Strengthening Local Pharmaceutical Production in Africa to improve and sustain Access to Medicines

Summary

- A strengthened pharmaceutical industry in Africa will contribute to improved access to new medicines.
- It is a cross-cutting issue that would facilitate improved access under different models being considered by the High-Level Panel.
- Africa's Leaders have identified the need for developing the industry, an agenda which is supported by WHO and UNIDO amongst other international organizations.
- Enhancing standards of production is central to improved access to quality assured medicines.
- This requires a comprehensive approach to the multifaceted challenges that industry faces.
- WHO and UNIDO have supported development of country level and continental strategies for the industry and are supporting their implementation. Regional Economic Community strategies for East and West Africa have also been developed.
- The African Union Commission has established a consortium of organizations supporting the Business Plan to accelerate implementation of the Pharmaceutical Manufacturing Plan for Africa.
- However, to accelerate and sustain progress requires deeper and broader collaboration between multiple parties and enhanced support from the international development community.

Introduction

The World Health Organization (WHO) and The United Nations Industrial Development Organization (UNIDO) believe that strengthening the pharmaceutical manufacturing industry in Africa has an important role to play in contributing to improved access to quality assured, affordable, safe and efficacious essential medicines. The organizations think that dynamics around local production are crucial for the High Level Panel to consider within its mandate of addressing "the misalignment between the rights of inventors, international human rights law, trade rules and public health where it impedes the innovation of and access to health technologies" specifically with reference to Africa.

Supporting the development of international standard pharmaceutical manufacturing in Africa will contribute to improved access in a number of ways. These include increasing security of supply for priority essential medicines such as those procured with resources from the Global Fund to Fight AIDS TB and Malaria (GFATM). Implementing this agenda will also make an impact through establishing a source of supply of high quality pharmaceuticals across the Essential Medicines List that highly resource constrained National Regulatory Authorities can effectively oversee. The panel has already received a submission from Maureen Mackintosh [1] that goes into detail on other ways that local production

[1] Mackintosh M, Open University, Submission to the High-Level Panel

contributes to improved access such as through the increased penetration of locally produced products in rural areas.

Following the call for proposals the panel has received a wealth of submissions that outline diverse approaches to increase access covering issues related to the patent system and alternative ways of funding and structuring research and development.

This paper sets out how strengthening local production of essential medicines in Africa is a cross-cutting issue that in reality can facilitate the impact of many of the different models proposed, whether it is maintenance of the status quo, incremental adjustments to the current system or more far reaching recommendations that the panel may consider.

High Level Political Commitment in Africa and Support from International Leaders

African leaders have identified the need for strengthening the pharmaceutical industry on the continent. In 2007 at their summit in Accra African Union (AU) Heads of State and Government endorsed the Pharmaceutical Manufacturing Plan for Africa (PMPA)[2] in which the ambition to develop the industry to deliver improved public health was articulated. Strengthening the industry across the multiple different contexts that governments on the continent face is a very challenging undertaking. An initial activity under the PMPA was the establishment of the African Medicines Regulatory Harmonization (AMRH) initiative in 2009[3]. This collaboration between the New Economic Partnership for Africa's Development (NEPAD), the World Bank and WHO sought to support harmonization of regulatory requirements in different Regional Economic Communities. It recognized that defragmented sub-regional markets would be essential for local manufacturers to establish high quality facilities and processes and procedures that could be run efficiently and therefore competitively. Progress on the broader array of issues was less forthcoming and the fifth Conference of African Ministers of Health mandated the AU Commission (AUC) to develop a Business Plan for the accelerated implementation of the PMPA[4]. Such a Business Plan was developed with support from UNIDO and was endorsed by AU Heads of State and Government at their summit in Addis Ababa in July 2012.

The Business Plan recognizes the multifaceted challenges that need to be addressed to establish universal, sustainable, high quality pharmaceutical manufacturing (see below) and recommends that multiple actors, both continental and international organizations, need to work together to meet this objective. It also recognizes that establishing joint ventures and transfer of technology (an objective of the TRIPS agreement, 66.22) both North-South and South-South would have a critical role to play in the rapid development of the industry. The role that BRICS countries can play was highlighted in a joint Editorial by Mr. Sidibe, Mr. LI and Dr. Chan in the World Health Bulletin in June 2014 entitled "Commodities for better health in Africa – time to invest locally"[5].

[2] African Union, Pharmaceutical Manufacturing Plan for Africa, Addis Ababa, 2007.
[3] For further details see: http://amrh.org/
[4] African Union Commission, Pharmaceutical Manufacturing Plan for Africa Business Plan, Addis Ababa, 2012.
[5] Sidibé M, LI Y, Chan M, Commodities for better health in Africa – time to invest locally, *Bulletin of the World Health Organization* 2014; 92:387-387A.

The relevance of developing international standard local production not least for priority products is recognized in the Global Fund to Fight AIDS, TB and Malaria's (GFATM) market shaping strategy. This includes measures to encourage supply of high quality essential medicines from African manufacturers for long term access to safe, efficacious, affordable priority medicines for these pandemics.

There have been a number of different initiatives to support African countries and Regional Economic Communities to develop and implement strategies for the strengthening of their pharmaceutical manufacturing industries. The Economic Community of West African States (ECOWAS) has developed the ECOWAS Regional Pharmaceutical Plan with support from UNAIDS.

WHO supported the Ethiopian Government to develop its National Strategy and Plan of Action for development of the county's pharmaceutical industry. His Excellency President Mahama by letter to The AUC Chairperson, Her Excellency Madam Dlamini Zuma, invited early implementation of the Business Plan in Ghana through collaborative intervention of the consortium of partners supporting the AUC's PMPA.

There have been other interventions including the development of strategies for Zimbabwe, Kenya, the East African Community as well as targeted technical assistance on specific issues such as by the United States Pharmacopeial Convention (USP) which has supported regulatory capacity building. It has also established its Centre for Pharmaceutical Advancement and Training (CePAT) in Ghana to develop the human resources required by the industry and regulators.

Access to quality assured local produced medicines

Quality of essential medicines is critical for their efficacy and safety. Adherence to Good Manufacturing Practices (GMP) and other quality assurance mechanisms are required to consistently manufacture high quality medicines. National Regulatory Authorities are mandated to inspect facilities regularly to ensure compliance with these practices. The challenge in resource constrained environments for regulators to regularly inspect numerous manufacturing sites across distant geographies represents a significant threat to public health. Limited studies on quality of medicines in different countries in Africa such as WHO's survey on quality of antimalarials in six sub-Saharan countries in 2011[6] and USP's 2013[7] joint study with the Ghanaian Food and Drugs Authority on quality of the uterotonics oxytocin and ergometrine (inter alia for the emergency treatment of post-partum haemorrhage) raise serious concerns that locally sourced and intercontinental imports are too often sub-standard.

The WHO prequalification scheme provides quality assurance oversight for specific priority products financed by major drug procurement funds. It also supports more advanced African manufacturers to achieve international standards. For example Universal Corporation in Kenya has been prequalified for its Lamivudine Zidovudine fixed dose combination. In 2014 four companies in Nigeria were found to be

[6] Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Saharan Africa. Geneva. World Health Organization; 2011.

[7] Post Market Quality Surveillance Project Maternal Healthcare Products (Oxytocin and Ergometrine) on the Ghanaian Market, Report of the First Round. Accra. Ghana Food and Drugs Authority and The Promoting the Quality of Medicines Program; 2013.

in compliance with WHO GMP requirements. Further, Quality Chemicals International in Uganda (wholly owned by Cipla of India) has an additional site license to manufacture Cipla's prequalified products.

These companies represent the few who have managed to overcome the many challenges that African manufacturers face in order to achieve international GMP requirements.

Other manufacturers are striving to meet such standards and governments and regional economic communities recognize the need to support and require attainment of these practices. Issues that manufacturers need to contend with include accessing affordable finance to invest in the sophisticated facilities required for GMP compliant manufacturing, developing the human resources and complex internal processes and procedures required to produce quality assured medicines, funding their working capital given the need for importing many inputs from India and China, policy incoherence across government institutions with for example often uneven playing fields regarding tax and duties when compared to imported finished formulations.

Creating a conducive environment for local manufacturers to address the challenges that they face requires a systemic approach to supporting and requiring the industry to upgrade, with Governments Regional Economic Communities, and Continental and International organizations all having a role to play. Some of the major issues include ensuring policy coherence in support of the industry, enhanced regulatory oversight (not least as investors need to be reassured that as more rigorous quality standards are put in place, they will not be faced with competitors that are not keeping up), human resource development both for skilled employees such as industrial pharmacists and microbiologists as well as semi-skilled workers such as machine operators, reliable market data to inform investment and strategic management decisions. Other requirements include defragmented markets to enable efficient production, investment promotion to encourage for example foreign direct investment, and time limited incentives to support companies to continue to compete whilst making significant long term capital investments. Addressing such an array of different issues requires coordinated action by multiple parties, a challenge which to date remains a work in progress.

To support local industry and regulators to plot a pragmatic path for upgrading standards to WHO GMP, UNIDO has developed a GMP roadmap methodology[8] that establishes a step-wise approach for industry to follow based on the current status of manufacturing. This has been implemented in Kenya[9] and work is ongoing in Ghana. Furthermore, expressions of interest have been received from regional economic communities to support the development of regional frameworks for the GMP roadmap approach, and NEPAD is convening an expert committee on regional GMP roadmap frameworks in June this year.

WHO has developed a tool for assessing the level of risk to public health represented by production of different products at different levels of GMP compliance. UNIDO and WHO are currently working together to combine these two tools so that regulators can mitigate the risk to public health as local pharmaceutical manufacturers transition to international standards of production.

[8] White Paper on UNIDO's GMP Roadmap Concept. Vienna. UNIDO; 2015.

[9] Kenya GMP Roadmap, A Stepwise Approach for the Pharmaceutical Industry to Attain WHO GMP Standards. Republic of Kenya and UNIDO. Nairobi; 2014.

Contribution of Local Production under different policy recommendations from the Panel

Two top line principles of strengthening local production in Africa are: 1) quality of medicines is of paramount importance and requires strong regulatory oversight and sophisticated manufacturing operations; and 2) the proximity of production is important as it allows for regular inspections by resource constrained regulators. Over the next 15 years the context in Africa and globally will change significantly with the expected rapid economic development and changing global priorities. Therefore economically and politically feasible sources of high quality priority medicines are of strategic importance for long term public health in Africa.

However, it is clear that for many countries in Africa lack of local capacity to manufacture medicines under voluntary or compulsory licenses is a key barrier. For example, as mentioned in WHO's recent report on "The role of intellectual property in local production in developing countries"[10]

> *"Given the confrontational approach of production under compulsory license, a country needs to set up good quality production without any technical assistance from the patent holder."*

The same report also notes that:

> *"Collaboration by patent holders has increased in recent years. Licensing has become common in the area of HIV/AIDS and we have also seen cooperation in the area of hepatitis C."*

Hence strong manufacturing capabilities are required to benefit from opportunities to implement compulsory licenses or to use voluntary licenses for local manufacturing. Even with increasing voluntary licensing opportunities for public health priority products technology transfer is not a trivial matter. It requires a detailed process and collaboration between skilled parties to ensure that formulations manufactured at a new plant comply with the specifications within a product dossier and that the resulting medicine is equivalent to the originator. Furthermore, originator companies will most likely only be prepared to enter into voluntary licenses with companies that comply with international standards of production.

The top level issues highlighted above apply for other submissions to the panel that recommend incremental change to the current system such as expanding and simplifying the use of compulsory licenses, increasing the utilization of patent pooling mechanisms and limiting the impact of TRIPS+ legislation. For these and other recommendations quality of production and the ability to develop or receive technology are of critical importance as is the proximity of production.

The panel has also received submissions describing new models for stimulating innovation including de-linkage and abolition of the current patent system. However, under any new system the need for universal high quality local production and enhanced regulatory oversight would seem to also be critical.

[10] The role of intellectual property in local production in developing countries, Opportunities and challenges. Geneva. WHO; 2016.

Ongoing work showing promise

WHO and UNIDO continue to work closely together in support of strengthening production of essential medicines in Africa. WHO's local production initiative has been developed in the context of the Global Strategy and Plan of Action on Public Health Innovation and intellectual Property (GSPA-PHI)[11] implemented by WHO and its partners. Its local production activities to improve access to quality assured health commodities have been carried on in Ghana, Tanzania, Ethiopia, Nigeria, Kenya, Senegal and South Africa. It has also developed a number of tools such as the EML risk assessment mentioned above and a framework for policy coherence across health and industrial policy. This work has been supported by the European Commission and a WHO Director General's strategic grant as part of the collaboration with the Bill & Melinda Gates Foundation.

The German Government has provided support for UNIDO to implement a project on strengthening production of essential medicines in developing and least developed countries. This has enabled the organization to support the development of the PMPA BP, support country level strategy development and implementation in Kenya[12], Ghana and elsewhere, and develop tools such as the GMP roadmap mentioned. Another undertaking is pilot scale development of a business linkages platform to facilitate multiple types of different Business to Business relationships that can contribute to the strengthening of the industry.

The benefit of industrial development and public health expertise and mandates coming together can be seen in the case of Ethiopia. WHO supported the development and launch of a 10-year National Strategy and 5-year Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia (NSPA-Pharma)[13]. It is providing ongoing technical and coordinating support to the Government which is implementing the strategy within the framework of the PMPA.

Ethiopia is a pilot country for UNIDO's mandate for Inclusive and Sustainable Industrial Development as endorsed in the Lima Declaration of 2013[14]. It is working closely with the government to implement the Programme for Country Partnerships (PCP), recognizing that for industrial development in general multiple parties need to work together across different mandates and capacities. The NSPA – Pharma, which has been identified by the Deputy Prime Minister as the flagship programme for the country's second Growth and Transformation Plan (GTP2) will soon be incorporated into Ethiopia's PCP.

There is a need for deeper and broader collaboration for sustainable development in local production to improve access

Establishing universal high quality production of essential medicines in Africa requires coordinated and complementary south-south, north-south collaboration and partnerships between African and

[11] For more information see: http://www.who.int/phi/implementation/phi_globstat_action/en/
[12] Kenya Pharmaceutical Sector Development Strategy. Nairobi. Republic of Kenya and UNIDO; 2012.
[13] National Strategy and Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia (2015–2025). Addis Ababa. Federal Democratic Republic of Ethiopia Ministry of Health and Ministry of Industry; 2015.
[14] Lima Declaration, Towards inclusive and sustainable industrial development. Lima. 15th Session of the UNIDO General Conference; 2013.

international organizations. The AUC/NEPAD has convened a consortium of partners for implementation of the PMPA Business Plan which as well as WHO and UNIDO includes UNAIDS, the African Development Bank, USP, The African Network for Drug and Diagnostic Innovation (ANDI), UNDP, UNFPA and the Federation of African Pharmaceutical Manufacturing Associations. A collaboration framework has been developed by these partners. However, scaling up support for implementation of the PMPA BP or other regional and national strategies requires more robust partnerships be established and that central resources can be identified to facilitate close collaboration between multiple parties.

Conclusion

This paper is submitted following the receipt of submissions by the HLP and the hearings and global dialogues that took place in London and Johannesburg. It highlights that strengthening local production of essential medicines in Africa has a significant contribution to make to improve access to medicines on the continent. It also suggests that as the panel looks to consider how to address the misalignment between the rights of inventors, international human rights law, trade rules and public health it could consider emphasizing the cross cutting role that enhanced local production could play. Further, the requisite coordination structures and resource requirements to deliver on these objectives could be identified.