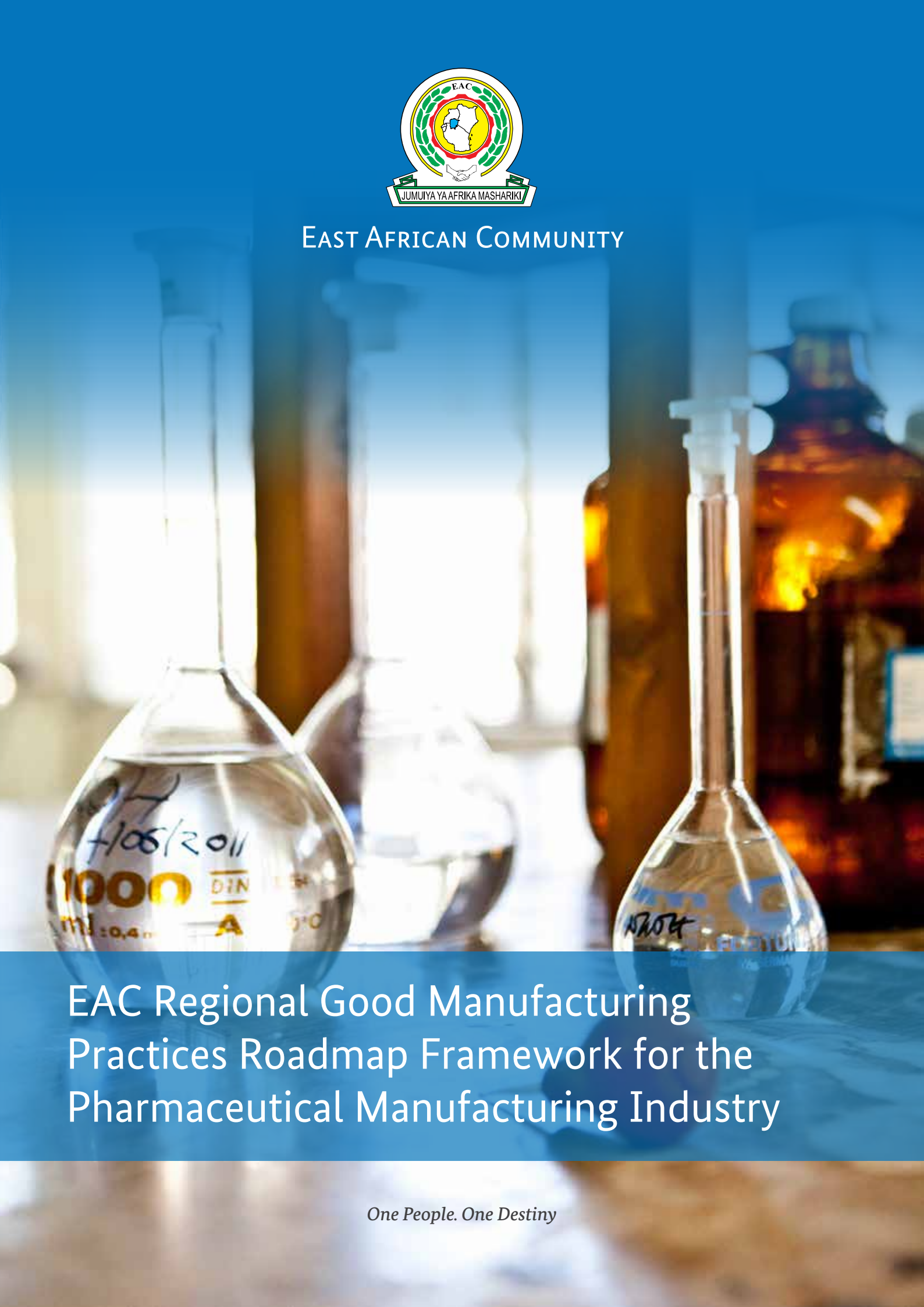

EAST AFRICAN COMMUNITY

EAC Regional Good Manufacturing Practices Roadmap Framework for the Pharmaceutical Manufacturing Industry

One People. One Destiny

East African Community

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One People. One Destiny

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List of abbreviations

API	Active Pharmaceutical Ingredients
CAGR	Compound Annual Growth Rate
CAPA	Corrective and Preventive Action Plans
CRS	Chemical Reference Standards
EAC	East African Community
EAC RPMPOA	East African Community Regional Pharmaceutical Manufacturing Plan of Action
FEAPM	Federation of East African Pharmaceutical Manufacturers
FDI	Foreign Direct Investment
FPP	Finished Pharmaceutical Products
GIZ	Deutsche Gesellschaft für Internationale Zusammenarbeit
GMP	Good Manufacturing Practices
HVAC	Heating, Ventilation, and Air Conditioning
JV	Joint Ventures
MIT	Ministry of Industry and Trade
MRH	Medicines Regulatory Harmonization Programme
NDA	National Drug Authority
NMRA	National Medical Regulatory Authority
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PTB	Physikalisch Technische Bundesanstalt
QA	Quality Assurance
QMS	Quality Management System
QC	Quality Control
SCTIFI	Sectoral Council on Trade, Industry, Finance and Investments
SOP	Standard Operating Procedures
TFDA	Tanzanian Food and Drug Authority
UNIDO	United Nations Industrial Development Organization
WHO	World Health Organization

Foreword

Our EAC Partner States comprising the Republics of Burundi, Kenya, Rwanda, Uganda, South Sudan and the United Republic of Tanzania, aspire to develop their pharmaceutical industry as part of the regions', social and political integration agenda. As a region we recognize the strategic importance of developing local production of pharmaceutical products in promoting access to affordable quality essential medicines. Moreover, pharmaceutical manufacturing provides quality jobs in a high-tech sector and facilitates technology and knowledge transfer. Its intersectoral character contributes to reaching both Sustainable Development Goal 3.8 and 3.b on Universal Health Coverage and access to medicines, as well as 9.2 and 9b on industrialization and technology development. Further, local manufacturing can be an important part of resilient health systems, as it may improve the reliability of supply and enable the production of appropriate, high quality and affordable medical products. It is in this regard that we developed an EAC Regional Pharmaceutical Manufacturing Plan of Action (EAC-RPMPOA), 2017-2027 to serve as a road map to guide the community towards evolving in to an efficient and effective regional pharmaceutical manufacturing industry. The EAC-RPMPOA prioritizes the strengthening of regional capacity to produce quality medicines and its implementation is supported by other regional policies such as the EAC Medicines Registration Harmonization (EACMRH) Programme and the EAC Industrialization Policy and Strategy (EACIPS).

As part of the EAC MRH project and in support of the implementation of the EACIPS, we developed regional Good Manufacturing Practices (GMP) guidelines modelled after the internationally recognized World Health Organization (WHO) standards. As a region, we understand that adhering to these standards is both important for public health and market reasons and that production sites that fail to fulfil GMP requirements may impair medicine safety or efficacy. We recognise that the majority of the EAC pharmaceutical manufacturers strive to adhere to the EAC/WHO GMP requirements within their own financial, technical and managerial capacities necessitating the requirement of the region to develop a regional risk-based stepwise approach to GMP compliance. In order to support our pharmaceutical sector in adhering to the EAC/WHO GMP requirements, we developed an ***EAC Regional GMP Roadmap Framework*** which was adopted by the EAC Sectoral Council on Trade, Industry, Finance and Investments (SCTIFI) of 13th September 2019. As a prerequisite to the Regional Framework, we supported the development of the national GMP Roadmaps in the EAC Partner States.

In this document, we present the ***EAC Regional GMP Roadmap Framework*** for the East African Community's (EAC) pharmaceutical manufacturing sector. The Framework combines data from all national GMP roadmaps in the EAC Partner States, compares industry GMP compliance and challenges across the region and highlights regional technical or policy support measures. The roadmap informs manufacturers, regulatory bodies and other stakeholders on how to best attain compliance. The Regional Framework is based on GMP gap assessments conducted in all active pharmaceutical manufacturers in the region. The assessments in Kenya were conducted in 2015 with the support of UNIDO and German development cooperation (GIZ) while the inspections in Rwanda, Tanzania and Uganda took place in 2017 in cooperation with GIZ and the German medical aid organization action medeor. The active pharmaceutical manufacturer in Burundi was assessed in 2018 by the German medical aid organization action medeor in cooperation with the Federation of East African Pharmaceutical Manufacturers (FEAPM).

The Regional GMP Roadmap Framework outlines regional interventions that incentivize and facilitate more investment into GMP compliant production and respective manufacturing sites including; fiscal and non-fiscal incentives; attracting foreign direct investments on GMP Compliant facilities; human resource capacity building and regulatory cooperation in line with priority intervention areas detailed in the EAC-RPMPOA: 2017-2027.

The successful implementation of the plan will require concerted efforts of all EAC Partner States, National Ministries of Health, Trade and Industry as well as National Medicines Regulatory Authorities, Pharmaceutical Manufacturers 'Associations, Pharmaceutical industries and International Development Partners. In view of the importance of the regional pharmaceutical sector with regards to improvement of health and overall well-being of the people of East Africa and its contribution to industrial development, I urge all the stakeholders to take necessary actions as outlined in the plan for successful implementation of the Plan.

Ambassador Liberat Mfumukeko
Secretary General
East African Community

Acknowledgement

The publication of the EAC GMP Regional Roadmap Framework is a significant step in the implementation of the 2nd EAC Regional Pharmaceutical Manufacturing Plan of Action (EACRPMPOA): 2017 – 2027. It is a road map for the community towards evolving in to an efficient and effective regional pharmaceutical manufacturing industry. In recognition of the important role played by the pharmaceutical sector in the industrialization policy the EAC GMP Roadmap Framework was prepared in close consultation with various national, regional and international stakeholders. The report was prepared through a gap assessment and a consultative process that took into account the views of stakeholders and ongoing developments in sector in the region. In this regard, the Secretariat, wishes to acknowledge and thank the participation, dedication and commitment by the EAC Partner States in the development of Roadmap Framework. Key national stakeholders were drawn from National Ministries of Industry, Health and East African Community Affairs; National Medicines Regulatory Authorities (NMRAs), National Investment Promotion Agencies, Academia, Pharmaceutical Manufacturers' Associations, local Pharmaceutical Manufacturers and International Development Partners. The support and active participation of the EACRPMPOA focal points and the National Coordination Committee members in the Partner States is also acknowledged.

The invaluable technical and financial support provided by the Federal Republic of Germany through the GIZ Programme and implemented by GFA Consulting Group is highly acknowledged and appreciated. Last but not least, the EAC Secretariat recognizes the tireless efforts of the EAC staff from the Directorate of Productive Sectors especially the Industrial Development Department on the successful development of the Roadmap Framework.

In conclusion, I wish to emphasize that we will ensure a coordinated and collaborative approach by all the relevant departments of the EAC Secretariat (Health and Industry), Partner States' National Ministries and Institutions, Pharmaceutical Manufacturers' Associations as well as development partners for the successful implementation of the Roadmap Framework. This coordination will seek to synergize and harness existing national, regional and international initiatives towards strengthening local production of pharmaceuticals. The EAC Secretariat will take the lead in mobilizing and optimally deploying the necessary resources including personnel for the successful implementation of the Roadmap Framework.

Hon. Christophe Bazivamo
Deputy Secretary General
(Productive and Social Sectors)
East African Community

I. Executive Summary

Upgrading the pharmaceutical industry has become a prominent goal on the African continent and in particular in East Africa where the pharmaceutical sector is among the six priority intervention areas[1]. Compliance with internationally acceptable GMP standards is a key requirement for upgrading the sector– for both public health and market access reasons. This document presents the Regional Good Manufacturing Practices (GMP) Roadmap Framework for the East African Community's (EAC) pharmaceutical manufacturing industry. It is part of the strategic interventions that aim to improve the quality of pharmaceutical production in the EAC-Regional Pharmaceutical Manufacturing Plan of Action 2017-2027. The GMP framework connects data from national GMP roadmaps in the EAC Partner States, compares the degree of industry compliance to the harmonized EAC GMP guidelines across the region, and works out where regional technical or policy interventions can support the industry on its path to full compliance with EAC GMP guidelines until 2027, as laid out in the RPMPoA.

The analysis is based on GMP compliance data from the 2015 Kenya GMP Roadmap (33 firms assessed), from GMP gap assessments undertaken in Tanzania (11), Uganda (14) and Rwanda[2] (1) in 2017 and from the assessment performed in Burundi (1) in 2018. All NMRAs registered manufacturers in Uganda, Tanzania, Rwanda, Burundi and Kenya are included except for few smaller firms in Kenya.

The following general results of the GMP assessments can be summarized:

1) A small portion of audited manufacturers, 3 out of 60 audited companies in EAC, is designated as highly GMP compliant. Most audited manufacturers are classified low compliance companies (44 out of 60).

2) The distribution of high- and low-compliance companies is very similar across the EAC:

   2.1) In all countries GMP deficiencies are most severe in quality elements related to *production site*. Most numerous are critical observations in the key quality elements "Utilities impacting GMP requirements" (in 63% of all audited manufacturers) and "Premises" (also 63%).

   2.2) Regarding *quality management systems*, three key quality elements stand out regionally as problematic on average. 43% of companies show critical observations for "Good practices in quality control" and 40% each for "Qualification and Validation" and "Materials".

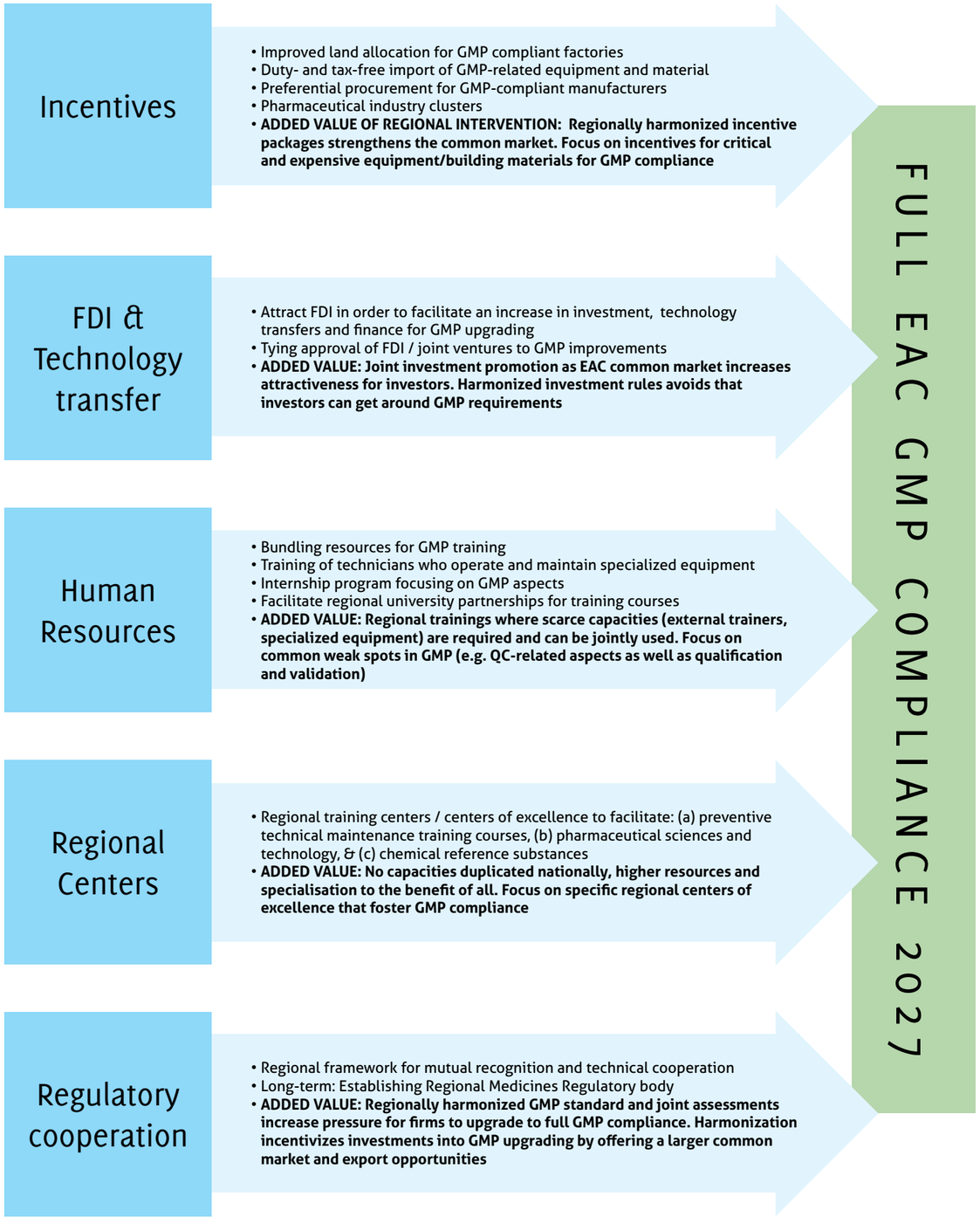
Due to the national mandate for GMP inspections, the majority of recommended interventions to increase compliance with international GMP standards target the national and firm level and are specified in national level GMP roadmap documents. The regional roadmap framework, however, points out priority areas where regional interventions have added value and ties them to regional activities such as the EAC Medicines Regulatory Harmonization Programme (MRH) and the EAC-RPMPoA 2017-2027.

As site-related aspects such as utilities and premises are by far the most critical areas, manufacturers need to invest in renovation and upgrade of existing manufacturing sites. The Regional GMP Roadmap Framework outlines regional interventions that incentivize and facilitate more investment into GMP compliant production and respective manufacturing sites. Moreover, we have identified a number of interventions related to other aspects like human resources, centres of excellence, regulatory cooperation where regional-level implementation has added-value. The recommendations are in line with priority intervention areas detailed in the EAC-RPMPOA: 2017-2027. The following figure summarizes recommended key interventions for the EAC and their added value of undertaking them on the regional compared to the national level.

[1] EAC Industrialization Policy and Strategy (2012-2032)

[2] South Sudan was not visited by GMP inspectors as no pharmaceutical manufacturers operate (see blue box below for more details). Yet, this framework is relevant for all EAC member countries as it shows investors for all countries where GMP challenges lay and indicates to policy makers how higher-quality medicines can be produced for the EAC common market.

Overview of recommended regional level interventions



1/Introduction

This document presents a Regional Good Manufacturing Practices (GMP) Roadmap Framework for the East African Community's (EAC) pharmaceutical manufacturing industry. For local pharmaceutical manufacturing to be successful, companies need to produce safe, high-quality and efficacious medicines. Complying with internationally recognized GMP is an effective way to ensure production quality and access to international markets. GMP roadmaps inform manufacturers, regulatory bodies and other stakeholders on how to best attain compliance to this standard.[3] **The Framework combines data from all national GMP roadmaps in EAC Partner States , compares industry GMP compliances and challenges across the region and points out where regional technical or policy interventions can support the industry on its path to full compliance with EAC GMP guidelines. Yet, it is not a roadmap with specific targets itself, as the mandate for GMP inspections remains on the national level.**

Pharmaceutical manufacturing on the African continent can look back on a long tradition. Recently, expanding and upgrading the industry has become a prominent goal on the continent's agenda both from a public health and an industrial development perspective. Local manufacturing can be an important part of resilient health systems, as it may improve the reliability of supply and enable the production of appropriate, high quality and affordable medical products. Moreover, pharmaceutical manufacturing provides quality jobs in a high-tech sector and facilitates technology and knowledge transfer. Its intersectoral character contributes to reaching both Sustainable Development Goal 3.8 and 3.b on Universal Health Coverage and access to medicines, as well as 9.2 and 9b on industrialization and technology development.

Several international initiatives and strategies have taken up the issue of promoting local pharmaceutical manufacturing in Africa. The African Union's Pharmaceutical Manufacturing Plan for Africa (PMPA) serves as the continental framework. Positive developments towards improving local pharmaceutical production capacities can be seen in the EAC. The EAC Secretariat and the Partner States recognize the strategic importance of the pharmaceutical sector in promoting access to affordable quality essential medicines. Thus, the EAC developed its first Regional Pharmaceutical Manufacturing Plan of Action (EAC-RPMPOA) 2012-2016 to guide the community towards building a successful regional pharmaceutical manufacturing industry. The implementation of the plan is supported by other regional initiatives as the EAC Medicines Registration Harmonization (MRH) Programme and the EAC Industrialization Policy and Strategy. The new phase of the plan (EAC-RPMPOA: 2017-2027) reviews the implementation progress and builds on the achievements of the industry and public sector and lays down strategic approaches for the EAC and the Partner States to address existing challenges and respond to emerging opportunities.

Part of the RPMPOA focuses on improving the quality of pharmaceutical production in the EAC. As part of the MRH project, the EAC developed its own regional Good Manufacturing Practices compendium modelled after the internationally recognized WHO standard. Adhering to these standards is both important for public health and market access reasons. Production sites that fail to fulfil GMP requirements may impair medicine safety or efficacy. Moreover, companies need to meet international GMP standards to qualify for large international tender markets. However, in reality EAC companies do not always adhere to the EAC/WHO GMP requirements, as their financial, human or management capacities may be limited. Thus, Kenya with support of the United Nations Industrial Development Organization (UNIDO) piloted the development of a risk-based stepwise GMP roadmap for its pharmaceutical industry. Such a roadmap outlines the path for the pharmaceutical industry to progress to compliance with internationally acceptable GMP standards. Given Kenya's positive experience, the RPMPOA 2017-2027 calls for the roll-out of this approach to the rest of the EAC region. As a result, in May 2016 the EAC Sectoral Council on Trade, Industry, Finance and Investments (SCTIFI) mandated the EAC Secretariat to develop a Regional EAC GMP Roadmap Framework. As a prerequisite for the Regional Framework, the EAC Secretariat in 2017 supported the development of national GMP Roadmap documents in EAC Partner States with an existing sizable pharmaceutical industry.

This document puts forward the Regional Framework based on GMP gap assessments in almost all active pharmaceutical manufacturers. The assessments in Kenya were conducted in 2015 with the support of UNIDO and German development cooperation (GIZ). The inspections in Rwanda, Tanzania and Uganda took place in 2017 in cooperation with GIZ and the German medical aid organization action medeor. The only active pharmaceutical manufacturer in Burundi was assessed in 2018 by the German medical aid organization action medeor in cooperation with the Federation of East African Pharmaceutical Manufacturers (FEAPM).

[3] See national GMP roadmaps for Kenya, Tanzania, Uganda and GMP assessment results for sole manufacturer in Rwanda and Burundi

2/Background[4]

2.1. Pharmaceutical manufacturing in the EAC

The EAC has a pharmaceutical market of 1.74 billion US$[5], which is rapidly growing. It demonstrated an estimated compound annual growth rate (CAGR) of over 10%[6] between 2007 and 2014. Kenya has the largest pharmaceutical market (740mn US$), followed by Uganda (450mn US$), Tanzania (400mn US$), Rwanda (100mn US$) and Burundi (75mn US$). With an estimated year-on-year growth rate of 15% Kenya is also the fastest growing market in the region.

Nonetheless, local manufacturing remains moderate in size. In total, the regional industry is composed of 60-70 actively producing companies. It is currently supplying less than 15% of the market in terms of value (EAC average). Kenya's local manufacturing share is slightly higher, as it has the highest number of manufacturing companies (>30). The market share for domestic medicines is around 30% (value-wise) while in Uganda and Tanzania it is 20% and 12% respectively. Uganda's local production capacity has recently been expanding. Yet, in Tanzania some companies closed down in recent years and the domestic share decreased from around 30% in 2007 to about 12% in 2017[7]. However, most local firms do not produce to full capacity. A survey[8] demonstrated that local firms could cater for a substantially larger part of the regional demand for pharmaceutical products, but underutilize their capacity by up to 60% in some formulations. This underutilization is partly attributed to a lack of competitiveness of local firms with regards to price and quality compared to foreign based firms that export to EAC markets. Among all dosage forms, only infusions and syrups/ suspensions experience capacity shortages.

Table 1: Pharmaceutical market overview (adopted from EAC RPMP0A 2017-2027)

Countries	Burundi	Kenya	Rwanda	S. Sudan[9] (estimates)	Tanzania	Uganda
Pharma market size (US$ million, 2014)	75	740	100	75	400	450
Compound Annual Growth rate (CAGR) 2007 to 2014	12.85%	15%	16.36%	NVAL	9%	8.5%
Market share of locally produced pharmaceutical drugs (% of overall market)	3%	30%	<1%	0	12%	20%
Market by segment	(Generic) 56% (Branded) 44%	(Generic) 62% (Branded) 38%	(Generic) 54% (Branded) 46%	(Generic) 60% (Branded) 40%	(Generic) 54% (Branded) 46%	(Generic) 80% (Branded) 20%
Number of local pharmaceutical manufacturers	1	44	1	0	11	14

[4] Based on information from the EAC RPMPoA 2017-2027
[5] IP Watch (2015). Policy Coherence To Boost East Africa Pharmaceutical Industry. http://www.ip-watch.org/2015/10/02/policy-cohernce-to-boost-east-africa-pharmaceutical-industry/
[6] 2014 estimates by industry associations in the EAC.
[7] Statistics from EAC RPMPOA 2017-2027 confirmed by Tanzanian RPMPOA Focal Point
[8] EAC - GIZ, 2011, Baseline Survey of the Local Pharmaceutical Manufacturing Capacity for Human and Veterinary Medicines and Medical Supplies within the EAC Partner States, (Unpublished report).
[9] South Sudan was approved for membership to the EAC in March 2016, and signed a treaty of accession in April 2016. It had six months to ratify the agreement, which it did on 5 September 17, at which point it formally acceded to the community. It does not yet participate to the same extent as the other members. South Sudan did not join the activities on the EAC GMP Roadmap so far.

EAC based companies are focusing on producing and packaging finished pharmaceutical products (FPPs) and do not engage in manufacturing active pharmaceutical ingredients (APIs). Moreover, they are currently limited to simple generic formulations instead of pharmaceutical products with higher value. The majority of companies produce multisource generic products, largely unbranded, that are less expensive than innovator or branded products. A small number of companies started to differentiate themselves by producing branded generics. Here over-the-counter medications play an important role. Given their similar product portfolios, most firms compete with each other in the small market segment of antibacterial medicines, analgesics, vitamins, cough and cold preparations. Expensive innovative medicines, such as anticancer drugs, immunosuppressive drugs, or blood components, are imported exclusively. Despite these limitations, local companies cover an estimated 66% of disease conditions. In terms of dosage forms EAC firms focus mainly on plain tablets, hard capsules, lotions and suspensions. Advanced formulations (sustained release, layered tablets, immune sera) have not yet been taken up in their portfolios[10]. Highly regulated product lines (sterile products, vaccines, and diagnostics) are each being manufactured by one manufacturer.

2.2. Regulatory environment

Medicines regulatory authorities have been established in all EAC Partner States including an independent authority for Zanzibar which is part of the United Republic of Tanzania. Recently, the national medicines regulatory authorities have made significant improvement in their facilities and equipment. This includes new offices and laboratory space for the NMRAs in Zanzibar, Kenya and Uganda. Burundi and Rwanda have made progress in the process of fully establishing their NMRAs. The National Quality Control Laboratories of Uganda, Kenya and Tanzania have received WHO prequalification and Kenya was accredited for ISO17025.

In the EAC, national regulators license local manufacturers. In this context companies require GMP certification for production of medicines by the respective NMRA. National regulators carry out inspections of companies to enforce quality standards. Despite the national mandates, the region is moving towards a harmonized medicines regulatory regime through the Medicines Regulatory Harmonization project. Several joint dossier evaluations and GMP inspections have already taken place. Reference is the regionally harmonized EAC GMP compendium, which is based on GMP requirements of the individual EAC countries, WHO and Pharmaceutical Inspection Co-operation Scheme (PIC/S) and other available literature[11]. The EAC Compendium has been prepared to enable effective implementation of GMP inspection activities under the EAC MRH programme. It is a guide for GMP inspectors in preparing for and performing GMP inspection activities of APIs and FPPs. In addition, the EAC Compendium outlines procedures to be followed when preparing and planning for joint inspection, reporting requirements including format and classification system adopted for non-compliances observed during GMP inspection. So far, a framework for mutual recognition is not in place, therefore the decisions taken through joint activities are non-binding to the individual Partner States. The key challenge is that not all NMRAs are at the same level of development, some are well established with a full control on the research, importation, production, storage, marketing and distribution of food, medicines, and medical devices, while others have recently established or are still in the process of establishing an NMRA. This may impede full implementation of agreed decisions.

Currently, only two companies in the EAC (CIPLA QCIL, Universal) have achieved WHO prequalification for selected products. Despite existing GMP regulation and regular inspections local companies do not always comply fully with the standards, as will be shown in the analysis section. Most regulatory agencies take a cooperative and risk-based approach of supporting companies towards upgrading to full GMP compliance. The GMP roadmap project is a way to structure this regulatory approach of using regulatory pressure to ensure medicine quality in a supportive way for business development.

[10] EAC-RPMPOA: 2017-2027
[11] EAC (2014). Compendium of Good Manufacturing Practices (GMP). Technical documents for harmonization of medicines regulation in the EAC, 2014. http://apps.who.int/medicinedocs/en/d/Js22313en/

3/Approach

Disclaimer: In order to ensure comparability the following paragraphs on the approach of the project 5.1 & 5.2 are strongly based on the text of the respective paragraphs in the Kenya GMP Roadmap[12] drafted by UNIDO consultants.

3.1. General considerations

This Regional GMP Roadmap Framework has been developed following a bottom-up approach. It is based on GMP gap assessments within manufacturing companies in the whole EAC region and resulting national GMP roadmap documents for Kenya, Uganda and Tanzania[13]. The Kenyan gap assessments took place in 2015 under a project implemented by UNIDO and co-financed by GIZ. The gap assessments in Rwanda, Tanzania and Uganda and development of national roadmaps took place under the EAC mandate for this Regional Framework in 2017 and were jointly undertaken by action medeor and GIZ. The remaining gap assessment in Burundi was performed in 2018 by action medeor and FEAPM. Given the time lag between the Kenyan pilot project and the regional project, the Kenyan data does not reflect any progress made since 2015. This needs to be taken into account when comparing the 2015 Kenyan data with the remaining 2017 and 2018 EAC data. However, the Regional Framework project has followed the approach and methodology taken by the Kenyan GMP roadmap pilot in order to facilitate comparability.

Adherence to Good Manufacturing Practice (GMP) is essential to ensure that quality, safety and efficacy of medicinal products is assured. Due to constraints in financial, technical and human resource capacities, pharmaceutical manufacturers in EAC Partner States are often overwhelmed by the vast array of GMP requirements causing companies not to operate in line with the internationally recognized GMP standard as outlined by the World Health Organization (WHO). WHO unified standards receive wide international acceptance and have been adopted by the EAC in the EAC GMP Compendium. Various initiatives have already offered training to manufacturers on general understanding of GMP and specific sub-topics. However, individual continuous training, support and consultancy have been missing. Therefore, roadmaps delineating a step-wise and modular approach to GMP compliance fit to the specific situation in each EAC Partner State with a sizable industry needed to be developed, setting out requirements, milestones and strategies for pharmaceutical manufacturers on their progress from the current level of GMP compliance to full EAC GMP compliance over a specified period of time.

In order to enable integrating the national roadmaps into a Regional EAC GMP Roadmap Framework, the approach follows the UNIDO pilot project for the Kenyan roadmap. Its methodology has initially been outlined in the "White Paper on UNIDO's GMP Roadmap Concept"[14].

The assessment of the compliance of existing manufacturing practices in the EAC region includes the following steps:

1. Definition of tools for assessment of pharmaceutical manufacturers and their evaluation regarding compliance with GMP

2. Assessment of results and evaluation

A note on Burundi, Rwanda and South Sudan

This analysis has been based on GMP gap assessments of existing and active pharmaceutical manufacturing sites in the EAC region. Given that the large majority of companies and their factories are situated in Kenya, Tanzania and Uganda the underlying analysis is based mostly on data from these countries. 58 out of 60 inspected companies are based in these three countries. The analysis included one company from Rwanda, but the comparability of results was limited, as the company was not actively producing at the time of inspection. Burundi's single manufacturer was actively producing during inspection, and since the assessment methodology used was the same used for other EAC manufacturers, the inspection results are fully comparable. South Sudan has no active pharmaceutical manufacturer at this moment and could not be integrated into the analysis.

Having said that, the Regional GMP Roadmap Framework is still highly relevant for EAC countries without active pharmaceutical manufacturing capacity. It shows potential investors where GMP-related challenges in the region are situated and how they can be best addressed. The Roadmap might offer additional information for manufacturers with distinctive plans for constructing new premises. During the gap analysis several existing manufacturers alluded to their plans of refurbishment. In addition, in Rwanda three new manufacturing sites are under construction. Moreover, the framework supports producers across the region to produce medicines of higher quality, which will serve each country when procuring in the Common Market.

[12] UNIDO (2014). Kenya GMP Roadmap. https://www.unido.org/sites/default/files/2014-12/Kenya_GMP_Roadmap_ebook_0.pdf
[13] Rwanda's and Burundi's single manufacturers have also been audited and supported in the development of a Corrective and Preventive Action Plan. However, it is not feasible to develop a distinct GMP roadmap based on only one existing manufacturer. Yet, their manufacturer's assessment results have been taken into account for the regional analysis.
[14] UNIDO (2015). White Paper on UNIDO's GMP Roadmap Concept. https://www.unido.org/sites/default/files/2015-09/White_paper_final_edit_content_table_print_0.pdf

3.2. Assessment tools

To have a full understanding of compliance with GMP, all active pharmaceutical manufactures in the EAC needed to be audited. The inspectors assessed the gap between the current company practices and the required EAC GMP standard according to set criteria. As mentioned earlier, the gap assessments in Kenya had already taken place between 2012 and 2015 and were undertaken by UNIDO, while data from Uganda, Tanzania, Burundi and Rwanda has been gathered in 2017 and 2018 through action medeor, GIZ and FEAPM. Thus, to ensure comparability action medeor inspectors followed the UNIDO methodology. However, while the Kenyan roadmap uses the WHO GMP standard as its reference, this Regional Framework orientates itself along the EAC GMP compendium. Yet, this compendium is modelled after the WHO GMP and works with the same key quality elements, which form the foundation of the assessments for the roadmaps. Thus, the different in reference compendia should not restrict comparability.

Inspections were carried out by international expert auditors commissioned by UNIDO in Kenya and action medeor in the remaining cases. Depending on the size of the manufacturing site, one or two international auditors were accompanied by one or more GMP inspectors of the respective NMRA. Partly, other stakeholders like Ministry of Industry representatives also joined the inspections. The inspections took one to two days depending on the size of the firm. Following the gap assessments, all companies received an inspection report by the international auditors and were expected to hand in Corrective and Preventive Action Plans (CAPAs) addressing the observations. Afterwards, the international auditors support the companies in optimizing the CAPAs.

The following tools were defined based on the Kenyan Roadmap tools and the EAC GMP guidelines:

- Definition of a GMP reference standard for assessment of companies
- Definition of key elements and focus areas during assessments
- Definition of rating of observations
- Definition of tools for evaluation of assessment results

3.2.1. GMP reference standard for assessment of companies

In Kenya the internationally recognized WHO GMP standard (as outlined by the World Health Organization (WHO) in the document "Quality assurance of pharmaceuticals. A compendium of guidelines and related materials. Volume 2, 2nd updated edition. Good manufacturing practices and inspection. World Health Organization, Geneva, 2007" and subsequently updated through the WHO Technical Report Series (TRS) especially TRS 961, Annex 3) was used as reference for the assessment of pharmaceutical manufacturers. UNIDO did not use the EAC Compendium in Kenya, as the project started before its publication.

The GMP standard used as reference for the assessment of Ugandan, Tanzanian, Burundian and Rwandan pharmaceutical manufacturers for human and veterinary medicines was the recognized GMP standard as outlined by EAC in the document "Compendium of Good Manufacturing Practices (GMP), Technical document for the Harmonization for medicines regulation in the East African Community, Document No: EAC/TF-MED/GMP/FD/COM/N1R0". It was selected, as this Compendium is meant to be the reference for NMRAs in all Partner States since September 2014. Moreover, its content is comparable to the WHO GMP compendium used as reference in Kenya.

3.2.2. Key quality elements, focus areas during assessment and assessment schedule

The underlying key quality elements in the EAC and WHO GMP compendia are similar. The assessment in all countries was based on seventeen key quality elements as laid out in both the EAC and the WHO compendium:

1. Quality assurance
2. Utilities impacting Good Manufacturing Practice (GMP)
3. Sanitation and hygiene
4. Qualification and validation
5. Complaints
6. Product recalls
7. Contract production and analysis
8. Self-inspection and quality audits
9. Personnel
10. Training
11. Personal hygiene
12. Premises
13. Equipment
14. Materials
15. Documentation
16. Good practices in production
17. Good practices in quality control

Each of the key quality elements were divided into sub-sections for which the focus of the assessment had been defined. This approach was then equally applied in all inspections to ensure comparability.

In all countries, assessments were conducted by a team of international GMP experts and GMP inspectors from the respective NMRA. Inspections took two days for each industrial pharmaceutical manufacturer, whereas smaller organizations (e.g. hospitals producing only one product) were assessed in one day. The respective inspection schedules can be found in the national roadmap documents.

3.2.3. Rating of observations

Observed deficiencies in Tanzania, Uganda, Burundi and Rwanda were rated based on the EAC compendium, "Compendium of Good Manufacturing Practices (GMP), Technical document for the Harmonization for medicines regulation in the East African Community, Document No: EAC/TF-MED/GMP/FD/COM/N1R0".

Critical Observation:
An observation describing a situation that will most likely result in a non-compliant product or a situation that may result in an immediate or latent health risk and any observation that involves fraud, misrepresentation or falsification of products or data.

Major Observation:
An observation describing a situation that may have an impact on the product but is not as significant as a critical observation. It may have an indirect impact in the strength, identity, purity or safety of the product. There is reduced usability of the product without a probability of causing harm to the consumer. Observation of a major deficiency puts a question mark on the reliability of the firm's quality assurance system.

Minor Observation:
An observation describing a situation that is a departure from GMP but has no significant impact on the product quality. It has low probability of affecting the quality or usability of the product.

In Kenya observed deficiencies were rated based on the compilation of EU community procedures on inspections and exchange of information (London, 25 May 2012, EMA/INS/ 9 KENYA GMP ROADMAP GMP/321252/2012 Rev 14). Here both approaches slightly diverge. The Regional Framework preferred to orientate itself along the EAC Compendium, but using EU community procedures would have created a similar number of critical, major and minor/other observations. The EU community procedures define observations as follows:

Critical Deficiency:
A deficiency which has produced, or leads to a significant risk of producing either
a product which is harmful to the human or veterinary patient or a product which could result in a harmful residue in a food producing animal.

Major Deficiency:
A non-critical deficiency,
which has produced or may produce a product, which does not comply with its marketing authorisation; or which indicates a major deviation from Good Manufacturing Practice; or which indicates a major deviation from the terms of the manufacturing authorisation;
or which indicates a failure to carry out satisfactory procedures for release of batches; or a failure of the Authorized Person to fulfil his/her legal duties; or a combination of several "other" deficiencies, none of which on their own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency:
A deficiency,
which cannot be classified as either critical or major, but which indicates a departure from Good Manufacturing Practice. (A deficiency may be "other" either because it is judged as minor, or because there is insufficient information to classify it as a major or critical.)

3.2.4. Tools for evaluation of assessment results

In order to evaluate the level of compliance of all pharmaceutical manufacturers with GMP and to identify main technical challenges across the range of pharmaceutical companies in the EAC, two tools developed for the Kenya roadmap were applied in the Regional Framework.

- Tool 1: Assignation of the level of GMP compliance for each key quality element
- Tool 2: Categorization of companies based on their compliance with GMP

Tool 1: Assignation of level of GMP compliance for each key quality element

Based on the rating of observations made during the assessment of the companies, a rating of the compliance of key quality elements with GMP was derived. Several sub-sections of each key quality element were individually verified and an overall rating was subsequently given to the key quality element. The rating was done as follows:

- Acceptable: Compliance of a key quality element with GMP was rated "Acceptable" if no or only "other" (i.e. "minor") observations were found on areas related to this specific key quality element. This is overall graded with 1.

- Improve: Compliance of a key quality element with GMP was rated "Requires improvement" (short: "improve") if only few "major" observations (≤ 5) were found on areas related to this specific key quality element. This is overall graded with 2.

- Inadequate: Compliance of a key quality element with GMP was rated "Inadequate" if at least one "critical" and/or a considerable number (> 5) of "major "observations were found on areas related to this specific key quality element or the entire quality element not available at a company. This is overall graded with 3.

This tool allows an overall grading of each key quality element and highlights weaknesses and strengths of pharmaceutical manufacturers regarding compliance to GMP. It therefore identifies areas in which the manufacturers face difficulties the most or non-compliance to full GMP and those where the least efforts need to be done. The tool can be found in Appendix IV.

Tool 2: Categorization of companies based on their compliance with GMP

Depending on the financial, technical and human resource capacities available to pharmaceutical manufacturers, the level of GMP compliance varies significantly among pharmaceutical manufacturers in the EAC. Some companies are fully compliant while others have several critical issues to address.

The broad spectrum of GMP adherence requires to evaluate the level of compliance associated with the pharmaceutical manufacturers that were assessed. Thus, a tool for compliance level categorization has been developed for the Kenya roadmap and was also used for this Regional Framework.

The key quality elements have been assigned to two aspects of compliance, namely 'Site' and 'QMS' (see Figure 2). The term Site mainly refers here to physical entities which are components of the pharmaceutical manufacturing industry and comprises all elements related to premises, utilities and equipment; whereas the term QMS refers to procedures, processes, and resources needed to implement a quality management, this includes Quality Assurance, Complaints, Product Recalls, Contract production/analysis, Self-inspection and Audits, Personnel, Training, Personal Hygiene, Documentation, Good practices in production and Good practices in quality control. However, a clear distinction is not possible for five key quality elements, notably Sanitation and Hygiene, Qualification and validation, Materials, Good practices in production and Good practices in quality control, These 5 key quality elements have been assigned to QMS for a matter of convenience and because they all focused on procedures rather than facilities or instrument. The physical parts have been already taken into account in the Site related key quality elements. Nevertheless, there is a correlation between QMS and Site. The quality of a finished pharmaceutical product can only be assured by a compliance of both the Site and QMS elements to GMP standards.

It needs to be noted that the Kenyan roadmap does not clearly specify how the quality elements were assigned to Site and QMS for its analysis. This may limit the comparability of the Kenyan results with the data gathered in the other EAC countries to a certain extent. This Regional Framework will summarize the results nonetheless, assuming that the overall compliance evaluation for Site and QMS should not vary strongly.

Figure 1: Key quality elements per category

The classification uses a matrix to categorize companies based on the two aspects of GMP compliance.

- Compliance of site with GMP standards
- Compliance of quality management systems with GMP standards

A score of "1", "2" or "3" was assigned to both site and quality management system to describe their compliance with GMP, with a score of "3" representing a high compliance level and a score of "1" representing a low compliance level.

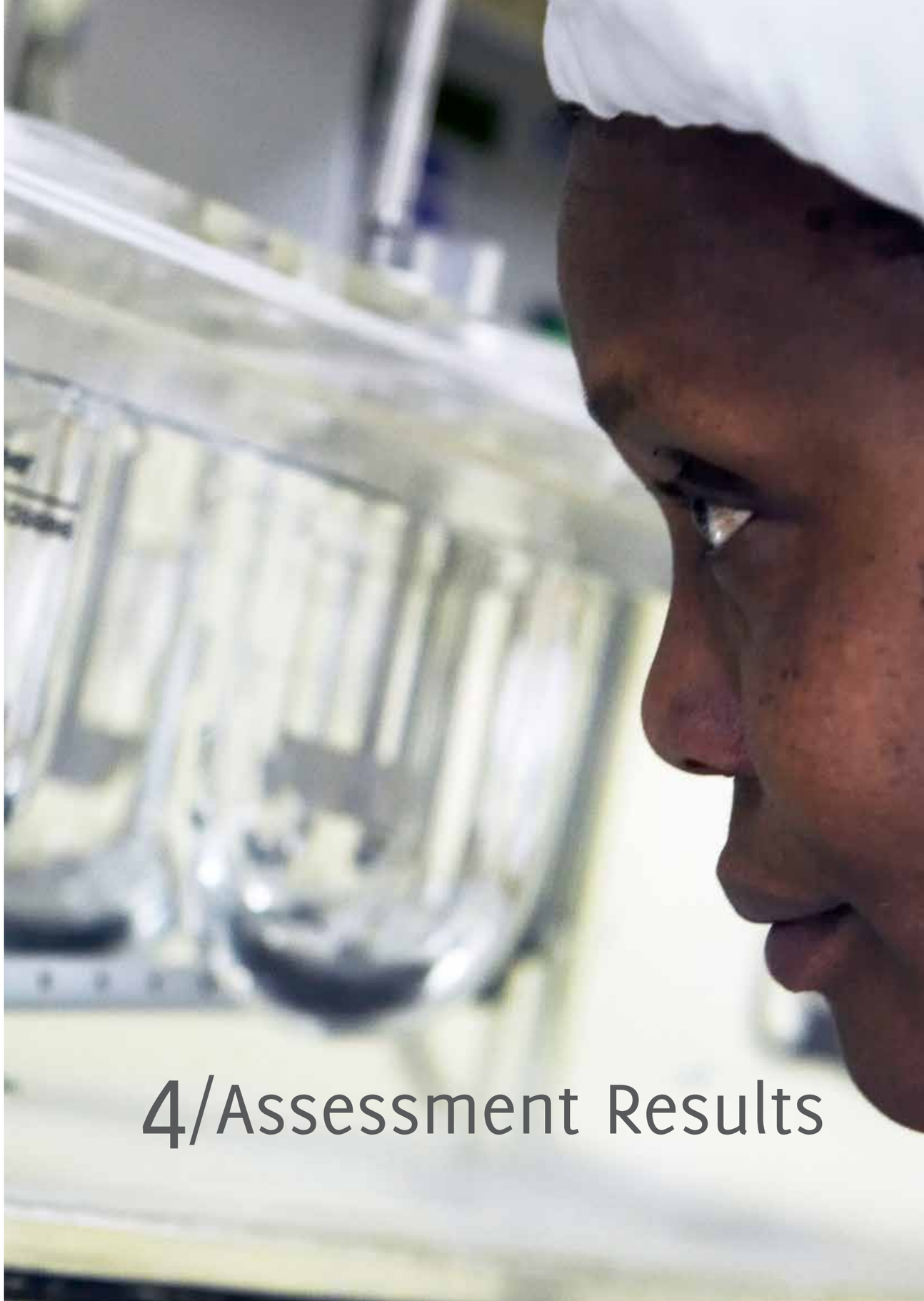
Furthermore, a matrix, as shown in Figure 3 below, was used for combining these two scores in order to generate an estimate of the compliance level associated with a pharmaceutical manufacturer. The resulting compliance ratings were "A", "B" and "C". A rating of "C" indicates companies with low levels of GMP compliance. A rating of "A" indicates companies, where the existing approach towards pharmaceutical manufacturing is, in general, in line with GMP requirements.

Figure 2: Compliance level categorization tool

Quality Management System (QMS) / Site	3 No QMS in place	2 Requirements are implemented sporadically only, a systematic approach to GMP is not in place	1 A systematic approach in line with GMP in place and implemented
1 - Site is generally compliant with GMP	C	B	A
2 - Site shows significant deficiencies in GMP, does not impair production safety	C	B	B
3 - Site unsuitable for pharmaceutical manufacturing	C	C	C

A: Existing approach towards pharmaceutical manufacturing in general in line with GMP requirements.
B: Existing approach towards pharmaceutical manufacturing results in medium levels of GMP compliance.
C: Existing approach towards pharmaceutical manufacturing not in line with GMP.

Both tools 1 and 2 can be used to monitor the level of GMP compliance and the improvements undertaken towards GMP compliance.



4/Assessment Results

Assessments were conducted in 60 firms in total. With 33 companies, Kenya makes up the largest share in this sample. While in Kenya several smaller firms were not able to take part in the exercise, the Framework covers all companies in Uganda, Tanzania, Burundi and Rwanda. The audits incorporated both manufacturers of human as well as veterinary medicines and vaccines. Data from Kenya was gathered two years before audits were conducted in the remaining countries. Thus, comparability of the data is limited.

Table 2: Number of companies inspected

Country	Timeframe of inspections	Total	Human	Veterinary	Both
Kenya	Apr-Nov 2015	33	20	6	7
Rwanda	Jun 2017	1	1	0	0
Tanzania	Jun-Jul 2017	11	9	2	0
Uganda	Jun-Aug 2017	14	12	2	0
Burundi	Dec 2018	1	1	0	0

First of all, the authors compared the number of firms in which inspectors found critical observations across the whole EAC. Critical observations mean that a company produces at a high risk for medicines safety and should thus be seen as priority areas for interventions.

Figure 3: Number of firms with critical observations in EAC

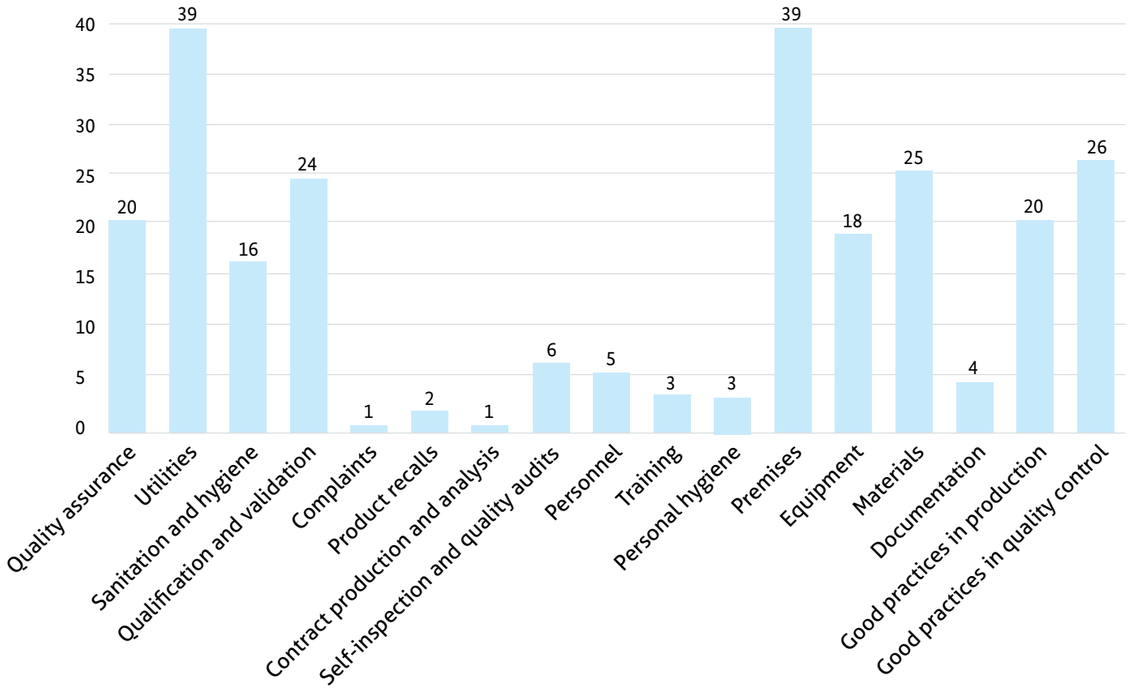


Figure 3 shows that no single key quality element without a critical observation were noted. Generally, the challenge appears to be more on site-related items across the whole region. The key quality elements "utilities impacting GMP", and "premises" are by far the most critical areas, with equipment" ranking 8th in most critical areas. In QMS, quality assurance and quality control are a matter of concern as well: "good practices in quality control", "qualification and validation" and "quality assurance" show relatively high number of critical observations.

Challenges might differ from country to country. For example, while "qualification and validation" scored low in Kenya, companies in the other countries demonstrated less critical observations. This may be partially explained by regional training activities that have been tailor-made to address key findings from the Kenyan GMP Roadmap, including regional hands-on trainings in calibration and validation[15].

Applying tool 2 and ranking the companies according to compliance levels shows that the large majority – 44 out of 60 companies – have to be classified as low compliance companies. 13 are medium compliance companies meaning that their existing approach to GMP is not in line with EAC GMP standards, but show a lower risk to production safety. 3 companies in the EAC region are generally compliant with EAC GMP standards (see Table 3). Due to the investments that have been undertaken by some Kenyan companies, a small number of companies might have moved up or down a category, which could not be shown with the 2015 data used for this analysis[16] .

Table 3: Number of firms in each compliance category: RW, TZ, UG data from 2017; KE data from 2015

	A	**B**				**C**						
Site score	**1**	**Total**	1	2	2	**Total**	1	3	2	3	3	
QMS score	**1**		2	1	2		3	1	3	2	3	**Total**
TZ	**0**	**2**	0	0	2	**9**	0	0	0	6	3	**11**
UG	**2**	**3**	0	2	1	**9**	0	1	0	7	1	**14**
KE	**1**	**8**	3	4	1	**24**	0	0	1	14	9	**33**
BI	**0**	**0**	0	0	0	**1**	0	0	0	0	1	**1**
RW	**0**	**0**	0	0	0	**1**	0	0	0	0	1	**1**
EAC	**3**	**13**	3	6	4	**44**	0	1	1	27	14	**60**

Table 3 also shows that the major compliance limitation lies in regional manufacturing sites being unsuitable for pharmaceutical manufacturing, while quality management systems fare better and are seldom the main issue with regards to GMP compliance. This is a problem across all countries even though Kenya and Uganda score a bit better than Tanzania, Burundi or Rwanda. Low compliance QMS is much rarer than low compliance sites. Moreover, while Kenya has the highest number of A and B companies in absolute terms (9 companies), Uganda scores highest as a share of the total number of manufacturers (36% of Ugandan companies score A or B).

[15] GIZ, PTB and MRH projects have contributed significantly to skills upgrade in the sector by supporting targeted trainings on dossier evaluation, GMP Inspection, Proficiency Testing, Calibration and Validation, amongst others. In total, over 300 technical personnel have been trained during hands-on workshops and technical seminars. Some of the trainings specifically targeted findings from the Kenyan GMP roadmap.

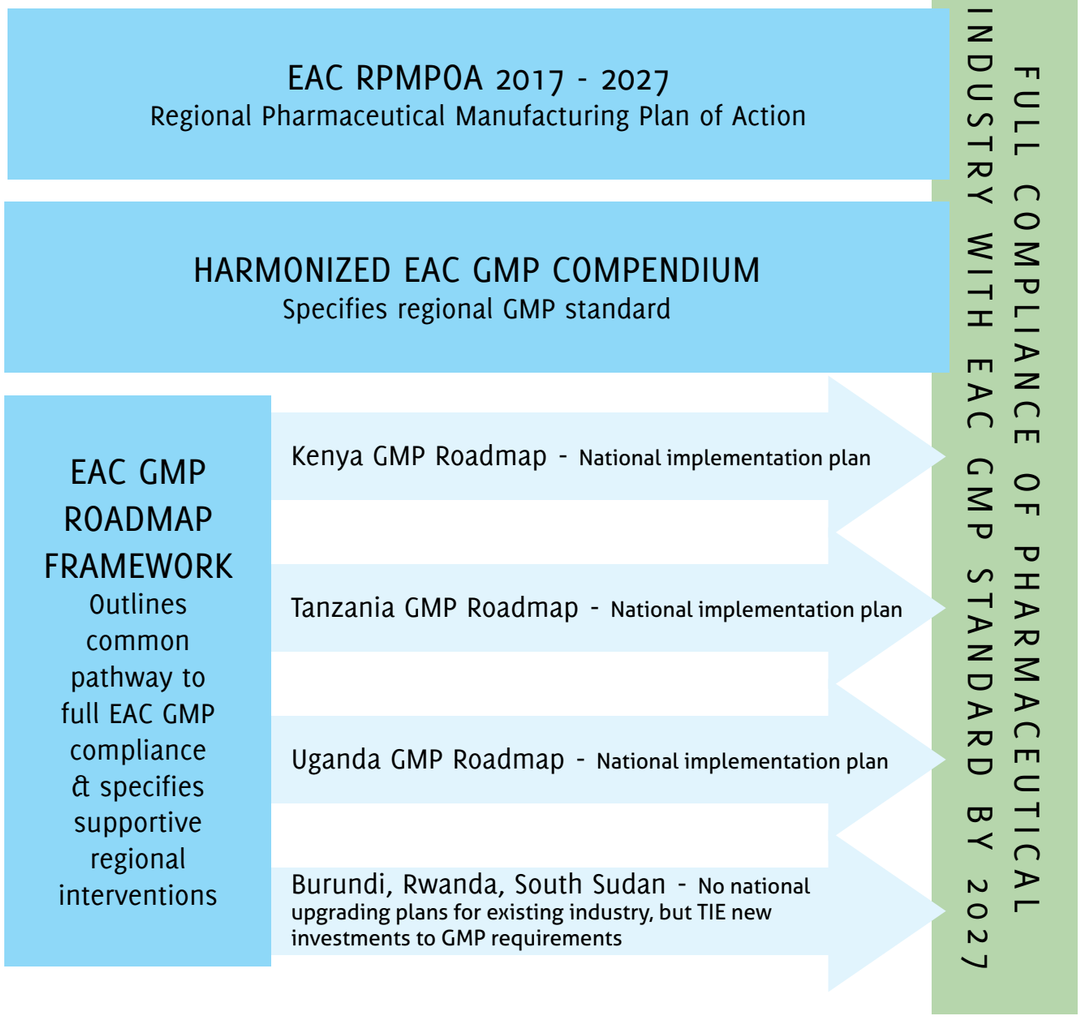
[16] Data on the progress is not available at this stage due to a legal argument between the Kenyan National Quality Control Laboratory and the Pharmacy and Poisons Board about the mandate for follow-up.

5/Conclusion and Recommendations

The EAC pharmaceutical industry has a comparatively strong manufacturing base that provides a platform for future pharmaceutical industry development and which deserves investment attention. The EAC partner states also have a strongly developing pharmaceutical regulatory infrastructure as well as a favourable investment risk assessment. However, the pharmaceutical sector in the region faces a number of barriers and constraints for its future development. What is missing are coordinated (cross-ministry and inter-governmental) policy implementing frameworks supported by technical assistance, cost-effective investment, effective measures to eliminate the many barriers and constraints that the local industry faces and strong incentives to encourage local producers to invest in quality assured production and innovation.

While the EAC-RPMPOA:2017-2027 provides a holistic approach for the future development of the pharmaceutical sector in the region, this regional GMP framework focuses on a number of key interventions specifically related to improving quality-assured production in line with stringent GMP standards.

Figure 4: Support Structure to reach full EAC GMP compliance by 2027



With increasing regulatory cooperation and harmonization, the EAC has developed its own regional GMP compendium modelled after the internationally recognized WHO standard. Moreover, the region is moving towards a harmonized medicines regulatory regime through the Medicines Regulatory Harmonization project. Several joint dossier evaluations and GMP inspections have already taken place. However, so far, there is no framework for mutual recognition. Licensing and GMP inspections are national mandates and still mainly a task for the respective NMRA on country level.

It is in this respect that this **GMP roadmap framework points out priority areas where regional interventions have added value** in addition to national interventions, and ties them to regional activities such as MRH or the EAC-RPMPoA 2017-2027. Due to the national mandate, the majority of interventions, however, target the national and firm level and are specified in the national level roadmap documents. A summary of national interventions per country is given below.

National level:

Kenya's roadmap specified a 5-year long two-step process towards GMP compliance (2014-2019). Stakeholders should focus first on overcoming risky site-related challenges in the first three years and then finalize by addressing QMS-related issues. Its implementation plan involves creating commitment and a steering structure, review of licensing standards, CAPA development by companies, development of incentive package for upgrading, access to affordable finance, development of adequate educational technical curricula and possibilities for cooperation among manufacturers.

Tanzania's shows that high investments are needed across the industry. There is no single high compliance producer at the moment. Several small-scale producers need special assistance to reduce the risk and to improve the GMP level. This might also result in reshaping the business model. Based on the modular approach, the GMP Roadmap also outlines how Tanzanian Food and Drug Authority (TFDA), Ministry of Industry and Trade, Ministry of Health and other institutions should support the industry in its upgrading strategy. TFDA is the driving force and should be supported by the other stakeholders.

Uganda's roadmap stresses the modular approach of implementing the GMP roadmap. There are clear procedures on how to start CAPA clinic and implementation as well as the follow-up. Besides the manufacturers, the manufacturers association, National Drug Authority (NDA), Ministry of Trade, Industry and Cooperatives and other stakeholders need to play their role. The implementation plan proposes training measures for technical and management staff, a reconsideration of product range for low compliance companies, strong steering and ownership for GMP compliance in NDA and a stronger incentive framework for GMP upgrading and investments.

Rwanda's manufacturer is currently not in production, but large investments would be needed to upgrade its production lines to EAC GMP standards. The Rwandan government is advised to tie investment incentives and support for new manufacturing sites to building facilities in line with the regional GMP guidelines. It is most important that the potential investors get support from the newly established NMRA with regard to GMP compliant pharma site design.

Burundi's baseline assessment clearly shows that the single manufacturer at the moment of inspection has to focus firstly on QMS related issues to tremendously improve the GMP level. The MoH is greatly recommended to strengthen the NMRA with regards to the pharmaceutical regulations in the country, a new regulation body is in plan. The ministry of trade has to offer fiscal advantages to local pharmaceutical manufacturers during national medicines store's tenders, actually there is a 0-15% preference on locally manufactured goods by companies with at least 51% Burundian ownership. The single Burundian company does not benefit from this advantage. The government of Burundi is also advised to attract new investments in pharmaceutical manufacturing by creating a conducive environment such as sufficient energy supply, good business climate.

South Sudan currently has no pharmaceutical manufacturing sites. Its government is also advised to consider new investments in pharmaceutical manufacturing only if they are in line with EAC GMP standards from the beginning.

Regional level:

Site related aspects such as utilities and premises are by far the most critical areas. There are 42 companies on EAC level that have low compliance sites. Therefore, manufacturers need to invest in renovation and upgrade of existing manufacturing sites.

The Regional GMP Roadmap Framework outlines regional interventions that incentivize and facilitate more investment into GMP compliant production and respective manufacturing sites. Moreover, we have identified a number of interventions related to QMS aspects where regional-level implementation has added-value.

The recommendations are in line with priority intervention areas detailed in the EAC-RPMPOA: 2017-2027. An activity matrix follows in Annex 1.

TAX AND FISCAL INCENTIVES

REGIONAL ADDED VALUE:
Regionally harmonized incentive packages foster common market development. Focus on critical and expensive equipment/building materials for GMP compliance.

a) On regional level, an **EAC model for pharmaceutical sector incentive packages** should be developed. While the EAC-RPMPOA: 2017-2027 details broader incentive packages for the pharmaceutical sector development, this GMP framework emphasizes the need to incentivize investment into GMP compliant production, existing and new product lines and general upgrade of manufacturing sites. The regional model for a GMP-related incentive package needs then to be tailor-made for the respective national demands and implemented on national level. The following aspects may be considered, their feasibility and appropriateness on regional and national level needs to be analysed:
   - Import free of customs and taxes for all required inputs (APIs, excipients, packaging and labelling materials) as well as critical equipment and machine spare parts (analytical tools, HVAC, etc) dedicated for upgrade of facilities needed for GMP compliance.
   - Tying land allocation for green field projects / set up of new manufacturing plants to a GMP-compliance condition. This should count for green field projects and where the costs for upgrading an existing manufacturing plant exceeds the cost for a setting up a new site. The EAC and the PS support respective costs analyses.
   - Establishment of pharmaceutical industry clusters, which will enable manufacturers to jointly use GMP relevant quality infrastructure, supporting industries and collaborating institutions. This includes utilities, packaging, innovative equipment and instruments, R&D infrastructure and testing labs, among others.
   - Rewarding/incentivizing companies to attain GMP compliance by restricting certain tenders (national/cross border) to companies that meet EAC GMP standards. Moreover, restricting import of selected medicines through tariffs and quotas for which sufficient EAC GMP-compliant production capacities exist.

b) Development of an EAC policy paper and subsequently an EAC policy directive on specific financial needs of the industry and suitable financing / loan options for GMP-related investments. The policy paper should be developed with support from the regional manufacturers association FEAPM and be based on a scoping study and consultative meetings (industry, national and regional key stakeholders).

FDI/tech transfer

REGIONAL ADDED VALUE:
Joint investment promotion as EAC common market increases attractiveness for investors. Harmonized investment rules avoids that investors can get around GMP requirements.

c) The EAC can play a crucial role in attracting **foreign direct investment (FDI) and technology transfer** into the EAC pharmaceutical sector. Foreign direct investment can be an effective way to access capital for GMP upgrading projects and catalyses faster access to regional and international markets. Moreover, it plays a critical role in facilitating technology transfer, technical expertise and relevant capacity building measures, including in GMP related aspects.
  - To facilitate FDI, JV and tech transfer that foster GMP compliance, the EAC could organize trade and industry visits to potential investor countries/firms.
  - Moreover, regular industry networking meetings can be organized and match making and brokering facilitated by EAC institutions.
  - Approval of new pharma FDI or joint ventures should be tied to GMP Compliance or upgrade towards compliance. The joint ventures or FDI must clearly demonstrate a pathway to GMP Compliance.

HUMAN RESOURCES

REGIONAL ADDED VALUE:
Hold regional trainings where scarce capacities (external trainers, specialized equipment) are required and can be jointly used. Focus on common weak spots in GMP (e.g. QC-related aspects as well as qualification and validation).

d) **Human Resource Development** is a fundamental necessity for the overall development of the local pharmaceutical manufacturing industry including GMP upgrades.
  - On national level, in-country training programmes for industry and regulators need to be created which have adequate and appropriate funding support and address local training needs in a cost-effective manner and also sustains future sector development.
  - On regional level, an EAC benchmark strategy for promoting availability of appropriate skills mix for the local pharmaceutical manufacturing industry should be developed (see EAC-RPMPOA).
- Certain capacity development measures and trainings have value added when conducted on regional level, in particular where there is a shortage of expertise that needs to be brought in from abroad and /or where specific hands-on training equipment is scarce in the region. It is EAC's role to facilitate those capacity development measures and source respective expertise and support from international partners, where required. With regard to GMP relevant trainings and capacity development on regional level, we recommend to focus on QC-related aspects (such as trouble shooting, preventive maintenance, repair, calibration of high tech equipment and instruments) as well as qualification and validation. As a background: there is a lack of suitably skilled technicians for repair and maintenance of a wide range of complex equipment required for GMP compliant production. Moreover, there is no easy access to original equipment manufacturers engineers and when repairs or maintenance are required, such engineers are required to be brought in from abroad. .
- The EAC should identify and designate a regional training centre / centre of excellence to for the establishment of pharmaceutical technology preventative maintenance training course in East Africa. This will help to make available in the region a pool of well-trained equipment maintenance and repair personnel for the pharmaceutical sector as well as establish an institutionalized, accredited and sustainable training program.
- The EAC Secretariat should foster partnerships between universities and schools of pharmacy in the region to improve their trainings on GMP-related issues and allow for a regional exchange of knowledge.
- The EAC with its network of international partners could also facilitate structured GMP-relevant internship and exchange programs with industry and academia outside the EAC region. Recommended areas include GMP for herbal medicines, bioequivalence testing, among others.

Centers of Excellence

REGIONAL ADDED VALUE:
No capacities duplicated nationally, higher resources and specialization to the benefit of all. Focus on specific regional training center / centers of Excellence that foster GMP compliance.

e) Based on the findings from the EAC-RPMPOA 2017-2027, the EAC should facilitate the development of **specific centres of excellence** that cater for the identified HR and technical needs for full EAC GMP compliance. The EAC is responsible for developing the framework for designating /establishing such centres; the EAC should also develop a respective business plan and facilitate budget. With regards to attaining GMP compliance, the following three specialized centres could play an important role:
  - The establishment of a regional training centre / centre of excellence for the establishment of pharmaceutical technology preventative maintenance training course in East Africa.
  - Moreover, we recommend the establishment of a regional centre for pharmaceutical sciences and technology as detailed in the EAC-RPMPOA:2017-2027. This centre could cover GMP aspects outsourced from local manufacturers to the centre, including development of GMP relevant documentation (SOPs, dossiers) and pilot projects (e.g. R&D, API production).
  - Another centre that has already been identified through fact-finding missions and needs assessment is the regional centre for production of Chemical Reference Substances (CRS) (see EAC-RPMPOA: 2017-2027). The respective studies identified difficulties in procurement, delays in delivery and high costs of procuring the CRS (for national QC laboratories and manufacturers), impacting cost-effective and GMP compliant production of medicinal products in the region. The adoption of international best pharmaceutical practices requires the use of chemical reference substances.

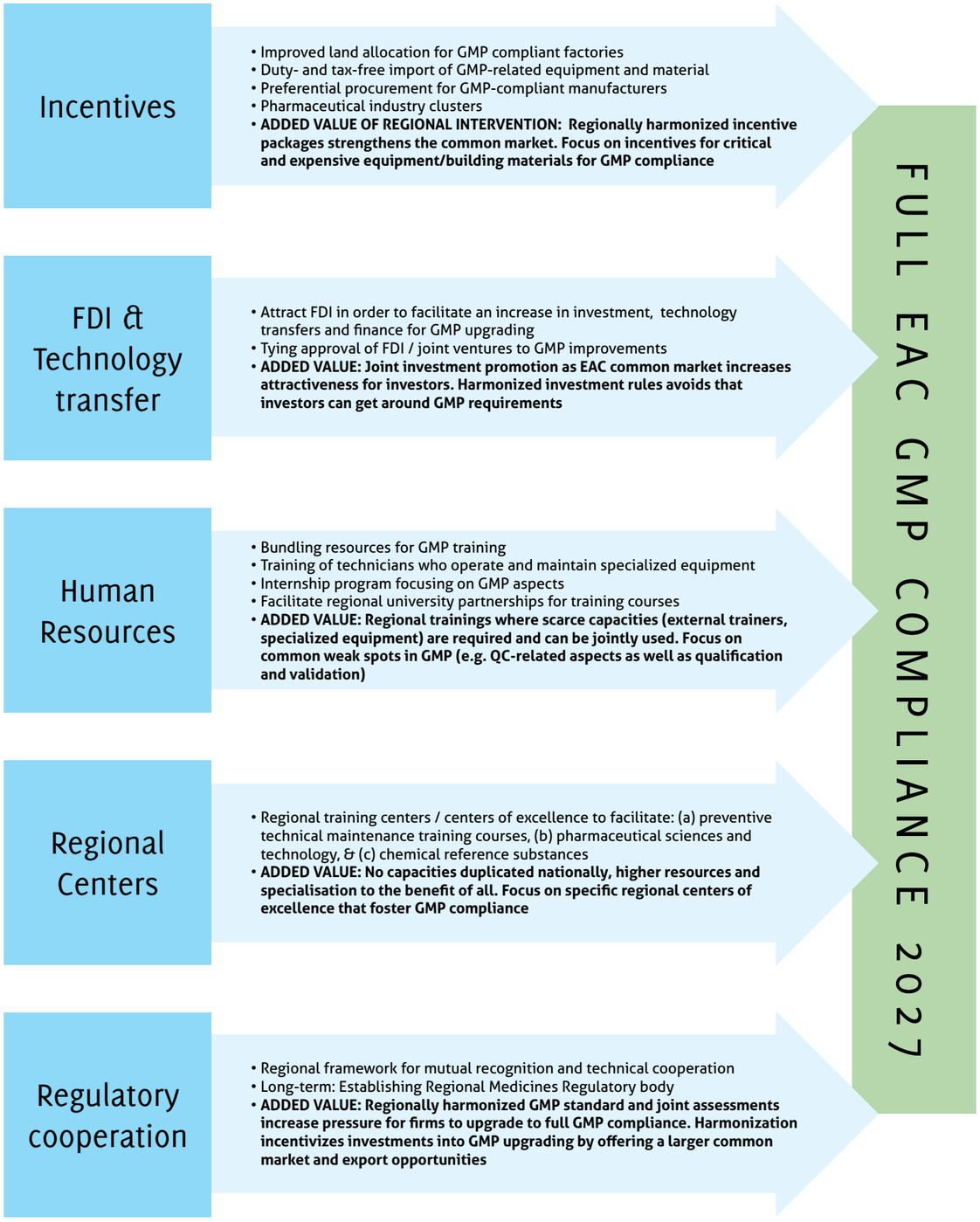
Regulation

REGIONAL ADDED VALUE:
Regionally harmonized GMP standard and joint assessments increase pressure for firms to upgrade to full GMP compliance. Harmonization incentivizes investments into GMP upgrading by offering a larger common market and export opportunities.

f) Regulatory cooperation and harmonization is a viable way to improve regulatory oversight by NMRAs. It aims to improve and streamline regulatory requirements - including GMP compliance - by shifting from a country-focused approach to a collaborative, cross-country approach. The EAC region is moving towards a **harmonized medicines regulatory** regime and through the MRH project joint dossier evaluations and GMP inspections are being conducted. However, decisions taken through joint activities are non-binding to the individual Partner States as there is not yet a framework for mutual recognition in place.
  - Therefore, the EAC needs to establish a regional framework for mutual recognition and technical cooperation on harmonized registration of medicines and other regulatory decisions on which to anchor the medicines regulation harmonization process at regional and national levels.
  - The EAC should develop a regional policy on mutual recognition and on technical cooperation agreements.
  - As a mid to longer term goal, the EAC should pursue the establishment of a regional medicines regulatory body, as detailed in the EAC-RPMPOA: 2017-2027.

g) As a cross cutting issue, the EAC should **strengthen the role of the pharmaceutical manufacturers association** (FEAPM). FEAPM can play an increasing role in galvanizing action for development of local pharmaceutical production. FEAPM is mandated and equipped to actively represent the local industry as well as acting as a major force for development and implementation of effective GMP-related policies on regional level.

Figure 5: Overview of recommended regional level interventions



Steering & Monitoring

All roadmaps should be implemented and full compliance to EAC GMP standards across the whole region should be reached by 2027 at the latest. On national level, Partner States may decide to set earlier targets for full GMP compliance.

In order to steer the implementation of the Regional Framework, there is a need to establish **steering committees** (comprising of Permanent/Principle Secretaries of the Ministries responsible for Health, Industry, Finance and EAC) on the national level. These may meet biannually or when need arises.

National technical committees meet on a regular basis. Technical committee membership reflects the national coordination committee of the EAC RPMPOA.

On the regional level, **the EAC RPMPOA steering committee** is responsible for monitoring the regional interventions, since GMP compliance of the pharmaceutical manufacturers in the EAC is one crucial part of the EAC-RPMPOA: 2017-2027.

Regular national monitoring on the progress of manufacturers towards GMP compliance needs to be undertaken by the NMRAs in accordance with the respective national GMP roadmap's specifications. The NMRAs with support of the national RPMPOA Focal Person should annually report on the implementation of their respective roadmap to the RPMPOA steering committee as a part of the RPMPOA monitoring structure. Progress reports should be composed at the three monitoring timepoints of the RPMPOA: 2021, 2024, 2027.

Costing and Funding

EAC Partner States need to support the implementation of their respective GMP roadmaps from their own budgets. However, much can be achieved with indirect incentives that do not require additional funding like tax-free import of capital goods required for GMP compliance or facilitating working with international GMP experts. Moreover, companies will need to make the highest investments themselves. Here Table 4 rates the costs and benefits of different possible activities. Site-related investments are more costly than addressing QMS issues, but will also have a higher impact on risk-reduction, as the assessment showed.

Table 4: Cost-benefit analysis of steps towards GMP compliance

	Financial efforts	Personnel effort	Time required		Risk reduction	Production efficiency
Effectiveness of Training	low	medium	high	→	high	high
GMP adherence and reporting	low	high	high	→	high	high
Supervision and governance (top-down quality and communication culture)	low	high	high	→	high	high
Documentation	low	high	high	→	high	medium
Maintenance of production equipment	high	medium	high	→	high	high
Maintenance on clean rooms	high	medium	medium	→	high	low
Maintenance on utilities	high	medium	medium	→	high	medium
Process optimization	medium	high	high	→	medium	high

Annex 1: Activity Matrix for Regional Level Interventions

	Activites	Inputs	Outputs	Timeframe			Responsibilities	Est. Budget 2018-2021
				2018-2021	2022-2024	2025-2027		
Tax and Fiscal Incentives	Develop and implement a harmonized incentive package for GMP upgrading (including tax incentives for import of machinery, tax incentives for investments in facility upgrades, industry clusters)	Consultative meetings, cost-benefit analyses, policy directives.	Harmonized incentive policy.				EAC Secretariat, FEAPM	200,000
Access to finance	Development of an EAC policy paper and EAC policy directive on specific financial needs of the industry and suitable financing / loan options for GMP-related investments	Consultative meetings, policy directives	Policy Paper on financial needs				EAC Secretariat, FEAPM	50,000
FDI / tech transfer	Organize matchmaking and study tours to potential investor countries	Expressions of interest for tours, travel logistics	Memoranda of Understanding with partner countries				EAC Secretariat, FEAPM, Embassies	50,000 / tour
	Organize annual industry networking meetings and conferences including international investors	Conference logistics, networking with international investors	Conference reports				EAC Secretariat, FEAPM,	100,000 / event
	Reach regional agreement to tie land allocation for greenfield projects & license for new manufacturing sites to condition of GMP compliant design	Consultative meetings, policy directives	Regional agreement, regulatory directives in each Partner State				EAC Secretariat, Investment Authorities, NMRAs	100,000

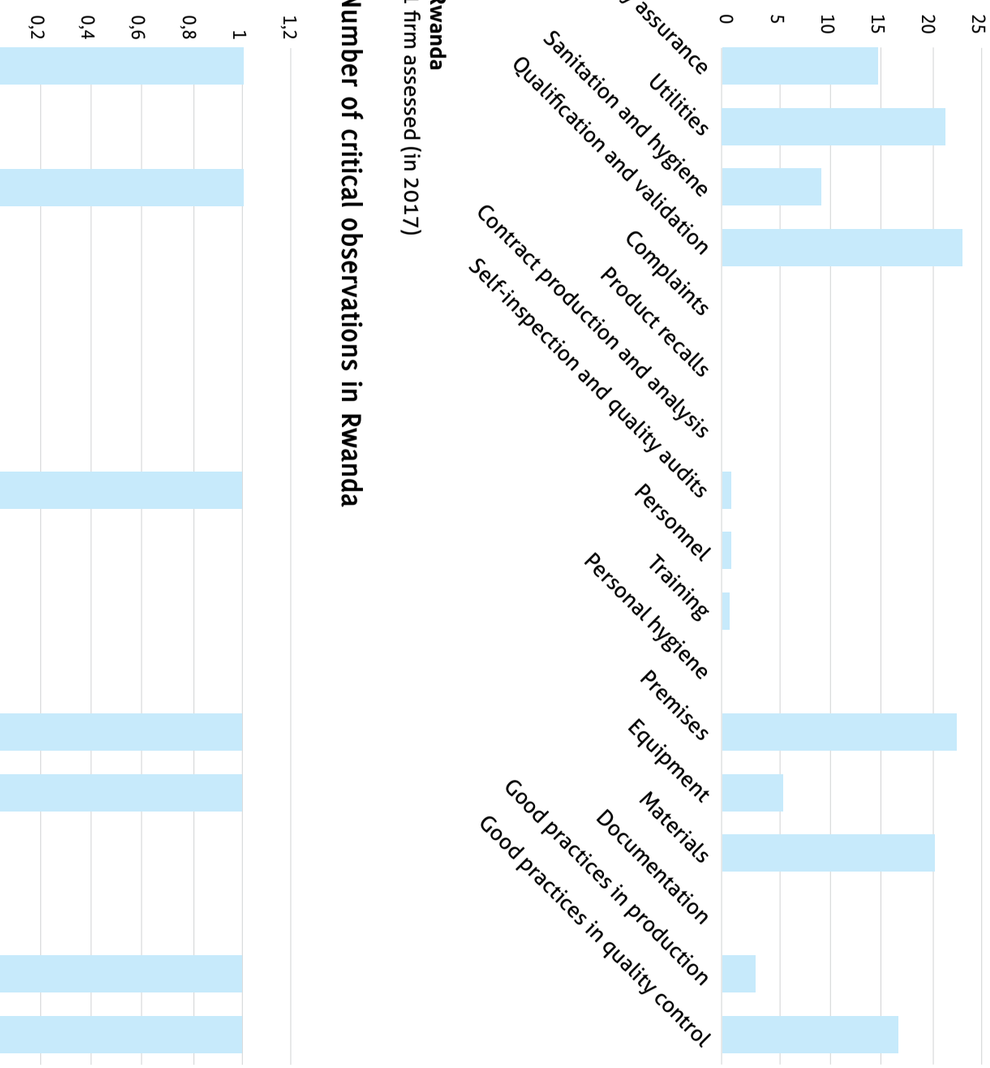
	Activites	Inputs	Outputs	Timeframe			Responsibilities	Est. Budget 2018-2021
				2018-2021	2022-2024	2025-2027		
Human Resource Development	Develop EAC strategy for promoting availability of appropriate skills mix for the local pharmaceutical manufacturing industry taking into account GMP skills.	Skills Gap analysis; Consultative meetings; Trainings and industrial attachments; Exchange programs (North-South and South-South linkages); Pharmaceutical Industry experts' diaspora returnee program; Identify and designate regional training centers for the required pharma skills mix	Gap analysis conducted; HR development strategy in place and being implemented; Data bank for potential returnee for pharmaceutical experts				EAC Secretariat; National ministries; Schools of pharmacy, physical sciences and engineering; FEAPM; National manufacturer associations; International partners	500,000
	Host capacity-building trainings, where regional need exists and resources can be shared (QC-related aspects such as trouble shooting, preventive maintenance, repair, calibration of high tech equipment and instruments & qualification and validation)	Training concepts, training materials, experts	Training reports				EAC Secretariat, FEAPM, international partners	30,000 / training
	Foster partnerships between universities and industry to develop joint courses on GMP	Exchange meetings, curricula development	Additional courses, curricula				EAC Secretariat, FEAPM, universities	30,000
	Facilitate structured international internship program with international industry in areas where EAC needs more expertise (Bioequivalence, formulation development etc.)	Consultative meetings, curricula development	Running program				EAC Secretariat, FEAPM	30,000

	Activites	Inputs	Outputs	Timeframe			Responsibilities	Est. Budget 2018-2021
				2018-2021	2022-2024	2025-2027		
Centers of Excellence	Establish Regional Training Center / Center of Excellence for pharmaceutical technology preventative maintenance courses	Consultative meetings, curricula development	Center established, course in place				EAC Secretariat, National Ministries, International partners	150,000
	Establish a regional center for pharmaceutical sciences and technology	Consultative meetings, curricula development	Center established, courses in place					300,000
Regulation	Establish a regional framework for mutual recognition and technical cooperation on harmonized registration of medicines and other regulatory decisions on which to anchor the medicines regulation harmonization process at regional and national levels	Consultative meetings, development of regional policy, review of national legislation	Mutual recognition of regulatory decisions				EAC Secretariat, National Ministries, NMRAs, International Partners	300,000
	Establish a regional medicines regulatory body	Consultative meetings, policy directive, development of policy and legal framework	Establishment of regulatory body				EAC Secretariat, National Ministries, NMRAs, International Partners	500,000
							Total 2018-2021	**2,340,000+**

Annex 2: Summary of national level assessment results

Kenya
33 firms assessed (in 2015)

Number of critical observations in Kenya

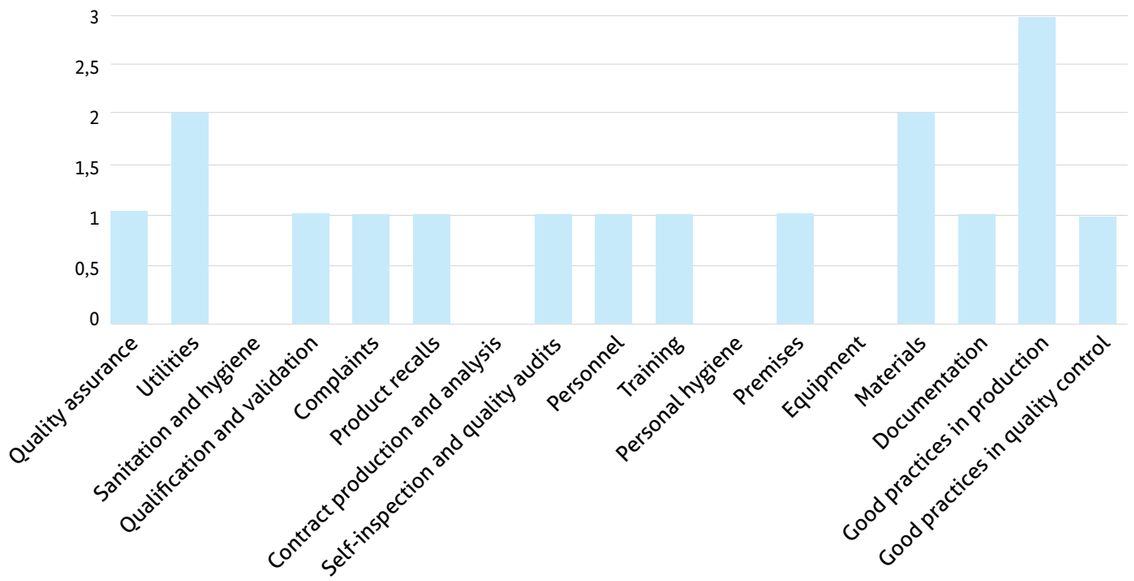


Rwanda
1 firm assessed (in 2017)

Number of critical observations in Rwanda

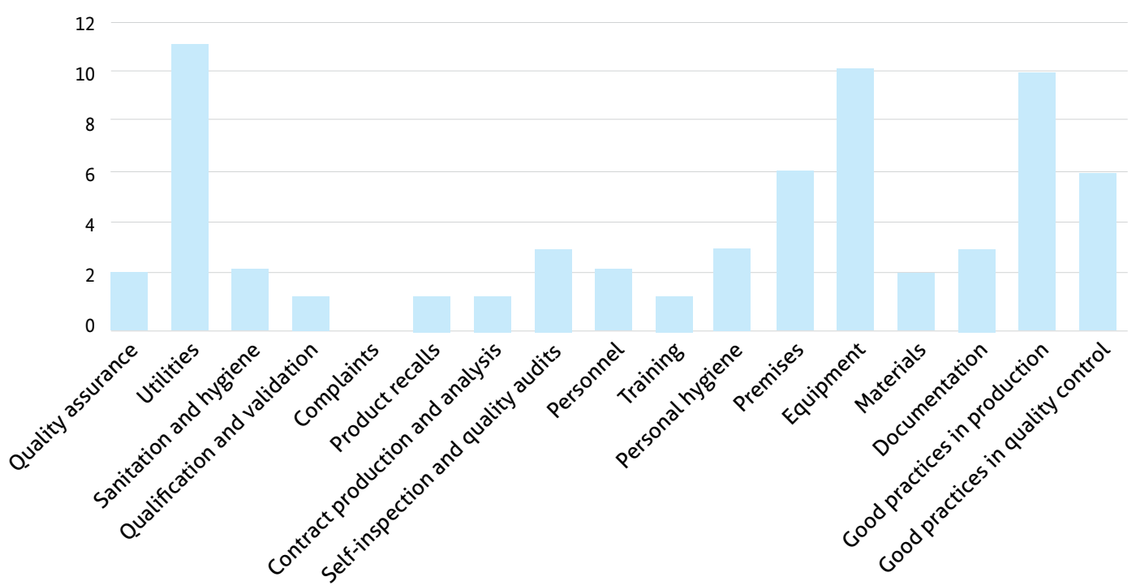
Burundi
1 firm assessed (in 2018)

Number of critical observations in Burundi



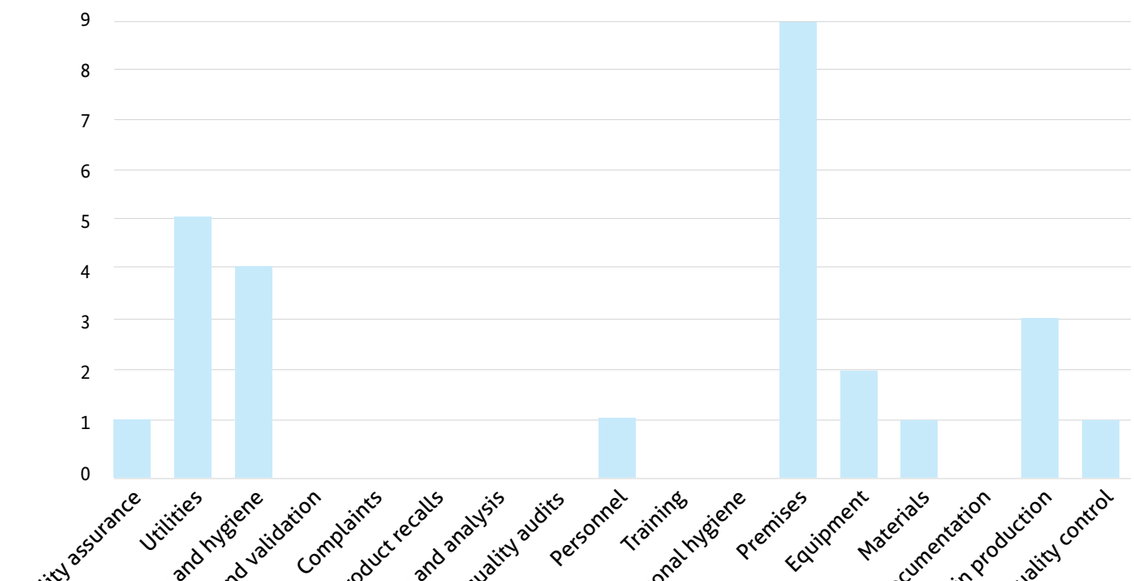
Uganda
14 firms assessed (in 2017)

Number of critical observations in Uganda



Tanzania
11 firms assessed (in 2017)

Number of critical observations in Tanzania



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