Pharmaceutical Manufacturing in Africa

Knowledge gaps and emerging research issues

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Introduction

This brief is an abridged version of a research report, *"Pharmaceutical Manufacturing in Africa: Towards a Research Agenda on Competitiveness and Social Inclusion"*. It highlights the key research issues as identified through a series of interviews with a wide range of stakeholders in the policy domains, private sector, civil society, industry associations, development partners and research organizations. The prioritized topics have further been supplemented with extensive literature reviews on the current status of pharmaceutical manufacturing in Africa and a mapping of the activities, foci and priorities of most research and development partners operating in the continent. The resultant research agenda has been subjected to stakeholder reviews and feedback and presented at regional forums for validation and refinement.

The research agenda proposes that to become 'globally competitive', African pharma manufacturing should address the following: (i) Financing, Upgrading and Capacity Utilization – the need for long-term investment in technology upgrading, R&D laboratories and associated infrastructure, affordable financing mechanisms including a better understanding of 'the politics of lending' and strategies for promoting widespread innovation and commercialization (ii) intellectual property rights, and technology transfer – including flexibilities in international agreements such as TRIPS, R&D collaborations and academia – private sector linkages and (iii) Research, Innovation and Skills Development – how to build, incentivize and retain talent and scientific research excellence in the continent, including harnessing the opportunities provided by scientific cooperation and the role of the African diaspora.

Similarly, to be 'socially inclusive', new research is required into the following issues: (i) Affordability – including how to use public health procurement as a tool for enhancing local production and the variety of pricing models and their impact on the ability to serve the poor and marginalized; (ii) Access – including the distribution patterns and supply chains and whether local manufacturers can better serve the rural and marginalized communities and (iii) Quality – including whether standards and regulations lead to technological upgrading or constitute entry barriers for local manufacturers, role of technology and policy in curbing counterfeits, and learning and intelligence sharing on pharmaco-vigilance and post market surveillance.

The Context

Despite the recent gains and positive outlook on Africa, including a rejuvenated economic performance, a growing middle class, a youthful population and political support for local pharmaceutical manufacturing, the continent still faces several challenges that undermines the realization of its full development potential. Africa's disease burden continues to be the highest, the non-communicable diseases (NCDs) are on the rise and predicted to be worse over the next 30 years; disease outbreaks such as the recent Ebola in West Africa exposes the continent's under-belly and the level of unpreparedness in the face of disasters. The political support demonstrated at the continental and regional levels (through AU and RECs) rarely translate into policies, programmes and projects at the national level. As such, the private sector continues to suffer the weight of incoherent, and sometimes, punitive policies that undermine the development of endogenous capacity.

The investments in health R&D, innovation and financing remains far below recommended levels; skills and technical capacities are sub-optimal; markets remain segmented and disjointed. Even though regional integration and harmonization efforts are taking root, implementation of the harmonized regulations and protocols still face opposition in some countries. The linkages between academia (and other institutions of higher learning and research) and industry has remained weak and ineffective, hampering the free flow of knowledge within national economies. The private sector are getting more organized but their capacity to engage in policy advocacy remains weak, partly because of their inability to generate, package and use evidence to back their policy demands.

While international agreements such as the Trade-related Intellectual Property Rights (TRIPS) provides opportunities for technology transfer and has in-built flexibilities that could be exploited for national interest, only a few of African countries have taken advantage of such opportunities. Intellectual Property is viewed largely as a hindrance, rather than a facilitator in the manufacture of medicines, even though WHO reports that up to 95% of drugs in its essential medicines list (EML) are off-patents[1].

This mix of challenges and opportunities demands renewed momentum and targeted action backed by solid evidence if Africa's economic take-off is to remain on a sustainable trajectory. It is in this context that the research agenda has been crafted. It takes note of the progress made so far, the new and emerging challenges, the knowledge gaps and suggests areas that call for new inquiry in order to generate the empirical evidence that will inform policy, investments and trade decisions.

[1]Kinsley, 2009

Knowledge Gaps and Emerging Research Issues.

Affordability

One of the key challenges facing local pharmaceutical manufacturers is under-investments and under-resourced public health systems. A study by ref. Chataway, Banda, Cochrane and Manville (2015) have noted that public procurement is viewed as a potent mechanism to direct the demand for goods and services, and therefore a tool for achieving both industrial policy and innovation policy goals.

The authors have identified two broad types of public procurement: regular public procurement i.e. purchase of goods and services ordinarily produced within the country and public technology procurement i.e. purchase of goods and services that could be new to the world or new to the country. While both create markets for goods and services, they may have different developmental and learning outcomes.

A number of questions spring to mind:

- How can African governments use public health procurement as a tool for enhancing local pharmaceutical production?
- In cases where countries have experimented with this tool (e.g. in South Africa and Ethiopia), what has been the effect on production and consumption patterns?
- What are the actual effect/experiences on firm financial cash flows of the various drug procurement methods i.e. advance payments; cash on delivery or credit terms?
- What is the effect of public procurement policies on the growth and capabilities of local manufacturing of pharmaceuticals?
- How do these policies affect the ability of local manufacturers to serve the poor?
- The role of development partners in supporting local pharmaceutical manufacturing has come under sharp focus. Studies are required to establish the full effect of donor policies and generate evidence that would support African governments not only in negotiating with their development partners but also in crafting their own domestic industrial and health policies.

Access

Skills and capacities that can support effective distribution of medicines and ensure that patients get the drugs they need, at the right place and time, are largely deficient. The key challenges range from lack of infrastructure such as roads; to the fact that only very few distributors reach out to low-income communities and the very low numbers of skilled experts in the medicines logistics and supply chain management.

Besides, there is limited data and studies addressing the scope of local manufacturing to improve access to medicines, especially for the rural and disadvantaged populations. In most parts of Africa the rural areas constitute a disproportionately large number of poor and

disadvantaged households. A study finding by ref. Mujinja et al, (2014) – that locally produced medicines have higher chances of reaching the rural areas as compared to imports – warrants further investigation into the distribution strategies, partnerships and other factors that have made this possible.

One other area that has largely been ignored in the debates on access is the issue of 'patient acceptance' i.e. whether medicine is packaged and presented in a manner that is acceptable and sensitive to the cultural norms of the patient. Issues of culture, gender, religion and their influence on patients' receptivity to drugs have been pointed out as a key consideration for enhancing access and call for deeper inquiry.

Standards and regulations

The quality standards to which companies in SSA produce vary both across different countries, regions as well as within individual countries. One of the key findings from a recent pilot study in Kenya, India and South Africa show that while standards for the pharmaceutical industry are sometimes seen as independent drivers of technological capability upgrading, the reality is far more complex. Standards change over time and are shaped by a complex mix of firms' innovations, lobbying, procurement politics and market protection. The study concludes that 'standards may both help to ensure safe and efficacious medicines, and also act as an undesirable market entry barrier' (ref. Mugwagwa et al, 2015).

Several research questions arise:

- What is the role of standards on innovation and technological upgrading? In which contexts and under what conditions have standards been applied as drivers of technological capability building and upgrading?
- What is/has been the impact of various standards on access to medicines in developing countries? Are there cases where standards have been used as a technical barrier to trade and how have these been resolved?
- Harmonization of standards and regulations is on-going and has been concluded in some cases. What are the implementation challenges that arise from these harmonized standards? How are regions responding to such challenges?

Counterfeits and sub-standard medicines

Due to the discrepancies in national definitions for counterfeit pharmaceuticals, misclassification of substandard drugs and a reliance on the results of studies with varied methodological quality, the exact scale of the problem and prevalence of counterfeit pharmaceuticals in SSA is yet to be established. Further, the globalization of the pharmaceutical market, high prices for genuine drugs, lack of pharmaceutical regulation

and inadequate jurisdiction against counterfeiters contribute to the high prevalence of counterfeit drugs in SSA. There is also a scarcity of official documents that analyze the prevalence of counterfeits drugs around the world.

New studies are needed to determine the scale of the problem and prevalence levels; the role of technology in detection and deterrence and international cooperation/coordination mechanisms amongst other issues.

Pharmacovigilance and Post market Surveillance

In 2010, WHO conducted assessments at national medicines regulatory authorities (NMRAs) in 26 African countries and noted that structures for medicines regulation existed in the countries assessed, and the main regulatory functions were addressed, although in practice the measures were often inadequate and did not form a coherent regulatory system (ref. WHO, 2010). The study also highlighted the lack of mechanisms and procedures that would enable NMRAs to benefit from the scientific assessments and inspections carried out by other well-resourced and established regulators. In almost all countries assessed, health budgets were low and lack of sustainable funding restricted the regulatory operations. On the whole, the countries did not have the capacity to control the quality, safety and efficacy of the medicines circulating on their markets or passing through their territories.

These issues call for further inquiry including:

- A detailed analysis of the extent to which regulatory functions are being performed/implemented in the different countries to identify gaps, training needs and share lessons of good practices.
- Review of the legal and regulatory frameworks to identify overlaps, inconsistencies and areas that need consolidation/coordination
- Mechanisms for information and data sharing that enable NMRAs to benefit from scientific assessments conducted by other well-resourced and established regulatory counterparts
- Role of technology and innovation in product/supplier selection; pre- and post-shipment inspection and analytical/ pharmaceutical testing

Financing, Upgrading and Capacity Utilization

There are minimal theoretical and empirical studies on financing of local pharmaceutical manufacturing in Africa (ref. Banda, 2013). This constitutes a major research gap since lack of knowledge on who finances this sector; the extent of such funding; the terms and conditions for lending; the interest rates, duration and margins limits the choices and options for local firms wishing to access these services.

Besides, as Banda (2013) has argued, there has been very little consideration of the "politics of lending", in other words, the institutional considerations that determine decision-making on whether to fund, at how much, under what terms and conditions. This lack of understanding of the politics behind the lending process undermines the chances of African firms in accessing some of these loans. While the numbers may be minimal, some firms have successfully obtained financing from local banks and other financial institutions.

Studies are required to elucidate:

- What has been their experience and what could other firms learn from it?
- How about those who have accessed external financing from international institutions and lenders, what have been their experiences?
- What are the policy options for African governments wishing to support local pharmaceutical production?
- How does dependence on external financing for essential medicines affect the chances of local manufacturers?

The available production capacity in SSA is underutilized by most manufacturers, averaging 40% in most countries. This implies that there is a large volume of underutilized manufacturing capacity which could be applied to produce new products upon demand. In spite of this expansion potential, African local pharmaceutical production accounts for only 30% of the local demand. This under-utilization of installed capacity is attributed mainly to the failure of local companies to meet international GMP standards and achieve WHO pre-qualification standards in order to benefit from international tenders and compete against their Asian counterparts.

While there is pressure on local firms to upgrade and attain WHO-GMP standards, and WHO pre-qualifications, this is expensive and often leads to local firms becoming less competitive and out placed as suppliers by imports. There have been concerns that while the pressure to upgrade and attain GMP is welcome, the responsible agencies are raising the regulatory standards without thinking about the level of investment required. Studies are required to establish the mix of policies, incentives and support structures required for local pharma to upgrade and still maintain their competitiveness.

Intellectual property rights and technology transfer

A number of companies in SSA are venturing into collaboration and partnership for technology transfer utilizing TRIPS flexibilities to acquire the skills required for drug development. Article 7 of TRIPS requires that "the protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare,

and to a balance of rights and obligations. Similarly, Article 66.2 encourages developed countries to provide industry incentives for pharmaceutical technology transfer and capacity building in developing countries (ref. WTO, 1994).

It is not clear, to what extent the provisions of article 7 and article 66.2 have been fully utilized in the African context. In cases where there have been technology transfer agreements involving north-south collaborations, it would be worth studying the effect of these agreements on domestic capacity to manufacture medicines locally. Equally interesting would be a comparison (where possible) between north-south collaborations and south – south collaborations (involving India, China, Brazil etc).

In 2001, Aspen Pharmacare (from South Africa) became the first in the world to receive a voluntary license for ARVs, followed by Cosmos Ltd. in Kenya in 2004. Similarly, other African countries including Zimbabwe, Mozambique, and Zambia issued compulsory licenses for ARVs. Tanzania, Ethiopia and Uganda, have utilized TRIPS transition period to manufacture generic ARVs. These examples of technology transfer arrangements require in-depth empirical analysis to elucidate the circumstances (in the domestic contexts) that led to their negotiation, to draw out the experiences and lessons from the countries/parties involved. These could provide useful exemplars for other African countries and firms.

Similarly, there have been complaints of predatory tendencies by big pharma when engaging in voluntary licensing. For example they may grant the license to a local company but go ahead and cut the price of the innovator molecule to the level where the licensee is unable to produce profitably.

Moreover, most ARVs are under multiple product and process patents, so even though a company may get a voluntary licence, a crucial process may not be accessible due to existing patent protection. A key question is whether the voluntary licences in Africa have contributed to improving access to medicines. In-depth case studies involving companies that have experimented with such voluntary licensing/technology transfer such as Cosmos, Universal, QCIL – may highlight the links (or lack thereof) between these voluntary licences/technology transfer agreements with profitability and access.

Research, Innovation and Skills Development

The contribution of Africa's rich biodiversity to drug development has not been fully studied and capacity building is still needed for handling of traditional medicines and phytomedicines and cultivation of medicinal plants. This includes capacity development of national regulatory authorities, including expertise in taxonomy, quality control of medicinal plants and microbiology. Whereas it has been suggested that herbal medicines are a potential source of new APIs, R&D should aim at characterisation, purification,

standardisation and chemical engineering to make them not only relevant in industrial application but also for new treatments.

There are centres of research excellence (created mainly through ANDI) and centres of regulatory excellence (spearheaded by NEPAD). More work needs to be done to understand the workings of these centres; pick their lessons in R&D partnerships, lessons on collaborations and how that model can be improved, replicated in other situations so that such partnerships are the norm rather than the exception in Africa. There's also the need to determine the role of the knowledge institutions and research networks such as universities and specialized laboratories (both in developing countries, as well as in the developed countries) in supporting local pharma.

Finally, there is limited work on the role of the African diaspora in the pharmaceutical manufacturing sector. Studies on how India and other Asian countries have harnessed the skills and expertise from their diaspora, including the incentive and reward structures put in place to attract and retain talent would be useful lessons for Africa.

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