ZAZIBONA STAKEHOLDERS' ENGAGEMENT MEETING, 18 JULY 2023

QUESTION & ANSWER

Section I: Administrative Issues

1. **Q: Why is the validity of the ZAZIBONA product recommendation limited to only 1 year?**

   A: The validity period is based on the premise that one year is reasonable timeframe not to expect any changes/variations to the product/application which would result in the need for full review of the application. This period may be reviewed at the end of the pilot of the revised ZAZIBONA process.

2. **Q: Will confirmatory review only be a short administrative process respecting the NRA committed timelines?**

   A: It is important to acknowledge that ZAZIBONA has achieved regulatory harmonization but is still on the journey to regulatory convergence. The review process on submission of a product application at country level supported by a positive ZAZIBONA recommendation will indeed be an abridged process that all Active ZAZIBONA Member States have committed to complete within 90 days of receipt of an application. This abridged review will be limited primarily to non-technical issues that still have legislative requirements at country level. Each participating country will publish, by the start of the pilot, the process pathway and requirements for the abridged review, including any exemptions.

3. **Q: When is the pilot proposed to take place and what qualifies an applicant to participate in the pilot?**

   A: The pilot is proposed to start towards the end of October 2023.

   The pilot will be a window in which to receive applicants for regional joint assessment **without the requirement to submit a product application to any SADC country at that point.** This is to align the process with the outcome of the joint review, which is essentially a recommendation based on the comprehensive evaluation of the quality, safety and efficacy of a medical product.

   Any applicant that envisages applying for Marketing Authorisation to any SADC Member State is eligible to use this voluntary pathway. The prerequisite for using the pathway is paying the cost recovery fee of USD 2,500.

4. **Q: Who is performing the assessment? SADC assessors or assessors from NRAs?**

   A: Assessments will be conducted by a pool of assessors from the SADC region. Each ZAZIBONA Active Member State will avail assessors for the pool. These are essentially the same assessors as before, employed by the SADC NMRAs.

5. **Q: What are timelines for screening?**
   A: Screening shall be completed within 14 working days from the date of receipt of the application.

6. **Q: What is the eligibility criteria for the Joint Assessment Pathway (JAP)?**
   A: The regional collaboration focuses on leveraging resources for medical products that are of mutual public health interest. Anyone can apply through the JAP as long as they pay the relevant cost recovery application fees.

   Products eligible for review through this voluntary pathway are medical products used in the treatment of the following conditions; HIV/AIDS, tuberculosis, malaria, acute respiratory infections, diarrhoea, diabetes, pneumonia, cardiovascular, cancer, obstetrics, gastroenteritis and colic, reproductive health products as well as products included in the list of United Nations Commission for Life-Saving Commodities for Women and Children Final UN Commission Report_14sept2012.pdf (unfpa.org). Medical products that may be of public health importance from a regional perspective that do not necessarily fall into the categories specified above can still be considered for eligibility by applicants expressing an interest in their review.

   The JAP does not consider products that are WHO Prequalified as there are adequate processes based on reliance at country level. In response to industry requests, products approved by Stringent Regulatory Authorities (SRAs) can be considered provided that the applicant submits the full SRA assessment reports as well as associated documentation in line with the WHO SRA CRP process. Ref: https://extranet.who.int/pqweb/medicines/faster-registration-fpps-approved-sras

7. **Q: Is there a common template to be used for the application?**
   A: The WHO QOS-PD which is the basis of most of the QOS-PD documents used by SADC countries remains the template on which Quality assessments are conducted while the WHO-BTIF is the document for bioequivalence studies. For the purposes of central submissions, these documents from WHO will need to be submitted and can be accessed from the WHO Prequalification website. They will also be available for download from the ZAZIBONA website once the pilot starts.

8. **Q: Can we have information on how the 2500 USD is allocated for the different stages in the process?**
   A: The process will only be split into two (2) parts: screening and evaluation. The screening component will be USD 250. The balance of USD 2,250 is for the evaluation process that culminates in the recommendation. An application will be screened first before proceeding to evaluation. The screening fee will be payable regardless of the screening outcome. In the case of a positive screening outcome, the applicant will pay the screening and evaluation fee together. In the case of a negative screening outcome, the applicant will only be required to pay the screening cost recovery fee of USD 250.

9. **Q: Can participating NRAs perhaps commit within the MoU that they will implement recommendations in a fast administrative process without additional queries?**

   A: All Active ZAZIBONA Member States have committed to complete implementation of recommendations within 90days of receipt of an application. The abridged review that must be completed within the 90days will be limited to non-technical issues that still have legislative requirements at country level, such as labelling requirements. Each participating country will publish, by the start of the pilot, the process pathway, clearly outlining requirements for the abridged review, including any exemptions. This will be published on the individual Member State websites and jointly as a statement of commitment on the ZAZIBONA website. This will allow applicants to make an informed decision regarding use of this voluntary pathway.

   The ZAZIBONA initiative has further committed to recourse through a discounted fee for a subsequent application where there is failure to meet commitment to this and the other timelines.

10. **Q: Is there a recommended or maximum timeline for applicants' response to queries?**

    A: The applicant will be expected to respond within two (2) months of receiving queries. ZAZIBONA will start and stop the clock such that the 9months to recommendation is a cumulative total of regulator evaluation time. Applicants can be granted extensions upon request. Any application whose queries have not been resolved within 18months of initial submission shall be closed. The applicant will be notified of closure of the application and the reason for closure shall be denoted as failure to respond to queries raised during the evaluation process.

11. **Q: Will you not be accepting further applications once the window closes? Or this will only apply for the Pilot?**

    A: There will be a temporary suspension for the receipt of applications once the window closes. Review of the pilot will be simultaneous and ongoing and will inform the next steps.

12. **Q: Will SRA have shorter timelines to approval?**

    A: It is likely that SRA approved products which meet all the requirements in terms of providing the information/documentation required as per the WHO SRA CRP process will take a shorter time to approval.

13. **Q: How do you mitigate the timeline from individual countries after getting ZAZIBONA certificate as some countries take 3-4 months for validation?**

    A: The prerogative of issuing marketing authorization ultimately rests with the country where an application is ultimately submitted. The Heads of Agencies in all the Active ZAZIBONA NRAs have committed to finalise an application submitted on the basis of reliance on the ZAZIBONA recommendation within 90 days. Applicants are encouraged to ensure they meet the declared country specific requirements on submission to ensure that each NRA is able to finalise the application within the 90days. The country specific requirements will be published by all the NRAs.

14. **Q: What happens if ZAZIBONA certificate expires in mid of process with NMRA?**

A: An applicant will have a window of 1 year to utilize the ZAZIBONA recommendation. This means that the applicant must submit the application to the NMRA before the recommendation expires. Once submitted, the NMRA is obliged to complete abridged review within 90 days. As long as the product is received within the validity period, the applicant will get the benefits of the new system.

15. **Q: What is your decision process on rapporteurs?**
    A: Each ZAZIBONA Active Member State will avail assessors for the pool. Entry into the pool will be based on competency. ZAZIBONA internally utilizes a competency framework developed by WHO.

16. **Q: Can ZAZIBONA halt the next application if company has not paid the previous product's screening fee?**
    A: It is not clear from the question why an applicant would not settle the screening fee timeously. We do not envisage such a scenario. For the entire process communication will be key. Such a scenario will be handled on a case-by-case basis.

17. **Q: Can we implement the screening fee right at the beginning of the process prior to screening in order to make the process efficient? This also justifies the transparency on the fee allocation for the entire process.**
    A: ZAZIBONA is wary of and wants to avoid a backlog resulting from applicants that fail screening. It will not be possible to evaluate such applications and the initiative does not want to get bogged down with processing refunds. After 14days of receipt of the application, an applicant will receive a proforma for either screening only or screening and evaluation, depending on the outcome of the screening process.

18. **Q: Will ZAZIBONA issue new set of guidance documents and forms required to be used?**
    A: Yes. These will be published on the website.

19. **Q: What will be the proposal for renewal of dossiers which registered through ZAZIBONA pathway where re-registration process is applicable?**
    A: At present, the collaborative initiative conducts routine joint inspections as a means of continued oversight on products approved on the basis of a ZAZIBONA recommendation. Marketing Authorisation and renewal of the same is currently not within the scope of the ZAZIBONA initiative.

20. **Q: For dossier submission fees, will each country still require their individual filing fees and additionally the US $ 2500 fee?**
    A: Yes. Marketing Authorization remains the prerogative and responsibility of the concerned Member State. Thus, an applicant will pay USD 2,500 to ZAZIBONA for the recovery of costs associated with evaluation to obtain the ZAZIBONA recommendation. At the time when the applicant decides to submit an application to any of the Member States they will be required to pay the applicable application fees.

21. **Q: Can you use the ZAZIBONA process for new products that are not yet registered in the country of origin?**

A: It will be possible for these [products to be assessed on a case-by-case basis but it is worth noting that registration in the country of origin is required by the countries before approval is granted. Effectively products may be recommended for approval on the basis of acceptable technical requirements but marketing approval in the countries will not be granted before registration has been granted in the country of origin.

22. **Q: So, the ZAZIBONA process fees are Admin fees of $2500 + any additional inspection fees + country specific fees for MAH approval?**
    A: The ZAZIBONA pathway attracts cost recovery fees for evaluation of the product dossier and joint inspection fees.

    Country specific Marketing Authorisation fees will also apply at the time of submitting an application to the selected Member States.

23. **Q: Is the eligibility criteria that the application should not have been submitted at country level an absolute criterion? If an applicant is willing to participate and 'resubmit' under the pilot, can they request for exemption from this eligibility criteria?**
    A: Applicants interested in getting the benefits of the new system that centralises the dossier, will, at the start of the pilot, have the option to pay for products submitted recently and prior to the change in this criterion. The stage at which the application is at will be given consideration and the matter discussed with the applicant.

24. **Q: Is there any assurance from the NRAs on acceptability of these recommendations from ZAZIBONA as this does not have legal or government endorsement?**
    A: All Active ZAZIBONA Member States have committed to complete implementation of recommendations within 90days of receipt of an application. The abridged review that must be completed within the 90days will be limited to non-technical issues that still have legislative requirements at country level, such as labelling requirements. Each participating country will publish, by the start of the pilot, the process pathway, clearly outlining requirements for the abridged review, including any exemptions. This will be published on the individual Member State websites and jointly as a statement of commitment on the ZAZIBONA website. This will allow applicants to make an informed decision regarding use of this voluntary pathway.

    The ZAZIBONA initiative has further committed to recourse through a discounted fee for a subsequent application where there is failure to meet commitment to this and the other timelines.

25. **Q: Suggestion for future plans: Given raised concerns on the centralized fee - perhaps different fee tiers depending on location of manufacturer? Somewhat like the West Africa Harmonization initiative.**
    A: The suggestion is noted and will be considered as the pilot is reviewed and with further stakeholder engagement.

26. **Q: So, with the central process, we are no longer going to submit to the 2 member states but rather one dossier to ZAZIBONA and once recommendation received submit the ZAZIBONA dossier to the various members with recommendation letter for MAH approval?**
    A: Yes, that is correct.

27. **Q: If a dossier is submitted in July or August will it be taken as part of the pilot or still the old review process?**
    A: Such a dossier will be part of the old review process. However, applicants interested in getting the benefits of the new system that centralises the dossier, will, at the start of the pilot, have the option to pay for products submitted recently and prior to the change in this criterion. The stage at which the application is at will be given consideration and the matter discussed with the applicant.

28. **Q: Would you consider applications already submitted to NMRAs but still pending ZAZIBONA Assessments/feedback if the applicant is willing to pay the central fee?**
    A: Yes, this will be possible. The stage at which the application is at will be given consideration and the matter discussed with the applicant.

29. **Q: Regarding the 90-day timeline for registration following a recommendation, it may be helpful for the individual countries publish on their website a guideline for the registration of products submitted through the ZAZIBONA collaborative process giving requirements and committing to the 90-day timelines.**

    A: Indeed. This will be done.

30. **Q: Could you please share a full flow chart/text of the process for the submission and assessment procedure including Q&A?**

    A: The flow charts are shared separately with this Q& A document.

<u>Section II: Technical (Dossier evaluation)</u>

1. **Q: USD2500 per product. Please advise me if this is per strength? In the case of an application with multiple strengths how will the fee be calculated?**

   A: Multiple strengths/line extensions will be charged an additional USD 1250 per application and not the full USD 2500.

2. **Q: Will the fees be the same as 2500 USD even for NCE, or generic, Biological all category of products?**

   A: The evaluation fee will be the same for NCEs and generics. However, a cost recovery structure for biologicals is yet to be determined. Applicants desiring to use the collaborative process for biologicals should approach the ZAZIBONA initiative to engage on this matter.

3. **Q: What about meeting country specific requirements such as dissolution for products with biostudies?**

   A: There are a few country specific requirements that are technical. Each country will declare how they will deal with them.

4. **Q: Will ZAZIBONA have a preferred submission format, will eCTD apply?**

   A: Guidance documents and forms for the submission process will be published on the website prior to the start of the pilot.

5. **Q: Would samples be required?**

   A: Samples are an integral part of a product submission and evaluation. The centralised process will require sample submission to the coordinating NMRA, MCAZ. The details of how this will be done will be contained in the guidance documents.

6. **Q: Regarding the assessment part: what is being assessed, CMC and Clinical? If clinical is not reviewed, the 90 days will not be met by some of NRAs as clinical reviews also take time. From a practical perspective, for countries who review clinical information, how will the process be as dossier is centrally submitted.**

   A: The assessment will include clinical assessment. The pool of assessors will include clinical assessors.

7. **Q: Will more guidance on biological products fees be made available. Will biological products be included in the pilot? Will there be standardized fees for biological product review?**

   A: Yes, more guidance will be availed on biological product review. Applicants desiring to use the collaborative process for biologicals should approach the ZAZIBONA initiative to engage on this matter.

8. **Q: How will Post Approval Changes (PACs)/variations be handled for applications submitted centrally? Will there also be a process and a central fee for these?**

   A: A regional guidance document is in place for post approval changes. However, given the timelines in place for the PACs at country level, ZAZIBONA may not be able to exceed these timelines.

   Where applicants have a significant multi-national presence and would specifically want collaborative review, this can be accommodated provided applicants appreciate that it may not be possible to complete the process in 60-90days as is the case at country level.

9. **Q: Who can we get clarity on biological products as some member counties consider certain molecules as biologicals and other not?**

A: The technical Assessments Coordinator for ZAZIBONA is Mr Farai Masekela. Specific technical queries can be channeled to him via email: fmasekela@mcaz.co.zw

10. **Q: The products listed on the website is for all essential medicines and medicines used in the treatment of the SADC priority diseases. What about other products ophthalmic, dermal and OTC, etc.?**

    A: The regional collaboration focuses on leveraging resources for medical products that are of mutual public health interest. Medical products that may be of public health importance from a regional perspective that do not necessarily fall into the categories specified on the website can still be considered for eligibility by applicants expressing an interest in their review. These special cases however do not include over-the-counter products.

11. **Q: Are you referring to the public assessment or unredacted assessment report?**

    A: With respect to the evaluation of products approved by stringent regulatory authorities, ZAZIBONA will review the products only if the full assessment report from the stringent NMRA is submitted with the application. The process to be followed is in line with WHO SRA CRP procedure. Ref: https://extranet.who.int/pqweb/medicines/faster-registration-fpps-approved-sras

Section III: Technical (GMP Inspections)

1. **Q: We do need a clear pathway on audits leading to GMP approval for all the countries in the review.**

   A: This is noted and will be published on the website. The ZAZIBONA website contains information on inspections under the FAQ section.

2. **Q: Please clarify inspection fees**

   A: ZAZIBONA cost recovery inspection fees are determined jointly by the Heads of Agencies (SADC Medical Products Regulatory Forum). The current fees, which are based on the dosage forms under consideration per block, are as follows:

Non-injection with less than 3 dosage forms:	**USD 8, 000**
Injectable plant:	**USD 10, 000**
Plant with 3 dosage forms:	**USD 10, 500**
More than 3 dosage forms:	**USD 12, 000**
Desk review:	**USD 4,000**