

20th DCVMN Annual General Meeting
21 - 23 October 2019, Rio de Janeiro, Brazil

AVAREF progress in clinical trial review, reporting standards and status of convergence for vaccine registration

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World Health
Organization

Background

- AVAREF was established in 2006 as a network of African NRAs and Ethics Committees to build capacity and to promote harmonized practices
- The regulatory environment has since evolved significantly: there are more CTs, complex products, and trial designs
- New ToRs were endorsed in 2016: new governance structure, expansion and alignment with AMRH
- Vaccine clinical trials against diseases with a high burden in Africa were authorized: meningococcal serogroup A meningitis, malaria, rotavirus, pneumococcal pneumonia, and Ebola virus
- Some of these vaccines are also licensed for use in the continent
- Diversification to other types of medical products, safety and vaccine registration

Statutory meetings



5TH MEETING OF THE TECHNICAL COORDINATING COMMITTEE AND STEERING COMMITTEE OF THE AFRICAN VACCINE REGULATORY FORUM (AVAREF)
ENTEBBE-UGANDA 24TH - 28TH SEPTEMBER, 2018



5TH MEETING OF STEERING COMMITTEE OF THE AFRICAN VACCINE REGULATORY FORUM (AVAREF)
ENTEBBE-UGANDA 24TH - 28TH SEPTEMBER, 2018



Statutory meetings of the governing bodies, the TCC and SC, were regularly convened in Feb and Sep 2018, and Feb and July 2019

Development and piloting of guidelines and harmonized tools

- <https://www.afro.who.int/publications/avaref-tools>
- Guideline for joint and assisted review of CTAs provides guidance to NRAs, ECs, trial sponsors and their investigators on a joint review model in Africa
- CTA form for the sponsors
- CTA checklist for the sponsors and NRAs
- Templates for assessors to evaluate the quality, i.e. chemistry manufacturing and control (CMC), nonclinical, biostatistical, and clinical aspects of a CTA
- GCP inspection guide and checklist for NRAs

CLINICAL TRIAL APPLICATION FORM
African Vaccine Regulatory Forum (AVAREF)

Clinical trial application form

Trial's full title	
Short title	
Protocol No.	
Version No.	
Investigational medical product	
Sponsor	
Contact person	
Address	
Telephone No.	
Fax No.	
Cell No.	
E-mail address	
Date of application	

Harmonized Clinical
Trial Application
Form

African Vaccine Regulatory Forum (AVAREF)

QUALITY ASSESSMENT

Study's full title	
Short title	
Protocol No.	
Version No.	
Investigational medical product	
Date of the review	
Reviewer's name	

Reviewers Guide –
Quality (CMC)

Reviewers Guide –
Clinical

& Non-Clinical

African Vaccine Regulatory Forum (AVAREF)

CLINICAL ASSESSMENT

Study's full title	
Short title	
Protocol No.	
Version No.	
Investigational medical product	
Date of the review	
Reviewer's name	

African Vaccine Regulatory Forum (AVAREF)

NON-CLINICAL ASSESSMENT

Study's full title	
Short title	
Protocol No.	
Version No.	
Investigational medical product	
Date of the review	
Reviewer's name	



GCP INSPECTION GUIDE & CHECKLIST

AVAREF

GUIDE FOR THE INSPECTION OF CLINICAL TRIALS

DRAFT FOR COMMENTS

Working documents will be sent out electronically only

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AVAREF

CHECKLIST FOR THE INSPECTION OF CLINICAL TRIALS

DRAFT FOR COMMENTS

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Domestication Efforts

Sep 2018

Endorsement of the tools by AVAREF SC

Feb 2019

Domestication workshop for the ECOWAS countries

May 2019

Domestication workshops for the SADC/EAC countries

June 2019

GCP inspection guide and checklist piloted in Ethiopia

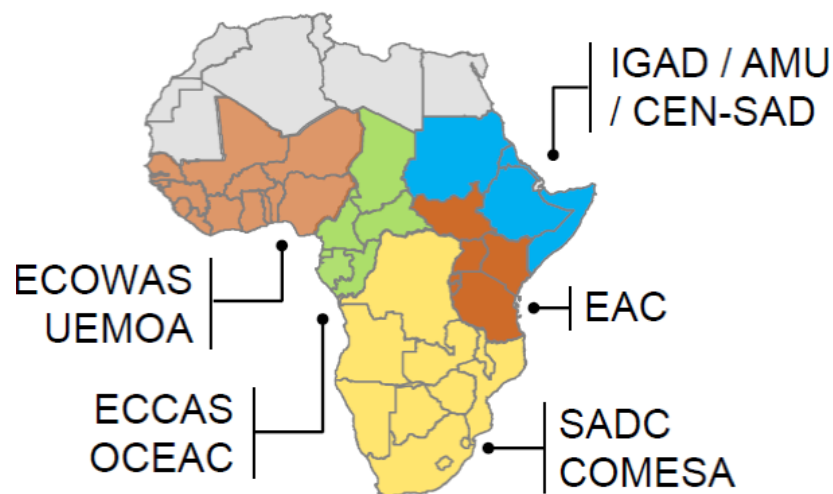
July 2019

Endorsement of the revised joint review guideline by AVAREF SC

Use of the tools by NRAs (Ghana, Kenya, Zambia, Nigeria, Uganda, South Africa, etc.)

Workshops to domesticate the adopted regulatory tools

- Purpose: To discuss the documents and to define a strategy to incorporate these tools into the countries' regulatory environment
- Ensure full implementation and domestication of the harmonized documents to entrench uniform processes in the jurisdictions of the Member States



Domestication workshop for ECOWAS

- ECOWAS/WAHO: 25 to 27 February 2019



Domestication workshop for the Southern African Development Community

Johannesburg 14 to 16 May 2019



Workshop on domestication of the African Vaccine Regulatory Forum (AVAREF) guidelines and tools for SADC Member States

Southern Sun OR Tambo, Johannesburg, South Africa,
14 May - 16 May, 2019



Domestication workshop for the East African Community

Johannesburg, 20 to 22 May 2019



Joint reviews

- RTS,S in Feb. 2018; reviewers from Ghana, Kenya, and Malawi
- Candidate to treat visceral leishmaniasis (DNDi), in Addis Ababa, Ethiopia in August 2018; NRAs and ECs of Ethiopia, Kenya, Uganda, and Sudan
- Candidate rotavirus vaccine (PATH) in Addis Ababa, Ethiopia in April 2019; reviewers from Ghana, Zambia, and Malawi
- TB vaccine trial is planned
- Common electronic platform – DataCol – used for the joint reviews improved efficiency of the review process

CT review times

- Monitoring of CT review and approval timelines
- Web data collection tool being developed to allow countries to provide information on real time to track the progress with regard to timelines for clinical trials review and authorization
 - Conducted with the support of CEPI/University of Applied Sciences & Arts Hanover
 - Easier way to obtain and analyze the data
 - Goal: To enable NRAs and ECs to store study data and to prompt upcoming timelines via a reminder function

Convergence for vaccine registration

Registration of the Merck Ebola Vaccine

- In February 2019, the SC agreed to a WHO-facilitated review process, in parallel to the EMA review process, to accelerate the registration decision
- Development and implementation of a roadmap for African countries' registration for Merck's Ebola Virus Disease (EVD) vaccine
- The roadmap explains the process and steps is available on WHO's website: <https://www.who.int/medicines/en/>
- WHO meeting to facilitate registration of rVSV-ZEBOV EVD Vaccine in Kigali, Rwanda in July 2019

Janssen EVD Vaccine

- Is at the EMA pre-submission stage. The procedure is expected to start in November 2019
- The company requested WHO and AVAREF to be observers in the assessment process
- WHO will prepare and share a roadmap for the process
- AVAREF nominated country representatives/experts to participate in the EMA assessment
- Involvement of African regulators of potentially affected countries in the review of the J&J vaccine

Regulatory pathway for Malaria vaccine

- Plan for regulatory support to countries in relation to RTS,S vaccine implementation pilot
- Joint regulatory review by the NRAs of Ghana, Kenya and Malawi, convened under the AVAREF on 28 Feb. 18
- Assessment for issuance of a special authorization for use in MVIP and regulatory oversight of the RTS,S vaccine
- Regulatory approvals granted in April and May 2018

VACCINE SAFETY - Establishment of an AACVS

An African Advisory Committee on Vaccine Safety (AACVS)
established

Mandate

- To provide independent expert advice on technical issues related to the safety, effectiveness and use of approved and new vaccines

Conclusion

- AVAREF has served as vector of cooperation and harmonization mechanisms and procedures between countries, NRAs and ECs.
- AVAREF activities have contributed to strengthen:
 - capacity of NRAs and ECs,
 - regulation of clinical trials, approval, registration, and timelines.
- The adoption of the new tools by African NRAs and ECs will promote standardized CT applications and assessments.
- This will ultimately lead to the countries meeting AVAREF's timeline of 60 working days
- And improve the quality of reviews
- As a key player of product development in Africa, AVAREF is **'open for business'**



**World Health
Organization**

REGIONAL OFFICE FOR

Africa

Thank you !