POLICY BRIEF

TheScinnoventCentre
SCIENCE, INNOVATION AND ENTERPRISE

NO.9/2020

INITIATIVES TO SUPPORT LOCAL PHARMACEUTICAL PRODUCTION OF QUALITY ESSENTIAL MEDICINES IN EAST AFRICA

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EXECUTIVE SUMMARY

Global and national initiatives have worked concurrently to support and sustain local pharmaceutical production (LPP) to ensure access to quality essential medicines.

Categorisation of the LPP is a key catalyst for growth of the sector in terms of product range, security of the medicines, access and availability of quality essential medicines.

A stimulus scheme to support and sustain LPP must 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 and development, human resource development and attract investment in the sector. The scheme should inform the levels of quality performance and risk categorisation.

INTRODUCTION

Access to essential medicines is a global campaign. 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 medicines, particularly against HIV/AIDS, TB and malaria. Since 2002, an annual amount of more than US$4 billion has been invested in the purchase of the fixed dose combinations in ARV and anti-malarial drugs. This has led to a significant drop in treatment cost and considerable increase in the number of people on treatment. In sub-Saharan Africa, there was a 13-fold increase from 1% in 2002 (300,000 out of 11 million adults) to 37% (5 million from 10.4 million eligible for ARV treatment).

It is important that these gains are not only realised, 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 categorisation approach provides a robust evidence-based, scientifically sound way to manage pharmaceutical manufacturers, to ensure they attain WHO good manufacturing practice (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 Nations Industrial Development Organisation (UNIDO) has also emphasised that many deaths could be prevented if safe and efficacious medicines were readily available to treat patients, and that inaccessibility would be increased 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 considerations, and interests must be carefully actuated. However, there is good justification that local pharmaceutical producers (LPPs) can reduce the disease burden of a country and improve the health status of its citizens. Local pharmaceutical production facilitates industrial and economic growth through infrastructure development, market access with potential for insulation against the unpredictable burden of new diseases and epidemics (e.g. Ebola) that may require unprecedented solutions.

LPPs provide:
a) Secure source of quality medicines and supplicants 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

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

non-communicable diseases, and offers a sustainable source beyond donor programmes.

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 programmes for the manufacturing sector to attain WHO GMP standards, and Health Action Internationals (HAI) pharma commercial viability/ improvement studies. They are 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 such as AMRH[2,3], have also been developed. They are aimed at promoting the regulation of medicines in Africa and sharing experiences, technical know-how and capacity building especially in 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 return contribute towards access to affordable medicines at the right time. Additionally, companies that have invested heavily to be GMP compliant as per the regulatory requirements feel that a level-playing field lacking due to the cost of compliance, which 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 previously been raised with regulators by the stakeholders[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 that the future for LPP growth will rely heavily on national governments and collaboration with global and regional agencies. The report articulates 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. This will help 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 a key component to the success of LPP.

To this end, there is an opportunity to develop a quality GMP-linked incentive mechanism, to not only boost access to affordable medicines, but to ensure that the industry also aspires 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

- 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 below international standards. Helping to 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*

[2]WHO Drug Information Vol. 28 No. 1, 2014.
[3]AMRH Newsletter 1Q 2019
[4]Discussions with CEOs from the pharma companies
[5]UNIDO Report on Boosting Pharmaceutical Production

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

There was also need to 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 incentivise the local manufacturers to invest in quality improvements and respond to the national health needs.

APPROACHES 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 the pharmaceutical industry, institutions of research, academia and policy makers in the Ministry of Health/ Ministry of Trade and 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 semi-solids (ointments, creams).

- Only 28% of the listed essential medicines are produced.
- About 56% of these products are solids and 63% are for management of non-communicable diseases.
- There were about three manufacturers of sterile products at the time of the study.
- The production capacity in this industry is underutilised. The average production capacity utilisation of local pharmaceutical producers (LPP) in Kenya (2-Shift basis) is ~43% (tablets, 48%, capsules, 28% and liquids, 52%).
- There is adequate skills-mix for the current levels of production of essential medicines.
- Many manufacturers are upgrading their facilities to comply with local and international GMP standards, and it 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 maintains quality and supports improvements. Some of the constrains include:

- Lack of clear and pragmatic government policy to support LPP leading to apprehensive behaviour when it comes to investing in their factories.
- Inadequate incentives on pharmaceutical inputs including the 15% public procurement.
- Lack of pragmatic strategies for product development in the industry, which has resulted into common 'me too' products.

3. *Collaborations and partnerships in pharmaceutical manufacturing*

All multi-national corporations' growth in terms of market, products and strength in research, development and innovations is a result of value-adding collaborations and partnerships with other institutions.

- This is uncommon, though it has been acknowledged as important towards enhancing GMP compliance, market penetration and improvement of product portfolio. These partnerships involve technical transfers. Examples include Universal Corporation Limited/Strides-Shasun Merger, Quality Chemicals /CIPLA Quality, and an intended PPP between Dawa Group, Merck and Government of Kenya geared towards the production of vaccines.
- In addition, there is 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 also not necessarily aligned to the technical needs of the dynamic industry needs, e.g. technological advancements.

IMPLICATIONS AND RECOMMENDATIONS

Based on the study, it was clear that there is need to review and improve on the exisitng pharmaceutical industry's relevant policies so as to make them practical and tenable.

They include:
(i) Developing a tangible framework for investment in the pharmaceutical sector and auxilliary industry;
(ii) Establishing a framework for attainment of stringent regulator status of the National Medicine Regulatory Authority (NMRA) for international recognition and benchmarking GMP compliance of companies;
(iii) Developing a harmonised incentive regime to catalyse growth and expansion of LPPs (expounded below)
The latter is the basis for the policy incentive mechanism proposed below.

Quality ranking and risk categorisation of LPP proposal

The categorisation 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 categorisation into A; B; C was meant for determining the root cause of inferior quality, fixing

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

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: Categorisation and Benefits *Source: author adapted from Kenya GMP Roadmap*

quality problems, and even for GMP inspector/regulator to use 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 categorisation is to ensure a level playing field for all manufacturers within the manufacturing environment, that comply with GMP requirements for site and quality management systems (QMS) (Exhibit 1). This, admittedly, would reduce the risk of entry of poor quality products to the distribution chain. Based on the results of the study, there is need to have an incentive approach for LPPs.

Exhibit 1 illustrates a potential quality-based incentive vehicle for LPPs. It is a risk-based categorisation model that has three classes; class A, B and C in terms of GMP compliance, derived and based on site and QMS related GMP requirements. The licensing for manufacture would take into consideration the suitability of a facility to manufacture specific products. Highrisk facilities will manufacture low risk products, for example, disinfectants and increasingly adopt other products.

The categorisation model will empower the national medicines regulatory authorities in EAC to be the means of industrial growth, and to stimulate the attainment of international standards. It is a 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, on its own, should develop a quality culture with growth patterns and alignment to health priorities that take cognisance of the SDG No. 3 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 by GMP inspectors. Upon the findings, facility-based CAPA will be developed and a project map agreed upon between the regulatory agency and the manufacturer, with clear timelines and milestones.

There will be a periodic review on the progress but more importantly, a qualification assessment to determine the quality status of both site and quality management systems as the criterion for categorisation. A scenario will be set where good performance will raise their quality status to full compliance, and likewise prevent a fall back to lower quality through regulatory controls that will be applicable.

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

Exhibit 2: Risk categorisation model stakeholders and their functions

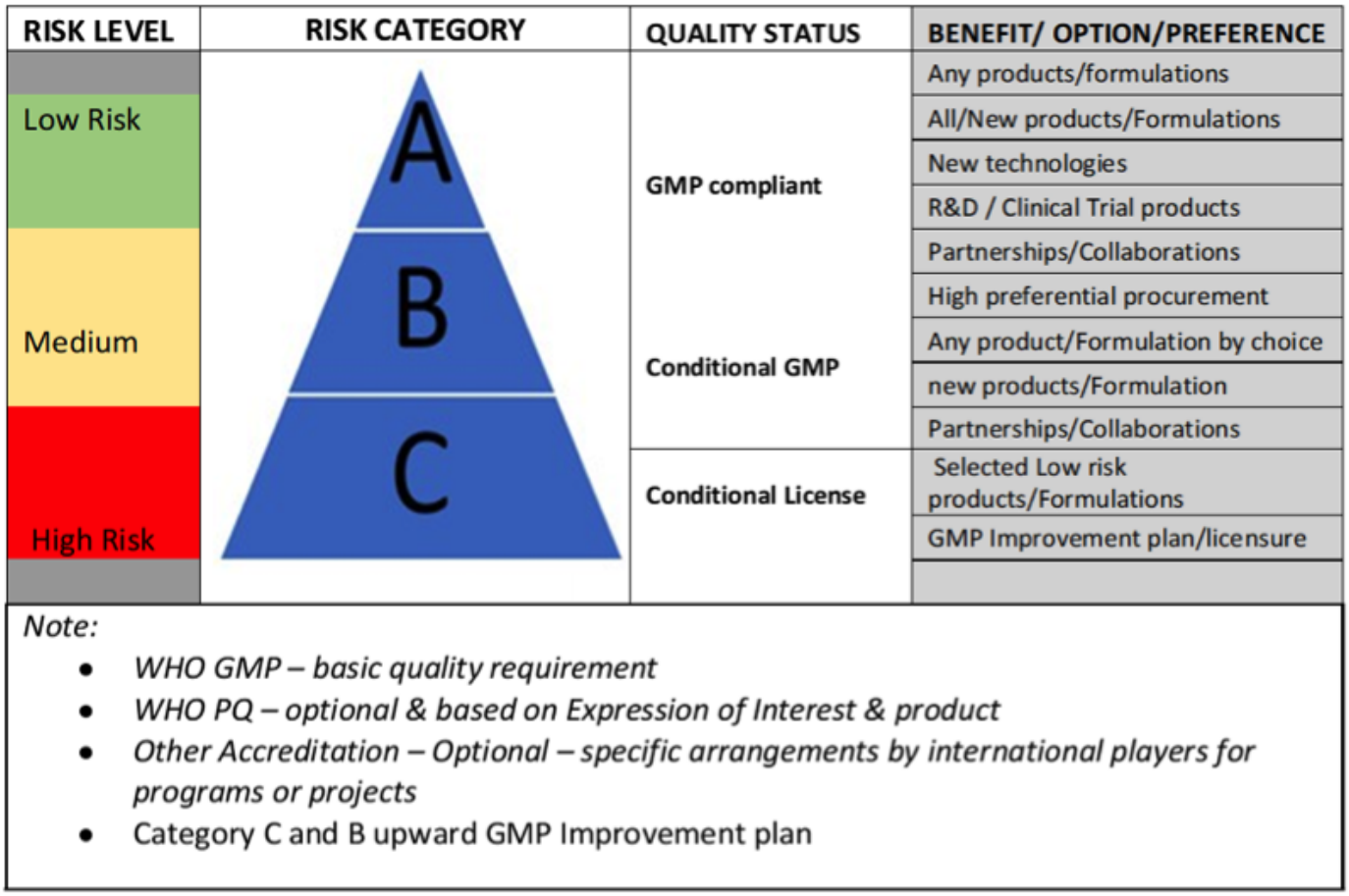


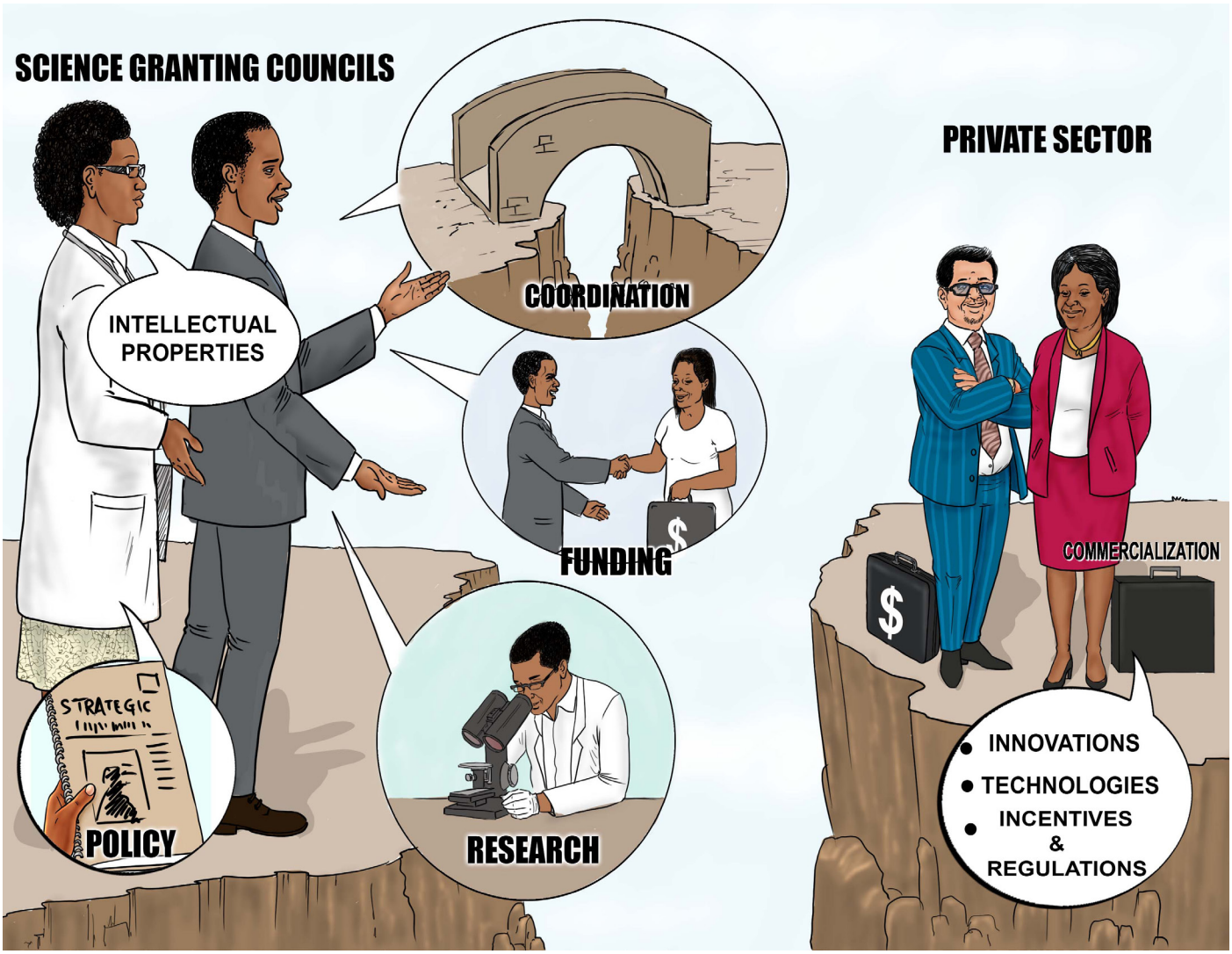
Exhibit 3: Risk Categorisation model for Sustainable LPP of high-quality medicines

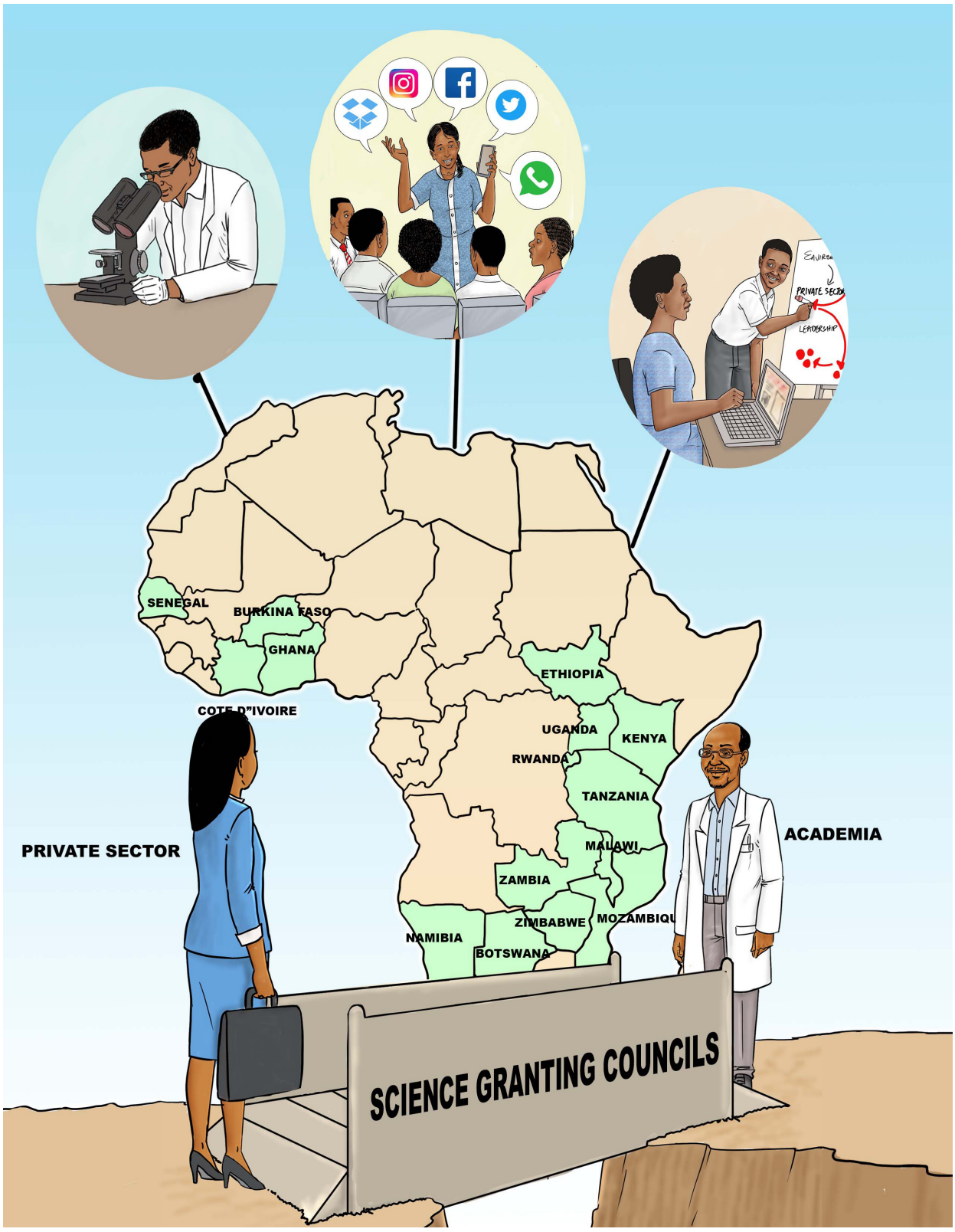
CONCLUSION

This risk categorisation is a suitable tool for benchmarking GMP compliance of companies and can also be used 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 corrective actions and preventive actions (CAPAs) and follow-up on implementation and review the GMP compliance levels.

A means of structured incentive can be used for different levels of categorisation to drive compliance. Additionally, 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 categorisation is therefore a stimulus scheme that promotes industrial growth and rewards quality improvements, and assures access to quality essential medicines.

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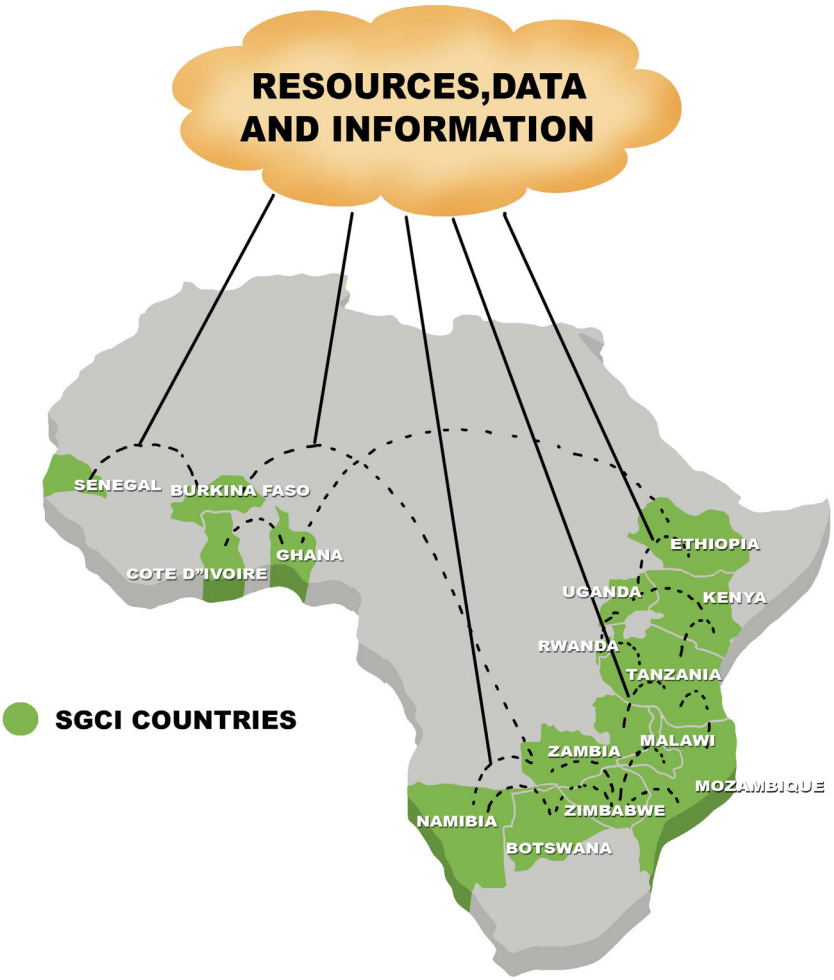

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