AVAREF’s role in facilitating regulatory system strengthening in Africa

Chinwe Iwu-Jaja (PhD)
AVAREF
• Background
• Overview of AVAREF
• Objectives of AVAREF
• Joint review procedures for clinical trial applications
• Other offerings
• 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 lifecycle of products; clinical trials, GXP – 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**
  - AdA.COV2.S
  - 8 April 2021
  - 23 countries

- **Moderna**
  - mRNA-1273
  - 24 May 2021
  - 13 countries

- **Sinopharm**
  - SIIIF-CovV
  - 16 June 2021
  - 17 countries

- **Sinovac**
  - CoronaVac
  - 30 June 2021
  - 19 countries

- **Pfizer/BioNTech**
  - CoronaVac (Proposed)
  - 23 July 2021
  - 17 countries

- **Novavax**
  - Covavax & Novavix
  - 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.**
  - CONVODECIA
    - COVID-19 Vaccine, [Ad5-Cov2-S (Recombinant)]
    - July 2022
    - All countries
• 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.

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

**Pre-submission meeting**
Countries confirm their participation in the joint-review.

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

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

All stakeholders are notified about successful screening. National stakeholders are prompted to indicate their willingness to participate.

AVAREF promptly screens application the same day.

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

**Joint review (2 days)**
- 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)**
- 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)**
- National authorities review responses to questions and identify queries that should be further discussed in joint review (1 day).
- National authorities take decision regarding application.
- ...And communicate decision within emergency timeline (3 days).

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

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

**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).**

**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 Procedures for Clinical Trial Applications

Authorization process can take up to 6m-1y when conducted at the national level

**Regular**
Expected timeline: +60 days

**Expedited**
Expected timeline: +30 days

**Emergency**
Expected timeline: 10 or 15 days


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

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

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

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

Dr Kwasi Nyarko: nyarkok@who.int
Dr Chinwe Iwu-Jaja: iwujajac@who.int
THANK YOU