Ending disease in Africa

AVAREF's role in facilitating regulatory system strengthening in Africa

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Universal Health Coverage/Communicable and noncommunicable Diseases

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.

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

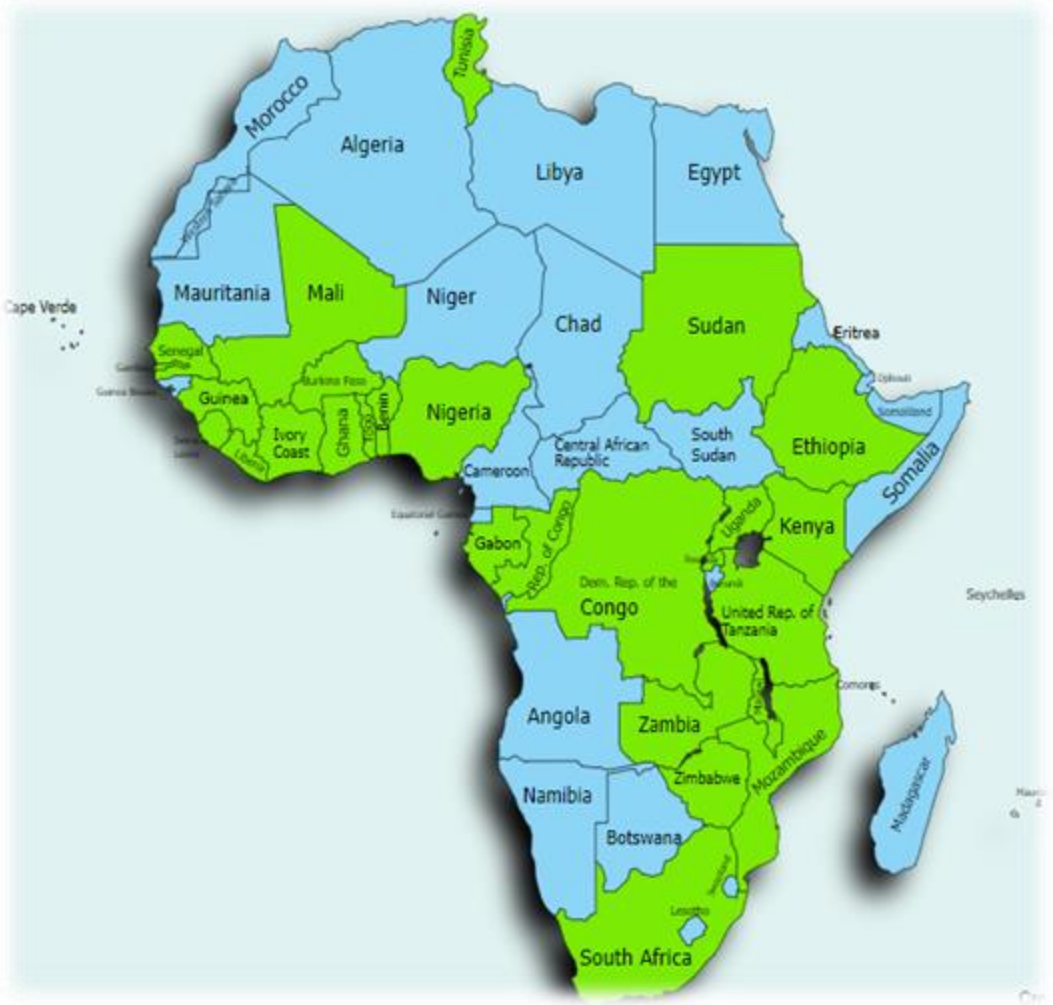
- Technical Committees for development of guidelines, check lists and guidance documents
- Advisory Committee setting workplans, adoption of developed guidelines and tools
- Adoption and implementation of AVAREF Tools and Guidelines

AVAREF Achievements

- Extensive contribution to regulatory harmonization through the development of tools and guidelines which have been adopted by over 26 member states
- AVAREF has supported authorization several multi-country clinical trial applications for neglected diseases such as Monkeypox, Lassa fever, and Rift Valley Fever
- AVAREF has used its platform in emergencies for the authorization of clinical trials as well as registration of products such as Ebola, Covid-19, Malaria vaccine, etc.
- Active calendar of events including regular webinars, country support, etc.

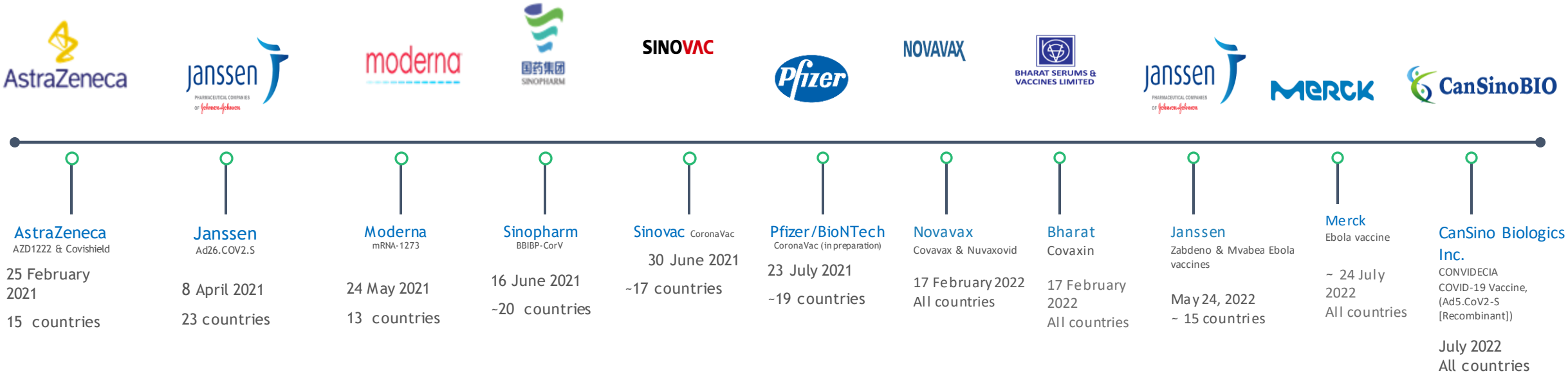
AVAREF Achievements

15 Multi-Country Joint Reviews between June 2020 to Dec 2023 in 26 countries



- Continental (trans REC)
- Capacity building initiatives
- Average country size = 6
- Maximum to date = 17 countries from 5 RECs
- Average days to decision = 10 days
- Well defined processes and perfected over last 16 years …

AVAREF Platform used to facilitate emergency registration of COVID-19 vaccines 2021-2022



AstraZeneca
AZD1222 & Covishield
25 February 2021
15 countries

Janssen
Ad26.COV2.S
8 April 2021
23 countries

Moderna
mRNA-1273
24 May 2021
13 countries

Sinopharm
BBIBP-CorV
16 June 2021
~20 countries

Sinovac CoronaVac
30 June 2021
~17 countries

Pfizer/BioNTech
CoronaVac (in preparation)
23 July 2021
~19 countries

Novavax
Covavax & Nuvaxovid
17 February 2022
All countries

Bharat
Covaxin
17 February 2022
All countries

Janssen
Zabdeno & Mvabea Ebola vaccines
May 24, 2022
~ 15 countries

Merck
Ebola vaccine
~ 24 July 2022
All countries

CanSino Biologics Inc.
CONVIDECIA
COVID-19 Vaccine, (Ad5.CoV2-S [Recombinant])
July 2022
All countries

AVAREF Facilitation of Clinical Trial Joint Reviews

- Joint-reviews and selected assisted reviews of clinical trials within Africa.

- AVAREF Secretariat convenes African NRAs & ECs and coordinates timely and efficient review of clinical trial applications.

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

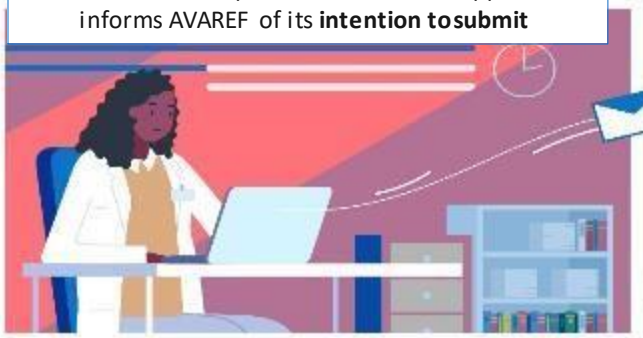
Benefits

- Scientific and ethical robustness of the collaborative review- the protection of human research participants
- Significant amount of time saved in undertaking reviews
- Knowledge and experience sharing among regulators as well as ECs
- Use of standardized formats

Joint-Review process of clinical trial application (1/2)

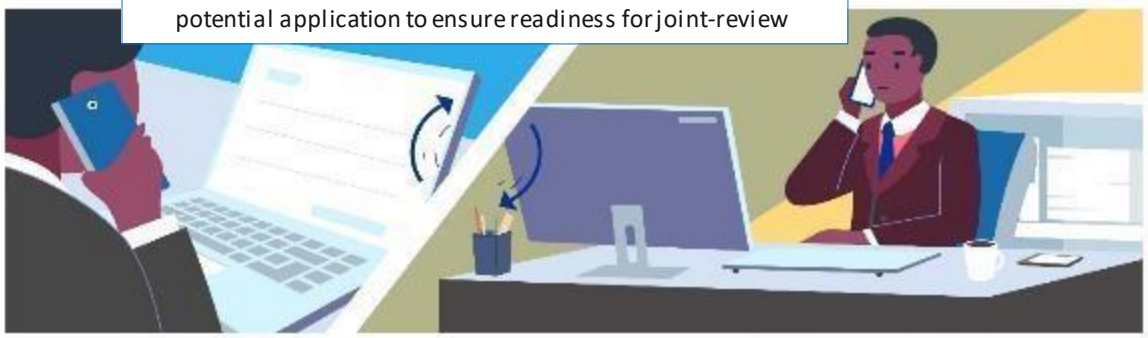
Intention to submit

At least 2 weeks prior to submission, applicant informs AVAREF of its **intention to submit**



AVAREF notifies the applicant about **submission requirements** for national authorities of potential target countries

AVAREF **notifies national stakeholders** (NRA and EC) about potential application to ensure readiness for joint-review



Application

Applicant **submits application** for emergency joint-review to AVAREF

AVAREF **promptly screens application** the same day

All stakeholders are **notified about successful screening**, national stakeholders are prompted to indicate their willingness to participate

Pre-submission meeting

Countries **confirm their participation** in the joint-review

During the pre-submission meeting, applicant share application key info, stakeholders **agree on responsibilities and on submission requirements** and the **joint-review timeline is finalised**

Joint-Review process of clinical trial application (2/2) with emergency joint review timelines

Country screening and review (4 days)

DAY 0

Applicant submits **application to national stakeholders** following country-specific guidelines – clock starts once the application is submitted to every target country

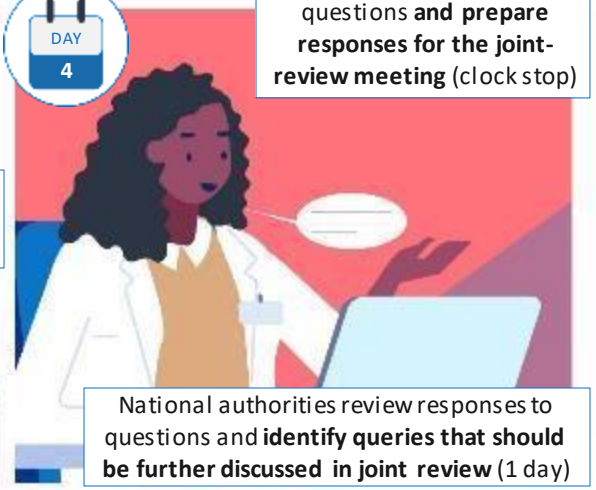
DAY 1-3

After **screening application** to ensure completeness (1 day)…

…all national stakeholders **review the application** and upload their questions to the applicant on the platform (2 days)

DAY 4

Applicant reviews the list of questions **and prepare responses for the joint-review meeting** (clock stop)



National authorities review responses to questions and **identify queries that should be further discussed in joint review** (1 day)

Joint review (2 days)

DAY 5-6

During the **joint-review meeting**, national authorities and applicant discuss the application…

…with appointed **Discussants presenting LoQs** for allocated section and **applicant sharing its responses**

Resolution of questions (1 day)

DAY 7

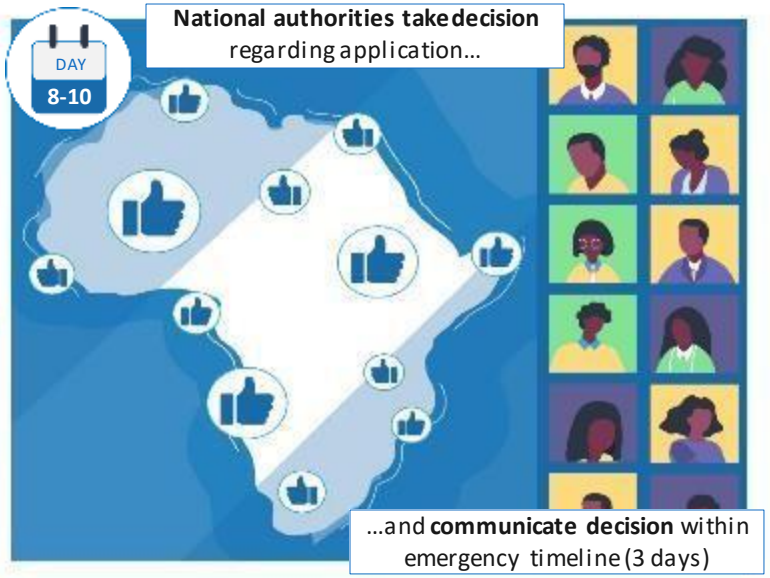
Should some questions remain unanswered, the **clock stops** and applicant indicates time required to **provide answers**…

…And all national stakeholders participate a **review finalisation meeting** (1 day)

National Authorization (3 days)

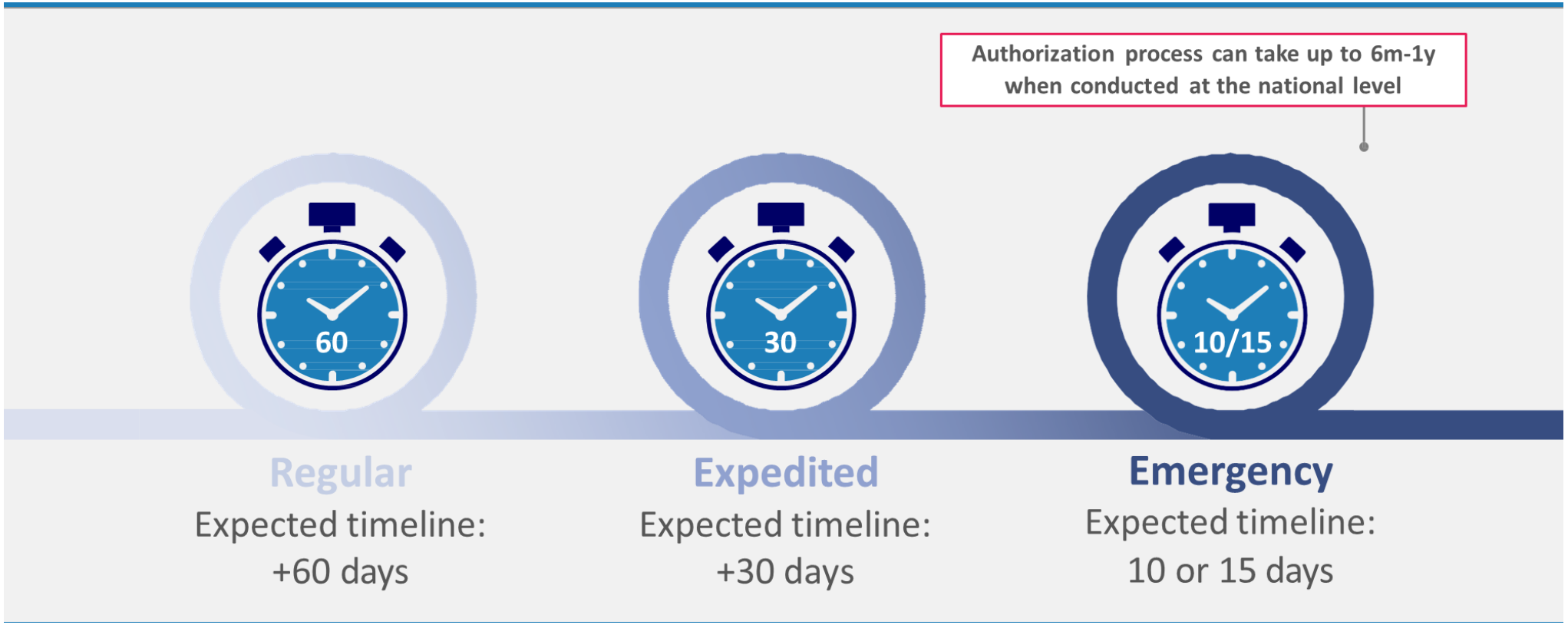
DAY 8-10

National authorities take decision regarding application…



…and **communicate decision** within emergency timeline (3 days)

Joint Review Procedures for Clinical Trial Applications

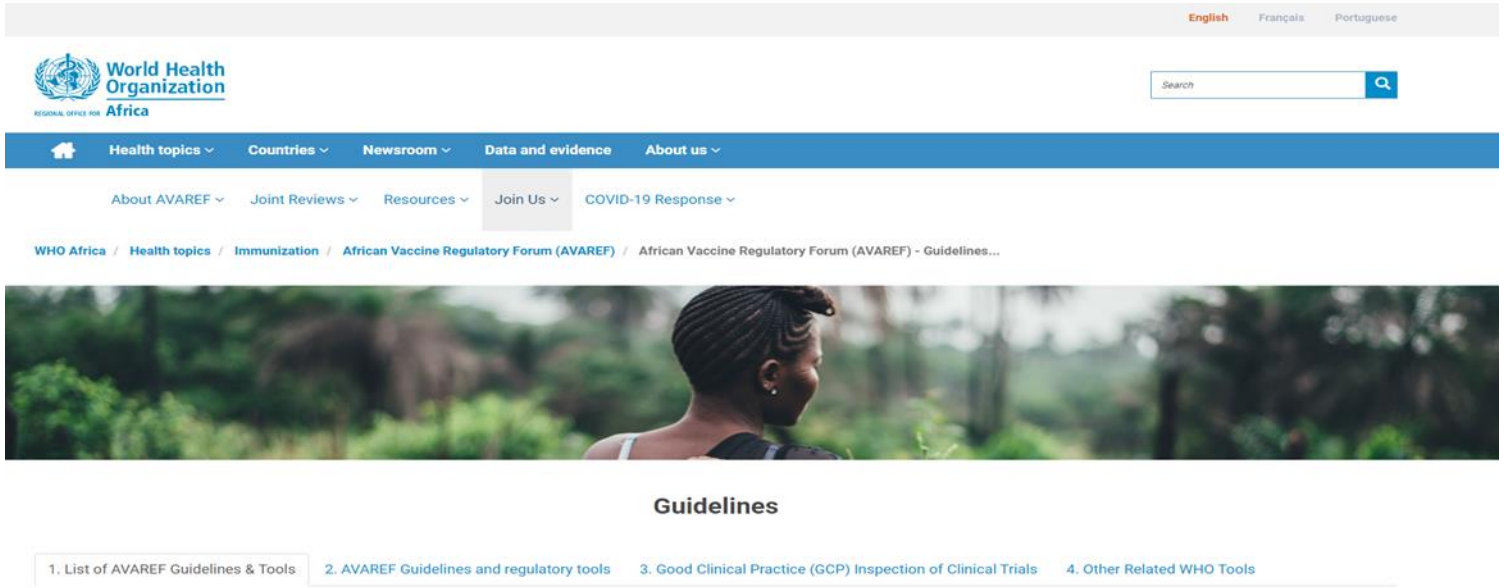


https://www.afro.who.int/sites/default/files/2020-05/9-Avaref_Joint_review_guideline_version2_Sept2019.pdf

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

AVAREF Guidance Documents and forms for joint reviews

AVAREF Tools for Review of Clinical Trial Applications



English | Français

Documents

Strategy and Guidance for Emergency Preparedness

1. Avaref Clinical trial application form checklist
2. Avaref Clinical trial application form
3. Avaref Clinical assessment template
4. Avaref Nonclinical assessment template
5. Avaref Quality assessment template
6. Avaref Statistical assessment template
7. Avaref GCP inspection checklist
8. Avaref GCP inspection guide
9. Avaref Joint review guideline

Final One-pager AVAREF regulatory tools

https://www.afro.who.int/health-topics/immunization/avaref/guidelines

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

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World Health Organization African Region

Other offerings

Ethics Committees training course

- Virtual training course for ethics committee members
- AVAREF GCP Inspections course, available in English, French and Portuguese, on OpenWHO
  - African Vaccines Regulatory Forum clinical trials inspections | (openwho.org)

AVAREF Webinars

Quarter	Date	Title/Topic TBC
1	22 February 2024	Descriptive Research Study of the Adverse Events Following Immunization (AEFIs) Surveillance System in Zimbabwe
	14 March 2024	PACTR +PAVM
2	16 April 2024	Webinar for Developers + DAC Informativeness tool
	23 May 2024	Post-market surveillance and the role of the regulator
	20 June 2024	LARISSA I and II
3	16 July 2024	Clinical Trials
	22 August 2024	Importance of Biostatistics : clinical trial data
	26 September 2024	Update on AU3S
4	17 October 2024	Controlled Human Infection Model
	21 November 2024	DAC Informativeness tool for NRAS and Ethicists

AVAREF Webinars are uploaded here: https://www.afro.who.int/health-topics/immunization/avaref/webinars

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THANK YOU