factories established in 1996 GC by British and Sudanese investors with the intention of producing human and veterinary medicines.

Pharmacure PLC

Established in 1998, Pharmacure PLC, is an Ethiopian-Saudi investment. It produces large-volume parenterals.

Sino-Ethiop Associate (Africa) PLC

Sino-Ethiop Associate (Africa) PLC (SEAA) was established in March 2001 as a joint venture between an Ethiopian company, Zaf Pharmaceuticals PLC, and two Chinese companies (China Associate Group and Dandong JINWAN Group) SEAA produces empty hard gelatin capsules and sells to pharmaceutical factories in Africa and the Middle East.

Cadila Pharmaceuticals Ethiopia PLC

In 2007, Cadila Pharmaceuticals Ethiopia PLC (CPEL) was established by Cadila Pharmaceuticals Ltd (India) and Almeta Impex PLC (Ethiopia), owning 57% and 43% of the company, respectively.

Julphar Pharmaceuticals

Julphar Pharmaceuticals Manufacturing Ethiopia PLC is another company established as a joint venture. The joint venture is formed between an Ethiopian company, Medtech Pharmaceuticals PLC, that holds 45% of the shares, and a United Arab Emirates (UAE) company, Gulf Pharmaceuticals (Julphar), that holds 55% of the shares. The UAE partner is producer of various pharmaceutical products in the Middle East and in its other subsidiaries in Algeria. Julphar maintains a network of 11 manufacturing plants based in the UAE, with developments under way to open additional facilities in strategic countries such as Saudi Arabia, Ethiopia and Algeria.

Through the initiative of joint ventures, a fore-closed factory revived, an old factory was upgraded, new factories were established, and enhanced technology transfer included localization of technical knowledge within Ethiopia. The Ethiopia scenario is a classic illustration of viability of pharmaceutical joint ventures.

6.1.2 Pharmaceutical Manufacturing in Tanzania

Item	Information
Population	Approximately 58.01 million, up from the 2014 estimate of 50.8 million, ranking 25th in the world (2019)
Annual pharmaceutical market in Tanzania (2018) (CAGR of ~5% per annum)	• Valued at USD 496 million • Drug expenditure per capita over USD 8.7 in 2017 • Forecast USD $730 million by 2022 with CADR of 8%.
Market share of Local manufacturers	• 12-16% (Generic 54%; Branded 20%) • 30% of the company's products are bought by the Medical Stores Department During the years 1990s to 2005, domestic pharmaceutical production supplied approximately 30%. This has reduced due to lack of competitive advantage in the market price of locally produced products.[1]
Number of importers	Over 50
The number of active manufacturers. (Please note: there are nil PI production in Tanzania)	12 firms
Production facilities and products categories	There are no multinationals, and only one joint venture with an external partner. Among the registered plants, only five were categorized as TFDA GMP compliant in 2019.
Oldest plant inception	1960's
Product range	• Dosage forms; Tablets, Capsules, syrups and externals common in EAC • focus on less sophisticated medicines such as antibiotics, cough and cold preparations, analgesics and antipyretics, sedatives, nutraceuticals, anti-helminthic and antimalarials. • However, one company (TPI) produces ARVs, anti-Malarial and anti-TB medicines pharmaceutical products not produced include IV fluids, antibiotics like cephalosporins.
Total output supplied to the private sector (From LP)	No data found

Tanzania industry pharmaceutical exports in 2015	USD 972,000 compared to USD 430,125,000 (2015) i.e. 0.25%
Company ownership	Private and partnerships
Production capacity utilization	• About 71 percent of MSD purchases come from abroad. The only advantage offered to local manufacturers is the 15 percent price preference, which does not provide much of an advantage as foreign manufacturers are still able to remain price competitive. • Manufacturing capacities are grossly underused and local manufacturers are largely restricted to production of over-the-counter medicines. • For example, Mansoor Daya Chemicals uses only 52 percent of its capacity, Keko Pharmaceuticals, 39 percent and Shelys, 36 percent.[2]
Number of employees	• No data on number of employees. • Inadequate personnel for specialized skills. • Access to technology and information is constrained.

National Pharmaceutical Strategy Plan: Supports Pharmaceutical Sector

The Government of Tanzania's National Medicine Policy of 2006 emphasizes the need for efficient quality assurance with the aim to establish a quality assurance system which is constrained by production capacities and low investment and hence the need

- to ensure that medicines reaching the patient are safe, effective and of acceptable quality. This applies to imports and LPP in accordance with the WHO Certification Scheme on the quality of pharmaceutical products moving in international
- The policy further aims at strengthening the National Medicines Regulatory Authority (the TFDA) through
    a. The establishment of Medicines Quality Control Laboratories
    b. The utilization of "Accredited Regional Quality Control Laboratories"
    c. The enforcement of GMP regulations
    d. Strengthening of a market surveillance system at all levels of supply chain of medicines and related supplies
    e. The establishment of "a system aimed at preventing infiltration of substandard and/or counterfeit medicines in Tanzania"

Policy Coherence

The existence of the policy demonstrates the important the pharmaceutical sector and is supported by stakeholders and donors. However, not all the proposed activities are actively supported for example, demand on subsidies like soft loans and guarantee schemes for the promotion of the sector.

Good manufacturing Practice (GMP) for Tanzania LPPs

It is reported that Tanzanian Food and Drug Authority (TFDA) appear to be relatively strong compared to other East African region because National regulation authorities are inadequately resourced, lack institutional performance and have weak monitoring systems.

TFDA provides free technical support and regularly inspecting industries (although this is limited due to budget constraints) in Tanzania and East Africa. Local industries must register all drugs produced every year after showing that they have achieved GMP.

Quality control has been a key challenge faced by local manufacturers. Sometimes leading to sanctions e.g. closures or suspensions. There are constrains and impediments to surveillance due to administrative lapses and finances and challenges in the distribution chain. Some policy changes have been recommended as in

- Focus on improving the public-sector distribution system by leveraging private sector
- Wholesale and Retail mark-up regulation
- Further strengthening of TFDA
- Strengthening and Consolidation of the Wholesaler market
- Special Incentive programs for Rural Distribution and Rural Pharmacies
- Overall credit facilitation for pharmaceutical wholesalers and retailers

In November 2017, the TFDA launched 10 minilab kits that will be used to strengthen its Quality Assurance Programme for rapid medicine quality verification and counterfeit medicines detection in the field which had a substantial reduction of substandard and counterfeit medicines from 3.7% in 2005 down to less than 1.0% in 2017.

In 2019 there was a major policy shift in the regulations as Tanzania harmonized regulatory bodies' roles, forms drug authority[3] due to regulatory overlapping. The TFDA was amended in Section 130 of the Standards Act No. 2 of 2009, food and cosmetic products, currently under Tanzania Food and Drugs Authority (TFDA), will be regulated by Tanzania Bureau of Standards (TBS), effective 1 July 2019. TFDA has been renamed as Tanzania Drug and Medicinal Authority (TMDA) and will be responsible for controlling medicines, medical supplies and reagents in the country.

Human Capacity Development

There is a general lack of highly skilled human resources in Tanzania.[4] The capacity and number of professional staff is very low. There is need for development of local capacity in terms of technical and managerial skills

Tanzania hosts the only Industrial Pharmacy Teaching Unit in East Africa; Kilimanjaro School of Pharmacy – (IPTU)[5] at Saint Luke's Foundation, Moshi is an Advanced Training Program in Drug Development, Drug Manufacturing, Regulatory & Quality Compliance in the Pharmaceutical Industry and include the GIZ support to the Muhimbili School of Pharmacy and the Kilimanjaro School of Pharmacy in setting up a

formulation development laboratory and a GMP-compliant pilot production facility respectively.[6] The training program entails and provides in-depth in industrial pharmacy albeit not available elsewhere in East Africa. The development of IPTU program is a joint effort with Purdue University, USA. Successful candidates are eligible to pursue master's program at Purdue University supported by UNIDO.

Government Incentives

There is lack of clear incentives and policies that promote local pharmaceutical production" has been one of the key policy gaps in Tanzania.[7] Typical incentives include

- 10 percent import duty tax on formulations (except for antiretroviral medicines, antimalarial medicines, anti-TB medicines and MSD imports),
- 9.9 percent VAT on raw materials BUT refundable, although the refund process takes time. This is negated by interest rates at nearly 20%.
- packaging materials, the manufacturers need to first pay the 18 percent refundable as above
- 15% price preference offered by MSD seems to be the only incentive provided to local
- Manufacturers. the advantage provided by the 15 percent price also negated by marginal cost pricing offered by some large importers.

Tanzanian authorities are seeking collaborations with international pharmaceutical companies to promote the local development of medicines. Zanzibar, a semi-autonomous region offers a 5-10 year tax holiday to investors.

Partnerships

TPI/Medeor Partnership

This partnership focuses on building local manufacturing capacity for anti-malarials and ARVs, between Tanzania Pharmaceutical industry (TPI) and Medeor but also covers training of the domestic pharma industry as it facilitates building technical expertise.

TPI with Action Aid Medeor implements two projects:

- manufacturing affordable artemisinin-based anti-malarial drugs for adults and paediatrics, (started in 2003); and
- producing good quality and affordable ARV fixed-dose combination, TT-virus (started in 2005).

The contractual arrangement with TPI specifies that all ARVs produced will be made available for public health sector but thereafter handed over to TPI after 40 months preferred marketing strategies

Keko Pharmaceutical Industries

Keko Pharmaceuticals was set up in 1968 as a unit under the Ministry of Health and Social Welfare (MOHSW) to supply tablets, capsules and large volume parenteral to the government procurement agency, Central Medical Stores (now MSD).[7] At that time, its products were distributed at public healthcare facilities. In 1997, the government sold off 60% of Keko to the private sector. Keko is a PPP, with 40% government-owned shares and a 15% preferential treatment in the MSD tendering process.

Mansoor Daya Chemicals

Mansoor Daya Chemicals is private-owned and manufactures large range of products mainly aerosols and over the counter preparations. These include antibiotics, antihelmintics, antiseptics and disinfectants, anti-fungal, analgesics, cough and cold preparations, vitamins, sedatives, bronchodilators, oral hygiene products, nasal and ear preparations, insecticides and insect repellents.

Shelys pharmaceuticals Ltd Tanzania

Shely's exists as part of Aspen Sub Saharan Africa group in the countries namely Tanzania, Zambia, Malawi, Democratic Republic of Congo (DRC), Rwanda, Burundi, Mozambique, Madagascar, Mauritius, Djibouti, Uganda and Kenya. In 2012, Aspen Pharmacare Holdings Limited (Aspen) acquired the remaining share in Shely's Pharmaceuticals Limited providing for a 100% shareholding both Tanzania-based Shely's and Beta Healthcare based in Kenya. The product brands include therapeutic categories such as cough and cold, anti-infectives, nutraceuticals, antimalarials, gastro-intestinal, pain management, fever and topical inflammation, disinfectants, cardiovascular and erectile dysfunction.

Zenufa

The Zenufa Group has pharmaceutical manufacturing facilities located in two strategic locations within Africa, the Democratic Republic of Congo (Kinshasa) and Tanzania (Dar-es-Salaam), with an additional ground distribution presence in five countries.

The Catalyst's acquisition of Zenufa is the fourth investment in Tanzania and second investment in the healthcare sector. In 2014. The media report[8] of 2016 reports that Zenufa acquired Kenya's Mimosa Pharmacy, which was later rebranded Goodlife Pharmacy and has rolled out across the region with an investment of $125 million (Sh12.5 billion) private equity firm, Catalyst. Zenufa manufactures over-the-counter (OTC) and prescription drugs for the Tanzanian market.

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6.1.3 Pharmaceutical Manufacturing in Uganda

Item	Information
Population	~42 million people (NSSP report, 2018)
Annual pharmaceutical market in Uganda (2018) (CAGR of ~5% per annum)	USD434 million
Market share of Local manufacturers	25%-30%
Number of importers	(Data not available)
The number of active manufacturers. (Please note: no API production in Uganda)	11 factories
Production facilities and products categories	• 15 different production lines with majority of local manufacturers specializing in oral and topical liquid preparations (UNIDO report) • There are about 19 sites, and only 11 engaged in commercial production of pharmaceuticals;
Oldest plant inception	1990s
Product range	• Like her EAC counterparts, Uganda LLPs do not produce all products in the national EML (674); with companies having 10 – 80 registered products. • Main products: diagnostic kits, large & small volume parenterals, tablets, capsules, oral liquids, capsules, dry powders as well topical ointments, and surgical gauze (NDA Uganda report) • Dosage forms; Tablets, Capsules, syrups, externals.
Total output supplied to the private sector (From LP)	(No data)
Uganda industry pharmaceutical exports in 2015	Approximately USD 66,500 (0.54% of the total exports)
Company ownership	Ownership of companies is a mix of locals and JV from international and regional companies, e.g. Quality Chemicals that is partnered with Cipla for production of

	ARVs and Medipharm EA that has shareholders from Kenya.
Production capacity utilization	In a self-assessment by the industry, Uganda LPPs indicated general underutilization of their capacities, especially for liquid/cream and ointments at < 40% in 2013. Tablets and capsules were above 60% in the same period. With the entrance of Cipla to partner with Quality chemicals and other self-driven improvements, the situation is likely to have improved at the time of this report even though no official data has been released on the same currently.
Number of employees	Approximately 1800 in 2014

National Pharmaceutical Strategy Plan: Supports Pharmaceutical Sector

The 3rd National Pharmaceutical Sector Strategic Plan of 2015-20 and the National Medicines policy 2015 provides opportunity to improve pharmaceutical production in Uganda. They are linked to Uganda's aim to achieve Universal Health Coverage (UHC) with essential services, using a Primary Health Care approach. As such, The NPSSP III, focuses on several healthcare enablers that includes medicines supply chain, financing, pricing and appropriate use. Domestic manufacturing is also highlighted in the document and two main objectives for improvement cited are;

1. To promote the development and growth of domestic production of pharmaceutical products of assured quality, safety and efficacy and,

2. To develop and empower the domestic pharmaceutical industry to satisfy national needs, and to promote economic and industrial development

To achieve the above two objectives, the following strategies were developed,

- Implementing tax incentives or subsidies for domestic manufacturers of essential medicines.
- Encouraging national and international procurement agencies to consider domestically produced essential medicines
- Minimizing imports of essential medicines that can be sufficiently produced in Uganda at a fair price.
- Ensuring that LPPs maintain Good Manufacturing Practice (cGMP).
- Supporting LPPs to obtain additional regulatory certification that includes WHO prequalification of products.
- Developing mechanisms to allow for harmonisation of policies and their reciprocity on domestic pharmaceutical manufacturing among EAC countries.

Some of the Challenges faced by LPPs in Uganda include but not limited to:

- Pharmaceutical industry remains weak

- Limited access to affordable financing
- Limited access to markets. For instance, donors and international NGOs still hesitant to purchase products from the LLPs
- Slow harmonization of regulations in the region.
- Technology and the associated high skilled expertise is not adequate.
- Nearly all the pharmaceutical inputs are imported.

Policy Coherence

There is general coherence and complementarity of policies between key sectors in Uganda. This supports health related initiatives that includes UHC and even commodity security (which included local manufacturing). There is a singular story from all the ministries that responds to the national development plan.

6. Human Resource Development Planning (Ministry of Education)
7. Science, Technology and Innovation Policy (Ministry of Science, Technology and Innovation)
8. National Industrial Policy (Ministry of Tourism, Trade and Industry)
9. National Intellectual Property Policy (Ministry of Industry)
10. National Health Policy (Ministry of Health)

Good Manufacturing Practice (GMP) for Uganda LPPs

- Most companies have the National Drug Authority GMP certification
- Only one manufacturer, Cipla Quality Chemical Industries limited, has international (WHO) GMP certification in Uganda;
- Uganda GMP roadmap is still being developed.

Human Capacity Development

Uganda is keen to improve the pipeline of pharmacists, engineers and technologists to serve in the Health sector. For the pharmaceutical manufacturing sector, the following initiatives are an indication of governments to rope in all stakeholders to ensure the pharma sector receives support.

- Uganda has invested in science-based health innovation that is meant to bridge the gap between research and industry as evident from two major initiatives namely, the Millennium Science Initiative (MSI) and the Presidential Support to Scientists Fund started in the 2000s. This was preceded by the establishment of the Med Biotech Labs in 1995 to undertake research on diseases that affect the Ugandan population, build capacity in biotechnology and medical research and to facilitate technology transfer. Through these establishments, Uganda continues to witness a pharmaceutical workforce pipeline growth that will certainly contribute to the health sector including pharmaceutical manufacturing.

- There are also clear initiatives taken by both university and industry to increase the number of Pharmacy graduates/experts in Uganda. For instance, the Pharmaceutical Society of Uganda and pharmaceutical companies have partnered with academic institutions to administer a scholarship program that supports about 10 pharmacy needy students in Public universities. The scholarships are from the Pharmaceutical companies in Uganda.

- It is also noteworthy that the National Pharmaceutical Sector Strategic plan of 2015-2020 indicates addresses human resources components, especially touching on the pharma sector. It lists training of all relevant industry staff in cGMP as one of the priorities in order to ensure robust quality domestic manufacturing.

Government Incentives

- All exports of goods and services are zero-rated for VAT. This enables them to reclaim VAT expended on all inputs used in the process of producing and processing exports.
- Manufacturers can produce under bond (without paying taxes) by using their imported raw materials for the manufacture of good/services for exports.
- There is a 10-year corporation tax holiday for pharmaceutical manufacturers investments and other priority sectors;
- Duty exemption on raw materials, plant and machinery and other inputs;
- Stamp duty exemption;
- Duty drawback applies on input of goods from domestic tariff area. This enables manufacturers/exporters, to compete in foreign markets by excluding duties paid on imported inputs in the final export price.
- Exemption of withholding tax on interest on external loans; and on dividends repatriated, to provide relief from double taxation.

Incentives specific to Pharma sector include;

- Plant and machinery are exempted from import duty. Additionally, VAT is deferred for one year. VAT deferment it can also be extended upon application provided that the value of the import stands at ≥US 22,500 when imported. Withholding tax is also exempted on plant and machinery
- Annual allowable deductions such as, assets depreciation, carried forward losses and one-off upfront start-up costs (start-up expenditure), and scientific research expenditure is at a rate of 25% for four years from the day it is incurred.
- Tax exemption on training expenditure for employees of the company not exceeding the aggregate of four years – for both citizens and permanent residents of Uganda is at 25%.
- Other tax exempted costs include, Accountant fee, Registration of business fee, promotion and advertising activities costs.
- Uganda also extends a 5% allowable deduction on industrial building, 40% on computers and data handling equipment, 30% on automobiles (i.e. plant and machinery) and 20% on office furniture and fixtures and any depreciable asset.
- Favourable income tax to employees in the pharmaceutical manufacturing sector

Partnerships

Uganda is keen to ensure that the local pharmaceutical manufacturing s in line with the aspiration of the PMPA strategy by partner states. As such, Uganda has encouraged partnerships in the sector. Furthermore, it has established the “Buy Uganda-Build Uganda” (BUBU) initiative with about 40 products prioritized for local manufacturers to produce. Through this initiative, the government also procurers form LLPs for the public sector. Some of the success stories are highlighted below.

Abacus Parenterals Drugs Limited (APDL)

It is a 100% foreign owned factory with major shareholding being Indians at ~75% and Kenyans 25%. It employees about 400 people and deals with large and small volume parenterals and eye drops. They are known to have strong regional market access because of their unique products. They operate in Tanzania, Kenya, Rwanda, Burundi and Uganda.

APDL has also demonstrated some form partnership capability by representing several pharmaceutical manufacturing companies of medicines, surgical / non-surgical products companies spread across India, China, Middle East, Pakistan, UK and Kenya.

APDL is the largest parenteral manufacturer in the EAC region and its success is exemplified by a ~30% wholesale price reduction of 500ml bottle of fluid, five months post production indicating the viability of local production.

Kampala Pharmaceutical Industries Limited (KPI)

Started in 1996, it is now owned by the Aga Khan Development Network (AKDN). It employees over 300 people with 50% being permanent staff. They have about 80 registered products comprising of oral liquids, tablets, capsules and creams. KPI has been working towards improving access to essential medicines and is planning to improve access to NCD products by exploring various partnerships with international partners.[1] It enjoys the support of one of the largest private hospitals in the region, i.e. Aga Khan Hospital (based in Kenya).

Quality Chemicals Industries Limited (QCI)

QCI is co-owned by Cipla of India, Quality Chemicals Ltd of Uganda, and the Government of Uganda. This was established to help in the manufacture of ARVs locally in a bid to localize ARV production while creating jobs? It focuses majorly on ACTs and ARVs. QCI is a WHO GMP certified facility. It is a demonstration of how partnership can accelerate not only development but quality improvements of factories. CIPLA was able to employ their expertise to accelerate quality improvements in this factory.

Rene Industries Limited

Started in mid-90s it is a fully locally owned company with over 500 employees and is the largest generic manufacturer in Uganda. The firm manufactures various Non-Beta Lactam & Beta Lactam dosage forms including tablets, capsules liquid orals, dry syrup, dry powder suspensions and external preparations. Rene has over 120 products, covering over 22 therapeutic ranges. It has market authorization in Burundi, Rwanda, DRC and South Sudan. Interestingly, Rene has leveraged on the BUBU initiative of government to improve their sales. It a demonstration that, with the right policies and partnership between government and industry, there opportunity for affordable quality medicines in the region.

Reference

1. Based on discussions with industry experts, 2019.

6.2 Questionnaires

PharmaQ Limited, Kenya

Date:

Dear _____

Re: Letter to Respondents

PharmaQ Limited, Kenya is conducting a study on ***Pharmaceutical Partnerships for Increased Access to Quality Essential Medicines*** *in the East Africa region.* 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 [illegible] United Nations. Access to medicines encompasses the consistent availability of appropria[illegible]quality and affordable essential medicines at health facilities. In the recent years the [illegible]eral interventions to support the Local Pharmaceutical Production. However, there is [illegible]e done at facility, country, regional levels to overcome the myriad of issues for the o[illegible]ment of the sector to not only attain international GMP standards, but also to offer [illegible]ality products. The **Science Granting Councils Initiative (SGCI)** through African Cent[illegible]gy Studies (ACTS) is conducting a study to explore how Pharmaceutical Partnershi[illegible] increased access of Quality Essential Medicines in the East Africa region. This [illegible]erall objective of finding mechanisms to strengthen the ability of SGCI to support [illegible]nange with the private sector for improved outputs. The main objectives of the study [illegible]:

1. To determine the level of produ[illegible]ce of the pharmaceutical industry in East Africa region in regard to manufactu[illegible]essential medicines.
2. Identify policies and regulati[illegible]t innovation and development of new products in the local pharmaceutical in[illegible]
3. To establish mitigation s[illegible]duce the product gap between the national essential medicines lists and me[illegible]manufactured.
4. To explore how coll[illegible]ancing, research links, and technology transfer can be harnessed to not on[illegible]roduction of quality essential medicines in the EAC region, but also increase a[illegible]able medicines.

We are inviting you to p[illegible]s research by completing the attached questionnaire. Please answer all questions as [illegible]ssible. The data will be used for research purposes only. To this end, your participatio[illegible]nsuring that we advocate for improved policy environment as a result of the good ide[illegible]by the sector with a view of unlocking growth in the pharma sector - while improving a[illegible]able quality medicines to the populace.

Yours faithfully,

PharmaQ Limited

QUESTIONNAIRE A- (Pharmaceutical Manufacturers)

Questionnaire on Pharmaceutical Partnerships for increased access to Quality Essential Medicines in the East Africa region

Details of the Company

Name of Company:	
Country:	
Name of person filling this form:	
Designation:	
Signature and Date:	

Part 1: Production competence level of the pharmaceutical industry in East Africa region

A: Product range

i. State the number of products manufactured in your facility

……

Please indicate the number of products in the following dosage forms produced at your facility

Solids	*Liquids*	*Semi-solids*	*Sterile*	*Nonsterile*
☐	☐	☐	☐	☐

(Please provide product list to accompany the above information)

State the number of products manufactured at your site that are used for management of ... nicable diseases listed

	Diabetes	*Hypertension*	*Osteoporosis*	*Cancer*	*...*
Number of Products					

ii. How many new product registration approvals have you received f... drug authority in the last 5 years? Do you have any new products under developme... ation applications awaiting evaluation and approval in the last five years? Yes/No.

Indicate the number in the appropriate section in the table belo...

Year	***Number of products***				
	Under development	*Applied registration*	*Registered*	*Used in Communicable diseases*	*used in Non-communicable diseases*
2014					
2015					
2016					
2017					
2018					

iii. Briefly describe the strategy for developing new pr... facility

……

……

……

iv. Do you envision growth in your product portfolio to improve access to essential medicines as envisaged by the Kenya pharmaceutical policy? ***Yes/No.***

Please, explain [hint; plans on the way (for yes) or challenges (for no)]

……

vi. Do you have a mechanism at your facility for follow up on off-patent products? ***Yes/No.***

v) Do have any experience with using TRIPS flexibilities to improve your product portfolio?

If Yes*, please explain.*

……
……
……
……

B: Number of employees at your facility

i. Indicate the number of persons in each department and their qualification in the table below.

Department	***Number of personnel***	***Qualification (indicate number of persons)***				
		PhD	*MSc*	*BSc*	*Diploma*	*Others*
Production						
Quality Assurance						
Quality Control						
Research & Development						
Maintenance						
Other special skills						
Total						

Explain others:

……
……

ii. In your view, is the R& D department at your f… adequately equipped? Explain briefly

……
……

iii. List the major equipment in your R&D d…

……
……

C: Production capacity

What is the designed capacity of y… plant and what capacity is currently utilized (as percentage) for the dosage fo… manufactured at your facility on 24hr basis?
……

Type of formulation	*Designed capacity*	*Percent (%) utilization*	*Remarks*
Tablets			
Capsules			

iv. Do you envision growth in your product portfolio to improve access to essential medicines as envisaged by the Kenya pharmaceutical policy? ***Yes/No.***

Please, explain [hint; plans on the way (for yes) or challenges (for no)]

……

vi. Do you have a mechanism at your facility for follow up on off-patent products? ***Yes/No.***

v) Do have any experience with using TRIPS flexibilities to improve your product portfolio?

If Yes*, please explain.*

……
……
……
……

B: Number of employees at your facility

i. Indicate the number of persons in each department and their qualification in the table below.

Department	***Number of personnel***	***Qualification (indicate number of persons)***				
		PhD	*MSc*	*BSc*	*Diploma*	*Others*
Production						
Quality Assurance						
Quality Control						
Research & Development						
Maintenance						
Other special skills						
Total						

Explain others:

……
……

ii. In your view, is the R& D department at your f… adequately equipped? Explain briefly

……
……

iii. List the major equipment in your R&D d…

……
……

C: Production capacity

What is the designed capacity of y… plant and what capacity is currently utilized (as percentage) for the dosage fo… manufactured at your facility on 24hr basis?
……

Type of formulation	*Percent (%) utilization*	*Remarks*
Tablets		
Capsules		

Liquids			
Ointments/Creams			

D: Current Certification/Authorizations

i. Please list in the table below the GMP inspection approvals that your company has achieved so far.

Regulatory (NDRAs)	***Non statutory (e.g. ICRC; procurement agencies etc.)***
1	*1*
2	*2*
3	*3*
4	*4*
5	*5*

ii. What has been the impact of GMP accreditation on market access for your products?

……
……

E: Factors impacting pharmaceutical manufacturing

(i) *To what degree do you agree or disagree with the following statements on their impact on pharmaceutical manufacturing. State reason/comment for opinion*

	Strongly Agree	**Agree**	**Disagree**	**Strongly disagree**	**Comment /Reason**
Human Resource and manpower					
Technology /Machinery					
Status of facility/ premises					
Process of manufacturing					
Source of starting materials					
Quality of starting materials					
Manufacturing environment					
Access to affordable Finance					
Stringent pharmacy Law enforcement					
Categorization of industry into groups (A,B,C) based on level of GMP compliance					
Policy coherence to support Local Pharma Production					
Working environment					

Quality culture					
Pharmaceutical Partnerships					
Access to markets					

(ii) *Please indicate whether you agree or disagree with the issue statements in the table below in regard to production of essential medicines*.

Issue statement	YES	NO	Explain or comment
In general, there are adequately trained personnel with satisfactory knowledge in GMP.			
There are other specialized areas with skills not commonly available. State any special skills required but not available.			
On-job training for key personnel, (Production, QC, QA etc.) is adequate.			
Other professions are adequately trained for support services (maintenance, Water, HVAC etc.).			
The institutions available (public or private) are capable of producing skilled manpower for the sector.			
There are certified trainings for skills and capacity building.			
Our company has felt the need for recruitment of special skills but has been unable to procure.			State the special skill required
The interventions steered by the international community in quality improvement has resulted into the expansion of the industry and local procurement.			State briefly how and what could be done differently
The financing models available for development of sector are appropriate and affordable (cost issue).			Explain
Some of the listed essential medicines are not manufactured at your facility.			
It is a known fact that there is a cost associated with improvement of quality. This impacts access to medicines.			Explain
Other (specify)…….			

Part 2. Identify policies and regulations that impact innovation and development of new products in the local pharmaceutical industry.

i. Please indicate whether you agree or disagree with the issue statements in the table below in regard to production of essential medicines.

Issue statement	Yes	No	Explanation (if any)
Policies and regulations are necessary for the industry.			
There are policies directly related to the pharmaceutical manufacturing industry.			Please specify
There are other supportive policies that are sector-wide and could be leveraged for pharma sector.			Please specify

There are other supportive policies that are sector-wide and could be leveraged for pharma sector.			Please specify
There is adequate consultation with experts when formulating policies.			
Are Policies/regulations that impact on local manufacturing industry coherent?			Explain
What would make policy & regulation work better for the sector?			Please explain
The incentive policy is adequate for the sector.			
The policies in industrialization, local production and public procurement support each other.			
The promotion of buy Kenya build Kenya has resulted into increased demand of local products.			
Others (specify)……			

art 3. Mitigation strategies to reduce the [illegible] between the national essential medicines lists and medicines that [illegible]ured locally.

i. Please indicate whether you agree or di[illegible]e issue statements in the table below in regard to production of essential medici[illegible]

Issue statement	Yes	No	Explanation (if any)
The national Essential Medicine List updates are the basis for development of new products.			
Development of new products is based on our own market research.			o Own market Research ( )
Development of new products is based on partnerships.			o Partnership with University or research Institution o Joint venture o PPP
We monitor the expiry of patents and use the TRIPS flexibilities to place new products from off/near off patent expiry.			List product (optional)
Our new products are a result of MOH policy for new treatment guidelines and epidemiology .			
Policy initiatives to support Local Pharmaceutical Production such as (EACRMPOA; Ke-GMP Roadmap) have impacted Quality, production Capacity, product range, skills, human capacity building etc.			
Access to affordable financing for new products is available.			
Other (specify)……			

ii. Please, provide comments on the statement o[illegible]ceutical production below;

a) It is a known fact that there a cost associated with improvement of quality. To what extend is this true?	
b) Has your company invested in any project on improving quality of production?	
c) Optional: Can you give examples of investment to improve quality at your facility?	
d) What has been the impact of either regional or national programs on improvement of quality of manufacturing and what could have been carried out differently?	
e) Is your company in any partnership with other entities on improvement of capacity and/or quality? Please give examples, status and results.	
f) What initiatives are currently in place to sustain improvements in your company in terms of;	
i. Availability of trained and skilled staff	
ii. Know-how and technology transfer	
iii. Availability of affordable finance	
iv. Regulatory enforcement	

Part 4. Collaborations, research links and technology transfer be harnessed to boost local production of quality and affordable essential medicines

i. Please indicate whether you agree or disagree with the issue statements in the table below in regard to production of essential medicines.

Issue statement	YES	NO	Explanation (if any)
Collaboration with a company which has been approved by a stringent regulatory Authority (SRA) can improve quality & growth			*(tick the type of improvement)* o Tech transfer advantages o Co-development of products o Improved operations o
Our company has a link partnership with other institutions			(*Tick if any*) o University o R&D o Joint venture o Other
			The link Partnership is based on; o Technology Transfer o New products o Transfer of Skills & Know-how o New investment Explain …….

Any success with your partnerships so far?			If Ye (hint; is it in production, APIs, te oducts, skills?)
			xplain why? ighlight 3 major challenges
Collaborations require investments			s applicable ○ New Machinery & Equipment ○ Quality of product ○ Personnel training & skills development ○ Others
There exists an information sharing platform in relation to research institutions and the pharmaceutical industry which support production of quality essential medicines			Explain…….

i. Any other opinion

……

END

Questionnaire B-(Policy and Regulatory)

Questionnaire on Pharmaceutical Partnerships for increased access to Quality Essential Medicines in the East Africa region

Name of company /Institution:	
Country:	
Name of person filling this form:	
Designation:	
Signature and Date:	

Part 1: Production competence level of the pharmaceutical industry in Eas[illegible]n

i. Please, give your opinion or explanation to the following statement

	Opinion or explanation
How would you describe the local industry in regard to its capability do manufacture products listed as essential medicines? (tick the option)	o Strongly capable o Capable o Fairly capable o Not capable
It is claimed that there are different levels of manufacturing standards in the pharmaceutical sector in the region. In your view what clearly describes this situation in terms of; a. Policy and Regulation b. Facility Infrastructure c. Management at facility level d. Regulatory enforcement e. Incentives to the sector	

Part 2: Identify policies and regulations that i[illegible]tion and development of new products in the local pharmaceutical [illegible]

i. Are you aware of any policies and re[illegible]ntives or any initiatives that support local manufacturing? Please descri[illegible]
……

ii. What have been the limiting factors in [illegible]lementation of the existing policies?
……

iii. Are you aware or have you participated in any invitation or Expression of Interest by any agency to add or include new products on the Essential Medicines List or annual procurement lists? If so, what was the basis of selection of products?

Aware/ not aware: Yes/No (tick one)

Explain:
……
…….....

i. Are you aware or have you participated in any for… new requirements and/or formulations or change of treatment regi… …es predominantly on a specific program (for example, mother-child he…

Aware/ participated: Yes/No (tick one)

Which one? Explain ……

Part 3: Mitigation strategies to reduce the pr… …tween the national essential medicines lists and medicines manufactured lo…

i. It is reported that about 40 % or the Esse… …s can be manufactured locally. What is your opinion or suggestion that wou… …he gap between local manufactured products and the Essential Medicines L…

Opinion:
……
……
……
……
……
……
……
……
……

ii. In your opinion will a … categorization stimulate or inspire local production so that manufacturers a… …d assessed against products commensurate with the in-build technology rat… …pen licensure?

……
……
……
……

iii. Similarly, what are the constrains or advantages in achieving the considerations listed in the table below in terms of closing the gap (should we re-write this to read; In relation to your answer to Part 3 questions, how do you think the following listed components affect the efforts to close gaps slowing increased essential medicines manufacturing?

	Advantage or benefit	**Constrain**
Technology		
Number of products		
Personnel skills and training		
International obligations (TRIPS-Utilization of the flexibilities)		

i. Do you know or have experience in working out Patents and/or TRIPS flexibilities? How long ago and what was your experience?

Experience, Yes/No

Please explain

……
……
……
……
……

Part 4. Collaborations, research links and technology transfer be harnessed to boost local production of quality and affordable essential medicines

i. Please indicate whether you agree or disagree with the issue statements in the table below in regard to production of essential medicines.

Issue statement	YES	NO	Explanation (if any)
Collaboration with a company which has been approved by a stringent regulatory Authority (SRA) can improve quality & growth.			(*tick the type of improvement*) o Tech transfer adv…ges o Co-development… o Improved oper… o
Is it important for pharmaceutical manufacturers to have partnership with other institutions?			(*tick examples)* o University o R&D o Joint ve… o other
			The link Partne…p is bas… o Tec… o Ne… o T…Know-how o *Explain*
Are these partnerships feasible?			*If ye…* (h… …ction, APIs, tech transfer, new p…
			…plain why? …ajor challenges
Collaborations require investments			…*applicable* o New Machinery & Equipment o Quality of product o Personnel training & skills development o Others
There exists an information sharing platform in relation to research institutions and the pharmaceutical industry which support production of quality essential medicines.			Explain ……..

i. Any other opinion

……

……

……

……

END

Questionnaire C- (Universities/Research Institutions)

Questionnaire on Pharmaceutical Partnerships for increased access to Quality Essential Medicines in the East Africa region

Name of company /Institution:	
Country:	
Name of person filling this form:	
Designation:	
Signature and Date :	

Part 1: Production competence level of the pharmaceutical industry in East Africa re

i. Please, give your opinion or explanation to the following statements**.**

	Opinion or explanation
a. How would you describe the local industry in regard to its capability to manufacture products listed as essential medicines?	b. Strongly capable c. Capable d. Fairly capable e. Not capable

What is your current interface with the local manufacturing industry in regard to access to quality essential medicines?	*Do you currently have a partnership or interactions?* ☐ **YES** ☐ **NO**
If **YES**, what forms of interactions?	a. Informal discu… …arma related project… b. Formal engag… …n MoUs for projects… c. Interaction… …e sharing platforms… …(e.g. confere… … d. Other…
How long have your partnerships/interactions been? (estimate in years)	a. …ear c. d. More …n 5 years
Please highlight/specify examples of the projects you have collaborated on (if any)	a. NCD or CD? b. Product formulation? c. Trainings? d. Other (please specify)
If **NO**, why?	e. We do not pharma research/work/trainings at the faculty f. Pharma companies are hard to collaborate with g. There is willingness, but funding for projects is a challenge h. No one is encouraging this partnerships (advocacy) Other (please specify)

Part 2. Mitigation strategies to reduce the product gap between the national essential medicines lists and medicines manufactured locally.

i. It is reported that about 40 % or the Essential Medicines can be manufactured locally. What is your opinion or suggestion that would help close the gap between local manufactured products and the Essential Medicines List?

Opinion:

……
……
……

ii. In your opinion what are the constraints in innovation and product development in terms of;

a. Technology	
b. Personnel skills and training	
c. International obligations (TRIPS)	

iii. Do you know or have experience in working out Patents and/or TRIPS flexibilities? How long ago and what was your experience?

Experience; Yes/No

Explain…….. …

Part 4. Collaborations, research links and technology transfer be harnessed to boost local production of quality and affordable essential medicines

i. Please indicate whether you agree or disagree with the issue statements in the table below in regard to production of essential medicines.

Issue statement	YES	NO	Explanation (if any)
Collaboration with a company which has been approved by a stringent regulatory Authority (SRA) can improve quality & growth.			(*tick the type of improvement)* o Tech transfer advantages o Co-development of products o Improved operations o Other__
It is important for pharmaceutical manufacturers to have partnership with other institutions.			*(tick examples)* o University o R&D o Joint ventur o Other__
			(*tick the basis of* o Tech o New o Tr o N *Explain …*
Are these partnerships feasible			ain briefly (hint; is it in , APIs, tech transfer, new skills?)

Are these partnerships feasible			lain briefly (hint; is it in , APIs, tech transfer, new skills?)
			uccess, explain why? ghlight 3 major challenges
Collaborations require investments			*as applicable*) ○ New Machinery & Equipment ○ Quality of product ○ Personnel training & skills development ○ Others
There exists an information sharing platform in relation to research institutions and the pharmaceutical industry which support production of quality essential medicines.			*Explain* ……

In your opinion, are there any other factors of emphasis that will help improve access to essential medicines and/or strengthen local manufacturing base in terms of quality and availability.

……

……

……

END

POLICY BRIEFS:

- Policy Brief Draft No. 1: Global and National Initiatives to Stimulate and Support a Sustainable Local Pharmaceutical Production of Quality Essential Medicines

- Policy Brief Draft No. 2: Improving Access to Essential medicines through Government-Industry-Universities/Research Institutions Joint Partnership

Global and National Initiatives to Stimulate and Support a Sustainable Local Pharmaceutical Production of Quality Essential Medicines

EXECUTIVE SUMMARY

Both global and national initiatives have worked concurrently to support and sustain Local pharmaceutical Production (LPP) to ensure access to quality essential medicines. Categorization of the LPP is a key catalyst for growth of the sector in terms of product range, medicines security, access and availability of quality essential medicines. A stimulus scheme to support and sustain LPP must also adhere to conformance to international standards of products, processes, facilities and regulatory function, in a manner that guarantees the value chain. The scheme must also be a foundation for innovation, Research & Development, human resource development and attract investment in the sector. The scheme should inform the levels of quality performance and risk categorization.

INTRODUCTION

Access to essential medicines is a global campaign to ensure availability of essential medicines. The global community has a milliard of initiatives that reduce the negative impact of pandemic diseases and support identification of quality sources in the value chain. The donor community response has supported the purchase of generic medicine more particularly against HIV/AIDS, TB and malaria. Since 2002 an annual investment of more than US$4 billion has been invested in the purchase of the fixed dose combinations in ARV and Anti-Malarial and this has led to significant drop in treatment cost and substantial increase in the number of people on treatment. In Sub Saharan Africa, a substantial increase of 13-fold from 1% in 2002 (300,000 out of 11 million adults) to 37% (5 million from 10.4million eligible for ARV treatment).

It is important that these gains are not only realized but also have sustainable mechanisms to ensure access of quality essential medicines via secure source(s) for continuous availability of quality essential medicines. The risk categorization approach provides a robust evidence based, scientifically sound way to manage pharmaceutical manufacturers to ensure they attain WHO GMP in their facilities.

The WHO report[1] states that one of the targets of the Sustainable Development Goals (SDGs) and a key factor in achieving Universal Healthcare (UHC) is access to safe, effective and quality medicines and vaccines. The United Nation Industrial Development Organization (UNIDO) has also emphasized that many deaths could be prevented if safe and efficacious medicines were readily available to treat patients and access could be worse by existence of substandard and counterfeit products on the market. At the same time, medicines have a business and health interface that evokes socio-economic

[1] Addressing the global shortage of, and access to, medicines and vaccines January 2018, Report by the Director-General.

considerations and interests must be carefully actuated. However, there is good justification that Local Pharmaceutical Producers (LPPs) can reduce disease burden of a country and improve the health status of its citizenry. Local pharmaceutical production facilitates industrial and economic growth through infrastructure development, market access with potential for insulation against unpredictable burden of new diseases and epidemics (e.g. Ebola) that may require unprecedented solutions. LPPs provide;

a) secure source of quality medicines and supplicant to substandard and counterfeits;
b) prevention of discontinued supplies or stock outs;
c) promotion of local value chain;
d) creation of jobs and technology transfer;
e) provision of service to the advancing non-communicable diseases and provide a sustainable source beyond donor programs.

- More than 2 billion people worldwide cannot get the medicines they need.
- LPPs can help vulnerable populations, especially those in remote areas, to access quality medicines, thus contributing to ''*leaving no one behind, and reaching the furthest behind first*'', the overarching principle of 2030 agenda for sustainable Development.
- LPPs can reduce the dependency on international donations and shrinking number of overseas companies who dominate the global market.
- LPPs are easier to monitor and control and can help curb the vast influx of sub-standard medicines into developing counties.
- While LPPs are widespread, most companies operate much below international standards. Helping upgrade their production contributes directly to people's health, as well as to inclusive and sustainable industrial development (ISID).

Source: UNIDO Pharmaceutical Production in Developing Countries

Several initiatives have been rolled out to help boost pharmaceutical manufacturing in Africa. They include efforts by WHO on TRIPS flexibilities, UNIDO's global project support programs for the manufacturing sector to attain WHO GMP standards, and Health Action Internationals (HAI) pharma commercial viability/improvement studies, geared towards strengthening local pharma production through quality improvement interventions, price preference, and policy shift amongst others. Furthermore, regulatory policies to support local manufacturing in Africa have also been develop such as AMRH[2,3] aimed at promoting medicines regulation in Africa and sharing experiences, technical know-how and capacity building especially for the pharma sector. However, these efforts have not translated to the growth of the sector as anticipated. This is not surprising though, because there is a disconnect between policy development and the practical implications. For instance, GMP improvements – a requirement for supply of medicines – is an expensive exercise. In most cases, access to financing hampers GMP improvements, emanating from the above-mentioned support programs. As such there is need to rethink on how governments could support LPPs in order for them to attain GMP and in

[2] WHO Drug Information Vol. 28 No. 1, 2014.

[3] AMRH Newsletter 1Q 2019.

return contribute towards access to affordable medicines at the right time. More so, companies that have heavily invested to be GMP compliance as per regulatory requirements feel that the is no level-playing field due to cost of compliance that makes them less competitive than non-compliant companies. For this reason, companies tend to avoid investing heavily in product development because of the regulatory gap. This concern has been raised with regulators by the stakeholders before.[4] To address this issue, there is need for a pragmatic industry accepted approach.

UNIDO recently published a report[5] highlighting how local pharmaceutical production could be boosted. It highlights the fact that future for LPP growth will rely heavily on national governments and collaboration with global and regional agencies. The reports articulate the need to ensure adherence to international standards; GMP roadmaps; GMP assessments and attainment of WHO-GMP. It also highlights the need for capacity building and more importantly the need for governments to set policies to harness opportunities within the health budget to prop up local manufacturing subject to quality and regulatory requirements. For instance, it shows that with regards to quality medicines, ensuring access to affordable financing is also very key to success of LPP. To this end, there is opportunity to develop a quality-GMP linked incentive mechanism to not only boost access to affordable medicines, but to ensure that industry also aspire to attain highest possible quality standards.

In the just concluded study, commissioned by ACTS, -Pharmaceutical Partnerships for Increased Access to Quality Essential Medicines in the East Africa Region – one of the key objectives was to identify policies and regulations that impact innovation and development of new products in the local pharmaceutical industry and propose mitigation strategies to reduce the product gap between the national essential medicines lists and medicines that are manufactured. Linked to this, was to make policy proposals that could be used to incentivize the local manufacturers to invest in quality improvements and respond to the national health needs.

APPROANCES AND RESULTS

A survey was conducted to determine the production competence level of LPPs, existing collaborations and pharma sector policy work in EAC. Information was obtained from pharmaceutical industry, institutions of research, academia and policy makers in the Ministry of Health/Ministry of Trade & Industry. Sixteen LPPs from Kenya participated in the study.

Summary of the Key Findings from the Study

1) Range of Products Manufactured by The Local Industry

The local industry does not manufacture all the products listed as essential medicines predominantly the Non-sterile products, solids (tablets, capsules), liquids (syrups, suspensions) and semisolids (ointments, creams)

- Only 28% of the listed essential medicines are produced.

[4] Discussions with CEOs from the pharma companies

[5] UNIDO Report on Boosting Pharmaceutical Production

- About 56 % of these products are solids and 63% are for management of non-communicable diseases.
- About three manufacturers of sterile products at the time of the study.
- The production capacity in this industry is underutilized. The average production capacity utilization of local pharmaceutical producers (LPP) in Kenya (2-Shift basis) is ~43% (tablets, 48%, capsules, 28% and liquids, 52%).
- There is adequate skills-mix is for the *current* levels of production of essential medicines.
- Many manufacturers are upgrading their facilities to comply with local and international GMP standards and is a capital-intensive process.

2) Policies and Regulations Impacting Innovation and Development of New Products

Policies and regulations within the government must work in a coherent manner with a clear roadmap to develop the LPP. They must ensure that the value chain maintain quality and support improvements. Some of the constrains include

- Lack of clear and pragmatic government policy to support LPP has led to apprehensive behavior when it comes to investing in their factories.
- Inadequate incentives on pharmaceutical inputs including the 15% public procurement There is lack of pragmatic strategies for product development in the industry has resulting into common 'me too' products
- Lack of pragmatic strategies for product development in the industry has resulting into common 'me too' products

3) Collaborations & Partnerships in Pharmaceutical Manufacturing

All multi national corporations growth in terms of market, products and strenth in R&D and innovations is a result of value adding colloberations and partnerships with other institutions

- This is uncommon, though acknowledged as very important as a means of enhancing GMP compliance, market penetration and improvement if product portfolio. These partnerships involve technical transfers. Examples include Universal Corporation/Strides Shasun r and Quality Chemicals /Cipla Qualityand an intended PPP between Dawa Group, Merck and Government of Kenya geared towards vaccine production.
- In addition, lack of clear guidelines and/or awareness on technology transfer, collaborations and partnerships
- Current training curricula and research priorities by local universities and research institutions are not necessarily aligned to the technical needs of the dynamic industry needs, e.g. technological advancements.

IMPLICATIONS & RECOMMENDATIONS

Based on the study, it was clear that there is need to review and improve on exisitng pharmaceutical industry relevant policies ino order to make them practical and tenable. They include (i) developing a tangible framework for investiment in the pharmaceutical sector and auxilliary industry; (ii) establishing a framework for attainment of stringent regulator status of the NMRA for international recognition and benchmarking GMP compliance of companies; and (iii) developing a harmonized incentive regime in

order catalyse growth and expansion of LPPs (expounded below). The latter is the basis for the policy incentive mechanism proposed below.

Quality Ranking and Risk Categorization of LPP Proposal

The categorization plan developed by UNIDO[6] in the Kenya GMP roadmap is a good starting point to ensure that GMP is adhered to while at the same time support companies to make incremental GMP improvents. This provides 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. While the GMP roadmap categorization into A; B; C was meant for determining the root cause of inferior quality, fixing quality problems, and even for GMP inspector/regulator to use it for licensing of premises and products, it can be enriched by turning it into an incentive vehicle to provide a win-win situation for the parties.

One of the fundamental ideals in Quality Ranking (QR) and risk categorization is to ensure a level play field for all manufacturers with the manufacturing environment that comply with GMP requirements for site and Quality management systems (QMS) (Exhibit 1). This admittedly would reduce the risk of poor quality of products entry to the distribution chain. Based on the results of the study, there is need to have an incentive approach for LPPs.

Exhibit 1. Categorization and Benefits. *Source: author adapted from Kenya GMP Roadmap*

Risk Category	Site	QMS	Benefits
A	Compliant site Low risk	WHO GMP certified	Regional GMP and products registered and trade
			Participate in national/regional/international tenders for all products
			New formulations/products and may produce for clinical trials & research products
			Maximum incentives
			Obligation to international GMP rules
B	Deficiencies but does not impair quality production Reduced Risk	Satisfactory QMS	Conditional licensure at national level
			Participate in national tenders on selected products
			Restricted exports
			Favourable and selected incentives
C	Unsuitable site High Risk	Unsatisfactory QMS	Limited low risk products for starters and time bound e.g. disinfectants
			general use being promoted for health, hygiene and sanitation
			National laws requirements

Exhibit 1 illustrates a potential quality-based incentive vehicle for LPPs. It is risk-based categorization model that have three classes; class A, B and C in terms of GMP compliance derived based on Site and QMS related GMP requirements. The licensing for manufacture would take into consideration the

[6] The consultant in this ACTs project was the author of the UNIDO report. Companies are ranked based on their GMP/quality positions. Categorization model has three classes, i.e. A, B and C, the latter being the lowest in quality.

suitability of a facility to manufacture specific products. High-Risk facilities will manufacture low risk products, for example, disinfectants and increasingly adopting other products.

The categorization model will empower the national medicines regulatory authorities in EAC to be means of industrial growth and stimulate the attainment of international standards. It is strategy to ensure compliance to international standards by all facilities via a stepwise approach for all manufacturers to attain the WHO GMP standards within a given period. It provides a growth pattern with the niche to achieve higher status of quality and a means of regulator enforcement. The industry of its own should develop a quality culture with growth patterns and alignment to health priorities that take cognizance of the SDG No. 3 of the and access to essential medicines. In a way it will realign the industry into categories that will stimulate upward growth, quality upgrades and investment to increase the product range within the Essential medicines list and other formulations. At the same time, LPPs will feel empowered because their improvements will be linked to potential increase in supply portfolios and competitiveness.

Implementation can be achieved by carrying out a baseline quality assessment of all or selected manufacturers with by GMP inspectors. Upon the findings, facility based CAPA[7] will be developed and a project map agreed upon between the regulatory agency and the manufacturer with clear timelines and milestones. There will be periodic review on the progress but more important a qualification assessment to determine the quality status of both site and Quality Management systems as the criterion for categorization. A scenario will be set where good performing will rise their quality status to full compliance and likewise prevent fall back to lower though regulatory controls will be applicable.

Exhibit 2. Risk categorization model stakeholders and their functions

Policy focus	Functions
Access to essential medicines	This a right which must be exercised by governments and public procurement agencies using the essential Medicines List but unlimited access in private sector
Medicines security	To ensure that all items on the EML are available and source is known for urgent and emergency supplies
Disease burden and morbidity	Focus on treatment regimens and ensure continuous availability of quality medicines from GMP certified and 'qualified' suppliers. Restriction of unlisted manufacturers to the market
Incentives to LPP	To be graduated and linked to quality improvements since the high-risk manufacturers with least investment in quality improvement. It provides a stimulus for quality improvement
Valuation of procurement tenders	Price valuation in identify and match import country export incentives and domestic levies, tariffs and non-tariff fees (if any) to off-set overheads for genuine price comparison

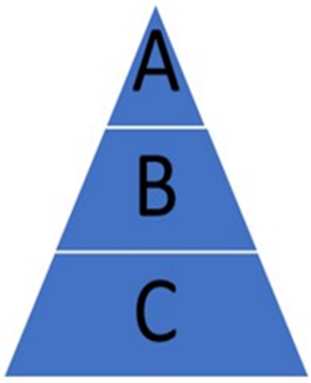
[7] CAPA: Corrective and Preventive Actions are set of actions taken by a pharma company to correct any issues highlighted during inspections, and actions taken to mitigate such occurrence or ensure they do not happen repetitively.

Quality ranking & Risk categorization	To stimulate quality improvements and give assurance of quality products in the distribution chain thus expanding market for compliant products

CONCLUSION

This risk categorization is a suitable tool for benchmarking GMP compliance of companies and can also be to monitor the companies' development towards full WHO GMP compliance. Suffice it to state that enforcement agencies can use their mandate to drive upgrades in domestic facilities by enforcing CAPAs and follow-up on implementation and review the GMP compliance levels. A means of structured incentive can be used for different levels of categorization to drive compliance. Moreover, a medicines security scheme, especially medicines in the disease burden regime, and determination of local capacity from reliable LPP can be derived from low risk manufacturers in category A and B. Risk categorization is therefore a stimulus scheme that promotes that industrial growth and rewards quality improvements and assures access to quality essential medicines.

Exhibit 3. Risk Categorization model for Sustainable LPP of high-quality medicines.

RISK LEVEL	RISK CATEGORY	QUALITY STATUS	BENEFIT/ OPTION/PREFERENCE
		GMP compliant	Any products/formulations
Low Risk			All/New products/Formulations
			New technologies
			R&D / Clinical Trial products
			Partnerships/Collaborations
Medium		Conditional GMP	High preferential procurement
			Any product/Formulation by choice
			new products/Formulation
			Partnerships/Collaborations
High Risk		Conditional License	Selected Low risk products/Formulations
			GMP Improvement plan/licensure

Note:

- *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

Source: author adapted from Kenya GMP Roadmap

<<END OF BRIEF>>

Improving Access to Essential medicines through Government-Industry-Universities/Research Institutions Joint Partnership

EXECUTIVE SUMMARY

Research & Development (R&D) is a critical aspect of innovation that is necessary for economic development and prosperity. Product development process is lengthy, costly and adherence to strict *regulatory requirements* is mandatory. Public-Private Partnerships (PPPs) have been identified as one of the solutions for addressing challenges in pharmaceutical innovation where capacity in research by the private sector is deemed insufficient. Industry-research institution partnerships should be established in the EAC region. EAC partner states should stimulate PPPs by directing the R&D agenda, funding pharmaceutical research and formulating policies that encourage product development.

INTRODUCTION

Pharmaceutical production is unevenly dispersed globally, with majority of the manufacturing work concentrated in a few sites mostly in developed countries. According to the World Health Organization (WHO) World medicines situation outlook, 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. The research-based multinational pharma companies from these countries have continued to spend, on average, ~17% of their revenues for R&D work to develop new medicines to save human lives. From such investments, tremendous reports on new formulations to address several ailments have been reported. The US Food and Drug Authority (US-FDA), through their Center for Drug Evaluation and Research (CDER), revealed that about 28 novel drugs were approved in the period 2005 - 2015 giving hope for hard to treat diseases.[1] Additionally, the International Federation of Pharmaceutical Manufacturers & Associations (*IFPMA*) show that there were 2.5million AIDS related deaths in 2005 compared to 1.1 million in 2015.[2] This was attributed to introduction of ARVs which were new at the time. Due to increase in the burden of non-communicable diseases (NCD), research-based pharma industry has also recognized this challenge and is committed to research in this area.

WHO has also identified 17 neglected tropical diseases (NTDs) that affect many people, predominantly from the poor setting, and have rallied all players including pharma to develop products to address the scourge. Considering that development of pharmaceuticals and new therapies is costly, there is need to leverage on partnerships to allow for concerted effort to ensure end-products are affordable. In this case, the support and funding for R&D for NTDs is mainly through collaborations and partnerships that bring together expertise from academia, industry, private foundations and governments and funded by philanthropic organizations, research-based industry. In 2014, the research-based industry invested over USD 543 million for NTDs research work. This demonstrates that industry-academia synergistic partnerships enabled by sound policies and regulatory systems are fundamental for development and

[1] CDER January 2016 summary report

[2] The Pharmaceutical Industry and Global Health, Facts & Figures 2017

funding of robust health systems.[3] This in turn creates conducive climate for investment in the pharmaceutical sector. As such, forming strategic partnerships with different organizations is a crucial part of our research and development process. For instance, GlaxoSmithKline (GSK) has over 500 research *partnerships* with universities and *academic* institutions globally and provides support for science students through fellowships to advance scientific understanding and research capacity. GSK's approach is drawn from historical happenings of the 1940s when the transformation of the US pharmaceutical industry happened because government partnered with 17 manufacturers to produce penicillin, which was urgently needed.[4]

Just like in the US, India's pharmaceutical industry experienced meteoric growth when government proactively crafted policy interventions, i.e. tax, partnerships, technology and legal provisions for the manufacturing sector[5] that has made their pharma industry the largest provider of generic medicines globally. In India, R&D is realized through partnerships and joint ventures (JVs). This has led to growth of the domestic market that is projected to increase from an estimated US$11 billion in March 2009 to approximately US$30 billion by 2020.

On the other hand, African countries produce approximately 30% of the national's medicines requirement; yet of the more than two billion people worldwide that have sub optimal access to medicines they need, majority reside in Africa. The low investment of manufacturing in Africa is a function of many aspects that include technical capacity, human resource, financing and conducive policy environments for pharma manufacturing. Nonetheless, Africa Pharma have demonstrated some level of expertise and currently produce various products, i.e. finished products such as tablets, capsules, creams and ointments for various therapeutic uses. More supportive policies and local partnerships can help bolster the small gains achieved so far. The government of Ethiopia is leading the way in demonstrating this through their industrial policy and health policy attributes that have accelerated growth of local pharmaceutical producers (LPP).[6] Learning from previous policy lapses, the current policy under implementation is more progressive with positive successes in industrial development including improved quality infrastructure and availability of quality medicines. Similar efforts have been seen in Uganda, Tanzania and Kenya even though proactive research partnerships remain low. Furthermore, EAC governments have not been able to create a framework within which government priority needs are linked to industry/research/academia groups. This has been attributed to weak policy advocacy environment - both in public and private sector.

In view of the above, ACTs project was conceptualized to establish the innovation capacity of the East Africa pharmaceutical manufacturing industry, identify the barriers to Public/-Private partnerships and establish a framework for an impactful pharmaceutical cross-sector partnership system for improved access in essential medicines.

The main objectives of the study were;

[3] Local production of pharmaceuticals and health system strengthening in Africa; An Evidence Brief; A publication in the German Health Practice Collection.

[4] Younkin, P. (2008). Making the Market: How the American pharmaceutical industry transformed itself during the 1940s. University of California, Berkeley, Berkeley, November 2008.

[5] Global pharma looks to India: Prospects for growth; PWC Report.

[6] Pharmaceutical Sector Assessment in Ethiopia December 2017 WHO and World Bank

1. To determine the level of production competence of the pharmaceutical industry in East Africa region regarding manufacture of national essential medicines.

2. To identify factors that contribute to the product gap between the national essential medicines lists and medicines that are manufactured in the region.

3. To establish mitigation strategies to reduce the product gap between the national essential medicines lists and medicines that are manufactured.

4. To explore how collaborations, financing, research links, and technology transfer can be harnessed to not only boost local production of quality essential medicines in the EAC region, but also increase access to affordable medicines.

From the study, this policy brief was developed. It proposes a clear pathway and mechanisms for enhancement of engagements across several industries including research institutions in the EAC region.

APPROACHES AND RESULTS

A survey was conducted in the pharmaceutical manufacturing industry, universities and research institutions in the EAC region. Information was obtained through comprehensive literature review, use of questionnaires, and formal meetings with key stake holders including the pharmaceutical manufacturing industry, Health ministry and Ministry of Trade & Industry.

Local Pharmaceutical Production in EAC region

There are about 60 pharmaceutical manufacturers in EAC and Ethiopia and majority produce non-sterile products – both beta and non-beta lactams; thus, demonstrating their level of competence in production of medicines. The major focus is on solids (capsules/tablets). The industry is limited in the capability to manufacture whole range of essential medicines. This is mainly due to lack the technical, financial and human capacity to manufacture these products. Pharmaceutical partnership is a great collaborative strategy that manufacturers can use in order to exploit synergies in application and utilization of knowledge and resources in order to help increase the range of products that are manufactured. Technology transfer and joint ventures are initiatives that can be harnessed to improve access to essential medicines. Examples of successful technology transfer enterprises in the region are Universal Corporation Limited/Strides-Shasun merger (Kenya) and CIPLA/Quality Chemical Industries Limited (Uganda).

Like many African countries, Kenya lacks sufficient technical, financial and human capacity to produce adequate medicines to meet the country's demand. This study established that the local pharmaceutical manufacturers in Kenya produced only 28% of the national essential medicines.

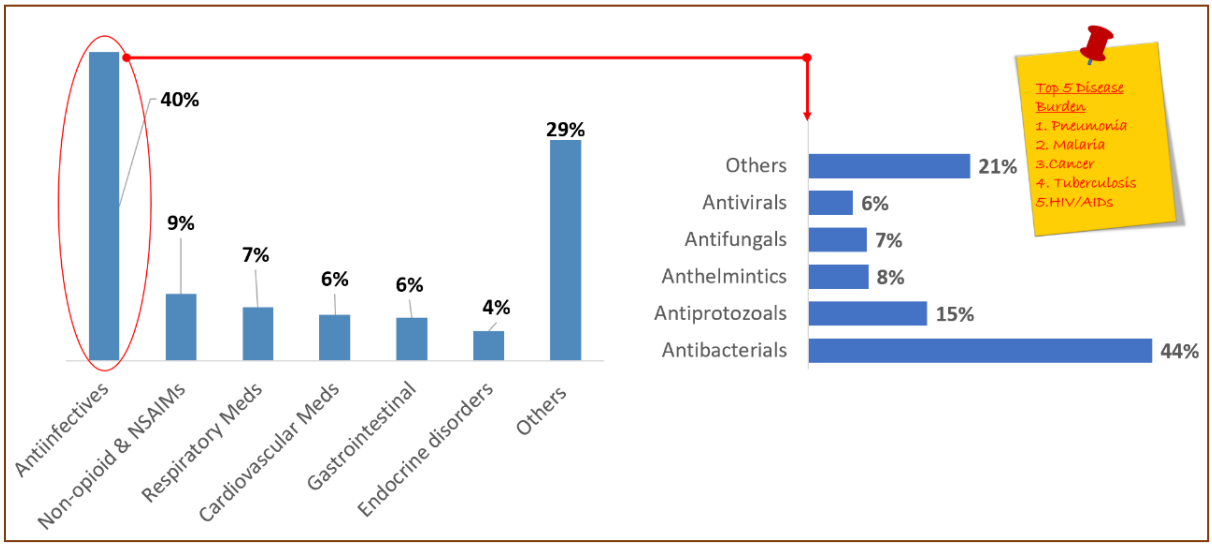


Exhibit 1. Pharmaceutical products manufactured in Kenya.

Notably, LPPs in Kenya focus on few therapeutic categories (Exhibit 1) at the expense of the bigger need as per the disease burden profile of the EAC region and country. It is also noteworthy that LPP are hesitant to engage in new molecule development that have high potential safety risks and/or narrow therapeutic indices and high product development costs. Most companies indicated that their product portfolio was based on market demand and not necessarily on the need to develop new products to address government priorities because they are unsure of government priorities and support. The industry's main agenda was tailored towards profit and not the needs of the country in regard to essential medicines.

There is potential for growth in pharma research in the region. There are efforts to promote R&D work at Muhimbili School of Pharmacy, the Kilimanjaro School of Pharmacy in Tanzania supported by GIZ and the Kenya Medical Research Institute (KEMRI) but are at nascent stages. Furthermore, the region has many universities with schools offering courses in biological and other sciences, chemistry and more than 10 schools of pharmacy that can collaborate with the pharma industry and work towards achieving the national research and medicines agenda.

However, the universities and research institutions in EAC have made no effort to create linkages with the pharmaceutical industry. Most of the research that is perfomed is for academic publishing and has not resulted in innovation that is useful for the pharma industry. There is a glaring disconnect between academia, research institutes, the pharmaceutical industry and the government. The LPP focus on a narrow set of products is an indication that there is no connection between the disease profile in the country and pharma manufacturing sector in terms of key priorities to address national disease burden. The disease burden of the country should determine the priorities in selection of products to be developed and the subsequent product quality requirements.

Partnerships Proposed by Pharmaceutical Sector

A symbiotic partnership is required (Exhibit 2). There is need to ensure that each player/stakeholder is benefiting from the partnership and this way it will be sustainable.

- Industry registers their needs with research institutions, e.g. product optimization, new formulations amongst others.
- Research/academic institutions use their research facilities to trial the work requested by industry.
- Once it is optimized and ready to be batch tested, the researchers send the compounds (test products) to the pharma company to use their R&D facilities to initiate the tests at a production site.
- If the product does well and process optimized, it is then scaled up to commercial scale production.
- To ensure success and sustainability, government shall commit to buy xx% of the FPP ensuing from this process.
- On their part, the private sector will contribute back ~xx% of their sales per unit that will be committed to R&D resource pool that supported the above work. The resource pool shall include already existing research funds from the National Research Fund targeted at health programmes
- The above cycle is repeated all through on a continuous basis.

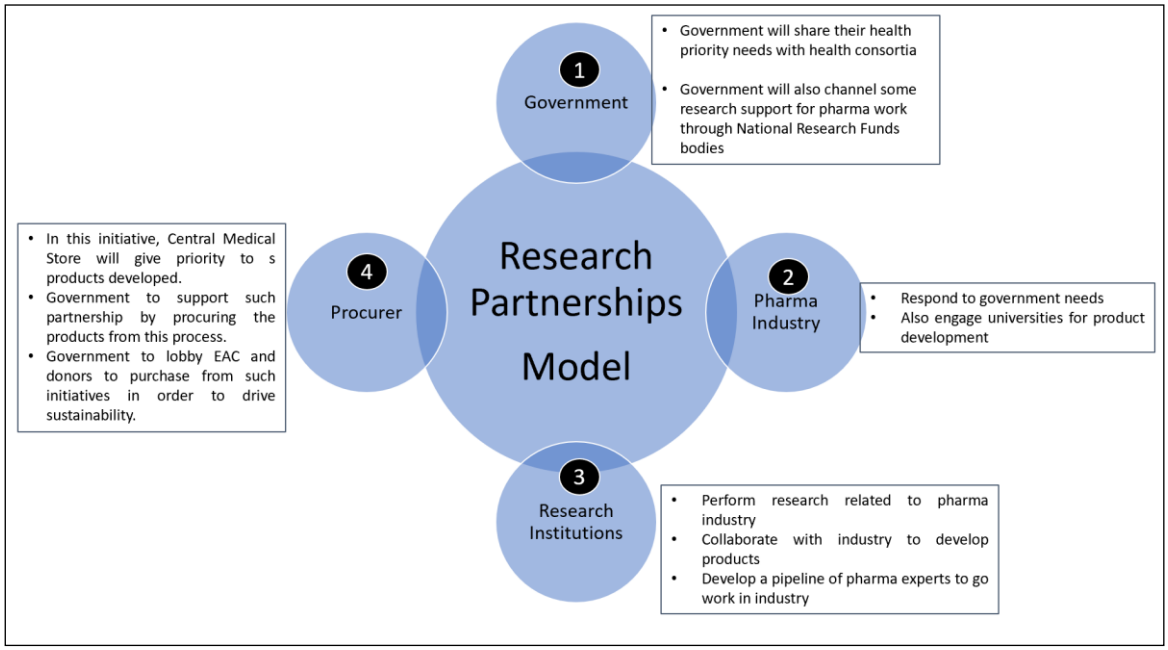


Exhibit 2. Proposed Academia-Industry-Government Model

Policy Implementation

There are several policy documents in Kenya which are consistent with vision 2030, an economic, social and political roadmap to move Kenya's economic status to a Middle-Income country. They include the Universal Health care, the Kenya Industrial policy and Kenya National Pharmaceutical policy. The driver for implementation in the pharmaceutical sector is the Kenya Pharmaceutical sector Development Strategy (KPSDS). The KPSDS is a holistic approach encompassing seven strategic components namely, setting out a roadmap for industry to achieve GMP Standards, strengthening mechanisms for quality assurance of medicines in the distribution chain, strengthening regulatory capacity, accessing necessary

financing for investment in the sector, devising time-limited incentives for industry, developing necessary human resources and developing common support services for the local pharma industry.

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 change.[7] This is because *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 programs[8] 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.

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. The weaknesses stated herein may be mitigated through the following actions, for enhancement of medicines access through pharmaceutical partnerships in the region.

IMPLICATIONS AND RECOMMENDATIONS

- A high level government advisory panel on pharmaceuticals development should be established that collects and collates and disseminates data necessary to attract investiment in the sector and provides a forum to bring government, industry and academic/research institutions to identify national priority needs relevant to the pharmaceutical manufacturing industry.

- Establish industry-research institution partnership for product innovation and research in line with the public health needs, especially essential medicines. This should include exploring traditional medicines as a source of medicines. This partnership shall run on the strength of product development, intellectual property agreements and assurance. Respective institutions and national governments should encourage, motivate and wherever possible facilitate the agreements, guarantees, especially those ralated to LPP and disease burden.

- The region should harness the potential of their research institutions capabilities to develop new products through structured collaborations & partnerships that can be public funded to address the priorities in line with the national disease burden. This structured approach should ensure that the positive outcomes of these research/devlopment work benefits the citizenry.

[7] Sarah Vugigi et al. Production Capacity of Pharmaceutical Manufacturing Industry in Kenya. East Cent. Afr. J. Pharm. Sci. 20, 2017, 3.

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

- Develop additional incentives and harmonise the incentive regime in order catalyse growth and expansion of LPP scope to address the UN Sustainable Development Goal No.3 and disease burden. For example, the need to consider tax rebates for LPP that invest in quality improvements and R&D and also fund basic research in this industry.

CONCLUSION

The government should derive the R&D agenda for the pharmaceutical industry. There is need to establish a structure process to collect, synthesize and disperse data that is vital to guide industry and academic/research institutions on national priority R&D needs. This necesitates a symbiotic linkage between universities/research institutions and the pharma industry on colloberative arrangements and sharing of knowledge in health and pharmaceutical research priorities for development targeted towards improved access to essential medicines.

<<END OF BRIEF>>