REQUEST FOR EXPRESSIONS OF INTEREST IN THE

PILOTING OF A CENTRALISED ZAZIBONA JOINT ASSESSMENT PATHWAY FOR MEDICINAL PRODUCTS

SUMMARY

The Southern African Development Community Medical Products Regulators Forum (SADC MRF) advises its stakeholders that the ZAZIBONA centralised process will be implemented from the **1st of January 2024.** From this date, the ZAZIBONA initiative will not be accepting any applications except through the revised procedure, starting with this pilot phase. Applications will no longer need to be lodged at country level but will be **submitted centrally** through the ZAZIBONA portal. **A cost recovery fee will be levied for each product application**. Applicants will receive a scientific opinion on the quality of their product which will serve as a recommendation to the participating Member States. Positive recommendations can be used by applicants for expedited review and registration with the participating Member States at the time of lodging an application for registration (marketing authorisation). The pilot will accommodate thirty (30) product applications. Stakeholder engagement sessions for review and progress update on the pilot will be scheduled for June and November 2024.

BACKGROUND

ZAZIBONA is the collaborative initiative of the Southern African Development Community (SADC) focusing on joint dossier assessments and joint determination of the Good Manufacturing Practice status of the manufacturing facilities seeking registration of their products in the region. Founded in October 2013 with support from the WHO Prequalification team and various support partners, the initiative was formally endorsed by the SADC Ministers of Health in 2014 and became part of the SADC Medicines Registration Harmonisation (MRH) programme in 2015. ZAZIBONA membership has grown from the four founding countries,

namely Zambia, Zimbabwe, Botswana, and Namibia, to include all 16 SADC Member States that are now participating either as active or non-active Member States, based on their internal capacity to conduct assessments and current Good Manufacturing Practice (cGMP) inspections, or as observers[1].

The initiative has achieved some level of success in its 10years of existence, having held 44 joint assessment sessions and reviewed 410 applications to date, finalising 340 of those applications. The median time to recommendation is currently 12months. Growth of the initiative has not been without challenges, the main ones being

- the extension of the target timeline to recommendation from 9months to 12months as well as variability and inconsistency in meeting this timeline,
- failure by participating Member States to implement ZAZIBONA recommendations to register products in a timely manner and simultaneously, and
- the initiative's tracking system lacking the provision to separate agency time from the applicant company time.

Centralising the procedure is therefore aimed at improving efficiency both pre and post the recommendations thereby improving access to safe, effective, and good quality medicines in the region. In addition to improving efficiency, centralisation comes with introduction of a cost recovery fee for the dossier assessment evaluation. Introduction of this cost recovery is focused on ensuring a sustainable operating model.

Applicants are hereby invited to submit applications for dossiers for medicines through this revised procedure for the ZAZIBONA joint assessment pathway.

OVERVIEW OF THE PROCESS

ZAZIBONA has transitioned into a centralised process for the provision of either a positive or a negative scientific recommendation to the participating Member States on the quality and safety of the product under consideration. Under the centralised procedure,

- ❖ The pilot will accept up to 30 product applications. The window for submissions of EOIs opened from the 12th February 2024. The window shall remain open until 30 applications

[1] ZAZIBONA **Active Member States**: Botswana, DRC, Malawi, Mozambique, Namibia, South Africa, Tanzania, Zambia and Zimbabwe.
ZAZIBONA **Non-Active Member States**: Angola, Comoros, Eswatini, Lesotho, Madagascar, and Seychelles.
ZAZIBONA Observers: **Mauritius**

have been received. ZAZIBONA has over the years received approximately 30-40 applications per year, and this informed the number of applications for inclusion in the pilot phase.

- Dossiers will be submitted **centrally,** and not to individual Member States. Therefore, applicants are no longer required to submit applications to Member States to qualify to use the procedure.
- Applicants should not simultaneously lodge applications with any of the Member States. The joint assessment pathway is an alternative pathway. Lodging the applications simultaneously can result in counterproductive duplicate evaluation of the same product.
- A cost recovery fee shall be paid **centrally.** This fee shall be independent of application fees levied by the Member States should an applicant choose to use a positive recommendation to seek registration (marketing authorisation).
- Each product application will be evaluated centrally. Assessors evaluating the products will be drawn from a common pool of ZAZIBONA assessors seconded by the participating Member States.
- Assessment of product(s) submitted will include evaluation of:
    - product dossiers, which must include product data and information as specified in the SADC guidelines for submission available on the ZAZIBONA website.
    - manufacturing sites, which must adhere to good manufacturing practices (GMP)
    - clinical sites (if applicable), which must adhere to good clinical practices (GCP).
- Applications will be tabled at the quarterly joint assessment sessions whose tentative dates for 2024 are:
    - 26 February - 1 March
    - 27 - 31 May
    - 26 - 30 August
    - 11 - 15 November
    - Dates for the quarterly assessment sessions will be published on the ZAZIBONA website along with cut off dates for submissions, to allow applicants to align submissions with meeting dates.
- Queries will be deliberated on in the joint assessment session and the agreed list of queries communicated centrally.
- Applicants will be allowed two (2) review cycles, after which a recommendation will be made. An additional cycle may be added in exceptional cases. Requests for extensions on

the basis of generating new data cannot be granted – applicants are advised to submit complete applications from the onset.

- ❖ Tracking will facilitate separation of applicant response time and ZAZIBONA review time.
- ❖ The final decision remains a **recommendation,** which shall be valid for 12 months.
- ❖ The written positive recommendation can be used by the applicant to support expedited review and finalisation of the application by any of the member states that have product registration processes.
- ❖ Updating the dossier to reflect clarifications and commitments made during the review cycle shall be a pre-requisite to issuance of the written positive recommendations. Applicants are encouraged to work on this simultaneously as part of the review cycles. Only updated dossiers can be submitted for expedited review in seeking registration (marketing authorisation) from the participating Member States.

ROLES AND RESPONSIBILITIES

The ZAZIBONA centralised process will involve several stakeholders who have different roles in the process.

The role of the applicant/manufacturer

i. Compilation of current CTD dossier including completion of the supporting assessment documents in module 1 (including QOS and QIS).
ii. Payment of cost recovery fees (refer to the section on fees)
iii. Submission of a complete application through the online submission portal.
iv. Responding completely and accurately to queries raised and adhering to the prescribed response timelines and paying particular attention to submission cut off dates.
v. Updating the CTD dossier to address queries raised and to include commitments made during the centralised evaluation.
vi. Taking cognisance of the country specific requirements when submitting products for registration.

The role of the ZAZIBONA coordination office

i. Acknowledgement of receipt of the application fees and the applications
ii. Management of the product evaluation cycles.
iii. Communication with applicants on progress of applications

iv. Sharing of list of approved/rejected products with the Member States upon completion of the assessment process.
v. Issuance of written scientific recommendation to applicants. Positive recommendations shall only be issued upon receipt of an updated dossier from the applicant.

The role of NMRA staff

i. Seconding review experts for the primary and second review of applications and any responses to queries in line with assessment best practices.
ii. Deliberating and concurring on queries to be raised, and the final recommendation in terms of quality and safety of the product.
iii. Timely evaluation of initial submissions and responses.
iv. Recognising the ZAZIBONA recommendations and utilising them for reliance for expedited and abridged review of applications for registration (marketing authorisation).

SCOPE OF PRODUCTS

Products eligible for assessment under the ZAZIBONA initiative consist of all essential medicines and medicines used in the treatment of the SADC priority diseases or conditions listed below:

a. HIV/AIDS
b. Tuberculosis
c. Malaria
d. Acute respiratory infections
e. Diarrhoea
f. Diabetes
g. Pneumonia
h. Cardiovascular
i. Cancer
j. Obstetrics
k. Gastroenteritis and colic
l. Reproductive health products
m. 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 using this joint assessment pathway.

ZAZIBONA 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

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.

ELIGIBILITY

All applicants interested in obtaining marketing authorisation in the SADC region are eligible for the process on the condition that they pay the required cost fees and submit an Expression of Interest through the ZAZIBONA submission portal. Prior registration is required to access the Expression of Interest submission form on the ZAZIBONA submission portal.

APPLICATION PROCESS

a. Applicants must register in order to be able to utilise the ZAZIBONA submission portal.
b. Product dossier applications must be submitted in English and in the Common Technical Document (CTD) format (modules 2 to 5), electronically as a pdf searchable document centrally through the ZAZIBONA submission portal. Applicants must use the ZAZIBONA QOS and BTIF (where applicable).
c. The application will be screened first before proceeding to evaluation. The screening and evaluation steps are separated, with proforma invoices issued through the ZAZIBONA submission portal. The detailed process flow is available as Appendix I.
d. Compliance with cGMP will be determined either through inspections (on site or remote) or desk review in accordance with prevailing criteria. The specific route will be determined

after successful screening. The initial dossier evaluation will also take into account areas of focus.

e. Product samples will only be submitted upon request. Initial submissions will only need to be accompanied by mock-ups.

COST RECOVERY FEES

The Medicines Control Authority of Zimbabwe is the current Implementing Agency tasked with the responsibility to receive and verify cost recovery fees. Proforma invoices shall be generated and issued through the ZAZIBONA submission portal. Proof of payment must accompany submissions at each process step, as guided by the ZAZIBONA submission portal.

ZAZIBONA cost recovery fees are determined jointly by the Heads of Agencies (SADC Medical Products Regulatory Forum) and are as follows:

Dossier evaluation

Item No.	Service	Fees (USD)
1.	Screening	**250**
2.	Product dossier evaluation	**2 250**
	Total	**2 500**

cGMP determination

Item No.	Service	Fees (USD)
1.	Non-injection with less than 3 dosage forms	**8, 000**
2.	Injectable plant	**10, 000**
3.	Plant with 3 dosage forms	**10, 500**
4.	More than 3 dosage forms	**12, 000**
5.	Desk review	**4, 000**

TIMELINES

ZAZIBONA timeline from receipt of an application to the final recommendation (scientific application shall be no longer than 9months, excluding applicant response time. Specifically,

- ZAZIBONA Joint Assessment Sessions: as per specific dates published.
- Confirmation and acknowledgement of receipt of EOI: within 5 working days of submission.
- Screening: within 14days from receipt of the application and payment of screening cost recovery fee.
- Q1 assessment: within 90days of payment of the full evaluation cost recovery fee. Thereafter the evaluation report shall be tabled at the next available joint assessment session.
- Q1 List of Queries: within 7days from the completion of a Joint Assessment session. For an assessment report to be tabled at a particular Joint Assessment session, it must have been received 3months before the Joint Assessment session. Cut-off dates will be published to assist applicants to manage the timelines.
- Q2 assessment: within 60days from receipt of applicant response to first Consolidated List of Queries (c1LoQs).
- Q2 List of Queries: within 7days from the completion of a joint assessment session. For query responses to be tabled at a particular Joint Assessment session, they must have been received 2months before the Joint Assessment session. Cut-off dates will be published to assist applicants to manage the timelines.
- Final assessment: within 60days from receipt of applicant response to c2LoQs. This will culminate in the ZAZIBONA recommendation.
- Communication of recommendation: within 7days from the completion of the Joint Assessment session in which a final recommendation is made. Applications shall be notified of the intention to issue a positive recommendation upon receipt of an updated dossier. Negative recommendations shall be communicated in writing within 7days from the completion of the Joint Assessment session.

In the event that ZAZIBONA exceeds the timeline to recommendation beyond 11months, applicants shall be entitled to a 10% reduction of the cost recovery fee payment with the next application.

- Recommendation to feedback on final registration decision: within 90days of submission of application at country level, provided country specific requirements have been met.

CONTACT PERSONS

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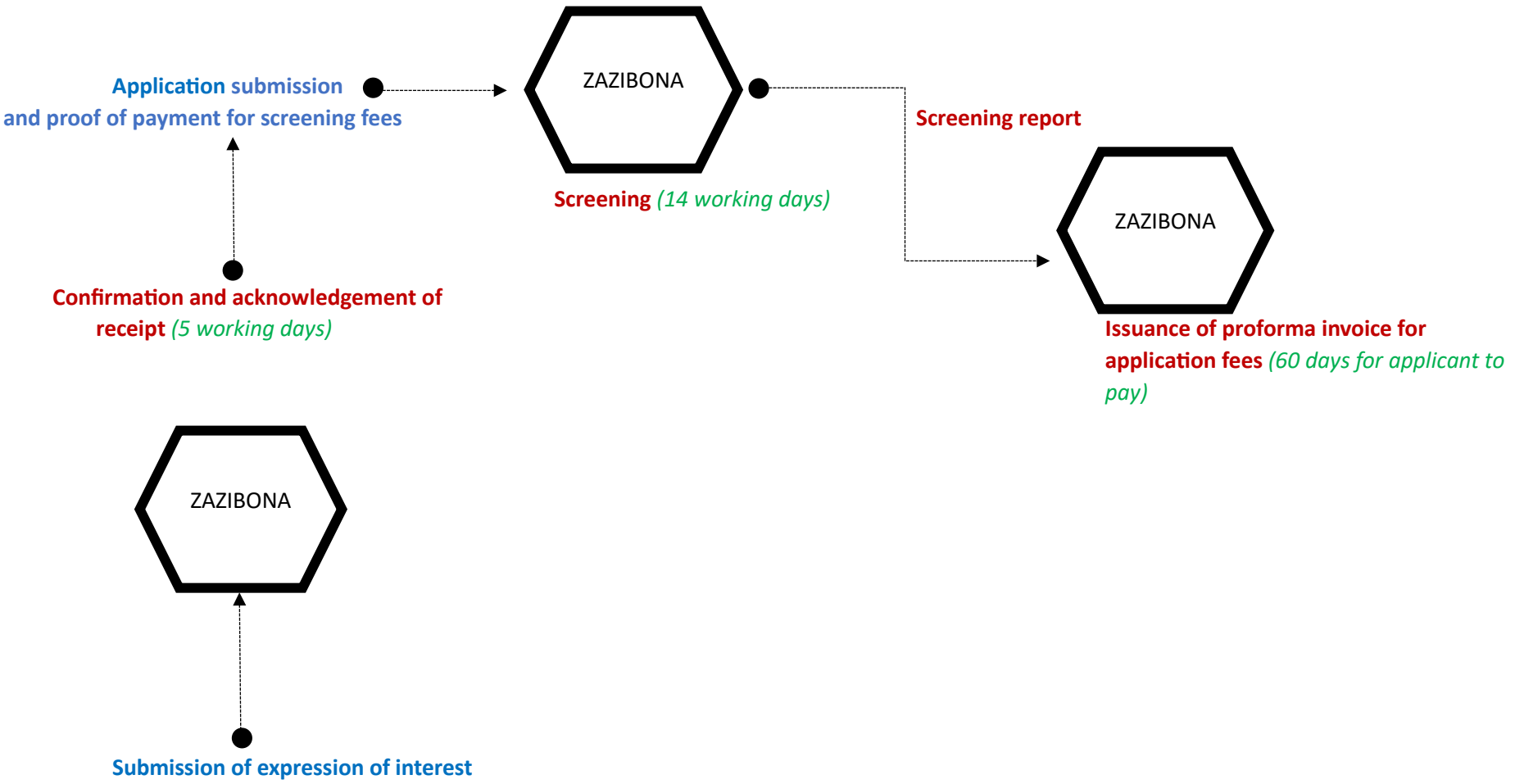
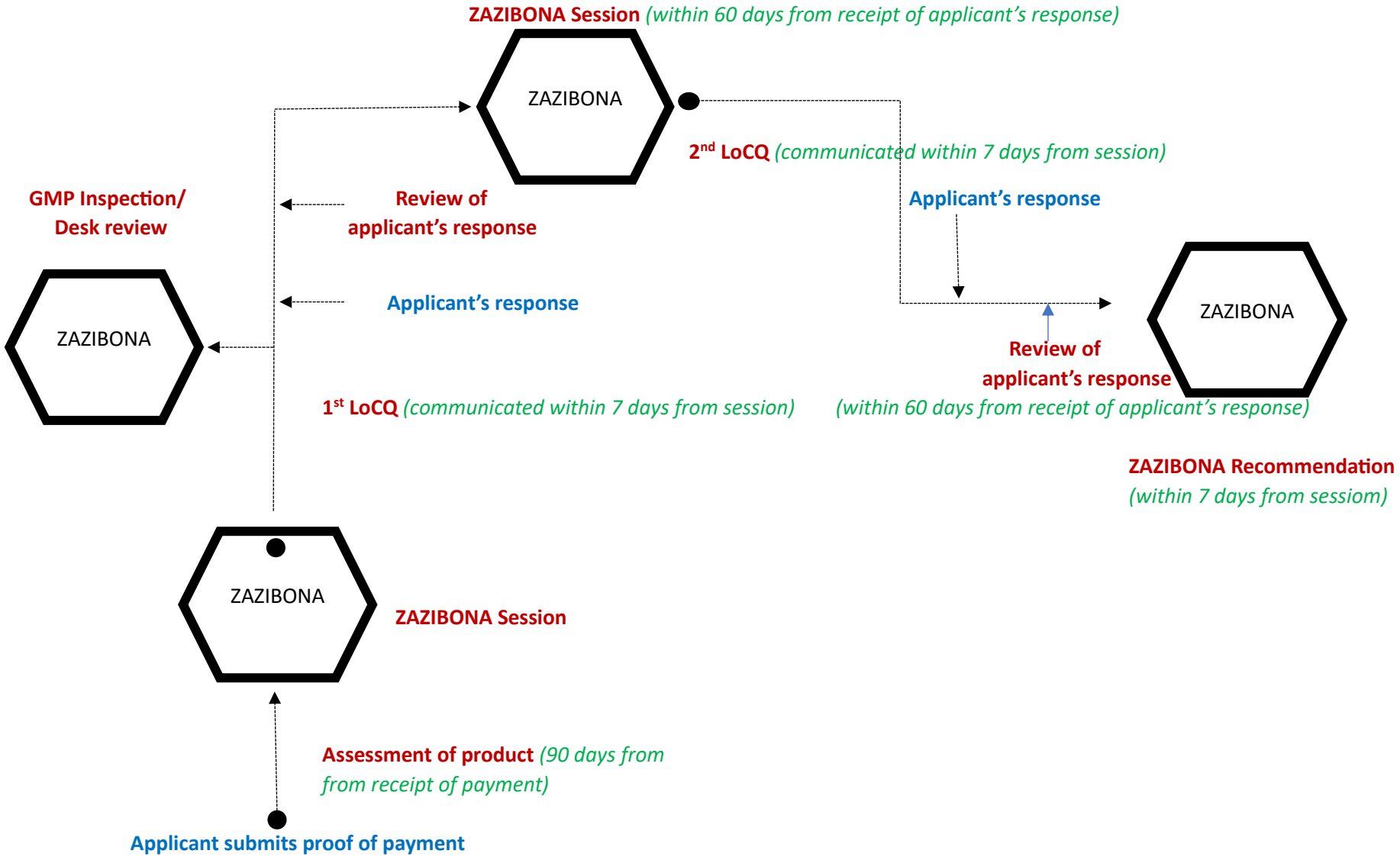
APPENDIX I – PROCESS FLOW

Part 1



Part 2


ZAZIBONA Session (within 60 days from receipt of applicant's response)
ZAZIBONA
2nd LoCQ (communicated within 7 days from session)
GMP Inspection/
Desk review
Review of
applicant's response
Applicant's response
ZAZIBONA
ZAZIBONA
Applicant's response
Review of
applicant's response
(within 60 days from receipt of applicant's response)
1st LoCQ (communicated within 7 days from session)
ZAZIBONA Recommendation
(within 7 days from sessiom)
ZAZIBONA
ZAZIBONA Session
Assessment of product (90 days from
from receipt of payment)
Applicant submits proof of payment