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Joint Medicines Regulatory Procedure in the East African Community: Registration Timelines and Way Forward

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ABSTRACT

A review of the East African Community (EAC) joint regulatory review process was conducted, registration timelines analyzed and key milestones, challenges and opportunities documented for the period of July 2015 to January 2020. A total of 113 applications were submitted for joint scientific review. Among these, 109 applications were assessed, 57 were recommended for marketing authorisation, 52 applications had queries to applicants and four applications were under review.

A total median approval time for all products ranged from 53 to 102 days. The maximum time taken by a regulator to review the dossier was 391 days and the minimum time was 44 days. For applicants, the maximum time to respond to queries was 927 days and the minimum time was nine days.

The total median time for granting marketing authorisation by the National Medicines Regulatory Authorities (NMRA) decreased from 174 to 39 working days in 2015 and 2019 respectively. However, not all EAC NMRA has granted marketing authorisation to all 57 products due to non-payment of applicable fees by applicants.

Long regulatory approval timelines were contributed by limited capacity for timely scientific review of dossier by some NMRA, lack of online portal to share dossiersand assessment reports, delay in responding to queries by applicants and deficiencies in dossier. The metric tool and register of medical products submitted for joint scientific review had incomplete data.

Challenges were identified and actions recommended to ensure regional regulatory system optimization, efficiency, transparency, sustainability and accountability.

Keywords: Registration, assessment, timelines, harmonization, regulatory review, medicinal Products, marketing authorization

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1. INTRODUCTION

Harmonization of pharmaceutical regulations and cooperation at regional and continental level contribute to increase availability of high-quality, safe and effective medicines in developed and developing countries (Pierre, 2014). Harmonization of regulations involves establishing an effective network of continental regional and national, or regulatory authorities. The networks facilitate sharing of scientific knowledge, best practices, skills and appropriate use of limited resources to avoid duplication of efforts, reduce cost to pharmaceutical industry and promote innovation and development of medicines for unmet medical needs (Ndomondo-Sigondaet al, 2017). The networks are important structures to build regulatory capacities and capabilities, trust and confidence between National Medicines Regulatory Authorities (NMRA). Conceptualization of harmonization of medicines regulatory frameworks in the East African Community started in 2009 during a continental meeting of Drug Regulatory Authorities (DRA) that was convened to discuss issues surrounding harmonization of drug regulatory requirements and systems in the African continent. The meeting was organized by African Union New Partnership for African's Development (AU-NEPAD Agency), under auspices of African Union Pan African Parliament (PAP), with support from the Bill and Melinda Gates Foundation (BMGF). The East African Community (EAC), with the main mandate of facilitating integration and harmonization of legal, policy and regulatory instruments, was better placed to coordinate the initiative to address regulatory and technical barriers on access to medicines, vaccines and health technologies. EAC is a regional inter-governmental organization of the six Partner States namely: The Republic of Burundi, the Republic of Kenya, the Republic of Uganda, the Republic of Rwanda, Republic of South Sudan and United Republic of Tanzania (www.eac.int). The six Partner States have a unique framework for regional cooperation, and integration in the health sector, as stipulated in the EAC Treaty, Chapter 21, Article 118 (EAC, 2000). The East African Community Medicines Regulatory Harmonization (EAC-MRH) programme was launched by the EAC Council of Ministers on 30th March 2012, with the goal of establishing a standardized and harmonized regulatory systems to ensure safe, efficacious, quality and effective medicines for treatment of priority diseases (S. EAC, 2010). The programme is implemented by seven National Medicines Regulatory Authorities (NMRA) and EAC Secretariat is the coordinating body. The implementing agencies include the Department of Pharmaceuticals and Medical Laboratories (DPML) of Burundi, Pharmacy and Poisons Board (PPB) of Kenya, National Drug Authority (NDA) of Uganda, Drug and Food Control Authority (DFCA) of South Sudan, Rwanda Food and Drugs Authority (Rwanda FDA), Tanzania Medicines and Medical Devices Authority (TMDA) and Zanzibar Food and Drugs Agency (ZFDA) of the United Republic of Tanzania. In addition, the African Medicines Regulatory Harmonization Partners (AMRH), namely the World Health Organization (WHO), African Union Development Agency (AUDA), formerly known as African Union New Partnership for Africa's Development (AU-NEPAD), the Bill and Melinda Gates Foundation (BMGF), the World Bank (WB), United Kingdom Department for International Development (UK-DFID), Swiss Development Corporation (SDC) and United States Agency for International Development (USAID) provided support to the initiative.

Technical partners include WHO and Swiss Agency for Therapeutic Products, while African Union Development Agency (AUDA) plays a high level advocacy role on medicines regulation harmonization in the continent working with Regional Economic Communities (REC) such as EAC, Southern African Development Community (SADC) and Economic Community of West African States (ECOWAS), Partners (BMGF, UK-DFID, WB, USAID and SDC) provide financial resources to AMRH Trust Fund to support AMRH initiative in different RECs.

The programme has six objectives:

a) To implement an agreed common technical document (CTD) for registration of medicines in EAC Partner States;

b) To implement a common information management system (IMS) for medicines registration in each of the EAC Partner States NMRA which are linked in all Partner States and EAC Secretariat;

c) To implement a quality management system in each of the EAC Partner States NMRA;

d) To build regional and national capacity to implement medicines registration harmonization in the EAC;

e) To create a platform for sharing information on the harmonized medicines registration system to key stakeholders at the national and regional level;

f) To develop and implement a framework for mutual recognition based on Chapter 21, Article 118 of the East African Community Treaty.

The initial phase of the EAC-MRH programme (March 2012 - December 2017) focused on:

a) establishment of regional governance structures to support implementation and sustain the programme

b) development of harmonized technical guidelines, procedures and tools for joint registration (EAC Common Technical Document-CTD) and joint good manufacturing practices (GMP) inspections

c) establishment of a quality management system in all EAC NMRA

d) institutional capacity building on regulatory sciences

e) high level policy advocacy for establishment of semi-autonomous National Medicines Regulatory Authorities (BCG, 2017).

EAC Joint Regulatory Procedure

EAC joint medicines regulatory procedure involves joint scientific evaluation of safety, efficacy and quality of medicinal products and joint inspections of pharmaceutical manufacturing facilities to assess compliance to Good Manufacturing Practices (GMP) standards.

The following procedures are undertaken under the EAC joint regulatory review:

a) Evaluation of medical product dossiers;

b) Joint physical inspections of manufacturing sites or desk review in line with EAC Compendium of guidelines for GMP (EAC, 2018);

c) Joint inspections of clinical sites, if applicable according to the Good Clinical Practices (GCP);

d) Joint post-marketing surveillance and safety reporting;

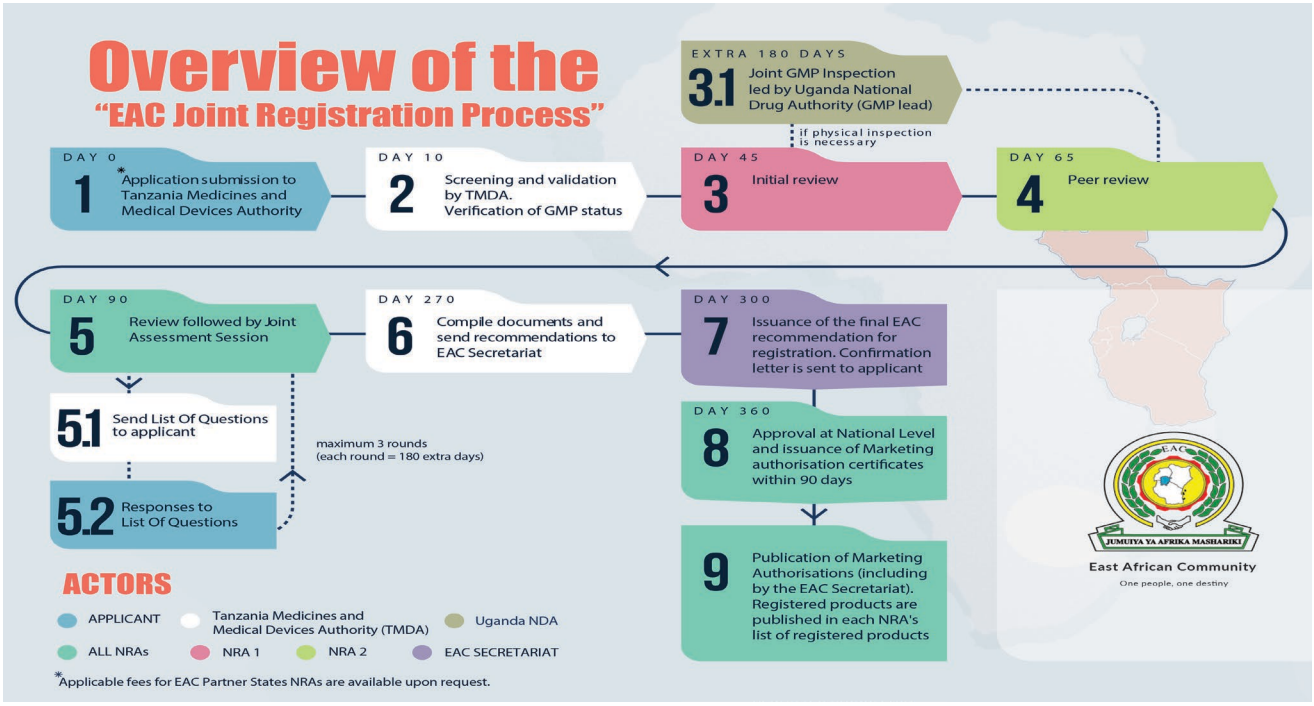
e) Enforcement of joint regulatory decisions by NMRA.

For the purpose of this study, the focus was on joint evaluation of medicinal product dossiers, which also involves joint inspections of pharmaceutical manufacturing facilities, depending on outcomes of dossier evaluation. The study narrowed down on analysis of registration timelines to evaluate if the process demonstrated efficiency and could be optimized to ensure predictability, consistency and accountability. The terms “joint assessment” and “registration” will be used interchangeably with joint registration procedure or dossier evaluation.

Submission of Dossier in CTD Format

The EAC joint assessment and registration process came to fruition in July 2015 after nine medicinal product dossier applications were lodged for joint evaluation and registration. The EAC procedure is highlighted in Figure 1. The procedure begins with submission of an application to TMDA, the lead NMRA for Medicines registration (Step) The medicinal product dossier should be in line with EAC guidelines on submission of documentation for registration of human medicinal products for preparation of marketing authorization application in the common technical document (CTD) (EAC, 2019a). Screening is conducted by the lead NMRA (Step 2) and the lead NMRA for GMP will be notified to verify GMP status and the applicant notified whether the dossier is accepted or rejected within 14 days. If the dossier is complete, the application will be assigned to 1st and 2nd assessor, as per EAC standard operating procedure for joint assessment, and scheduled for joint assessment. Dossier assessment will be conducted within three months following successful screening (Step 3, 3.1 & 4). The evaluation of additional data will be conducted within two months of receipt and a maximum of three rounds of queries is permitted (Step 5, 5.1 & 5.2). Following successful dossier evaluation and compliance with Good Manufacturing Practices, the experts will make recommendations to the EAC Heads of NMRA and will recommend to the EAC Secretariat to issue confirmation letter to the applicant/manufacturer (Step 6 & 7).

Figure 1. ***Infographic of EAC Joint Assessment Procedure***



National administrative procedure to grant marketing authorisation (MA) takes three months from the date of joint acceptance. The respective EAC Partner States NMRA will issue a certificate of MA, which confirms the final registration outcome (Step 8). Registered products shall be maintained in each NMRAs list of registered products and EAC Secretariat (Step 9). The EAC Partner States will then monitor the safety and quality of the products in line with the national policies and regulations. In addition, EAC Compendium of Pharmacovigilance Guidelines (EAC, 2019b) requires the applicant to ensure safety of their products they place in the EAC market and in this regard, the EAC NMRA will jointly monitor safety of the products registered through the EAC-MRH scheme using standardized tools and procedures.

According to the EAC joint assessment procedure, scientific evaluation of dossiers by a regulator should be carried within 181 working days. The applicant's response to queries is 180 working days. Once a regional positive outcome of the assessment is issued, alle EACNMRA are required to issue marketing authorization within 90 working days following a positive regional recommendation.

EAC Joint Good Manufacturing Practices Inspections

Initiation of EAC Joint GMP inspection may occur through three mechanisms:

a) A joint procedure in the framework of multiple applications for marketing authorization to more than one NMRA

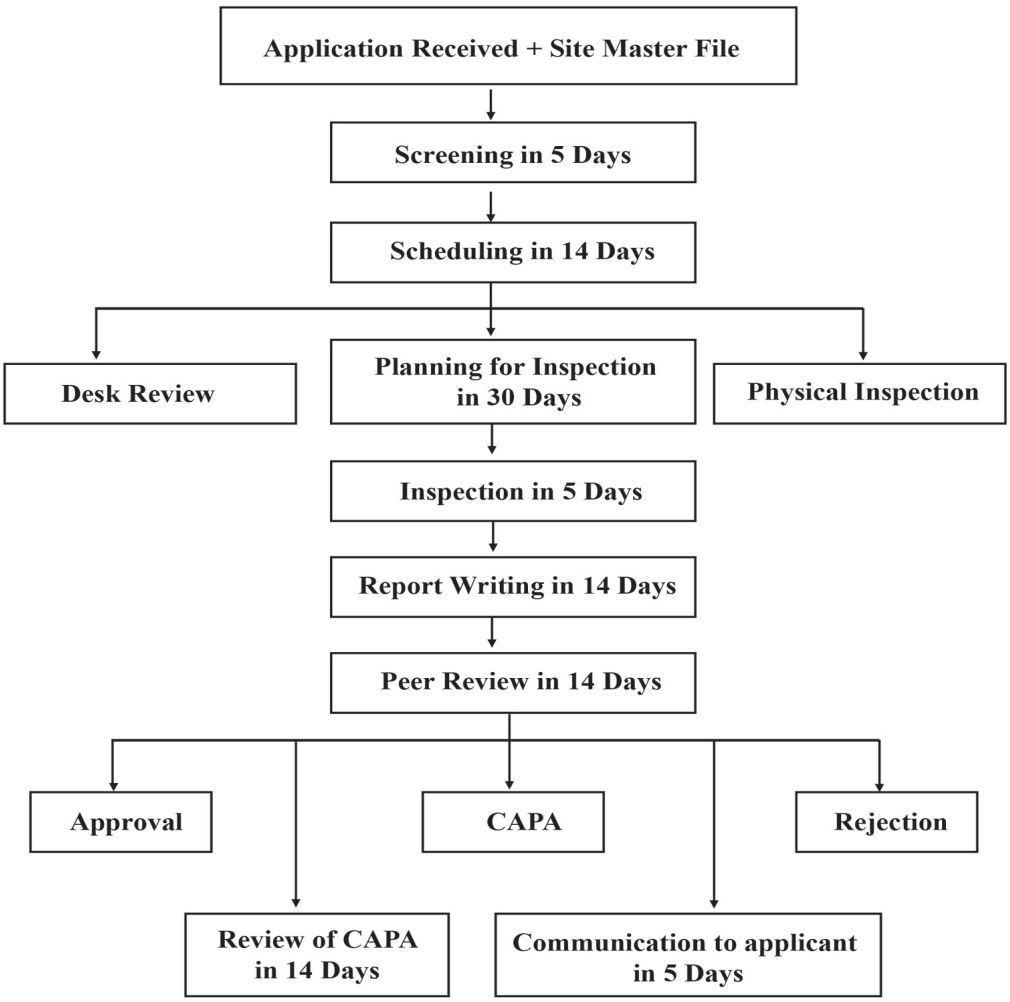
(joint assessment and registration);

b) An official request from a manufacturer;

c) A joint interest of at least two EAC Partner States NMRA.

The procedure for joint GMP inspections, as indicated in Figure 2, requires an applicant to submit an application including the Site Master File and applicable fees to the lead NMRA for GMP, National Drug Authority (NDA), Uganda and other NMRAs, as per their fee guidance. Scheduling of joint inspections will be done by the lead NMRA, while the maximum number of inspectors per site is three, drawn from two NMRAs. Communication of the inspection dates will be done within 14 days by the lead NMRA. Site visit and inspection will be conducted within 30 working days from the day of scheduling. Communication of the outcome of inspection will be within 42 working days from the dates of inspection. Review of Corrective and Preventive Actions (CAPA) and responses by the applicant will be completed within 90 working days.

Figure 2. ***EAC Joint GMP Inspection Procedure Flow Chart***



The letter, which confirms the final inspection outcome, will be communicated by the EAC Secretariat. National approval will be granted within three months from the date of joint acceptance; and respective EAC NMRAs will issue a certificate, which confirms the final inspection outcome. EAC NMRA will maintain the list of inspected sites and continue to monitor compliance to EAC GMP standards after every three years.

To ensure timely availability of quality medicinal products and effective medicines registration and marketing authorization, it is important to have timelines tracking the system to evaluate performance of the system and ensure compliance to agreed timelines. The EAC has developed a comprehensive metric tool to track timelines for joint registration and joint GMP inspections. The clock stop system is implemented to monitor the length of the review process.

Metric Tools to Track Timelines of Joint Assessment Procedure

The metric tool for joint registration procedure is an Excel sheet which contains six sections as indicated below:

(i) Section 1: Application Details

This section documents application number, brand name, generic name, pharmaceutical form, therapeutic class, type of product, applicant name, manufacturer, date of submission of dossier and date of notification to the EAC expert working group (EWG) for GMP.

(ii) Section 2: Screening Process *(14 days)*

This part covers the date of completion of the screening, date when the outcome of screening is communicated to applicant, date of receipt of updated dossier, final outcome (accepted/rejected) and date of acceptance/rejection of dossier.

(iii) Section 3: Evaluation Process

First Cycle of Evaluation

- Date the first assessment is completed *(21 days)*;
- Date second assessment completed *(14 days)*;
- Date the assessment report is discussed and finalized *(seven days)*;
- Date recommendations are communicated to applicants *(14 days)*.

Second Cycle of Evaluation
(First Round of Queries)

- Date additional information is submitted by applicant *(180 days)*;
- Date first assessment of query response is completed by first assessor *(14 days)*;
- Date second assessment of query response completed by second assessor *(seven days)*;
- Date when query response assessment report discussed and finalized at EAC *(seven days)*;
- Date when recommendation is communicated to applicant *(seven days).*

Third Cycle of Evaluation
(Second Round of Queries)

- Date additional information is submitted by applicant *(120 days)*;
- Date when first assessment of query response is completed by first assessor *(14 days)*;
- Date when second assessment of query response is completed by second assessor *(seven days)*;
- Date when query response assessment report is discussed and finalized at EAC level *(seven days)*.

Fourth Cycle of Evaluation
(Third and Final Round of Queries)

- Date additional information is submitted by applicant *(120 days)*;
- Date when first assessment of query response completed by first assessor *(14 days)*;
- Date when second assessment of query response completed by second assessor *(seven days)*;

(iv) Section 4: Final Recommendations

This section captures information on whether the product has been accepted or rejected. It also covers:

- Date when final recommendations are reached;
- Date when final recommendations are communicated to applicant.

(v) Section 5: NMRAs Implementation of Regional Recommendations

This section contains the following:

- Date when EAC Secretariat communicates final recommendations to all EAC NMRA *(14 days)*;
- Date when the product is granted marketing authorization (MA) by each individual EAC NMRA *(90 days).*

(vi) Section 6: Post Approval Process

The section document time period of communication made to theEAC expert working group (EWG) for pharmacovigilance (PV) and post-market surveillance (PMS) following approval for marketing authorization., This also applies for variations and renewals. If the product

is withdrawn from the market, then it should be documented in this section.

Metric Tool for EAC Joint GMP Inspections

The metric tool for EAC Joint GMP Inspections is an Excel sheet which contains five sections as highlighted below.

Section 1: Application Details

This section captures information on application number, name of applicant, site(s) address(es), contact person on site, category of medicines, registration status of products and number of production lines to be inspected.

Section 2: Screening Process

This part covers date of completion of screening (five days) and course of action (physical inspection/desk review).

Section 3: Scheduling

This section contains:

- Scheduling of inspections (14 days);
- Date of lead NMRA communicates to applicant on Schedule of Inspection;
- Date Lead NMRA communicates to Partner States on dates of joint inspections;
- Date the applicant confirms the inspection to be conducted (30 days);
- Submission of names of inspectors by EAC Partner States (seven days).

Section 4: Planning and Inspection

This section covers:

- Planning and preparation *(30 days)*;
- Inspection *(five days)*;
- Report writing *(seven days)*;
- Peer-review monthly reviews *(14 days)*;
- Recommendations communicated to applicant *(five days).*

Section 5: Review of Corrective and Preventive Action (CAPA)

- Date submission of CAPA is done by applicant *(90 days)*;
- Date review of CAPA concluded *(14 days)*;
- Date recommendations are communicated to applicant *(five days)*;

Clock Stop System for EAC Joint Assessment

The clock watch system for EAC joint assessment and registration is summarized below:

- First Cycle of Evaluation
  - **Clock Stop 1:** The evaluation is paused (first clock stop) while the applicant prepares the responses to EWG for Medicines evaluation and registration (MER).
- Second Cycle of Evaluation
  - **Clock Stop 2:** The evaluation is paused again for applicant to address outstanding issues.
- Third Cycle of Evaluation
  - **Clock Stop 3:** The evaluation is paused for applicant to provide clarifications on outstanding issues.
- Fourth Cycle of Evaluation
- Final discussion and adoption of scientific review opinion.

The evaluation process is a step-by-step process and the metric tool has been designed to document the time period (working days) of each step using a clock stop system.

Confidentiality of Manufacturers Data

Confidentiality of shared data is assured by mechanisms applied by participating parties (EAC NMRA). Participating NMRA create a written commitment that “any information and documentation provided to them by applicants will be treated as confidential and access to this information will be allowed only to persons involved in the joint assessment and registration procedure”. The expertsare bound by confidentiality statement and commitment as specified in Part 5 of the EAC Compendium of Quality Management System Technical Documents For Harmonization of Medicines Regulation in the East Africa Community, the EAC Code of Conduct for EAC Partner States NMRA (EAC/TF-MED/QMS/FD/COM/N3R0).

Timelines for EAC Joint Assessment Procedure

The time spent by EAC experts to conduct scientific evaluation is 181 working days and the time is interrupted by three clock stops during which the applicant prepares the answers to questions raised by an EAC expert working group for medicines

evaluation and registration (MER). The time for the applicant to respond to queries is 180 working days while national administrative procedures to grant marketing authorisation is 90 working days. The overall assessment of medicinal products usually takes approximately a full calendar year (360 days). Since commencement of joint assessment and registration procedure in July 2015, a total of 113 applications have been submitted for joint scientific review. Among these, 109 applications have been assessed, 57 have been recommended for marketing authorisation, 52 applications have queries to applicants and 4 applications are under review.

Studies have been conducted in relation to the East African Medicines Regulatory Harmonization Programme (Hiiti et al., 2020; Jane et al., 2020; Margareth et al., 2020). However, none focused on analysis of the registration timelines for the EAC joint evaluation procedure. This study therefore wasconducted with the following objectives:

(i) To document stages of the EAC joint regulatory review process;

(ii) To review the metric tool and analyse registration timelines;

(iii) To identify key milestones, challenges and opportunities.

Data collection template was developed to enable structured documentation of all relevant information extracted from the metric tool (Excel sheet) in a summarized manner. The template contained information on application number, pharmaceutical form, therapeutic class and type of product, date of submission of application, notification to EWG on GMP, type of assessment (full or abridged), round of assessment, date when final report was discussed and completed, regulators time (working days), applicant timelines (working days), final outcome (accepted /rejected) and date when final recommendation were communicated to the applicant. Regulators and applicant timelines were obtained by reviewing data in the metric tool for each product from the date of submission, date of clock start/stop and date of approval. Number of days were counted for each evaluation step, as indicated in the introduction section of the evaluation steps and rounds of queries. Timelines for the applicant and regulator were obtained considering clock start and stop system and summed up to get the total number of working days. Appendix 2 summarizes the findings and registration timelines of each product. Based on the metric tool and the EAC register of medicinal products, the 57 medical products were recommended for marketing authorisation hence they formed study sampling frame.

2. METHODS

Information on the total number of applications and approvals for the period of July 2015 to January 2020 was obtained from the register of medicinal products submitted for joint evaluation and registration (TMDA, 2015). Review of the metric tools for joint evaluation procedure and joint GMP inspections was done (RTO's & Secretariat, 2018a; 2018b). Analysis of regulatory approval times between July 2015 to January 2020 for 57 medicinal products recommended for registration was conducted. Retrospective review of other program documentations, such as guidelines, templates, standard operating procedures (SOP's) and reports, was conducted. Documents were available at EAC Secretariat and others were obtained from Tanzania Medicines and Medical Devices Agency (TMDA) and National Drug Authority (NDA).

Study Hypothesis

- There is a significant reduction in the regulatory approval timelines between 2015 and 2020 for EAC joint assessment and registration procedure;
- Long regulator timelines are associated with the type of evaluation process.

Data Collection

Statistical Analysis

Study data was processed in Microsoft Excel to test the hypotheses and examine associationsbetweenvariables.

3.RESULTS AND DISCUSSION

Scientific evaluation of safety, quality and efficacy data in the dossier was conducted by assessors from the seven EAC NMRA. Two experts from each EAC NMRA formed the EAC Expert Working Group (EWG) for Medicines Evaluation and Registration (MER). The primary mandate of this network of assessors was to provide technical guidance in all matters related to medicinal product registration to the Forum of Heads of EAC NMRA. This arrangement was adopted by the EAC Council of Ministers in September 2014, since there was no regional regulatory body that is mandated to oversee regulation of medicines in the EAC region.

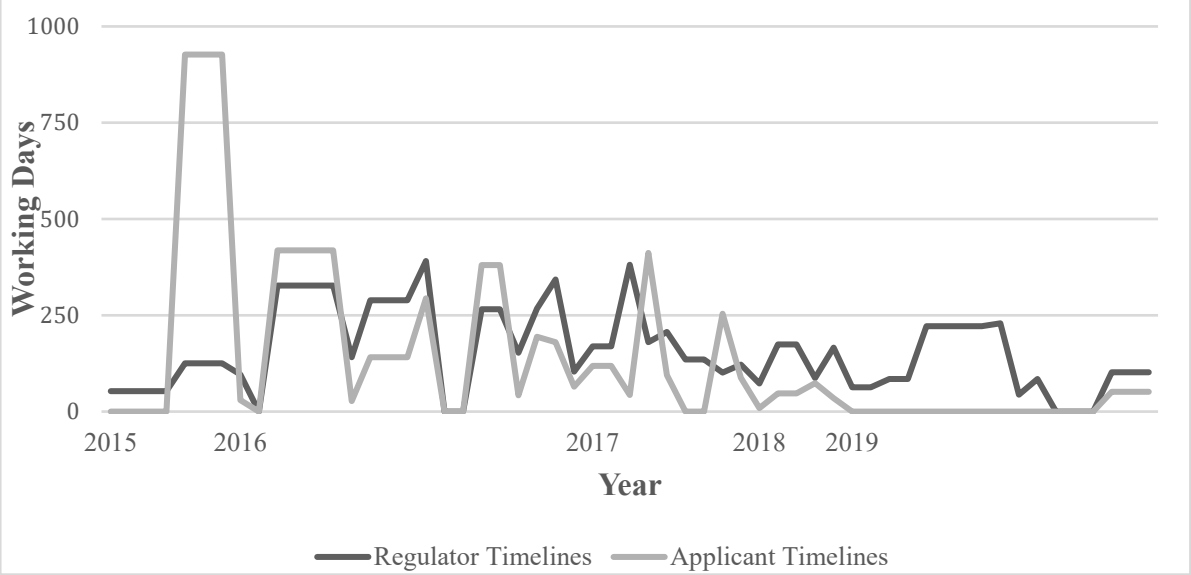
As indicated in Figure 1, once a dossier was submitted and accepted, it was assigned to first and second assessors. The assessors conducted evaluation at the national level and shared reports with other regulators. Then the assessment report

was reviewed and discussed during face-to-face meetings with assessors.

A total of 113 applications were submitted for EAC joint scientific review. Among these, 109 applications were assessed, 57 were recommended for marketing authorisation, 52 applications had queries to applicants and four applications were under review.

The highest number of products recommended for marketing authorization was in the year 2016 (n=19) and the lowest number was in 2018 $(n = 5)$, as indicated in Appendix 1.

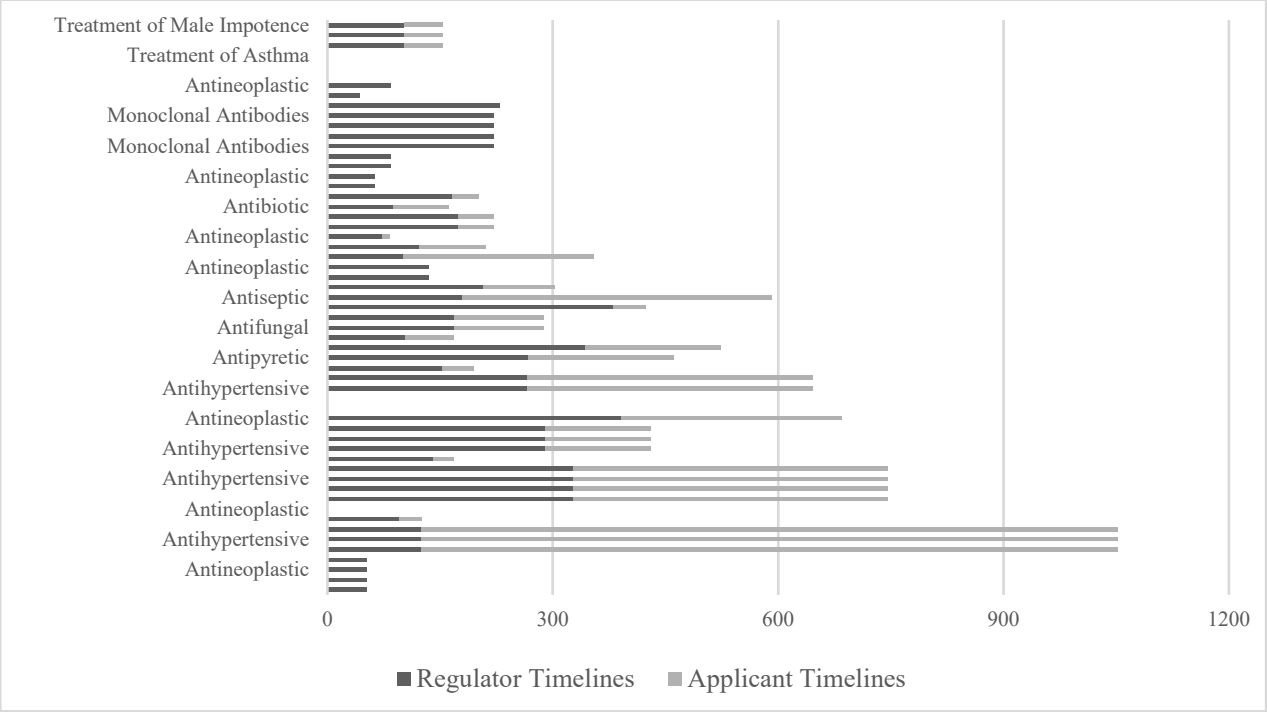
Figure 3. ***Trend of Regulator and Applicant Timelines for a Period of 2015 to 2019***



There was a significantly long regulatory approval timeline (1,052 working days) in 2016, as indicated in Figure 3 above. The main reason was the delay of manufacturers to respond to queries raised, which took 927 working days, while the regulator's time was 125 working days. A similar challenge was observed by Ahonkhai et al. (2016) in which long regulatory review period was due to delay to respond to queries by sponsor. In addition, the quality product dossier submitted had insufficient data, which led to more rounds of queries and negatively impact review period. The EAC assessors had an obligation to ensure the products submitted for registration met standards as stipulated in EAC guideline for registration of human medicinal products. The trend of timelines for regulators indicated a steady improvement throughout the years. This was contrary to the findings by Dansie et al. (2019), which indicated hesitation of manufacturing companies to use the EAC joint assessment procedure. The main reason was due to the length of time to receive the actual marketing authorization and unexpectedly higher quality standards than national procedures. For all 57 products, the longest time taken by a regulator to review the dossier was 391 days in 2016 and the shortest time was 44 days in 2019. For manufacturers (applicant), the longest time to respond to queries was 927 days (2015) and the shortest time was 9 days in 2018 (Figure 3 & Appendix 2).

For regulators, the root cause of long review timelines was mainly due to lack of an integrated information management system portal to support timely sharing of dossiers and assessment reports. In addition, the region had NMRA with different capacities and capabilities of assessors to conduct timely scientific reviews of medicinal product dossiers of different product categories. However, the EAC-MRH program continued to provide a greater opportunity for capacity building across the region to bridge the gap between highly skilled and less-resourced NMRA.

Figure 4. ***Therapeutic Category of Products Submitted for EAC Joint Assessment Procedure***

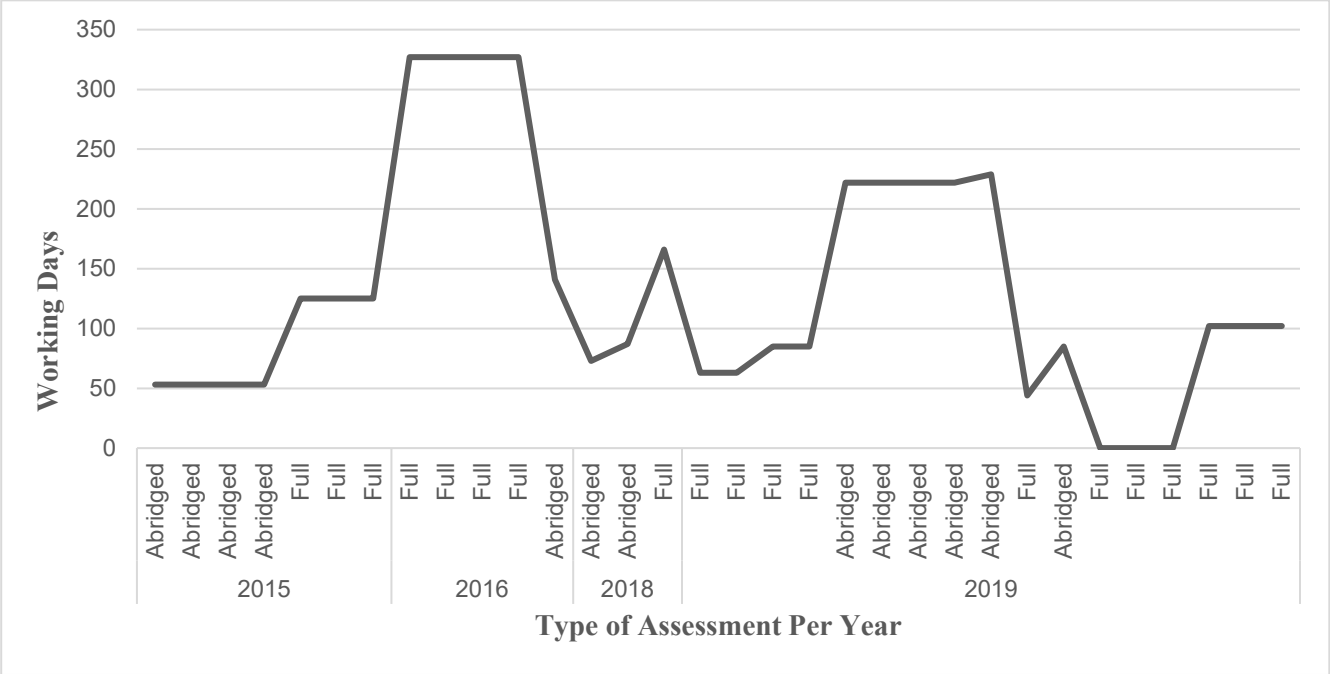


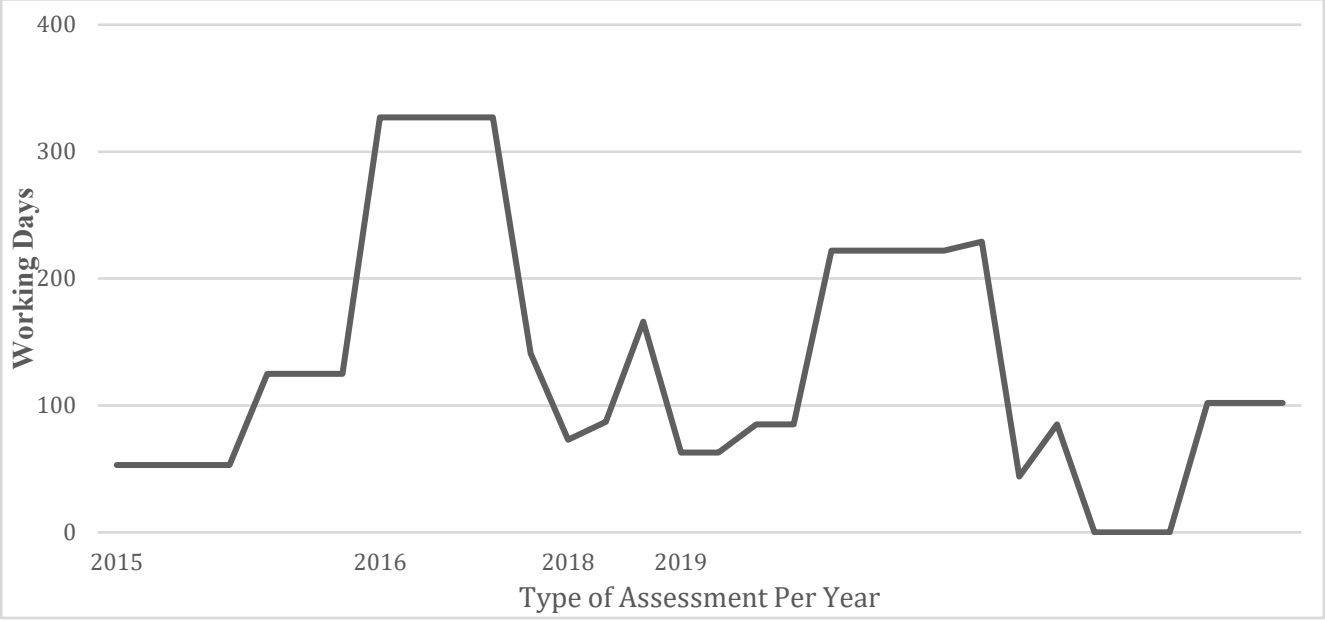
Therapeutic categories of products submitted for joint evaluation process for the past five years were mainly antineoplastic/biologicals, antidiabetics, monoclonal antibodies, antimicrobials and antihypertensives as indicated in Figure 4. The scope of products for consideration under the EAC joint assessment procedure included medicines, biotherapeutics and biosimilars. The priority was given to medicines to manage maternal, neonatal and children's health conditions, HIV, malaria, tuberculosis and neurological disorders. In addition, the EAC Expression of Interest have listed category of products for management of neglected diseases such as leishmaniasis, pneumocystosis, toxoplasmosis, filariasis and strongyloidiasis (EWG & Registration, 2020). Apart from the listed products, the EAC routinely conducted mapping of common applications submitted in at least two EAC Partner States NMRAs and requested the applicant to consent to participate in the joint review process.

A joint assessment procedure involved full and abridged evaluations. An abridged procedure was for medicinal products already approved by stringent regulatory authorities and the WHO prequalification program. For this procedure, the assessors employed a risk-based approach in the evaluation process and review of the quality information summary of the finished pharmaceutical product (QIS-SRA) submitted by the applicant. The reviewer focused on the main aspects of Active Pharmaceutical Ingredient (API) quality and stability. For finished pharmaceutical product, the assessor reviewed specifications, labelling and the manufacturing process. For any variations (post approval changes) to the products, the EAC guideline on variation to a registered pharmaceutical product or vaccine would be applicable.

Full evaluation involved review of all data related to quality, safety and efficacy of the drug product. For this study, data were analysed according to the type of evaluation to discover if this variable would have an impact on regulator timelines and determine whether the hypothesis was true. As indicated in Figure 5 below and Table 2 (Appendix 2), for the year 2019, full evaluations of product 040, 041, 042, 043 and 044 took a period of 166, 63, 63 and 85 working days respectively; while abridged assessment of product 045, 046, 047, 048 and 049 in the same year took 222, 222, 222, 222 and 229 working days respectively. In addition, in the year 2015, abridged evaluation of product 001, 002, 003 and 004 took 53 working days each, while full evaluations of product 005, 006, and 007 took 125 working days each. Based on the findings for the year 2015, 2016, 2018 and 2019, there was no correlation between regulators' timelines with the type of evaluation.

Figure 5. ***Regulator's Timelines Vs Type of Assessment Method for a Period of 2015 to 2019***





For the year 2019, abridged assessment took longer than 181 days, as per the standard operating procedure for joint assessment; while full assessment was less than 181 days for the five products mentioned above. For year 2015, both abridged and full assessment took less than 181 days. For 2017, the type of evaluation was not documented in the register of medicinal products submitted for the joint review process as indicated in Appendix 2. Incomplete data in the metric tool and other records should be addressed by the programme implementers so that future studies' findings can represent the real situation.

During the past 5 years, the total median approval time (submission through end of assessment) for all

products ranged from 53 days in 2015 to 102 days in 2019. There was a significant increase in the total median approval time (476 working days) in 2016, as indicated in Figure 6. Long median time was contributed due to the following reasons:

a) the dossier submitted by the applicant did not have bioequivalence data to demonstrate that a generic product submitted for registration is bioequivalent to its reference or originator product;

b) the package of products submitted did not meet EAC Common Technical Document (CTD) requirements;

c) there was a delay in response to queries by applicants

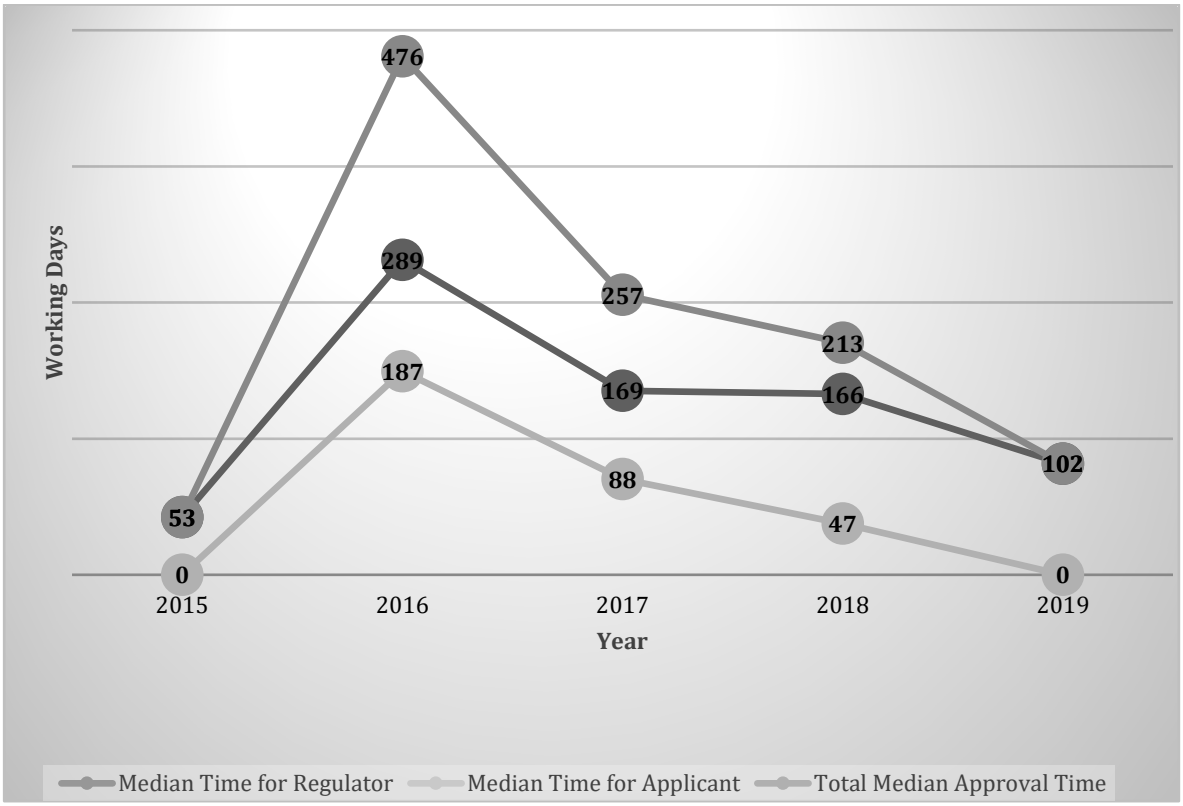
d) there was a delay in submission of assessment reports by assessors

e) stringency of regulators.

Deficiencies in the dossier were also observed by a study conducted by the WHO prequalification program (Wondiyfraw et al., 2012).

During the same period (2016), the median time for an applicant was 187 days while median time for a regulator was 289 days. The findings further indicated a decrease in total median time from year 2017 to 2019, as indicated in Figure 6. The median time for a regulator decreased from 169 days to 102 days and manufacturers ranged from 88 days to zero days. This showed improvements in the processes and high commitment by all stakeholders involved in the joint assessment procedure, which led to

Figure 6. ***Median Timelines for Regulator and Applicant Per Year***



improved efficiency and effectiveness of the whole process. Both regulator and applicant were compliant to the set timelines of 181 and 180 days, respectively. The results of this study were different from the study conducted in 2014 to evaluate central registration procedure by the Gulf Cooperation Council (Al-Rubaie et al,, 2014). The evaluation of the Gulf Centralized Procedure indicated an increase in median approval time from 107 calendar days in 2006 to 265 days in 2010. The increase was due to

a limited number of meetings by the Gulf Cooperation Council-Drug Registration (GCC-DR), and a delay of assessment reports due to a lack of standard evaluation templates for product assessment, which lead to an increase in correspondence by GCC-DR to the sponsor requesting additional information. A similar study conducted by Andrea et al. (2018) for a regulatory review process in the South Africa indicated overall regulatory median approval time decreased by 14% in 2017 (1411 calendar days) compared to 2016, despite the 27% increase in the number of applications. The findings of South Africa regulatory process further indicated the regulatory agency had no target for overall approval time of new active substance applications, no target for key review milestones and an abridged assessment procedure was not implemented.

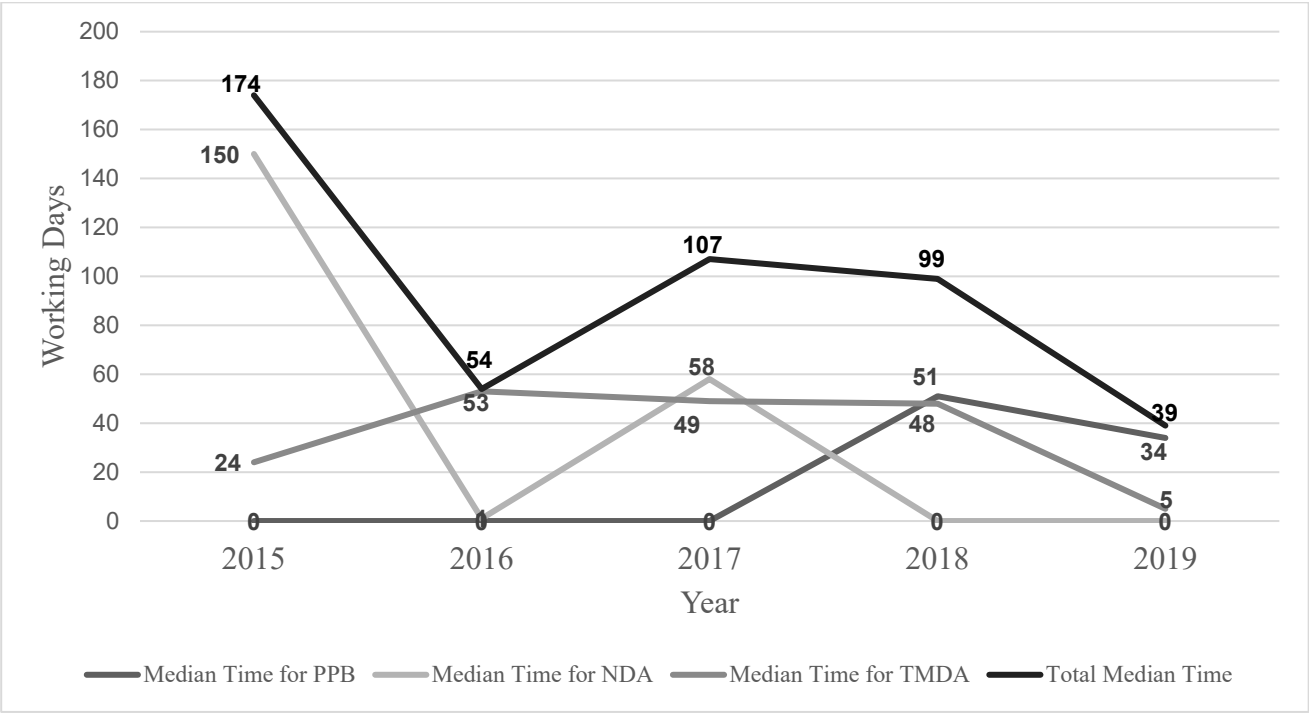
Among the seven NMRAs implementing the EAC-MRH program, only one (Tanzania Medicines and Medical Devices Agency) granted marketing authorisation to all 57 medicinal products recommended for registration at EAC level. Pharmacy and Poisons Board of the Republic of Kenya granted marketing authorisation to 35 medicinal products and National Drug Authority of Uganda granted marketing authorisation to 25 medicinal products, as indicated in Appendix 3. Rwanda Food and Drugs Authority (Rwanda-FDA) granted pre-registration to five antineoplastic drugs and one antiseptic solution. Among the antineoplastic drugs, four were approved at EAC level on 3rd October 2015 and one in September 2016. The antiseptic solution was recommended for registration at EAC level on 15th December 2017. In addition, two medicinal products were awaiting approval by Rwanda FDA which included an antihypertensive drug and a drug for management of overactive bladder. Both were recommended for approval on 7th December 2018.

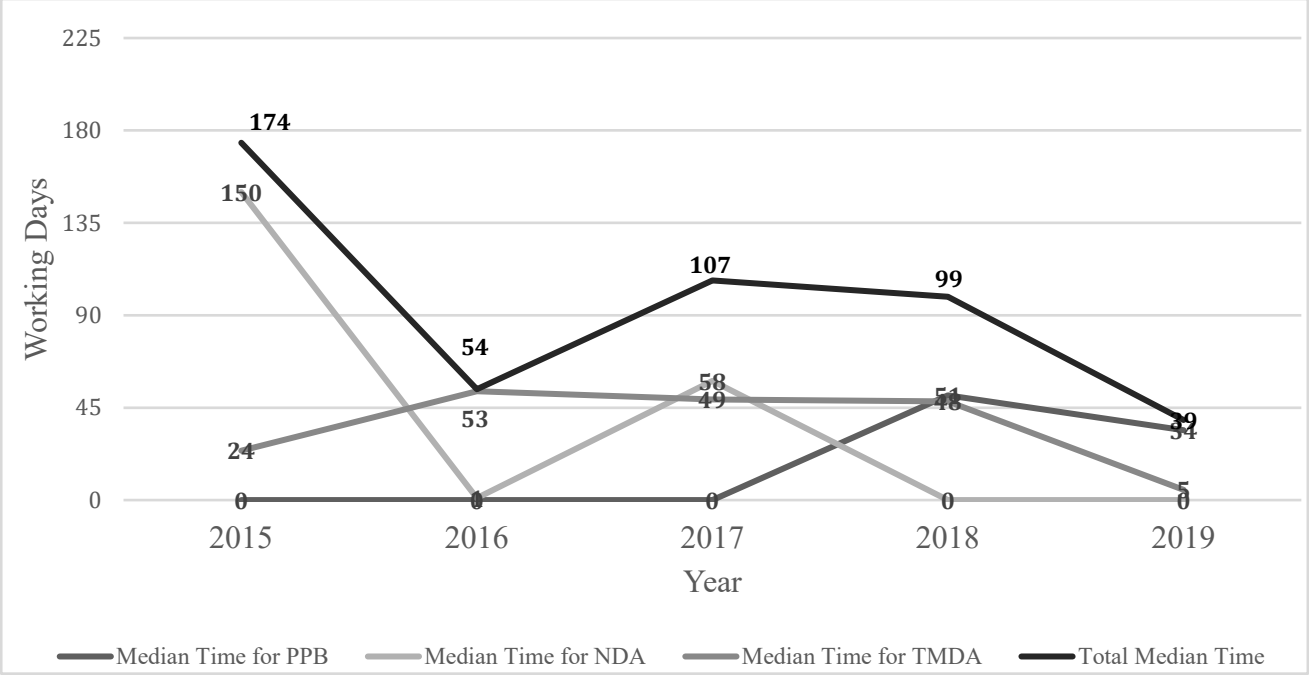
The Zanzibar Food and Drugs Agency (ZFDA) granted pre-registration to an antiretroviral drug which was recommended for approval in January 2018. The other NMRAs of the Republic of Burundi and Republic of South Sudan had not registered any medicinal products, as the applicants had not yet shown interest in placing their products in these countries' markets by paying applicable fees. Non-payment of fees by the applicants was also observed for other countries (i.e. Uganda, Kenya and Rwanda) as indicated in Appendix 3.

Once a regional recommendation was issued and communicated to the applicant, the manufacturer was required to pay the applicable fees for each of the respective EAC Partner States NMRA for their products to be placed in market. Each of the EAC Partner States have fee guidance and structure governed by that country's regulations and jurisdiction. Appendix 3 highlights the products in which the applicant had not yet paid fees for their products to be granted marketing authorisation (MA) by the remaining six NMRAs. Most of the products were granted MA by TMDA because it is the Lead NMRA for the program component of drug evaluation and registration. In this regard, TMDA received all applications for joint evaluation procedure and screened the dossier and distributes to assessors for evaluation. Since it was the primary point for the joint assessment procedure, most of the time, the applicant submitted the dossier as per EAC CTD and the applicable fee.

In order to encourage applicants to introduce their products in all EAC Partner States markets, the 19th EAC Sectoral Council of Minister of Health, held on 1st November 2019, recommended a two year window period for applicants to apply for marketing authorization from all EAC NMRA directive (*EAC/SCHealth/19/Directive/050)*. In this regard, the applicant had two years to pay the applicable fee in each NMRA for their products to be placed in the respective markets. In addition, the Council of Ministers of Health further introduced a priority voucher mechanism for applicants who made timely payment of fees to all Partner States NMRAs following positive outcome of EAC as per directive *EAC/SCHealth/19/Directive/053.* Once a marketing authorisation was granted by an individual NMRA, it was valid for five years, as per EAC guideline for registration of human medicinal products, and the applicant was able to apply for renewal once the validity expires using the same guidelines. However, the applicant needed to specify in the application form as "renewal" and not "new application."

Figure 7. ***Median Timelines for Granting Marketing Authorisation by NMRAs of Kenya, Uganda and United Republic of Tanzania***





The procedure recommended a period of 90 working days for each of the NMRA to grant marketing authorisation following a regional positive outcome and payment of application fees by the applicant. The median time for granting marketing authorisation for three NMRA was analysed using an Excel sheet and the findings indicated a decrease in total approval median time from 174 working days in 2015 to 39 working days in 2019. The median time for PPB ranged from 0-5 working days, NDA ranged from 150 -0 working days and TMDA ranged from 24- 5 working days (2015 to 2019). The reason for a long median timeline of approval for NDA was the delay for the applicant to pay the registration fee based on national requirements.

For the period of 2019, the median time for PPB was 34 working days, NDA was zero working days and TMDA was five working days. This showed

continuous improvements in the processes and high compliance to agreed timelines for granting marketing authorisation by NMRA.

EAC Joint GMP Inspection

Since commencement of EAC joint GMP inspections in July 2015, the region conducted (22) joint inspections of pharmaceutical manufacturing facilities in Uganda, Bangladesh, India, Palestine, Kenya, China, Germany, Italy, Belgium, Egypt, Morocco and Tanzania. Among these, only one joint inspection was triggered by a dossier application submitted for joint review. The other inspections were conducted based on the mapping of common backlog of applications in all seven NMRA and upon official request from the manufacturer.

Apart from steady progress in adhering to set timelines for the joint review processes, EAC region registered other key milestones in which some are part of initial project targets (Appendix 1) and others were part of program expansion phase. The key milestones included:

a) Harmonization oftechnical guidelines and procedures:
- EAC guideline for variations of registered vaccines and pharmaceutical products and similar biotherapeutic products;
- EAC procedure for Active Pharmaceutical Ingredient Drug Master File (APIDMF);
- EAC procedure for recognition of GMP decisions of other NMRA.

b) Regional institutions established and strengthened:
- Establishment of two semi-autonomous National Medicines Regulatory Authorities (NMRA) (i.e. Zanzibar Food and Drugs Agency [ZFDA] in 2017 and Rwanda Food and Drugs Authority [Rwanda FDA];
- Four EAC NMRA were ISO 9001: 2015 certified namely Tanzania Medicines and Medical Devices (TMDA), Zanzibar Food and Drugs Agency (ZFDA), Pharmacy and Poisons Board (PPB) and National Drug Authority (NDA);
- One EAC NMRA attained the World Health Organization (WHO) Maturity Level 3 (ML3) i.e. Tanzania Medicines and Medical Devices [TMDA].

c) Expansion of the program to include other regulatory functions such as Pharmacovigilance and Post Market Surveillance System Strengthening; and Clinical Trial Control Oversight with adoption of the African Vaccine Regulatory Forum (AVAREF) guidelines and tools for domestication in the EAC region.

4. CHALLENGES

Despite progress made by the initiative, there were some challenges identified by the study that should be addressed to ensure improvement in the system and optimize the processes to deliver the program goal and objectives. The challenges observed by this study are related to:

- Data Management: The study observed incomplete data in the register of medicinal products and the metric tool (registration). This indicated limited consistency in data entry to the metric tool when each step is initiated and finalized at both national and regional level. The metric tool was not automated, which hinders accessibility and timely entry of data by all NMRA and EAC Secretariat. Based on the current arrangement, the metric tool for registration was managed by TMDA and GMP metric tool was managed by NDA.
- Integrated Information Management System: Lack of regional integrated information management system (IMS) to support sharing of dossiers and assessment reports lead to a lag time.
- Capacity and Capabilities of EAC NMRA to Conduct Scientific Review of Medicinal Product Dossiers: limited capacity and capability of some NMRA to conduct timely scientific review of quality, safety and efficacy data contribute to delay in submission of assessment reports
- Quality of Dossiers Submitted by Applicants: Low quality of dossier submissions by applicants increase screening time due to rounds of correspondence between Lead NMRA and applicant.
- Submission of Queries by Applicants: Delay in response to queries by applicants contribute significantly to lengthy joint review process
- Scientific Advice to Applicants: The initiative did not provide scientific advice to applicants to improve the quality of dossier submission which ultimately will address lengthy screening process.

- Regional Fee for Joint Regulatory Activities and Central Mechanism for Collection of Fee: The region did not yet establish harmonized fee structure for joint regulatory activities. Lack of regional fee and mechanism for central collection of fee lead to administrative burden to the applicant and consequently limit the applicant to place their products in the market of all EAC NMRA.

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5. CONCLUSION

This study examined for the first time the joint regulatory process timelines for the EAC-MRH program. A clock-stop system was implemented, which provides data to measure performance of the system. However, the metric tools should be consistently updated to ensure data completeness. Automation of the metric tool is also key to ensure easy accessibility and timely data entry by NMRA and EAC Secretariat. Additionally, establishment of EAC integrated information management system would serve as a backup mechanism to track timelines of the joint regulatory process.

The findings (2015-2019) demonstrate substantial improvement in total median time for joint regulatory review process (53 to 102 working days) and marketing authorization by NMRAs (174 to 39 working days). This improvement indicates that the EAC-MRH initiative has potential to continue to improve regulatory efficiency in the region and subsequently improves patient access to new, innovative, safe, efficacious and quality medicines.

As EACregion moves towards implementation of joint regulatory review process for variations, biosimilars and Active Pharmaceutical Ingredient Drug Master File (APIDMF) system, it is crucial to establish strategic engagement and collaboration with pharmaceutical industry stakeholders. Additionally, there is a need to introduce a feedback and scientific advice mechanism for pharmaceutical industry stakeholders to improve future submissions.

Efforts should be made by the initiative to put a regional fee structure and central fee collection mechanism in place to reduce the administrative burden to the applicants and ensure sustainability of the EAC-MRH program.

5. RECOMMENDATIONS FOR NEXT STEPS

a) The EAC region should establish an integrated information management system (IMS) to facilitate timely sharing of dossiers and assessment reports.

b) The EAC needs to automate EAC metric tools to capture regulatory timelines and ensure consistency in data entry.

c) The EAC should establish strategic engagement and collaboration with industry stakeholders and feedback mechanism to address the quality of dossier to improve future submissions and decrease frequency of deficiency questions and, subsequently, shorten the time required for joint review.

d) Industry stakeholders are encouraged to take advantage of a two-year window period following a positive regional recommendation to place their products in all Partner States market by payment of applicable fees to all EAC NMRA. This will facilitate availability of high-quality medicines for the entire region.

e) EAC fee structure and a mechanism for central collection of fees should be explored to reduce administrative burden to applicants.

f) EAC should strengthen less resourced NMRA's capacity on regulatory sciences to ensure timely scientific review and submission of assessment reports.

g) Conduct further research studies to :

- evaluate regulatory timelines for joint GMP inspections;
- assess uptake of the initiative between domestic and multinational pharmaceutical manufacturers;

- compare system performance efficiency with other/similar international and continental initiatives.

6. REFERENCES

(BCG), B. C. G. (2017). *End Term Evaluation Report of EAC Medicines Regulatory Harmonization Program*. Retrieved from EAC SECRETARIAT, Arusha, Tanzania:

Ahonkhai, V., Martins, S. F., Portet, A., Lumpkin, M., & Hartman, D. (2016). Speeding Access to Vaccines and Medicines in Low- and Middle-Income Countries: A Case for Change and a Framework for Optimized Product Market Authorization. *PloS one., 11*(11), e0166515. doi:10.1371/journal.pone.0166515

Al-Rubaie, M. H., Walker, S. R., & Salek, S. S. (2014). Evaluation of the Gulf Cooperation Council Centralized Procedure: The Way Forward. *Therapeutic Innovation & Regulatory Science, 48*(6), 709-716. doi:10.1177/2168479014529572

Andrea, K., Joey, G., Sam, S., & Stuart, W. (2018). The Regulatory Review Process in South Africa: Challenges and Opportunities for a New Improved System. *Therapeutic Innovation & Regulatory Science, 52*(4), 449-458.

Dansie, L. S., Odoch, W. D., & Årdal, C. (2019). Industrial perceptions of medicines regulatory harmonization in the East African Community. *PLoS One, 14*(6), e0218617. doi:10.1371/journal.pone.0218617

EAC. (2000). *The Treaty for the Establishment of the East African Community*. Arusha, Tanzania

EAC. (2018). Compendium of Good Manufacturing Practices (GMP) Technical Documents For Harmonization of Medicines Regulation In East African Community (EAC/TF-MED/GMP/FD/COM/N2R1). In E. F. GMP (Ed.), (pp. 356). Arusha, Tanzania.

EAC. (2019a). Compendium of Guidleines for Medicines Evaluation and Registration for Medicines Regulatory Harmonization in East African Community (EAC/TF-MED/MER/FD/COM/N1R1). In EAC (Ed.), *2nd Edition* (Vol. 2, pp. 187). Arusha, Tanzania: EAC Secretariat.

EAC. (2019b). EAC Compendium of Harmonized Guidelines for Safety and Vigilance of Medical Products and Health Technologies. In E. Secretariat (Ed.), (First Edition ed., Vol. 1, pp. 173). 2019: EAC Secretariat.

EAC, S. (2010). *Project Document: East African Community Medicines Regulatory Harmonization Programme*. ARUSHA, TANZANIA

EWG, E., & Registration, M. E. a. (March 2020). 4th Expression of Interest for Submission of Application for Marketing Authorization of Medicinal Products [Press release]

Hiiti, S., Aggrey, A., Samvel, A., Chimwemwe, C., Joseph, K., Murray, L., . . . David, M. (2020). *Coming Together to Improve Access to Medicines: The Genesis of the East African Community's Medicines Regulatory Harmonization Initiative*. (2).

Jane, M., Vincent, A., Noel, A., Aggrey, A., Samvel, A., & Dan, H. (2020). *Eight Years of the East African Medicines Regulatory Harmonization Initiative:Implementation, Progress and Lessons Learned*. (3).

Margareth, S., Gugu, M., Margaret, A., & Emer, C. (2020). *A New Approach to an Old Problem: Overview of the East African Community Medicines Regulatory Harmonization Initiative*. (1).

Ndomondo-Sigonda, M., & Ambali, A. (2011). The African medicines regulatory harmonization initiative: rationale and benefits. *Clin Pharmacol Ther, 89*(2), 176-178. doi:10.1038/clpt.2010.299

Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Dodoo, A., & Kaale, E. (2017). Medicines Regulation in Africa: Current State and Opportunities. *Pharmaceut Med, 31*(6), 383-397. doi:10.1007/s40290-017-0210-x

Pierre, L. L. (2014). *International Cooperation, Convergence and Harmonization of Pharmaceutical Regulations*: Elservier Inc.

RTO's, & Secretariat, E. (2018a). *Metric Tool to Track Timelines for EAC Joint Assessment and Registration Procedure*.

RTO's, & Secretariat, E. (2018b). *Metric Tool to Track Timelines for EAC Joint GMP Inspections*.

TMDA. (2015). *Register of Medicinal Products Submitted for EAC Joint Assessment and Registration Procedure*. Tanzania: EAC

Wondiyfraw, W., John, G., Matthias, S., & Lembit, R. (2012). Deficiencies in Generic Product Dossiers as Submitted to the WHO Prequalification of Medicines Programme. *Journal of Generic Medicines, 9*(2), 63-74.

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Appendix 1

Table 1

EAC-MRH Programme Critical Milestones and Indicators of Success

Objective	Critical Milestones	Indicators of Success
1	EAC CTD implemented in at least 3 Partner States by end of year 3 and in all EAC Partner States by end of year 5	Eighteen (18) Medicines approved under joint assessment scheme by end of year 5
2	A common integrated IMS established and linked in all Partner States and EAC Secretariat by end of year 4	NMRAs and 1 regional websites regularly updated Centralized Portal to share information and work established
3	Quality management system implemented in each of the EAC Partner States NMRAs by end of year 3	Three (3) NMRAs ISO certified by the end of year 3
4	Institutional, human and infrastructural capacity built by end of year 5 Regulatory capacity building programs institutionalized into existing structures in Partner States NMRAs by the end of year 5 Regional capacity to coordinate the medicines registration harmonization strengthened by the end of year 5	Two (2) regional centre's of excellence in training assessors and GMP inspectors established in the EAC region by the end of year 5 25 NMRAs and EAC Secretariat staff trained on project management 24 assessors trained in assessment of quality, safety and efficacy of medicines by the end of year 5 24 inspectors trained on GMP inspection by end of year 5
5	Government commitment to EAC-RH Programme secured by end of year 5 Industry-buy in and commitment to EAC-MRH program secured by the end of year 5 Public awareness on EAC-RH created by end of year 5	Rwanda and Burundi semi-autonomous NMRAs established by end of year 5 100 applications submitted to NMRAs as per EAC CTD Partner States commitment to fund EAC-MRH programme
6	A framework for mutual recognition of regulatory decisions made by other EAC Partner States NMRAs developed and implemented by end of year 5	Seven (7) NMRAs recognizing regulatory decisions made by other NMRAs based on mutual recognition framework by end of year 5

Appendix 2:

Table 2

Summary of Product Registration Timelines (Submission to End of Assessment) for Regulator and Applicant

Product Number	Year	Product Category	Type of Assessment	Regulator Timelines	Applicant Timelines
001	2015	Antineoplastic	Abridged	53	0
002	2015	Antineoplastic	Abridged	53	0
003	2015	Antineoplastic	Abridged	53	0
004	2015	Antineoplastic	Abridged	53	0
005	2015	Antihypertensive	Full	125	927
006	2015	Antihypertensive	Full	125	927
007	2015	Antihypertensive	Full	125	927
008	2016	Antineoplastic	-	96	30
009	2016	Antineoplastic	-	-	-
010	2016	Antidiabetic	Full	327	419
011	2016	Antidiabetic	Full	327	419
012	2016	Antihypertensive	Full	327	419
013	2016	Antihypertensive	Full	327	419
014	2016	Antituberculosis	Abridged	141	27
015	2016	Antihypertensive	-	289	141
016	2016	Antihypertensive	-	289	141
017	2016	Antihypertensive	-	289	141
018	2016	Antineoplastic	-	391	294
019	2016	-	-	-	-

020	2016	-	-	-	-
021	2016	Antihypertensive	-	266	380
022	2016	Antihypertensive	-	266	380
023	2016	Antineoplastic	-	153	42
024	2016	Antipyretic	-	267	194
025	2016	Antiseptic	-	343	180
026	2016	Antibiotic	-	104	65
027	2017	Antifungal	-	169	119
028	2017	Antifungal	-	169	119
029	2017	Mineral Supplements	-	381	43
030	2017	Antiseptic	-	180	412
031	2017	Antineoplastic	-	207	95
032	2017	Antineoplastic	-	135	0
033	2017	Antineoplastic	-	135	0
034	2017	Antiretrovirals	-	101	254
035	2017	Antiallergics	-	122	88
036	2018	Antineoplastic	Abridged	73	9
037	2018	Overactive Bladder	-	174	47
038	2018	Overactive Bladder	-	174	47
039	2018	Antibiotic	Abridged	87	74
040	2018	Antiretroviral	Full	166	35
041	2019	Antineoplastic	Full	63	0
042	2019	Antineoplastic	Full	63	0
043	2019	Antineoplastic/Biological	Full	85	0
044	2019	Antineoplastic/Biological	Full	85	0

045	2019	Monoclonal Antibodies	Abridged	222	0
046	2019	Monoclonal Antibodies	Abridged	222	0
047	2019	Monoclonal Antibodies	Abridged	222	0
048	2019	Monoclonal Antibodies	Abridged	222	0
049	2019	Gynaecological Anti-infective	Abridged	229	0
050	2019	Antivertigo	Full	44	0
051	2019	Antineoplastic	Abridged	85	0
052	2019	Emergence Allergic Reaction	Full	-	-
053	2019	Nerve Agent & Insecticide Poisoning	Full	-	-
054	2019	Treatment of Asthma	Full	-	-
055	2019	Treatment of Male Impotence	Full	102	51
056	2019	Treatment of Male Impotence	Full	102	51
057	2019	Treatment of Male Impotence	Full	102	51

Appendix 3

Table 3

Registration Timelines at National Level (Marketing Authorisation) for Each EAC National Medicines Regulatory Authorities

Product Number	Year	Marketing Authorisation Timelines (Working Days)						
		PPB	NDA	TMDA	Rwanda FDA	DPLM	ZFDA	DFCA
001	2015	0	150	0	PR	NS	NS	NS
002	2015	0	150	30	PR	NS	NS	NS
003	2015	0	150	0	PR	NS	NS	NS
004	2015	0	150	30	PR	NS	NS	NS
005	2015	NS	43	24	NS	NS	NS	NS
006	2015	NS	43	24	NS	NS	NS	NS
007	2015	NS	43	24	NS	NS	NS	NS
008	2016	0	594	307	PR	NS	NS	NS
009	2016	0	47	1	NS	NS	NS	NS
010	2016	0	1	53	NS	NS	NS	NS
011	2016	0	1	53	NS	NS	NS	NS
012	2016	0	NS	53	NS	NS	NS	NS
013	2016	0	NS	53	NS	NS	NS	NS
014	2016	ND	NS	272	PR	NS	NS	NS
015	2016	0	NS	53	NS	NS	NS	NS
016	2016	0	NS	53	WA	NS	NS	NS
017	2016	0	0	53	NS	NS	NS	NS
018	2016	ND	0	53	NS	NS	NS	NS
019	2016	0	NS	25	NS	NS	NS	NS
020	2016	0	NS	25	NS	NS	NS	NS

021	2016	0	0	53	NS	NS	NS	NS
022	2016	0	0	53	NS	NS	NS	NS
023	2016	ND	340	108	NS	NS	NS	NS
024	2016	0	0	0	NS	NS	NS	NS
025	2016	0	NS	40	NS	NS	NS	NS
026	2016	0	498	83	NS	NS	NS	NS
027	2017	0	NS	49	NS	NS	NS	NS
028	2017	0	NS	49	NS	NS	NS	NS
029	2017	0	NS	40	NS	NS	NS	NS
030	2017	ND	NS	33	NS	NS	NS	NS
031	2017	0	0	48	PR	NS	NS	NS
032	2017	0	116	49	NS	NS	NS	NS
033	2017	0	116	49	NS	NS	NS	NS
034	2017	ND	0	27	NS	NS	NS	NS
035	2017	ND	NS	70	NS	NS	PR	NS
036	2018	51	NS	48	NS	NS	NS	NS
037	2018	51	NS	48	NS	NS	NS	NS
038	2018	ND	0*	1	WA	NS	NS	NS
039	2018	128	NS	27	NS	NS	NS	NS
040	2018	ND	NS	79	NS	NS	NS	NS
041	2019	ND	NS	155	NS	NS	NS	NS
042	2019	ND	NS	5	NS	NS	NS	NS
043	2019	ND	NS	5	NS	NS	NS	NS
044	2019	0	NS	79	NS	NS	NS	NS
045	2019	NS	NS	5	NS	NS	NS	NS
046	2019	NS	NS	5	NS	NS	NS	NS
047	2019	34	NS	0*	NS	NS	NS	NS

048	2019	34	NS	0*	NS	NS	NS	NS
049	2019	34	0	0*	NS	NS	NS	NS
050	2019	34	0	0*	NS	NS	NS	NS
051	2019	ND	NS	40	NS	NS	NS	NS
052	2019	ND	NS	40	NS	NS	NS	NS
053	2019	ND	NS	40	NS	NS	NS	NS
054	2019	ND	NS	40	NS	NS	NS	NS
055	2019	ND	NS	5	NS	NS	NS	NS
056	2019	ND	NS	5	NS	NS	NS	NS
057	2019	0	WA	5	NS	NS	NS	NS

Key to Appendix 3

PPB- Pharmacy and Poisons Board, Republic of Kenya

NDA- National Drug Authority, Republic of Uganda

TMDA- Tanzania Medicines and Medical Devices Authority, United Republic of Tanzania

Rwanda FDA- Rwanda Food and Drugs Authority, Republic of Rwanda

DPML- Department of Pharmaceuticals and Medical Laboratories, Republic of Burundi

ZFDA- Zanzibar Food and Drugs Agency, United Republic of Tanzania

DFCA – Drug and Food Control Authority, Republic of South Sudan

PR- Pre-registration pending fee payment by applicant

NS- Application for marketing authorisation not submitted by applicant

ND- No Data

WA – Submitted waiting NMRA approval

Zero (0) Days- Product already registered in country before EAC joint assessment

0* Days - Product registered between 5 to 30 days before regional recommendation