Addressing bottlenecks to local production of medicines: Issues for international co-operation in East and Southern Africa

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Abstract
African countries are highly dependent on imported medicines and related products despite a stated policy intention in the African Union and regional bodies to develop local pharmaceutical production, which is expected to facilitate responsiveness to local health needs and has stated advantages for employment, skills retention, and foreign currency savings. Noting these policy intentions, this paper explores how the stated policy of local production in African Union (AU), Southern African Development Community (SADC) and East African Community (EAC) policies is being implemented and the bottlenecks to implementation. The paper examines the efforts made in selected countries to overcome these obstacles and the role of international and south-south co-operation. Drawing upon document reviews and key informant interviews, it presents case studies of Uganda, Kenya and Zimbabwe and their co-operation agreements with China and India. The study found limited evidence of operational co-operation, especially that which is based on south-south collaborations, despite the potential contribution of such collaborations to overcoming bottlenecks to local medicines production. Although the evidence from the case studies had limitations, the research suggests that a convergence of interests between countries in east and southern Africa and emerging economies on trade and investment cannot be assumed and that national and regional economic and social interests need to be actively negotiated to overcome identified bottlenecks. We thus recommend measures to strengthen the enabling policy, legal, trade and investment environments, to strengthen oversight and regulation of medicines, and to enhance technical and strategic capacities in the east and southern African region needed to support local production of medicines.
Introduction
The United Nations Programme on HIV/AIDS (UNAIDS) has noted that African countries are highly dependent on imported medicines and related products, with more than 80% of antiretroviral medicines (ARVs) imported from outside Africa (UNAIDS, 2014). The organization highlights that local production is important not only for the AIDS response, but also for other existing and future health challenges faced by the continent. Total pharmaceutical spending for Africa in 2012 was an estimated US$18 billion and is expected to reach US$45 billion by 2020 (UNCTAD, 2011a). While the limits to local production may not be a barrier to medicine access in the short term, concern over the dependency on imported medicines and a desire to develop local manufacturing capacity has been articulated on the continent, given the advantages for employment, skills retention, foreign currency savings; and to facilitate responsiveness to local health needs (AU 2007; SADC 2007). The continent has 14% of the world’s population but produces only 3% of the world’s medicines. While the overall pharmaceutical market in sub-Saharan Africa is worth US$3.8 billion annually, the pharmaceutical manufacturing sector in Africa contributes only 25-30% of the continent’s needs (IFC, 2008).

In 2008, the World Health Organization (WHO)’s Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) observed that local production of pharmaceuticals was a key area for investment (WHO, 2011). The GSPA-PHI’s policy intention was to support local medicines production in Africa; and in doing so it called for investment, capacity building, identification of best practices, north–south and south–south co-operation and collaboration with the pharmaceutical industry, amongst other recommendations. The Southern African Development Community (SADC) Pharmaceutical Business Plan and the East African Community (EAC) Pharmaceutical Manufacturing Plan, which were developed in 2007 and 2011 respectively, also suggested policy measures to overcome barriers to access to medicines, including calling for pooled procurement to make medicines more affordable (SADC, 2007; EAC, 2011). In 2012 African governments, as member states of the African Union, adopted in 2012 the Pharmaceutical Manufacturing Plan for Africa (PMPA), which also includes a policy goal to create and sustain pharmaceutical industries whose operations are relevant to local economies and responsive to local disease burdens (AU, 2012). This paper explores the bottlenecks to implementation of these stated policies on local production at continental and regional economic community levels. It analyzes evidence from three country case studies and from a document review on national efforts made to overcome these bottlenecks, including advocating it as an issue for foreign policy, through international co-operation with India and China.

The ESA region has traditionally been dependent on Western economies for bilateral and multilateral support to the health sector, including for access to medicine. However, new diplomatic collaborations and agreements have been pursued between countries in east and southern Africa and Brazil, India, and China around trade, joint manufacturing, prequalification processes, and other areas of technical co-operation on medicines. These international relations provide opportunities for overcoming bottlenecks in important aspects of pharmaceutical manufacturing such as technology transfer, particularly when linked to manufacturing and capacity building initiatives within the region (WHO, 2006; WHO, 2011; Anderson 2010; Seiter 2005, UNCTAD 2011a).
We explored this within the Regional Network for Equity in Health in East and Southern Africa (EQUINET)’s research project on Contributions of global health diplomacy to equitable health systems in east and southern Africa.

Methods
The research carried out from 2013 to 2014 included a review of government and intergovernmental body policies, peer-reviewed journal papers, official documents and other published materials to identify and triangulate the policy positions, bottlenecks to local production and evidence of international co-operation in addressing these bottlenecks. Three country case studies were carried out through literature reviews and semi-structured interviews with key informants to identify bottlenecks to local medicine production in the region. In addition, in order to test reliability and validity, the authors of this paper organized a forum with policy makers from national and regional institutions to review and verify the findings.

The literature reviews included peer-reviewed journal articles, policy documents, book chapters, media articles, academic reports, briefing papers and parliamentary reports published in English between 1992 and 2012. The documents included were those that referred to local production of pharmaceuticals, south–south co-operation, access to medicines, global health diplomacy and those that referred to the role of India and China in access to medicines and local pharmaceutical production in ESA. The reports were obtained from Medline, the International Development Research Centre (IDRC), Google Scholar and EQUINET databases and through internet searches. Searches were also done on multilateral agency websites, e.g., those of the WHO, the World Trade Organisation (WTO), United Nations Industrial Development Organization (UNIDO), United Nations Conference on Trade and Development (UNCTAD), World Bank; continental and regional organisation websites, e.g., those of the AU, SADC, EAC, and the UN Economic Commission for Africa; and mainstream international and regional media. A final set of 58 documents met the inclusion criteria. The documents included are not exhaustive of all literature on access to medicines, local production and south–south co-operation. Additionally much publication in Africa consists of grey literature which is not accessible online. The fieldwork addressed this limitation in the case studies. We discontinued the collection of new data once saturation in the literature was reached and material was repeated across the literature reviewed.

At a policy dialogue forum organized at the 56th East Central and Southern Africa (ECSA) Health Ministers’ Conference in Arusha, Tanzania, in mid-December 2012, the authors obtained feedback from senior officials from ESA countries on the document review findings, which provided a measure of reliability testing.

Three country case studies were examined: A) in Uganda on the experience of the partnership between Cipla (India) and Quality Chemicals International Limited (QCIL)(Uganda); B) on local production in Kenya and the Kenya-China co-operation on medicines production; and C) in Zimbabwe, on the role of domestic private capital in local medicines production generally, and specifically through the experience of Varichem Pharmaceuticals [Pvt] Ltd., a local pharmaceutical company registered in Zimbabwe since 1985. We reviewed 30 relevant documents in Kenya, and carried out nine key informant
interviews with government officials at the Ministry of Health and specialized government agencies dealing with medicines, with respondents from the pharmaceutical industry (private sector and University of Nairobi School of Pharmacy) and civil society. We reviewed 20 documents in Uganda, and carried out thirteen key informant interviews with respondents from the same groups as in Kenya including stakeholders from the Cipla-QCIL co-operation, along with other domestic producers. In Zimbabwe, we reviewed 25 documents, and carried out three key informant interviews with government, private sector and non-state actors in the sector, given that the focus in this case was only on domestic production.

The document reviews and interview data were analysed thematically and the findings are presented here according to the most commonly expressed themes in the data. The qualitative semi-structured interviews allowed for the further exploration of themes identified within the literature review and policy analysis. Hence, despite the limited sample size, the interviews provided key insights and perceptions related to the themes identified from document review.

In Kenya, the Ministry of Health authorized the research. In Uganda, clearance was obtained from the National Council for Science and Technology. In Zimbabwe, individual interviewees gave consent for the interviews. All key informants (KI) received introductory letters in advance of the interviews detailing the background and purpose of the research, structure of the interview and information pertaining to data storage of the interview transcripts. The respondents signed consent forms agreeing to be interviewed. Anonymity is preserved unless respondents indicated that they were willing to be quoted.

Finally, consultations were carried out at the 2nd East, Central and Southern Africa Health Community (ECSA-HC) pre-World Health Assembly (WHA) preparatory meeting for senior officials from ministries of health held in Harare, Zimbabwe in April 2014. A set of discussion questions were identified from the preliminary research and used in structured interviews with senior officials from Swaziland, Uganda, Zambia and Zimbabwe, documenting their responses. The questions explored the policies, incentives, regulations, licensing requirements, institutional reforms, tax incentives, funding, training of personnel needed to support local production and draw benefits from south-south co-operation; the changes needed to domestic law and policy; and areas for regional trade agreements and protocols in the ESA region (EAC, SADC). As only four of the eight countries were available for interviews, we provided the full report to the ECSA HC and their members and integrated feedback comments.

The study faced a number of challenges in data collection. Despite documentation of south-south co-operation, we found such co-operation in place in only one country (Uganda), where comprehensive information was available on the nature, scope and extent of co-operation. The proposed Kenya/Sino pharmaceutical plant that we intended to study did not advance past the planning phase and the factors affecting this outcome were not always forthcoming or in the public domain. In Kenya and Uganda there were difficulties accessing all key informants, with an overall response rate of 76% across the three countries. The loss was due to respondents not being available in the time frames of the research visits, some involved in initial negotiations having left their posts and some hesitant to share
Barriers and bottlenecks to local production
The review and key informant interviews in the case studies offered several insights into the main bottlenecks to local medicine production in ESA. This was further supported by an analysis of the key regional and governmental plans by the AU, EAC and SADC cited earlier (AU, 2007; EAC, 2011; SADC, 2007) and by interviews with policy actors at the ECSA-HC and WHA meetings. While specific evidence on cost drivers and affordability was not found, the bottlenecks identified would affect price and affordability. Critically, the plans highlight that pharmaceutical manufacturers operating within the SADC and EAC regions generally produce at a higher cost compared to larger international generic manufacturers and are constrained by reduced scale, older technology, higher costs of financing, a lack of integration with active pharmaceutical ingredients suppliers and unreliable supporting infrastructure such as electricity, water and transport (EAC, 2011; SADC, 2007). General consensus on these issues as priority areas support existing policy perceptions that local production of medicines requires developed infrastructures, a sound legislative and regulatory framework, skills and capital. While the need for access to medicines is embodied as a principle, all plans reflected a preoccupation with considerations of commercial viability, with limited attention to how to address the balance between commercialization and the need to make access to medicines affordable (AU 2007; EAC, 2011; SADC, 2007). These bottlenecks, while domestic, have implications for diplomatic negotiations and international collaborations on the manufacturing of pharmaceuticals. The analysis of the data revealed five main bottlenecks to local production.

First, diplomatic and policy negotiations that focus on the willingness (or unwillingness) of the pharmaceutical industry to transfer its know-how and techniques are not sufficient to secure the successful transfer of technology (COHRED and NEPAD, 2009; WHO, 2011; UNCTAD, 2011b; EAC, 2011; Loewenson, 2011). This is because recipients of transferred technology must also have a minimum absorptive capacity to receive and effectively appropriate the technology transferred and ability to work in a policy and political environment conducive to pharmaceutical innovation. This absorptive capacity is determined by the existence of a sustainable and efficient cadre of highly skilled scientists – a capacity that remains underdeveloped within the case study settings, as discussed below.

A second constraint highlighted by the literature was the shortage of skilled professional personnel; and the literature pointed to infrastructure and skills as major issues affecting technology transfer, indicating the relevance of this area in international co-operation (COHRED and NEPAD, 2009; WHO, 2011; UNCTAD, 2011b; EAC, 2011; Loewenson, 2011). Key informant interviews and documents in the Kenyan setting highlighted the capacity to produce industrial scientists, but also a weakness in communication between training
institutions and the pharmaceutical industry to respond to the human resource needs of the latter (MoMS and MoPHS 2010:45).

Thirdly, the literature review exposed that there is debate on what technology transfer entails; and this debate also affects the content of foreign policy negotiations. GlaxoSmithKline has argued that technology transfer includes both resources and know-how (GlaxoSmithKline, 2011) – hence its position that collaboration with African research institutes to develop a malaria vaccine and clinical trials in the region constitute technology transfer. In response to criticism that collaboration is not sufficient, in a position paper the company questioned why disproportionate emphasis is placed on manufacturing capacity over other types of technology transfer, such as its collaboration on clinical trials (GlaxoSmithKline, 2011). For others, medical education satisfied the definition of technology transfer. For example, India offers world-class expertise at relatively low cost to African countries as a stated contribution to technology transfer (Lunogelo and Baregu, 2013). In the health sector, this has included medical expertise and support to local hospitals and health-related institutions, such as through telemedicine consultations with specialist hospitals in India (Lunogelo and Baregu, 2013). What these results suggest is that there remains considerable ambiguity regarding the definition of what constitutes technology transfer as well as what types of transfers best reflect general expectations. Clearly defining the goals for technology transfer is important for negotiations on pharmaceutical manufacturing.

Fourth, the research also found that local production supported by external (development) aid to local public sector producers can protect or direct funds to specific producers, and gains from mark-ups on imported pharmaceuticals can be diverted to private use, especially where civil society is weak and unable to ensure accountability of public funding (Bate, 2008). This draws attention to the regulatory frameworks and functioning of governance systems in the development and establishment of local pharmaceutical production, including in negotiations on aid for pharmaceuticals. In consultations, senior officials noted that donations of essential medicines produced outside the country, while important for health services, reduced the incentive to invest in local production. They suggested that a share of external funding could support local or regional procurement from firms prequalified by the WHO or used to subsidize a reduced price for locally produced medicines, making them more affordable.

Finally, patents on medicines were noted to pose a fifth potential barrier to local production, and have been raised as contributing to cost barriers to access to medicines (Elbeshbishi, 2007; WHO, 2011; Klug, 2012). While flexibilities within the WTO’s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) have been attained from prior trade negotiations, ESA countries are reported to have faced challenges in using them, such difficulties in issuing compulsory licences, due to cumbersome processes (SEATINI and CEHURD, 2013). ESA countries reported the importance of the Declaration on the TRIPS agreement and public health (“Doha Declaration”), adopted by the WTO Fourth Ministerial Conference in 2001, which extended the deadline for least-developed WTO members to grant or enforce pharmaceutical patents until at least 2016.
Senior state officials interviewed at the regional policy dialogue forum confirmed a number of the constraints identified from the literature review: the lack of working capital and higher costs of local production; lack of strategic public and private sector leadership and skills—especially industrial scientists and pharmacists—; high tariffs on inputs/raw materials; and weak purchasing power in the regional markets for medicines. Triangulating evidence across all the study findings, there were further bottlenecks to local medicine production, many of which are linked, including:

- A weak policy environment and limited government support for domestic investment in the pharmaceutical industry;
- High tariffs on imported inputs;
- High interest rates on credit;
- Aging and unreliable energy production facilities, water and transport infrastructure;
- Limited international linkages and mechanisms for the sourcing of active pharmaceutical ingredients;
- Gaps in the regulatory framework and in enforcement capacities to ensure quality-assured, safe and efficacious medicines;
- Small markets within individual countries, and;
- Weak or non-existent capacities for research and development.

These factors raise issues for the content of international co-operation and also affect the uptake of prior diplomatic gains, such as the TRIPS flexibilities.

**Findings from the country case studies**

Kenya, Uganda, and Zimbabwe are experiencing a number of challenges, including a lack of infrastructure, rising population, high levels of poverty and a high disease burden. In all three countries, there are challenges in ensuring the availability, quality, and affordable pricing of medicines – challenges which are exacerbated by trade rules and intellectual property protections (UNDP, 2011).

In Uganda it emerged that while there has been a significant increase in per capita expenditure on medicines from $0.5 in 2010/11 to $0.9 in 2012/13 this falls far short of the annual needs of the population, estimated at US$ 5.86 per capita (MoH Uganda, 2008, UNIDO 2010). Medicines in public health facilities are relatively more affordable than those in private health facilities, and the government has the primary role of ensuring access to essential medicines (MoH Uganda, 2010), albeit with high levels of external procurement (MoH Uganda, 2008; UNIDO, 2011). The Kenyan pharmaceutical industry register has 42 companies listed as local pharmaceutical manufacturers, but Kenya still imports about 72% of its medicines, mainly from India and China (MoMS and MoPHS, 2010).

**Uganda**

In Uganda, Quality Chemicals Industries Limited (QCIL), located in Kampala, was formed in 1998 and focused mainly on the importation of generic medicines from India. In 2004, Quality Chemicals and Cipla Limited, an Indian pharmaceutical manufacturer, entered into a joint venture to set up a pharmaceutical plant in Uganda. The factory was commissioned in 2007. QCIL is the only local manufacturer involved in the production of antiretroviral
and antimalarial medicines. These medicines are manufactured under a licence from Cipla and the plant is compliant with the WHO's good manufacturing practices for pharmaceutical products. In interviews, senior officials at QCIL emphasized that the plan is to compete in new pharmaceuticals.

The partnership between QCIL and Cipla set up a research and development unit with positive results for technology transfer. Through staff exchanges and on-site efforts, Cipla has trained QCIL staff. While initially the personnel at the joint venture may have been comprised of expatriates, QCIL currently has fewer than 10 expatriates working in the whole plant out of a workforce of about 220. These training and exchange programmes have helped develop skills capacities and human resource development in the pharmaceutical sector (Uganda KI 7).

QCIL is manufacturing under a license from Cipla, which creates an obligation to maintain high manufacturing standards. QCIL thus strives to maintain high standards of pharmaceutical manufacturing not only to enhance its prestige but to sustain its license to manufacture pharmaceuticals. Although there was no accessible evidence on any reduction in costs of medicines produced by QCIL, officials at QCIL mentioned that the plant will begin to manufacture and market certain medicines at a cheaper price than those imported from outside the country, due to benefits of the partnership with Cipla. According to KIs, the plant also seems to be moving towards more advanced processes, potentially leading to the manufacturing of active pharmaceutical ingredients (APIs), which could further reduce the cost of production, not only in Uganda but also in the whole east and central African region, since APIs are currently being procured from Asia at high cost (Uganda KI 7). Due to its partnership with Cipla, QCIL is now the leading manufacturer of antiretroviral and antimalarial medicines in the region. Further, the proposed upgrading to the manufacturing of APIs will strengthen QCIL's position in the market for the entire region. For example, according to QCIL’s corporate secretary, the government of Rwanda has expressed an interest in procuring APIs from QCIL, as have other governments in the region (Uganda K17).

Interviews with both officials from QCIL and the government indicated that the government of Uganda played a central role in arranging the joint venture (Uganda KI 7). The government provided a wide range of incentives that encouraged CIPLA to partner with QCIL, including free land for the plant site in Kampala and other financial support, such as the tax-free set-up of the entire infrastructure, an agreement to procure ARVs worth $30 million per year for seven years from the plant and a 10-year tax break for the joint venture.

While this specific example provided a positive case of local production, evidence suggests that it is not widespread in Uganda. While the law provides incentives for local production (Government of Uganda, Investment Code Act Cap 92:14), the national tax policy has not been set up to provide tax incentives for local investors and manufacturers, and there are no import restrictions on pharmaceutical products already in production (WTO, 2012). In 2002 the National Drug Policy (NDP) promised to create a system of incentives for local production of essential medicines, including training of personnel, but this has not yet been widely operationalized (MoH Uganda 2002; Uganda KI 7). KI respondents in Uganda
emphasized the high operating costs of manufacturing in the country as being particularly restrictive for the establishment of local pharmaceutical production, including the costs of transporting raw materials and unreliable energy supplies (WTO, 2012).

Kenya
In the 1980s the Kenyan government mooted a plan to build a pharmaceutical plant in Eldoret with the help of the Chinese government. This was intended as a government-to-government partnership with each party owning 50% of the equity in the proposed investment. The Kenyan government would provide the land while China would supply the equipment, technology and financial resources in the establishment of the plant. However, the project was not pursued and when the government explored reviving the project in 2004, it found that many of the terms were out-of-date, such as those on equipment. At the national level, the policy environment had shifted from state-controlled, state-owned companies to a more liberalized paradigm of private producers and state regulators. As a result, there are no current plans to revive the project (Kenya KI 6).

Kenya’s National Pharmaceutical Policy has identified multiple barriers to local production, including:
- Conflicting policies and laws;
- Poor infrastructure and high costs of power and other production inputs;
- Negative publicity on generics and on locally manufactured product;
- Limited technology transfer for manufacture of generics;
- Lack of full implementation of TRIPs flexibilities and;
- A limited pool of specialized pharmaceutical personnel to meet the research and development (R&D), industrial pharmacy, biotechnology, quality control and assurance needs of the industry (MoMS and MoPHS Kenya, 2012).

A paper by the Kenyan Ministry of Medical Services made clear that pharmacy training in Kenya does not adequately address the skills required for pharmaceutical manufacturing (MoMS and MoPHS Kenya, 2010), although the number of pharmacists graduating from the country’s academic institutions has increased (Thoithi and Okalebo, 2009). In addition, key informants and documents raised the issue of high electricity costs due to inadequate generation and distribution facilities (WTO, 2012b) and the lack of long-term public or private financing at affordable interest rates (Kenya KI 2, 10, 11).

Zimbabwe
The pharmaceutical sector in Zimbabwe is the second largest in the SADC region after South Africa in terms of size and development, and was included in this research for its contrasting example of a strong domestic sector created by local investment. In 2009, Zimbabwe locally produced more than 65% of the medicines on its Essential Drugs List (Zimtrade, 2009). Zimbabwe has a positive policy and skills environment. The state encourages generic medicines through issuing of compulsory licenses to manufacturers and has remittance measures to facilitate technology transfer, the infrastructure and facilities to train pharmacists, scientists and technicians and government-to-government agreements to recruit pharmacists, including from Cuba (Zimbabwe KI 15; WTO, 2011; Maonera and Chifamba, 2005; NECF, 2009). For example, after the Zimbabwe government
declared a period of emergency on HIV/AIDS in 2002 the Minister of Justice, Legal and Parliamentary Affairs of Zimbabwe invoked Section 34 of the Patents Act (which allows use of patented inventions for the service of the state). This measure was used in 2003 by Varichem to apply for and be granted a compulsory license to manufacture Combivir, an antiretroviral medicine (Maonera and Chifamba, 2005).

Since 2009, however, the industry generally has performed poorly due to a lack of funding for trade, competition from imported and donated medicines, declining government spending on medicines, prolonged registration times (about 24 months) and electricity supply shortages. A lack of credit lines has hampered the industry’s ability to effectively participate in the export market (WTO, 2011). In 2011, the chairman of the Pharmaceutical Manufacturers Association reported that the industry was collapsing due to:

- Low capacity utilization (0 to 40% of potential capacity to produce being used);
- Instability inherent in companies surviving through lines of credit from banks;
- Outdated facilities requiring upgrades or replacement;
- No new product pipelines and;
- A decline in the number of new companies entering the industry (Mujuru, 2011).

While Zimbabwe’s pharmaceutical manufacturers exported an average of 10% of output in the region in the early 2000s, this share has not grown. Local manufacturers are reported to be grappling with competition from cheaper Indian generics; liquidity problems, with no lines of credit available and externally funded imported pharmaceuticals (UNIDO, 2011; Zimtrade, 2009; Mujuru, 2011). Contrary to policy, there is a more favourable tariff regime on imported finished products compared to the raw materials for manufacturing (UNIDO, 2011), eroding the viability and competitiveness of local producers in key economic sectors.

Discussion

Learning from the study on overcoming bottlenecks to local production
The case studies highlight that some of the bottlenecks to local production are being addressed. Both Kenya and Zimbabwe produce pharmaceutical products that are consumed locally and are exported to other countries in the region, although with a fall in production in Zimbabwe. In all three countries, the legal and regulatory policy framework for the pharmaceutical sector has been improved, although the supportive measures have not been fully operationalized. There are research institutions with the requisite infrastructure to support the sector. In Uganda, the partnership between QCIL and Cipla shows the potential of south-south co-operation in establishing viable and WHO GMP-compliant production in the ESA region.

Respondents consistently highlighted that government has a key role in encouraging local production of pharmaceuticals, especially given dominant foreign competition. The low prices of foreign-produced products - due to subsidies from their governments - means that if local manufacturing is to grow, then ESA governments need to subsidize the costs of production, improve on the regulatory environment and galvanize markets for local
manufacturers. This is shown in the Uganda QCIL/CIPLA partnership and the enabling support by the government through land, tax waivers and market agreements.

The pharmaceutical industry is a high-skill, high-technology industry, requiring the development of skills and the negotiation of technology transfer in international co-operation. The evidence presented here indicates that the case study countries have developed pharmaceutical expertise and have the operational research capacities to adapt technology to manufacture generic medicines. Research institutes, such as the Kenya Medical Research Institute (KEMRI) and the Scientific Industrial Research and Development Centre in Zimbabwe are examples of this. Stronger linkages between academia, research institutes, professional associations and the industry, nationally and regionally, could facilitate collaboration in research and development and improved strategies for improved retention of skilled workers and quality improvements in practice (MoMS and MoPHS Kenya, 2012). The options for technology transfer and its impact on the bottlenecks and on costs and affordability are a matter for further study, including research on how countries in other regions, such as Brazil, have addressed bottlenecks in production.

In addition to the proposals in the AU, EAC and SADC plans for improving market size and infrastructure (AU, 2007; EAC, 2011; SADC, 2007), the case study findings point to the need to:

- Bring down the cost of utilities like electricity, water and other public services;
- Increase funding for research and development;
- Provide incentives and tariffs that support local manufacturers; and
- Use government procurement to support domestic producers.

These measures require governments to take a leading role in formulating strong policies and regulatory frameworks and implementing these policies. Many of these factors also point to the potential contribution that would come from regional co-operation in pharmaceutical manufacturing.

While local manufacturers have the capacity to produce quality essential medicines, they cannot compete with international manufacturers when it comes to price because they incur higher production costs. This was one area where QCIL had not noticeably benefitted from its partnership with Cipla, despite tax incentives. The fact that APIs are still not manufactured in Uganda (although QCIL is aiming to change this, as noted previously) but imported from abroad also drives costs up. In importing technology, key resources, such as raw materials, and operating at a lower scale for a smaller market, QCIL is still unable to compete on prices with other global manufactures, such as those from India.

Lessons learnt for international co-operation
Emerging economies and other developing countries that have succeeded in developing their local pharmaceutical industries provide crucial lessons for ESA countries in the quest to set up local production. They have invested in research and development, established a solid human resources base and tapped markets in the south, including those in Africa (Chaudhuri, 2008). It would appear that there is an opportunity for strengthened negotiations to link the heightened interest in medicines in Africa and the capabilities in
Brazil, India, China and other emergent economies through measures that address the bottlenecks to local production in ESA countries. The expertise, resources and capacities in the emergent economies can be tapped to incentivise medicines development, support smaller firms in international markets, support regulatory capacities, distribution channels, financing, and build links with international partners (Holt et al., 2012). Diplomacy can play a role in this, in negotiating agreements that address bottlenecks. From the constraints identified in this review, we suggest that negotiations with investors in medicines production, whether government or private, could address:

- Research and development to deal with the challenges of technology including investments in science education and local R&D infrastructure to spur innovation;
- Personnel skills and capacities to assess needs, invest in training and resource centres and train local professionals in the requisite fields to widen the availability of knowledge and skills, with incentives to attract and retain the necessary capacities for local production; and
- The development of producers and market expansion through agreements to enable a wider population base for the market and a mix of participation in production from large and small firms and link regional and international interests that exploit existing strengths.

These measures call for government support and policy frameworks that balance public health and business interests and that facilitate investment in this area, including through partnerships. Our recommendations imply that governments would have set laws and policies and built the capacity to ensure the quality of medicine production by developing national standards, strengthening quality management systems for regulatory authorities and ensuring that biotechnology development goes hand-in-hand with regulation.

While the literature suggests rising international interest in local production of medicines across African countries, especially in ESA countries (WHO, 2006; WHO, 2011; Seiter, 2005, UNCTAD, 2011b), in this study, whilst noting its limitations stated earlier, we found limited evidence of operational co-operation especially that which is based on south-south collaborations. Yet there is evidence that such collaborations may support local medicines production, as found in the Uganda case study. Although the official documents reviewed do not mention south-south co-operation as a strategy for developing the pharmaceutical industry, nor provide explicit incentives for this (MoH Uganda 2002; GovUganda 2000), the collaboration between the Cipla of India and Quality Chemicals of Uganda provides an indication of what such cooperation would yield if pursued within the context of structured formal cooperation and collaborations.

The QCIL-Cipla case does suggest that the technical expertise, resources and capacities that already exist in emerging economies could be tapped to incentivize medicines development, support smaller firms in international markets, support regulatory capacities, increase distribution channels, increase financing and build links with international partners (Holt et al., 2012). If co-operation in medicines production is to be established, then it could start in those areas where there are already some market structures in place.
However, emerging economies like India and China may be more concerned to consolidate their own trade position than to invest in building local production in ESA countries, as is also found in Brown et al.’s discussion of the role of BRICS co-operation in addressing health system priorities in East and Southern Africa (Brown et al., 2015). This is particularly so given a perception of weak or disabled local policy and regulatory environments. It suggests that African countries may need to negotiate exchanges that better position themselves for future benefit, such as in relation to the capacity building and infrastructure needed to facilitate future investment in local manufacturing. The Zimbabwean case further suggests that some countries can, with the right capacities and conditions, build their own pharmaceutical industry through domestic investors without relying on south-south co-operation.

Given the lack of implementation observed in this study, domestic and regional measures would require awareness, oversight and reporting of implementation of policies already in place in the region. This study indicates the need for strengthened dialogue among governments, pharmaceutical companies and training institutions on human resource requirements for the pharmaceutical industry in order to develop, implement and harmonize the national pharmaceutical strategies for meeting the workforce requirements for the sector. The measures further include implementing agreed projects to improve water, energy and transport infrastructures in the EAC and SADC regions and raising import taxes on imported pharmaceutical products that can be manufactured locally, while encouraging importation of products that local manufacturers do not have the capacity to make and exempting duty and value added tax (VAT) on imported raw materials and packaging materials, to stimulate local production. Ministries of trade and health could establish a database on essential medicines and whether they can be sourced from local production or imports; and negotiate for a share of funds from development aid or investments to be used for local procurement from companies prequalified by WHO. While international co-operation can support such measures, many call for strengthened co-operation between domestic private and public sectors within ESA countries and regional co-operation across ESA countries.

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**Disclaimer of interest**

The authors declare that they have no competing interests.
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Uganda KI17 Respondent, QCL, Kampala, November 2013.


Zimbabwe KI5KI Senior industry official, Zimbabwe, Harare, February 2014.