Ending disease in Africa

AVAREF's role in facilitating regulatory procedures for candidate vaccines and therapeutics for filoviruses in Africa

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African Region

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Outline…

- Background
- Overview of AVAREF
- Objectives of AVAREF
- Joint review procedures for clinical trial applications
- Other offerings

BACKGROUND

- Biomedical research in Africa has surged in the past decade
- A regulatory platform is needed to improve expertise, access to therapies, and regulatory efficiency.
- Regulatory efficiency- critical for epidemic/pandemic preparedness
- Stakeholder cooperation is vital, including funders, sponsors, researchers, regulators, and ethics communities.

OVERVIEW OF AVAREF

A Network of 55 member countries

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African Vaccine regulatory Forum (AVAREF)

- **The African Vaccine Regulatory Forum (AVAREF)**, a network of National Regulatory Authorities (NRAs) and Ethics Committees (ECs).
- Established in 2006 by the WHO to build capacity & improve the harmonization of practices in support of product development.
- Help NRAs, ECs, and sponsors to achieve consensus on regulatory and ethics questions surrounding R&D of medical products.

AVAREF Objectives

- To increase the efficiency and quality of reviews and inspections and the timeliness and transparency of regulatory decisions for all interventional trials conducted in Africa
- To promote patient safety
- To accelerate the African Medicines Regulatory Harmonization (AMRH) process, linking all Regional Economic Communities (RECs)
- To stimulate innovation and research in Africa
- To enhance emergency preparedness on the continent, in RECs and in individual countries

A Strong Record of AVAREF Capacity Building Activities

Multi-Country Joint Activities

- Scientific Advice for Clinical Trials
- Multi-Country Joint Review of Clinical Trial Applications (CTAs)
- Emergency Registration of Medicines such as Covid-19 Vaccines, Ebola Vaccines, Malaria Vaccines, etc.

Country Support

- Training of staff in review of life cycle of products; clinical trials, GXPs – GCP, GLP, GMP, GRPs.
- Training for ethics reviewers as well as effective synchronization of ethics reviews with regulatory reviews
- Optimization Exercises such as for clinical trial authorization

Harmonization

- Technical Committees for development of guidelines, check lists and guidance documents
- Advisory Committee setting workplans, adoption of developed guidelines and tools
- Adoption and implementation of AVAREF Tools and Guidelines

Offerings to developers - Scientific Advice

- Regulatory harmonization within the continent and alignment with good practice in regulation on a global level- priority for AVAREF

- Developers interested in conducting clinical trials in Africa require advice in designing clinical trials appropriate for the African context

- This advice is often not available or not easily accessible by developers at a country level, especially for novel IMPs

- Developers have indicated their interest in such a service being offered by AVAREF

AVAREF's Joint Review Process

- Letter of Intent to utilize AVAREF Process for Joint Scientific Advice or Clinical Trial Application, or Registration is submitted to RD, WHO-AFRO.
- Dossier is submitted to AVAREF Secretariat, as well as submissions made to each of the Countries as per their national procedures
  - Submission to NRA and/or National Ethics Committee
  - Payment of Applicable Fees
  - Use of standardized formats
- All supporting information such as reports from other NRAs, WHO-PQ, etc. loaded onto the portal for the review process
- Pre-submission Meeting
- Joint review using the AVAREF Platform

Role and responsibilities of the focal points

Focal points serve as interface between the institution they belong to, the WHO AVAREF Secretariat as well as with the applicant

1. Ensure process and timelines are followed as agreed
2. Attend the Joint-review related meetings on behalf of the team of reviewers of representing agency
3. Download the assessment reports and related documents from WHO PQ portal, and make these available to review team at NRA
4. Send the questions collected from review (from the team of reviewers at NRA) before the agreed deadline for the step
5. Respond to answers provided by the Applicant if satisfied or not satisfied
6. Provide regular and timely updates on the review progress to the WHO AVAREF Secretariat if there is any (expected) delays, as well as updates on the post review steps following the joint review meetings

Pre-Submission Meeting

Objective(s)

- Applicant presents the product for which marketing authorization is sought
- Agreement on submission of the relevant data package
- Agreement on facilitated registration review process and proposed timelines / meeting dates

List of documents requested from the sponsor

Type of Documents	Is provided for the submission	Will be provided during review	Will be provided before study starts	Could not provide
Protocol (English)				
Protocol Ancillary studies (if applicable)				
Country specific appendices (treatment arm or additional testing)				
Synopsis (English, French, Spanish Portuguese if applicable)				
Informed Consent Form (English, French, Spanish Portuguese if applicable)				
Summary of Product Characteristics/Patient Leaflet information				
Investigator's brochure				
GMP certificate for the site(s) producing the IMP(s)				
Certificate(s) of analysis of the IMP(s)				
Data Safety Monitoring Board charter and composition				
Proof of registration on PACTR or other primary accessible registry				
Synopsis (translation)				
Translated Protocol				
Translated ICF				
Signed Declaration by Sponsor				
Signed Declaration by the National Principal Investigator				
Active Clinical Trials insurance				
Study Budget				
Signed CVs for Regional or local Monitors – if applicable				
Signed joint financial declaration between the Sponsor and National PI				
Signed Declaration by each Investigator				
Signed CV for all site staff: Principal Investigator, Co-investigators, study coordinators, nurses				
GCP certificates for all investigators				
Signed declaration by the co-investigators and key staff participating in the clinical trial				
Proof of sponsor indemnification for investigators and trial site				
Proof of professional indemnity (Medical malpractice insurance to cover investigator's participation to the clinical trials)				
Workload forms for Principal and Co-Investigators				
Signed CVs for regional and local monitors at sites- if applicable				

+ Countries specifics requirements

Proposed timeline for AVAREF Clinical Trial Application
EXPEDITED Joint Review for filovirus candidate vaccine

(expected timelines : 30 working days)

Pre-submission meeting
30/04/2024
Virtual meeting to prepare joint-review and align on the timeline

Sponsor completes CTA submissions to Countries
(As soon as possible after the pre submission meeting)
30/04/2024

NRAs and ECs screen CTA
(3 days after CTA submission)
03/05/2024

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NRAs and ECs review CTA
(13 days after CTA screened)
23/05/2024
+1 day needed for AVAREF Secretariat facilitation step
24/05/2024

Sponsors prepare responses for reviewers and share them with AVAREF Secretariat
(CLOCK STOP suggested: *within* 5 days after the review)
31/05/2024
+1 day needed for AVAREF Secretariat to compile and share response to NRAs and ECs at least 3 days before the meeting
03/06/2024

Joint-review meeting (2/3 days)
A minimum of 14 working days should be considered between the submission completed and the joint review meeting
05-06/06/2024
Physical/Virtual meeting to conduct joint-review with sponsors, NRAs and ECs

Sponsors address unresolved questions
(CLOCK STOP suggested: within 5 days after the joint meeting)
13/06/2024
+1 day needed for AVAREF Secretariat facilitation step
14/06/2024

Post-review meeting
(As soon as possible after the AVAREF Secretariat addressed the Sponsor responses to the NARs and EC)
18/06/2024
Virtual meeting to answer questions unresolved during joint-review meeting

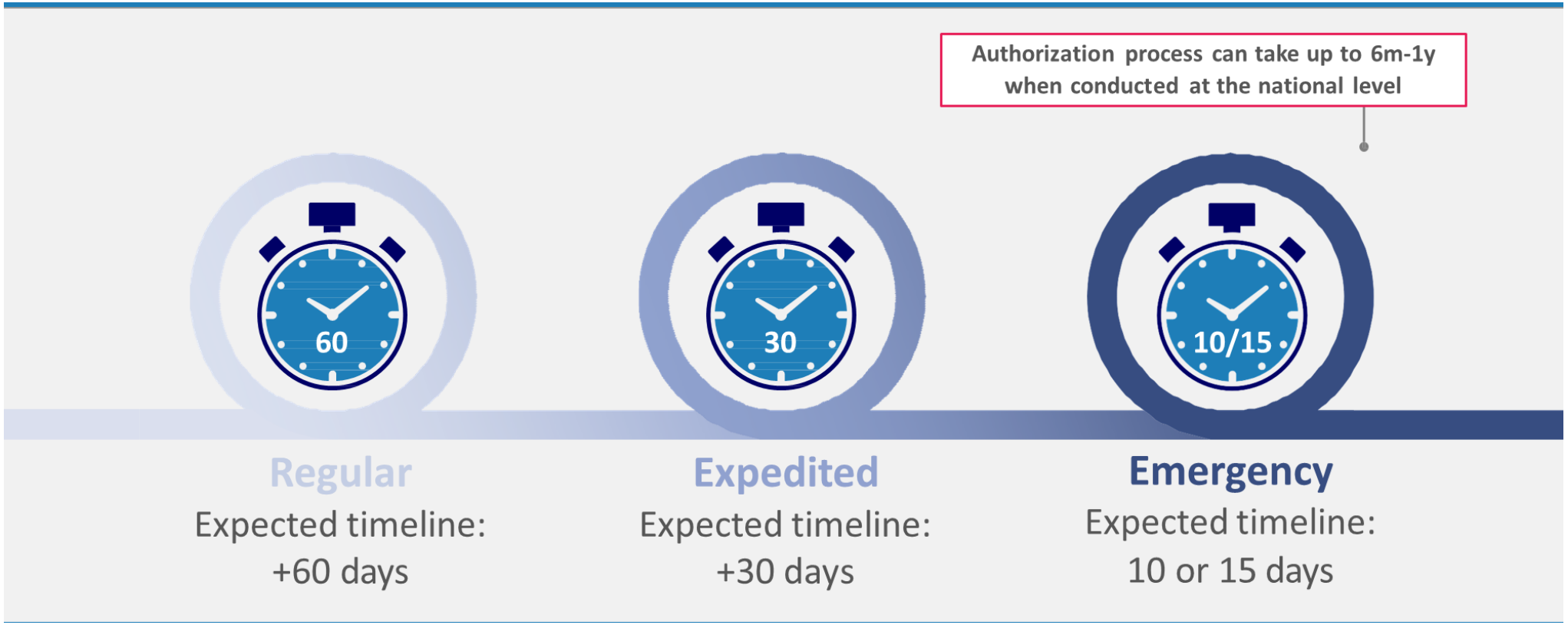
Countries deliver decision on CTA
(3 days after the post-review meeting)
21/06/2024

Joint-review finalised
A minimum of 10 business days should be considered between the joint review meeting and the joint review is finalized
21/06/2024

- Review to start using the uploaded document package.
- The CTA submissions to be made to countries according to local requirements.
- Focal Points will have access to the uploaded CTA immediately after country submissions are confirmed, or earlier if agreed upon during the pre-submission meeting

World Health Organization
REGIONAL OFFICE FOR Africa

Joint Review Procedures for Clinical Trial Applications



https://www.afro.who.int/sites/default/files/2020-05/9-Avaref_Joint_review_guideline_version2_Sept2019.pdf

African Vaccine Regulatory Forum (AVAREF) - Strategy and Guidance for Emergency Preparedness | WHO | Regional Office for Africa

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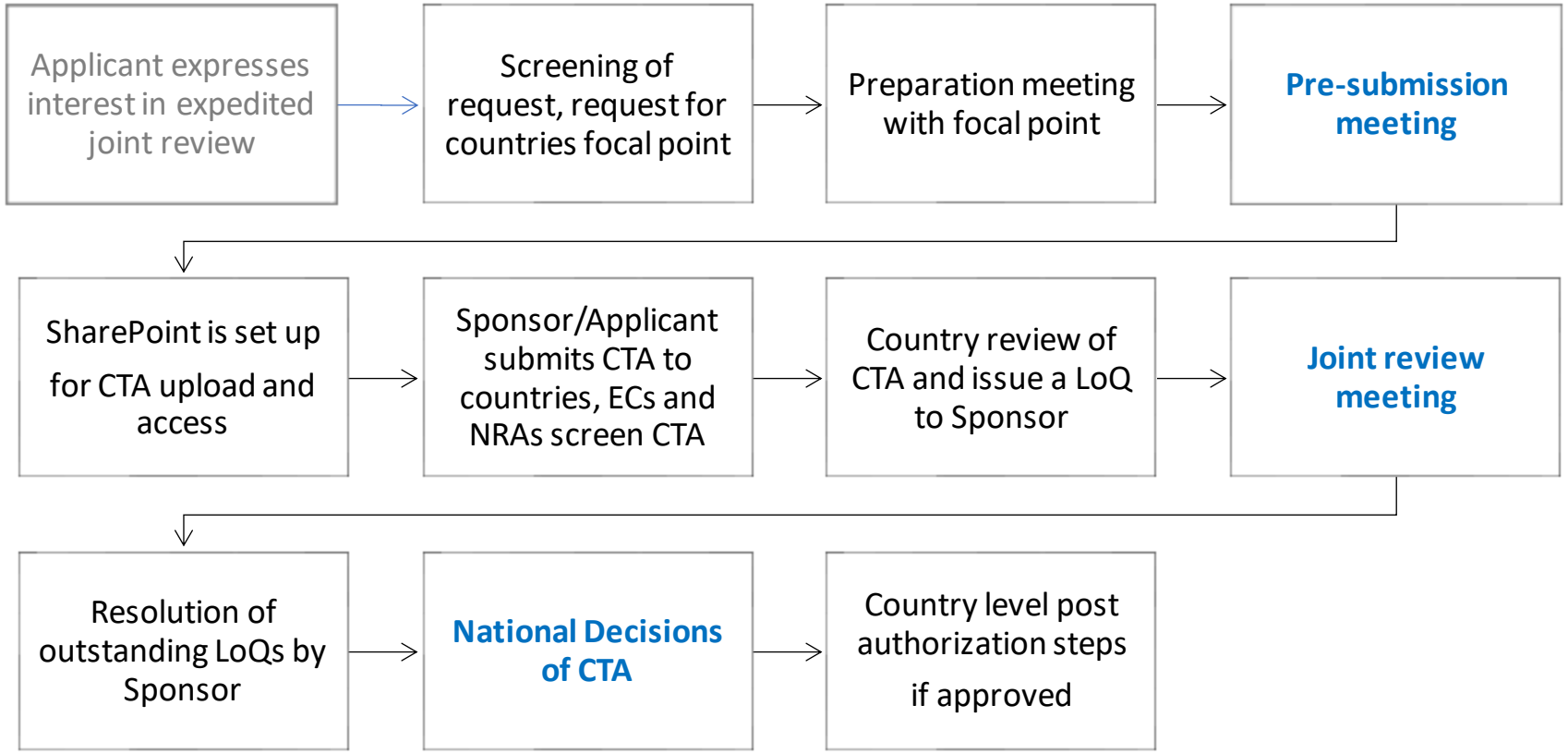
Principal Steps of AVAREF Joint Review Procedures



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