



Regulatory performance of the East African Community joint assessment procedure: The way forward for regulatory systems strengthening

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ABSTRACT

Background: Seven national medicines regulatory authorities in the East African Community (EAC) have embraced regulatory reliance, harmonization and work sharing through the EAC Medicines Regulatory Harmonization programme. Measuring the performance of regulatory systems provides key baseline information to build on regulatory system-strengthening strategies. Therefore, the aim of the study was to evaluate the regulatory performance of the EAC joint scientific assessment of applications approved between 2018 and 2021. **Methods:** Utilising a data metrics tool, information was collected reflecting timelines for various milestones including submission to screening, scientific assessment and communication of regional recommendations for biologicals and pharmaceuticals that received a positive regional recommendation for product registration from 2018 to 2021.

Results: Several challenges as well as possible solutions were identified, including median overall approval times exceeding the EAC 465-day target and median times to issue marketing authorisation following EAC joint assessment recommendation that far exceeded the 116-day target. Recommendations included establishment of an integrated information management system and automation of the capture of regulatory timelines through the EAC metric tool.

Conclusions: Despite initiative progress, work is required to improve the EAC joint regulatory procedure to achieve regulatory systems-strengthening and ensure patients' timely access to safe, efficacious and quality medicines.

1. Background

The three pillars of medicines regulation are quality, safety, and efficacy. To ensure that medicines and other health products meet these criteria, seven national medicines regulatory authorities (NMRAs) in the East African Community (EAC) region collaborate to jointly assess the safety, efficacy, and quality of medicines, in addition to inspection and surveillance along the entire supply chain. The EAC has embraced regulatory reliance, harmonization, and work sharing for medical products

since 2012, through the EAC Medicines Regulatory Harmonization (EAC-MRH) programme (Sillo et al., 2020). It is the first regional economic community (REC) to implement the African Medicines Regulatory Harmonization (AMRH) programme, which was initiated in 2009 and which is a model to be adopted by other RECs. The EAC-MRH initiative is in line with the EAC Treaty, Chapter 21, Article 118 (East African Community, 2000), in which partner states are committed to cooperate in the harmonization of medicines registration. The initiative has contributed to time and cost savings for both regulatory authorities

Abbreviations: AMRH, African Medicines Regulatory Harmonization; EAC, East African Community; EAC-MRH, EAC Medicines Regulatory Harmonization; GMP, good manufacturing practice; MA, marketing authorisation; Uganda NDA, Uganda National Drug Authority; NMRA, national medical regulatory authority; REC, regional economic community; TMDA, Tanzania Medicines and Medical Devices Authority; WHO-PQ, World Health Organization Pre-Qualification.

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and the pharmaceutical industry, reducing the duplication of efforts and capacity building of less-resourced NMRAs (Ndomondo-Sigonnda et al., 2017; Ngum et al., 2022). However, there is currently a lack of information regarding the efficiency of the review process, especially on the length of registration times for the joint scientific review process and the issuance of marketing authorisation (MA) by participating NMRAs once a regional positive outcome is reached (Dansie et al., 2019; Mashingia et al., 2020).

Therefore, the aim of this study was to evaluate the target timelines between the key milestones and the performance metrics for applications for the EAC joint scientific assessment that were approved between 2018 and 2021.

1.1. EAC joint assessment procedure

The EAC region developed and customised a common technical document, requirements, standards, and guidelines for the assessment of the quality, safety, and efficacy of medicines, vaccines, bioterapeutics and biosimilars (East African Community, 2019) to guide the joint scientific review process and joint inspections of pharmaceutical manufacturing facilities. Other guidelines, such as requirements for the regulation of medical devices, in-vitro diagnostics (East African Community, 2021) and pharmacovigilance can be accessed through www.eac.int/mrh. The joint scientific review of medicinal product dossiers and good manufacturing practices (GMP) inspections, which commenced in July 2015, have built trust and confidence between EAC NMRAs and paved the way for the recognition of each authority's decisions (East

African Community, 2018a).

There are two regulatory pathways that have been implemented by the EAC for the joint scientific review of a medicinal products. The full assessment procedure involves a full review of the medicinal product dossier, including scientific data for quality, safety, and efficacy by the first and second assessors, sequentially. The abridged procedure involves the benefit-risk assessment of products that have been approved by World Health Organization (WHO)-listed regulatory authorities or the WHO prequalification programme (WHO PQ) (East African Community, 2018b).

Fig. 1 summarises the steps and timelines for the EAC joint assessment procedure. Step 1 commences with the submission of the application to the lead NMRA, the Tanzania Medicines and Medical Devices Authority (TMDA). In step 2, the lead authority screens the application to check for completeness, including GMP status (Day 10). For step 3, the TMDA schedules the initial review, which also includes the GMP inspection led by the Uganda National Drug Authority (NDA; Day 45) and the GMP inspection under certain circumstances could take a further 180 days to be completed. In step 4 (day 65), an initial review is completed by two NMRAs and by day 90, a joint assessment session is held (step 5), with all representatives from the seven NMRAs. At this stage, when appropriate, a list of questions or queries are sent for an applicant response. A maximum of three rounds of reviews is implemented, with each expected to last about 180 days. In step 6, documents are compiled and recommendations from the joint assessment are sent to the EAC Secretariat (Day 270). By day 300 (step 7), the final recommendation is issued, and a confirmation letter sent to the applicant. In

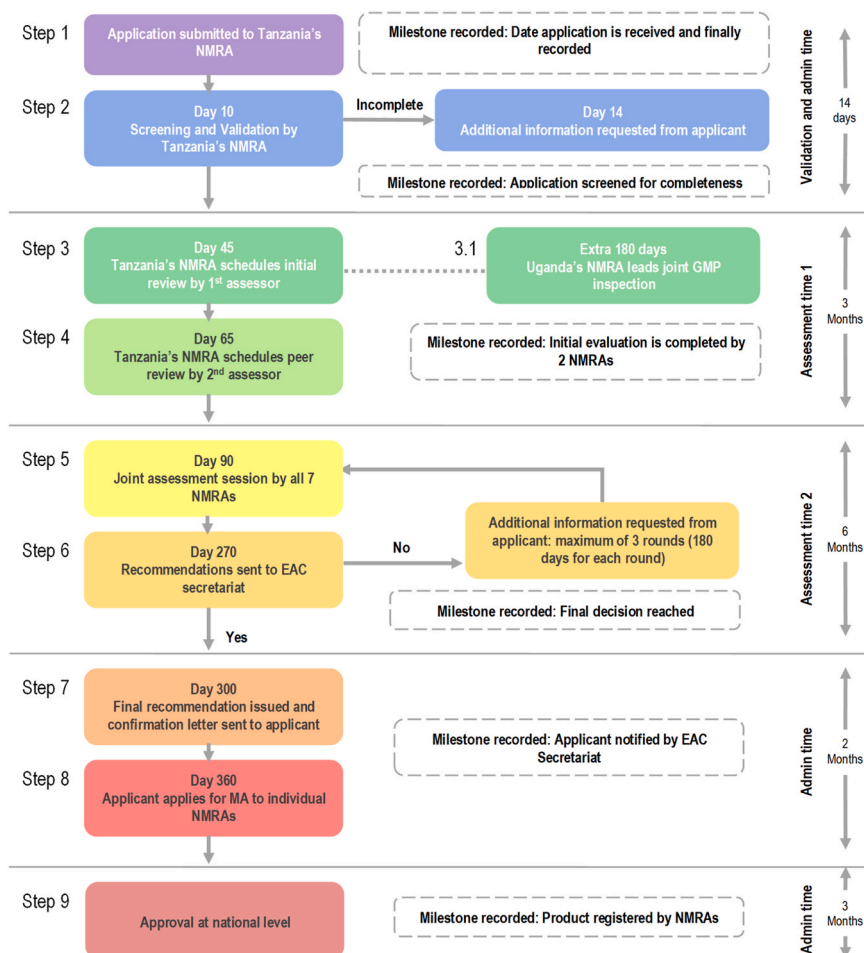


Fig. 1. Process map of the EAC joint assessment procedure. Reprinted from Ngum et al. (2022).

step 8 (day 360), the applicant is expected to apply for marketing authorisation to individual NMRAs, with subsequent approvals at national levels (step 9), which should take place within 90 working days.

1.2. Study objectives

The objectives of this study were to.

1. Evaluate the current review process of the EAC joint assessment procedure
2. Identify the key milestones and target timelines achieved in the review process
3. Evaluate the overall performance of the review models and different product types approved in the EAC joint assessment procedure
4. Identify the challenges as well as the opportunities for an enhanced EAC joint assessment procedure, with a view to expediting patients access to life-saving medicines
5. Determine the future direction of the EAC joint assessment for supporting the newly established African Medicines Agency

2. Methods

2.1. Data collection process

Data were collected reflecting the timelines between the various milestones for biologicals and pharmaceuticals that received positive regional recommendations during the period 2018–2021 such as submission to screening, scientific assessment, communication of regional recommendation to applicant, communication of recommendation to NMRA, and product registration by NMRAs.

These data were obtained using an EAC metric tool, which records timelines for each step of the joint scientific evaluation process, from submission of application to the national administrative procedure for granting marketing authorisation.

2.2. Data analysis

Data collected for applications that received positive regional recommendations between 2018 and 2021 were analysed and the category of medicinal products submitted for the EAC joint scientific review were described. The review type applied to each application, whether full or abridged assessment, was also identified. Timelines for each milestone for the regulator and applicant during the entire review process were analysed. Median times between milestones within the review process, as well as median overall approval times, were calculated. The intervals between milestones in the review process were defined as follows.

- *Start-up time*: date of submission of dossier, screening for date of distribution of dossier for first assessment
- *Scientific assessment time*: date of distribution of dossier for first assessment, time for second assessment, regional technical committee meetings, query responses by applicants to final recommendations reached
- *Communication of recommendation to applicant*: date when final regional recommendation was reached to final recommendation communicated to applicant by the EAC Secretariat
- *NMRA registration time*: date of communication of final recommendation to NMRA by the EAC Secretariat to date of an MA certificate issued by the EAC NMRA

Ethics approval

The study was approved by the Health, Science, Engineering and Technology ECDA, University of Hertfordshire, United Kingdom [Reference Protocol number: LMS/PGR/UH/04988]. All the national medicine regulatory authorities in East Africa approached to take part in

the study were satisfied with ethics approval obtained from the United Kingdom and did not require us to apply for any IRBs in East Africa.

3. Results

3.1. Characteristics of the study participants

The attributes of the seven NMRAs participating in the EAC joint assessment are described in Table 1. These authorities are characterised by different levels of regulatory maturity and the populations they serve range in size from the smallest, which is Zanzibar, to the largest, which is Tanzania. As a result, there is a wide range in the number of reviewers: from 3 in Burundi to 55 in Tanzania, with the most resourced authorities carrying out the majority of the regulatory reviews. This is further illustrated by the total number of applications that each NMRAs receive in addition to the joint assessments.

3.2. Overall approval times for biologicals and pharmaceuticals

Between 2018 and 2021, 69 medicinal products were recommended for MA by EAC NMRAs following joint scientific evaluation of their safety, efficacy and quality. The medicinal products were in the therapeutic categories of antineoplastic/biologicals, monoclonal antibodies, antidiabetics, antimicrobials, antihypertensives, anti-retroviral, antifungals and drugs for the treatment of asthma and male impotence. Twenty-five applications were reviewed using the abridged procedure and 41 were reviewed using the full assessment procedure. The overall median approval times (Fig. 2a) were 933 calendar days (2018), 311 calendar days (2019), 274 calendar days (2020) and 606 calendar days (2021).

3.3. Overall approval times for assessment and product types

The overall median approval time for the full assessment procedure in calendar days (Fig. 2b) was 568 (2018), 823 (2019), 244 (2020), and 638 (2021). Delays in the provision of query responses by applicants for products which were submitted for joint scientific review in October 2015 and August 2017 contributed to the long approval times for full assessment in 2018, 2019, and 2021. In addition, there were delays in distribution of dossiers by the lead NMRA to assessors to conduct the scientific review process. Most of the pharmaceutical product's applications were generics which underwent full assessment and the applicant was required to provide data for therapeutic equivalence with the innovator/comparator product. The applicants' failure to provide timely data on therapeutic equivalence of the generic product contributed to the long median time for pharmaceuticals in the year 2018, 2019 and 2021 with total approval median times of 947, 823 and 565 calendar days respectively (Fig. 2b).

The overall median approval time for the abridged procedure in calendar days (Fig. 2b) was 975 (2018), 311 (2019), 294 (2020), and 402 (2021). The long median time for abridged procedures in 2018 was due to delays in submission of query responses by applicants. For the period of 2019–2021, the use of reliance contributed to the short median time for abridged assessments, since monoclonal antibodies and other biologicals had already been registered by WHO-listed regulatory authorities. Reliance and convergence for biological applications led to short median approval time of 190, 216, and 57 calendar days for 2018, 2019, and 2020, respectively (Fig. 2b). The long median time (700 calendar days) for biologicals in 2021 was due to the long screening times, which took 162 calendar days, while the scientific assessment took 52 calendar days and communication of the outcome of assessment to applicants took 44 calendar days. The screening of dossiers took longer than expected due to the limited capacity of reviewing staff, as well as competing priorities at TMDA.

Table 1
Characteristics of the participating national regulatory authorities.

	Burundi	Kenya	South Sudan	Uganda	Rwanda	Tanzania (2020)	Zanzibar
Population	12,255,429	54,985,702	11,381,377	45,741,000	13,276,517	58,552,845	1,717,608
Authority staff	32	170	42	292	188	103	150
Number of reviewers	3	28	4	30	15	55	12
Total applications received in a particular year- 2021	68	909	0	849	615	858 (2019)	10
Fees new active substance	0	\$1000	NA	\$2,000	\$1250	\$2000	NA
Fees generic	0	\$1000	NA	\$2,000	\$1250	\$2000	\$1000

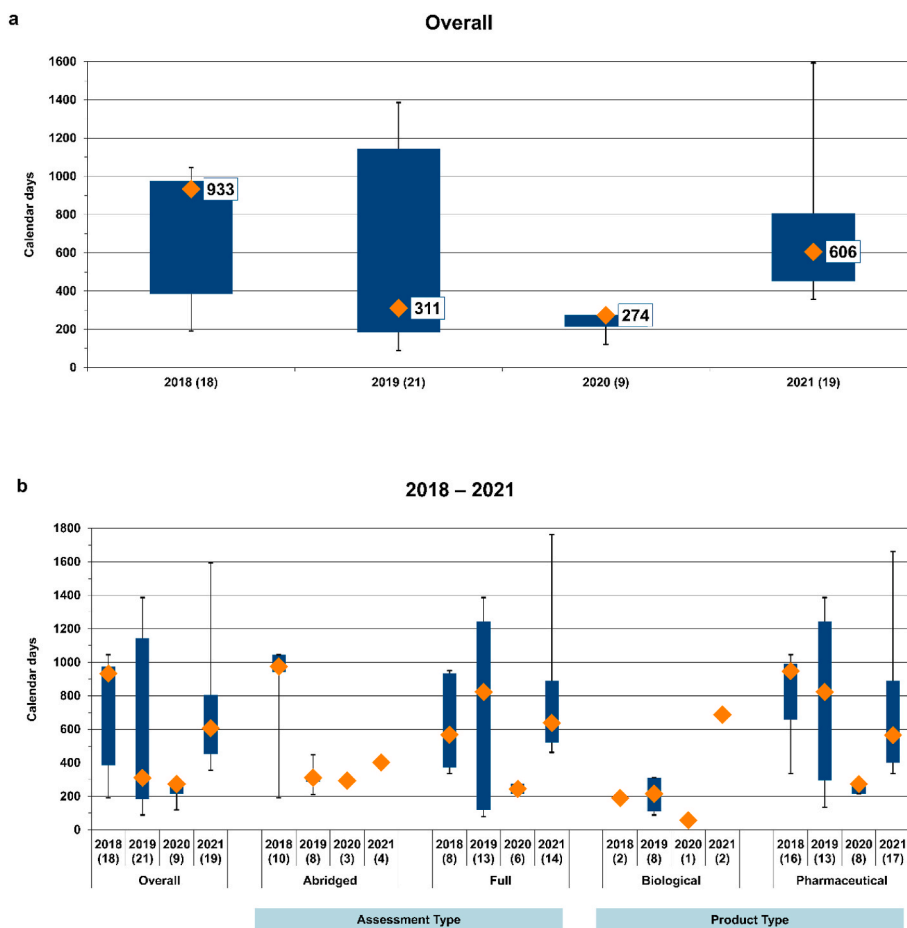


Fig. 2. a) Trend in approval times for pharmaceuticals and biologicals (2018–2021); b) trend in approval times, by assessment type and product type (2018–2021). Data are shown for applications that were approved ("Final recommendation reached on") between 01/01/2018 and 31/12/2021. (n) = number of drug applications. ◊ = Median. Where (n) is less than 5, only the median is displayed.

3.4. Overall metrics for various milestones

The timelines for key milestones were analysed for the individual years between 2018 and 2021 for applications that had complete data (Fig. 3a). The timelines for start-up, scientific assessment, and communication of recommendation to applicants were calculated and analysed for all product types (biologicals and pharmaceuticals), irrespective of the assessment type.

The overall start-up time for applications submitted for joint scientific review was 56.69, 53, and 78 calendar days for the years 2018, 2019, 2020, and 2021, respectively. For each year between 2018 and 2021, The EAC start-up (date of submission of dossier to date of distribution for first assessment) exceeded the target time of 20 calendar days and this gap could be addressed in the screening process (Fig. 3a).

The scientific assessment time, which covers cycles of evaluation, query responses by applicants (first assessment, second assessment, the EAC technical committee to review assessment report, query responses

by applicant, first and second assessment of query responses by regulators, and final recommendations) was measured. The scientific assessment time over the four-year period was generally below or aligned to the target, with the exception of 2018, when the longest scientific assessment time (891 calendar days) was observed. The long scientific assessment time for this year was due to delays in applicants responding to queries for the full assessment procedure. Communication to applicant on the final regional outcome of the joint scientific assessment is normally conducted by the EAC Secretariat using an official notification letter. The guideline requires the notification letter to be sent to the applicant no more than 30 calendar days after the final outcome of scientific assessment. For 2020 in particular, the results showed a long median time of 140 calendar days for communication of approval to the applicant (Fig. 3a), which was primarily the result of long bureaucratic processes for approving official letters by the EAC Secretariat.

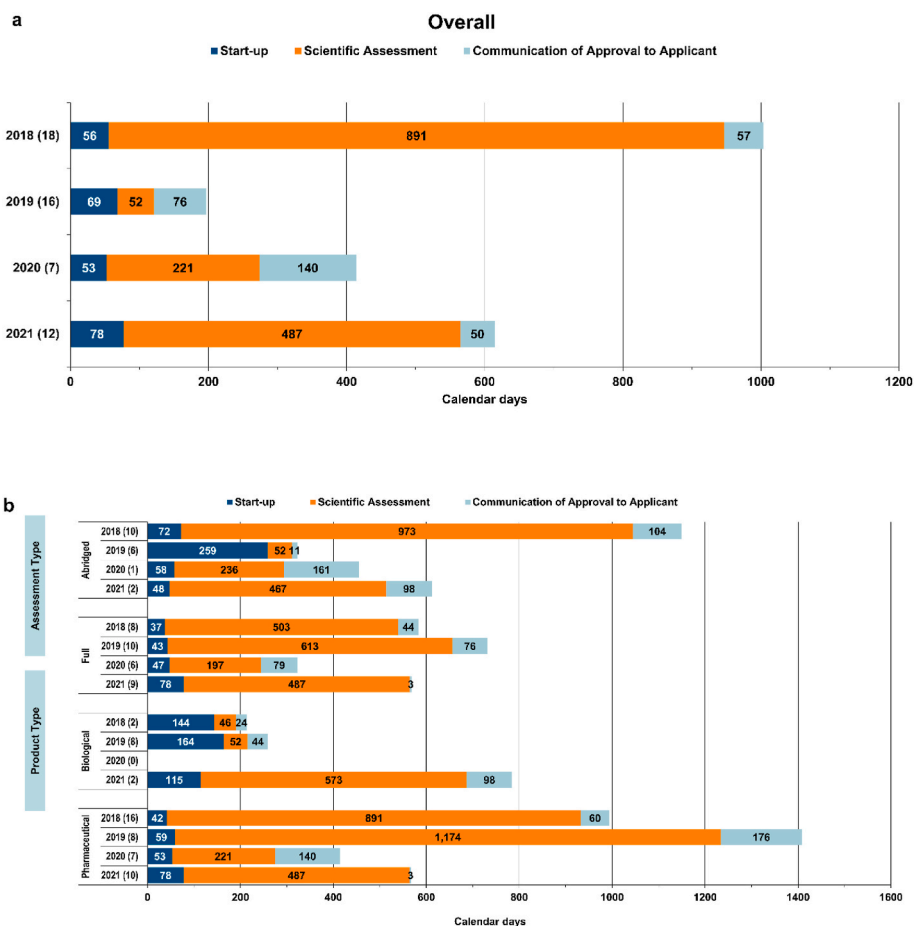


Fig. 3. a) trend in median times for start-up, scientific assessment, and communication of recommendation to applicant (2018–2021); b) trend in median times for start-up, scientific assessment, and communication of recommendation to applicant, by assessment type and product type.

3.5. Metrics for various milestones by assessment and product types

The median time for start-up for each type of assessment procedure (abridged and full) and each product type (biological and pharmaceutical) during the study period (2018–2021) exceeded the EAC target of 20 calendar days (Fig. 3b). In 2019, the start-up time for abridged assessment was notably long (259 calendar days). Median start-up times for biologicals for the years 2018, 2019, and 2021 were also notably long (144, 164 and 115 calendar days, respectively). The main reason was the long screening times at the lead NMRA for registration before a dossier was assigned to assessors related to the validation phase of biologicals. The long scientific assessment timelines for the full assessment procedure in 2019 (613 calendar days) is seen in Fig. 3b. The median time for full scientific assessment in 2018 (503 calendar days) was slightly above the target of 465 calendar days. The primary reason for the long median time for full scientific assessment was delays in responding to queries by the applicants. These delays were also the main reason for long median time for the abridged scientific assessment procedure in 2018 (973 calendar days).

The median time for the abridged scientific assessment procedure for biologicals in 2021 was 573 calendar days. This was greater than expected given that the abridged procedure is based on reliance of regulatory decisions from WHO-listed regulatory authorities. Again, the main reason for the long median time for abridged scientific assessment of biologicals was the delay in responding to queries by the applicants. Particularly long scientific assessment times for pharmaceuticals were observed in 2018 (891 calendar days) and 2019 (1,174 calendar days). Similar to those for abridged reviews, the main reasons were delays in responding to queries by applicants as well as the delays in conducting

the scientific evaluation and submission of assessment reports by assessors to guide the regional recommendation and outcome. The median time for the communication of approval to the applicant following the scientific assessment generally exceeded the EAC target of 30 calendar days (Fig. 3b). Exceptions include the abridged procedure in 2019 (11 calendar days), biologicals in 2018 (24 calendar days), and both the full procedure and pharmaceuticals in 2021 (3 calendar days). In each case, the main reason was the long bureaucratic process for the review and approval of the official notification letters to applicants.

3.6. Timelines for regulatory scientific assessment and applicant response

A comparison of median times for the regulator and applicant components of the period between “date of distribution of dossier for first assessment” and “final recommendation reached” is shown in Fig. 4a. The shortest median times for the period covering regulator scientific assessment and applicant response were observed for 2019 and 2020 (52 and 221 calendar days, respectively). For the year 2018, the median applicant response time (176 calendar days) was shorter than the median scientific assessment time of the regulator (327 calendar days), and again for 2021 (90 compared with 316 calendar days, respectively). Long median times for regulators’ scientific assessment were in part due to the requirement for physical inspection of the manufacturing facilities and delays in conducting scientific evaluation by assessors from less-resourced NMRAs.

Data are shown for applications that were approved (“Final recommendation reached on”) between 01/01/2018 and 31/12/2021. (n) = number of drug applications. Data limited to applications where all the following milestones are available and in chronological order: “Date of

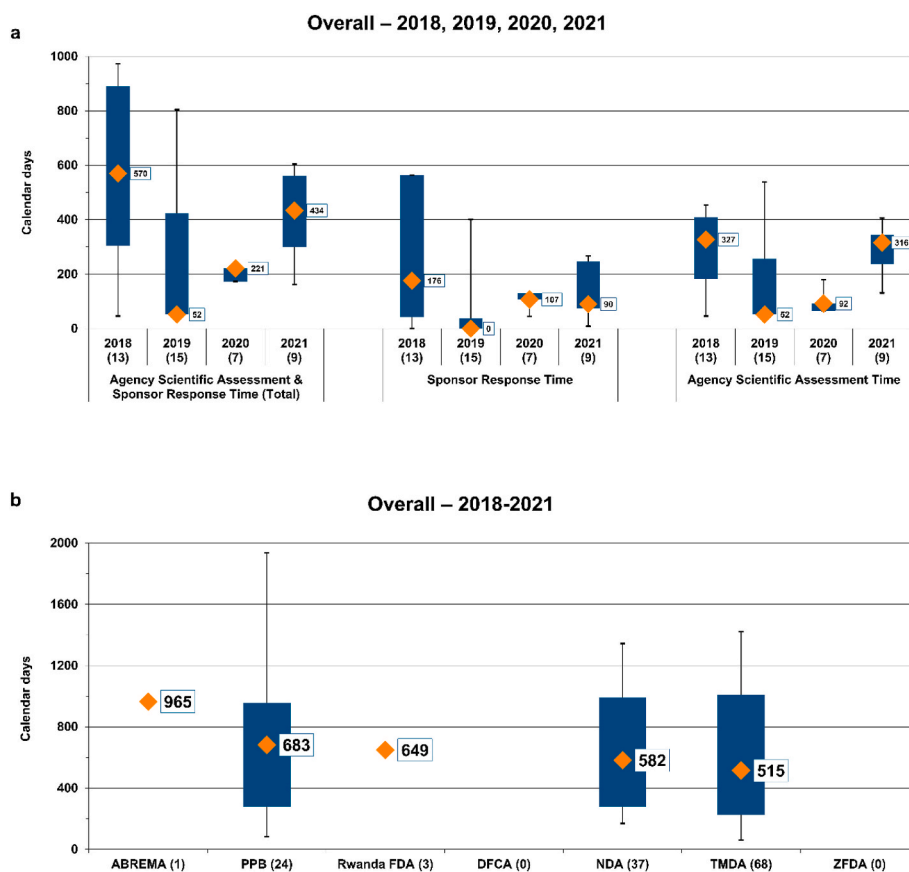


Fig. 4. a) trend in regulator scientific assessment time and applicant response time (2018–2021) b) timelines for granting of marketing authorisation by EAC NMRAs (2018–2021); data are shown for applications that were approved (“Final recommendation reached on”) between 01/01/2018 and 31/12/2021; “sponsor response time” includes applications where there is no sponsor response, (i.e., one evaluation cycle, which is represented in this figure by a sponsor response time of 0 days). For 2018, 2019, 2020, 2021, these represent: 2/13, 10/15, 0/7, 1/9 applications respectively. (n) = number of drug applications. ◊ = Median. Where (n) is less than 5, only the median is displayed. ABREMA = Burundi; PPB=Kenya; DFCA = South Sudan; NDA = Uganda; TMDA = Tanzania; ZFDA = Zanzibar.

submission of dossier”, “Date of distribution of Dossier for first Assessment”, “Final recommendation reached on”, and “Final recommendations communicated to applicant”. Start-up = “Date of submission of dossier”, “Date of distribution of Dossier for first Assessment”. Scientific Assessment = “Date of distribution of Dossier for first Assessment” to “Final recommendation reached on”. Communication of Recommendation to Applicant = “Final recommendation reached on” to “Final recommendations communicated to applicant”.

The time for granting MA by EAC NMRAs was analysed for products that had complete data captured in the metric tool (Fig. 4b). The median times for granting MA by Burundi (ABREMA), Kenya (PPB), Rwanda FDA, Uganda (NDA), and Tanzania (TMDA) were 965, 683, 649, 582, and 515 calendar days, respectively. Therefore, the EAC target time for granting the MA of 116 calendar days was far exceeded by all five authorities. The main reasons for long median times to grant the MA by the EAC NMRAs included long administrative procedures, such as NMRA requirements for product applications to be considered first by the scientific committee before a certificate of MA could be issued. In addition, applicants filing for a certificate of MA and then delaying paying the required fees contributed to these long median times.

4. Discussion

Measuring the performance of national and regional regulatory systems provides key baseline information to build on regulatory systems-strengthening strategy, ensuring patients’ timely access to safe, efficacious, and quality medicines. This analysis of the registration timelines for the EAC joint assessment procedure evaluates the performance of the procedure, identifies the challenges, and suggests possible solutions. The findings from this study indicate a particularly long median overall approval time in 2018 (993 calendar days), for which the main reason was delays by applicants (manufacturers) in responding to

queries raised by the regulators.

Eleven products of the 19 that were approved for MA in 2018 were submitted for the EAC joint scientific review between January to May 2016. A similar challenge with long median approval timelines was observed in the evaluation of the Centralized Procedure in other regions such as the Gulf Co-operation Council (GCC) (Ahonkhai et al., 2016; Al-Rubaie and Salek, S., Walker, 2015; Al-Rubaie et al., 2014). Several findings from research in regulatory systems in the GCC region have highlighted long regulatory review periods as a result of delays by sponsors in responding to queries. Insufficient data submitted in product dossiers, leading to more rounds of queries was also reported. For the year 2018, the overall median approval time for the abridged procedure was 975 calendar days, which was notably longer than EAC target of 465 calendar days. The main reasons were delays in distribution of the dossier to the first assessor for scientific review, delays in the response to queries by applicants, as well as the delays by the EAC Secretariat in communicating the final recommendations of joint scientific review to the applicants. Median overall approval times of biologicals were notably shorter for the periods 2018, 2019, and 2020 (190, 216 and 57 calendar days, respectively). For pharmaceuticals, the median overall approval time in 2020 was notably shorter at 274 calendar days, since a risk-based approach was applied during the scientific review process, in which the assessors relied on the regulatory decisions from WHO-listed regulatory authorities. For 2021, the overall median approval time of biologicals was particularly long (687 calendar days), due to delays by experts in conducting the scientific assessments. The lack of expert capacity to review biologic dossiers with increasing product complexity could also have contributed to delays.

Once a final regional positive recommendation is issued for a medicinal product, and communicated to the applicant, the applicant is required to file an application for an MA certificate at individual EAC NMRAs and pay the applicable fees to each of the respective regulatory

authorities in order to have their products placed on the market. Each of the EAC Partner States have fee guidance and structure governed by that country's regulations and jurisdiction. The findings of this study indicated that applicants do not file for a certificate of MA to all EAC NMRAs, resulting in significant variability in the availability of registered products among the seven NRAs. Tanzania have granted MAs for more medicinal products (68) than other authorities between 2018 and 2021, as TMDA is the lead NMRA for receiving, screening, and assigning medicinal product dossiers to the EAC assessors for evaluation.

The median times for granting MA by EAC regulatory authorities were longer than expected, largely due to long administrative processes at the NMRA level and delays by some applicants in paying the required fees after filing an application for MA. The EAC guidelines and procedures requiring EAC NRAs to issue the MA certificate within 116 calendar days of the applicant filing an application were exceeded by each of the five NMRAs where this could be calculated. The MA certificate is valid for five years and the applicant can renew its validity through a similar regional regulatory pathway. Following a positive regional recommendation, there is a two-year window for an applicant to place products in all EAC markets by filing an MA application and paying applicable fees to the individual NMRAs.

Despite the progress made by this initiative, several challenges have been identified by this study which should be addressed in order to ensure improvement in the joint regulatory procedure and to optimise the resulting processes, thereby delivering on the programme goals and objectives, including regulatory system strengthening. These challenges included incomplete data in the register of medicinal products recorded in the metric tool for registration. In addition, there is limited consistency in data entry when each step is initiated and finalised at both national and regional levels. The metric tool is not automated, which hinders the accessibility and timely entry of data by all NMRAs as well as the EAC Secretariat. The lack of a regional integrated information management system (IMS) to support the sharing of dossiers and assessment reports leads to a lag time and negatively impacts the overall review timelines. Long durations observed for scientific review indicate the limited capacity and capability of some NMRAs to conduct the timely scientific review of quality, safety and efficacy data, which contributes to delays in the submission of assessment reports. The poor quality of dossier submissions by applicants, with some dossiers having missing data on bioequivalence and stability studies, increases the screening time and scientific assessment time due to several rounds of correspondence and queries between regulator and the applicant. A delay in the response to queries by applicants contributes significantly to the lengthy joint review process. The initiative does not provide scientific advice to applicants to improve the quality of dossier submission, which ultimately leads to a lengthy screening and scientific assessment process. The initiative does not charge fees for joint scientific review of medicinal product dossiers. The applicant is required to pay fees applicable to all EAC NMRAs. The lack of a regional fee structure and mechanism for central collection increases the administrative burden to the applicant and consequently limits the applicant to place their products in the market of all EAC Partner States.

Optimisation in the joint regulatory process at a regional level is essential if such regional regulatory authority will be operating at the continental level under the auspices of the African Medicines Authority (AMA).

4.1. Recommendations

The following recommendations for the EAC joint assessment procedure were identified from the study.

- Establish an integrated information management system (IMS) to facilitate the timely sharing of dossiers and assessment reports.
- Automate the capture of regulatory timelines through the EAC metric tool to ensure consistency in data entry and to validate its accuracy.

- Implement rigorous timelines which would enable documentation of the regional scientific assessment as well as the applicant's response time. Such an approach would necessitate a "Clock Stop" system with specific timelines. This ultimately would reduce the delay in registration of products and improve patients' access to medicines.
- Establish strategic engagement and collaboration with the pharmaceutical industry stakeholders, including a feedback mechanism to address the quality of dossiers in order to improve future submissions, decrease the frequency of deficiency questions and subsequently, shorten the time required for joint scientific review.
- Encourage the pharmaceutical industry stakeholders to take advantage of the two-year window following a positive regional recommendation to place their products in all Partner State markets by paying applicable fees to all EAC NRAs.
- Finalise and conclude a fee structure and mechanism for the central collection of fees, reducing the administrative burden on applicants and ensuring sustainability of the EAC-MRH programme.
- Design and implement innovative processes to fast-track MA for products which received positive recommendation after a joint scientific review procedure.
- An appropriate way forward for less-resourced NMRAs is to implement a reliance strategy by taking into account assessment reports carried out by WHO-listed authorities for the same products or the EAC joint assessment procedure.

5. Conclusions

This study examined for the first time the joint regulatory process timelines for the EAC-MRH programme. The implementation of a clock-stop system enables performance to be assessed via data capture and subsequent analysis. Long regulatory scientific assessment timelines were driven by several factors, including delays in applicants responding to queries; insufficient data in the dossier, for example, bioequivalence and stability data, leading to more rounds of queries being issued by regulators; limited capacity of assessors to conduct timely scientific reviews; and the lack of a regional integrated information management system (IMS) to support timely sharing of dossiers and assessment reports. At a national level, delays in the payment of fees by applicants and long administrative procedures by NRAs contributed to the long median times for products to be granted certificates of MA. This study further identifies the gaps in the data within the metric tool, highlighting the need to streamline approaches to data sharing at a regional and national level and the need to automate aspects of data collection.

5.1. Limitations

Only five of the seven participating authorities had complete data captured in the metric tool. Although the sponsor time was calculated by the assessors, it was not easily identifiable for all the authorities took part in the study.

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CRedit authorship contribution statement

Jane Mashingia: Formal analysis, Data curation, Writing – original draft. **Nancy Ngum:** Validation, Writing – review & editing. **Margareth Ndomondo-Sigonda:** Validation, Writing – review & editing. **Adem Kermad:** Formal analysis, Validation, Writing – review & editing. **Magda Bujar:** Formal analysis, Validation, Writing – review & editing. **Sam Salek:** Conceptualization, Methodology, Validation, Writing – review & editing. **Stuart Walker:** Conceptualization, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Sam Salek reports financial support was provided by Bill and Melinda Gates Foundation.

Data availability

Data will be made available on request.

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References

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, e0166515. <https://doi.org/10.1371/journal.pone.0166515>.
- Al-Rubaie, M.H., Salek, S., Walker, S., 2015. An evaluation of the efficiency of the Gulf Cooperation Council's Centralized procedure by the Gulf regulatory authorities and pharmaceutical companies. *Ther. Innov. Reg. Sci.* 49, 560–568.
- Al-Rubaie, M.H., Walker, S.R., Salek, S.S., 2014. Evaluation of the Gulf cooperation Council centralized procedure: the way forward. *Ther. Innov. Reg. Sci.* 48, 709–716. <https://doi.org/10.1177/2168479014529572>.
- Dansie, L.S., Odoch, W.D., Årdal, C., 2019. Industrial perceptions of medicines regulatory harmonization in the East African Community. *PLoS One* 14, e0218617. <https://doi.org/10.1371/journal.pone.0218617>.
- East African Community (EAC), 2021. East African Community Medicines Regulatory Harmonization Programme. <https://www.eac.int/mrh/medicines-regulatory-guide-lines>. (Accessed 1 December 2022).
- East African Community (EAC), 2019. Compendium of guidelines for medicines evaluation and registration for medicines regulatory harmonization in East African community (EAC/TF-MED/MER/FD/COM/N1R1). In: second ed. EAC. EAC Secretariat, Arusha.
- East African Community (EAC), 2018a. Compendium of good manufacturing practices (GMP) technical documents for harmonization of medicines regulation. In: *East African Community (EAC/TF-MED/GMP/FD/COM/N2R1*. EAC, Arusha.
- East African Community (EAC), 2018b. EAC Guideline for Abridged Procedure for the EAC Joint Assessment and Accelerated National Registration (By the EAC Partner States) of Pharmaceutical Products Approved by Stringent Regulatory Authorities and the World Health Organization- Prequalification Program (WHO PQ). <http://www.eac.int/mrh>. (Accessed 1 December 2022).
- East African Community (EAC), 2000. The Treaty for the Establishment of the East African Community. Arusha: EAC. https://www.eala.org/uploads/The_Treaty_for_the_Establishment_of_the_East_Africa_Community_2006_1999.pdf. (Accessed 1 December 2022).
- Mashingia, J.H., Ahonkhai, V., Aineplan, N., Ambali, A., Angole, A., Arik, M., et al., 2020. Eight years of the East medicines regulatory harmonization initiative: implementation, progress and lessons learned. *PLoS Med.* 17, e1003134 <https://doi.org/10.1371/journal.pmed.1003134>.
- Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Doodoo, A., Kaale, E., 2017. Medicines regulation in Africa: current state and opportunities. *Pharmaceut. Med.* 31, 383–397. <https://doi.org/10.1007/s40290-017-0210-x>, 2017.
- Ngum, N., Mashingia, J., Ndomondo-Sigonda, M., Walker, S., Salek, S., 2022. Evaluation of the effectiveness and efficiency of the East African community joint assessment procedure by member countries: the way forward. *Front. Pharmacol.* 13, 891506 <https://doi.org/10.3389/fphar.2022.891506>.
- Sillo, H., Ambali, A., Azatyan, S., Chamdimba, C., Kaale, E., Kabatende, J., et al., 2020. Coming together to improve access to medicines: the genesis of the East African Community's Medicines Regulatory Harmonization initiative. *PLoS Med.* 17, e1003133 <https://doi.org/10.1371/journal.pmed.1003133>.