**POSITION PAPER**

Proposal to Applicants

DOSSIER PROCESSING FEE

SADC MRH Collaborative Registration Procedure Initiative

A stepwise approach to increased efficiency and effectiveness

**Preamble**

In 1999, the SADC Council of Ministers approved the harmonization of medicines regulation in the region in line with Article 29 of the Protocol on Health, under the African Medicines Regulatory Harmonization (AMRH) initiative. The SADC medicines regulatory harmonization (MRH) project is implemented within this broad continental initiative. The purpose of the SADC MRH project is to promote and protect public health through increased and sustainable access to safe, effective, and affordable essential medical products of acceptable quality. The project is implemented by the SADC Medicines Regulatory Forum (SADC MRF). The SADC MRF is made up of the heads of the National Medicines Regulatory Authorities (NMRAs) of the SADC Member States. It is the governing body that makes decisions in terms of the grouping of the NMRAs involved in the harmonization of medical product regulation within SADC, operating under and reporting to the AMRH initiative.

With technical and financial support from partners such as the World Bank, World Health Organisation (WHO), Bill & Melinda Gates Foundation, the African Union Development Agency (AUDA NEPAD), the SADC MRF has made significant progress in strengthening the regulatory framework for medical products, since 2013.The key successes of the SADC MRH project, which includes the ZAZIBONA initiative includes; 38 joint assessment sessions; 48 manufacturing sites jointly inspected by the NMRAS; 22 manufacturing sites approved through desk review; and 9 NMRAs participating in at least one regional joint inspection. Number of products registered in the active member states at country level; DRC (3) Botswana (132), Malawi (2), Mozambique (5), Namibia (117), South Africa (65), Tanzania (20), Zambia (121) and Zimbabwe (133).

**Introspection of the SADC MRH Collaborative Registration Procedure**

As part of the development of the 5Year Strategic Plan for Regulatory Harmonization and System Strengthening, a situational analysis was conducted. In the write up, Narsi and Sithole identified the successes and challenges of ZaZiBoNa, SADC regional collaborative initiative.

*ZaZiBoNa Successes*

The successes of the ZAZIBONA initiative according to the participating regulatory authorities and pharmaceutical industry are as follows (1, 2):

* the initiative has assessed over 330 products in its 8 years of operation, the highest number of products assessed by any regional harmonization initiative on the African continent.
* the median time to ZAZIBONA recommendation of 13 months or less inclusive of the applicant’s time has been achieved in all the years except 2018 and is lower than the registration times achieved by some of the individual participating countries.
* regulatory authorities have reported that participating in the initiative has increased their capacity to conduct assessments and good manufacturing practice inspections.
* the initiative has provided a platform for the sharing of information with other regulators.
* applicants have benefited from compiling one package (regulatory dossier excluding country specific requirements) for the initial submission as well as a single response package to the consolidated list of questions which saves time and resources.
* the ZAZIBONA initiative has achieved shorter timelines for the approval of medicines resulting in increased availability of quality-assured medicines for patients in the SADC region.
* the harmonisation of registration requirements and joint reviews have reduced the workload for both the pharmaceutical industry as well as the regulatory agencies
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*ZaZiBoNa Challenges*

The challenges of the ZAZIBONA initiative according to the participating regulatory authorities and the pharmaceutical industry are as follows (28, 29, 30):

* failure by countries to implement ZAZIBONA recommendations to register products in a timely manner and simultaneously.
* lack of tracking, monitoring, and evaluation of the time taken by participating countries to finalise product registration after a ZAZIBONA recommendation.
* the initiative’s tracking system was not able to separate the agency time from the company time.
* the lack of standardised review templates addressing benefit-risk assessment for new active substances and biosimilar.
* the lack of a centralized submission system and the tracking for applications.
* lack of clarity and information about the ZAZIBONA process in some of the participating countries.
* the operating model is unclear.
* labelling requirements are different in the participating countries.
* the lack of expertise in some countries to assess certain types of products.
* inadequate human resources.
* unequal workload among participating countries.
* the inability of the initiative to mandate central registration.

Taking the above into consideration, this position paper puts forward a proposal to build on the successes and address the challenges. This will improve the efficiency and effectiveness of the ZaZiBoNa joint review process’s operating model piloted since 2013.

**Proposal**

As the initial step to improve efficiency, the SADC Medicines Regulators Forum is proposing a semi-centralised approach to the joint assessment process as a means of improving process control.

The proposal entails introduction of a dossier processing fee which is being proposed to applicants through this position paper. The fee will be utilised to cover administration and technical prosing costs. The proposal is detailed below:

* **Proposed dossier processing fee: USD 2,500** per product
	+ Paid centrally, for cost recovery
	+ Fee will be in addition to (over and above) NMRA registration fee paid to each country where application is lodged
* No change in eligibility criteria
	+ Applicant **must** submit application in at least 2 participating Active Member States
		- To be declared in the Expression of Interest Form
* Benefits
	+ All participating Active Member States are committed to the ZaZiBoNa pathway becoming an expedited pathway
	+ Assured turnaround times: Guaranteed 1st review and List of Queries within 3months; guaranteed recommendation in 6-9 months, finalisation in 9-12moths.
		- Quarterly joint assessment dates to be published together with cut-off dates for submission of applications and query responses
		- Timeline dependent on the quality and adequacy of information submitted; and responsiveness of the applicant
	+ Abridged and expedited review in other Member States where the application was not lodged initially, based on reliance on the ZaZiBoNa recommendation and report
		- Abridged review to verify ‘sameness’ of dossier, and exclusion of post approval changes
		- Validity of recommendation: up to 12 months from issuance
	+ Variations/post approval changes for products approved through the joint assessment process will also be handled centrally but will attract a separate fee depending on the nature of changes
* Uses
	+ Administrative/secretarial support
	+ Technical processing: Screening; 1st and 2nd Reviews; Review of Queries and Finalisation at country level

The proposed process flow is summarised in Figure 1 below.

Fig 1: Proposed Process Flow

**Requested stakeholder feedback**

It is our intention to start piloting this new operating model in the 4th quarter of 2022. To proceed, we need feedback and consensus from industry. Existing and prospective applicants are requested to indicate their views on the proposal. Specifically, applicants should indicate their acceptance or rejection of the concept and acceptance or rejection of the proposed dossier processing fee by completing the Google Form survey on the link below. Stakeholders are further invited to attend the Stakeholder Engagement Meeting to be held virtually on the 12th October 2022.

*Google Form link:*

<https://docs.google.com/forms/d/e/1FAIpQLSfPTLBo02ZWaGCQAWr35apQayBuVWfNeaVLcMQZdi3zltEoJw/viewform?usp=sf_link>

*Stakeholder Engagement Meeting link:*

Topic: SADC MRH meeting
Time: Oct 12, 2022 08:30 AM Harare, Pretoria
Join Zoom Meeting
<https://us02web.zoom.us/j/86118717681?pwd=UVJZL2tPOWV5VHorTHd0VUpOTlRJZz09>

Meeting ID: 861 1871 7681
Passcode: 467016
Join by SIP
86118717681@zoomcrc.com

**References**

1. Sithole, T., Mahlangu, G., Walker, S. and Salek, S. 'Regulatory authority evaluation of the effectiveness and efficiency of the ZaZiBoNa collaborative medicines registration initiative: the way forward', Frontiers in medicine, 9 (2022).
2. Sithole, T., Mahlangu, G., Walker, S. and Salek, S. 'Pharmaceutical Industry Evaluation of the Effectiveness and Efficiency of the ZaZiBoNa Collaborative Medicines Registration Initiative: The Way Forward', Frontiers in medicine, 9 (2022).