WORKING WITH COUNTRIES TO BRING NEW PRODUCTS TO MARKETS

THE ACHIEVEMENTS OF AVAREF & REGIONAL HARMONISATION
Outline

• **Introduction**
  – Global Product Development Challenges
  – Key Regulatory Challenges

• **AVAREF**
  – History

• **The New AVAREF**
  – Governance Structure
  – Role
  – Achievements

• **The Future**
  – PV
  – Vector control products

• **Conclusion**
Global Product Development Challenges

- **Growing public health needs and limited resources**, demand faster, cheaper, and better treatments and vaccines.

- **Progressively increasing regulatory requirements over time** → increasing trial size and length → multiple country trials → multiplicity of regulatory requirements

- **Duplication due to overlapping reviews and inspections** of clinical/ manufacturing sites for similar purposes.
Global Product Development challenges

- Significant and rising portion of R&D budgets is spent on differing regulatory requirements across countries for the same therapy directed to the same disease with no obvious added benefits.

- **Harmonization of procedures** and processes is as not fast as preferred.
Additionally in LMICs

• Lack of clarity of roles between regulatory authorities and ethics committees
• Disparate application requirements and processes
• Limited technical expertise and capacity within individual NRAs and Ethics Committees
• Lack of data on review timelines for applications
• Lack of data on approval timelines for applications and ethics reviews
AVAREF History and Achievements

Jan. '05: Network approach to regulation of clinical trials proposed at NRA workshop organized by WHO

2006: Joint reviews of CTAs, joint GCP inspection of phase II trial of Men. A. conjugate vaccine using model procedure

2005/2006: Dev. of model reg. procedures for countries to adapt/adopt

Sept. 06: Birth of AVAREF (Accra), managed by WHO-HQ/AFRO

2007: Joint reviews of CTAs

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2007-2014: Annual meetings with review of RTS,S, TB vaccines, and others

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2015: New AVAREF strategy developed

2015: New AVAREF strategy launched

2014/15: Joint reviews of CTAs for Ebola interventions

Global, regional standards, strategies and plans
Encourage Parallel Submissions to Improve Timelines

Dialogue Among NRAs and ECs to Establish Common Guidelines and Understanding of Responsibilities

Build/Strengthen Capacity

Held Joint Reviews

Reference RAs invited to support on Technical Issues

Monitor Performance And Generate Performance Data

AVAREF 2006-2016
Joint Review Model

- A system for ECs and NRAs of more than one country to meet and undertake a review of an application.
  
  ➢ To enhance quality of reviews and optimize review timelines

  - Also serves as an opportunity for knowledge and experience sharing among regulators
  - Promotes work and resource-sharing among NRAs and Ecs
  - Promotes good regulatory practices through strict adherence to timelines
  - the opportunity to establish early-on mechanisms for information sharing once the trials begin.

Clinical Trials/Registration/GCP Inspections
Process, Report & Agreement

 Agreement among the countries involved to use the model and also agreement by manufacturer to review of the application together,

 WHO AVAREF Secretariat facilitates the joint review

 Experts from the NRAs and ECs of other the countries invited to the meeting as experts to support the process

 The sponsor (and investigators if trial site specific) will provide answers to queries raised at the meeting

➢ At the end countries endorse timelines to provide final outcome or review additional submissions

➢ Sponsors endorse timelines to provide additional responses as required

➢ Outcome of review is according to country regulations within the agreed timelines
AVAREF has Changed

• 2006 - Informal network
  – Necessary for quick decision-making
  – Whipped up enthusiasm
  – Achieved results
  – Minimized delays implementation

• 2010 – Formalized Network
  – Heads of NRAs and chairs of ECs signed ToRs in 2010
  – Slow implementation
  – Changes in profile of participants

  ➢ 2016 - New AVAREF
    ➢ New model and governance
    ➢ Strategic Direction
    ➢ New TORs
AVAREF Governance - Revolutionized

ASSEMBLY

STEERING COMMITTEE

TECHNICAL COORDINATING COMMITTEE (TCC)

TECHNICAL WORKING GROUPS

Meeting of heads NRAs & ECs in Africa

Provides Leadership and Strategic Direction

Identify Technical Needs, Develop Guidelines, make recommendations

Support TCC

AVAREF Governance - Revolutionized

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Support TCC
• Arab Maghreb Union (UMA)
• SADC
• East African Community (EAC)
• Economic Community of Central African States (ECCAS)
• ECOWAS
• Intergovernmental Authority on Development (IGAD)

54 countries — 6(8) regions — 1 continent
BRING NEW PRODUCTS TO MARKETS.....

What Role can AVAREF Play?
Even before approval of one of the Trials [in Ghana]
7 Strategic Objectives [+ Key Performance Indicators]

1. Improve regulatory outcomes and access to priority *medical products* (address gaps build capacity, improve timelines)
2. Promote the safety of patients. (databases of valuable AEs from CT ➔ post market)
3. Accelerate the AMRH process. [promote harmonisation]
4. Stimulate innovation & research in Africa. (early engagement improves quality, transparency, predictability and timeliness of regulatory activities and the value of regulatory decisions)
5. Enhance emergency preparedness. (ready platform of NRA/ethics/reference NRAs)
6. Strengthen AVAREF’s capacity building role. (support from partners/early engagement)
7. Promote awareness, sustainability and monitoring of AVAREF (commitment and ownership)
Achievements

• Harmonized NRA / Ethics Committee Technical Guidelines and Requirements developed for CTAs
  – Adoption of ICH-E6 R2 for common GCP
  – Development of common GCP Guideline, Checklist and Tools
  – Clinical Trial Application Form
  – Clinical Trial Application Reviewer’s Document

• EUAL Procedure Adoption
  – Better understand and use as a procedure for approval during a public health emergency

• Performance
  – Timelines for review and approval have been dropping steadily since 2016
Achievements

Methodology

• **Simple data collection tool sent to the NRAs and ECs.**

• **All clinical trial applications (Medicines, vaccines) from January to December 2017.**

• **21 countries contributed to the data.**

• **In addition, Guinea and Guinea Bissau reported absence of CT application in 2017.**
Achievements

• Timeline for Ethics Committee’s Review **35.9 days** (42 days in 2016)
• Timeline for EC Approval **68.6 days** (77 days in 2016)
• Timeline for NRA Review **36.6 days** (53 days in 2016)
• Timeline for NRA Approval **87.3 days** (82 days in 2016)
• Timeline for CT authorisation **135 days** (127 days in 2016).

Adjusted timeline would be close to 90 days (135-47) estimated delay between EC approval and submission to NRA is 47 days)
Examples of Joint Reviews by AVAREF

- Conjugate meningitis A vaccine clinical trial - 2006
- RTS,S malaria vaccine clinical trial - 2008
- Expedited review of conjugate men A and registration, 2011
- Expedited review of inactivated polio vaccine and registration – 2012
- Joint reviews of Ebola vaccine clinical trial application in Geneva 2014, Tanzania 2015, Sierra Leone, Ghana, 2015
- Assisted review of CTA for medicine against eumycetoma in Sudan
- Medicine against visceral leishmaniasis 2017
- RTS,S Mosquirix 2018 (Ghana, Kenya, Malawi)
WAY FORWARD
Why focus on patient safety?

- Increased stringency and data requirements for clinical trials
- Complexity of products and non-traditional designs
  - Vaccines against Ebola
- Global public health demands
  - Short timelines for development
  - Lower costs of clinical trials
- Weak ethics and regulatory systems of LMICs
  - Inadequate technical capacity
  - Inadequate resources to monitor
Why Focus on Patient Safety

S.O.2 - Promote the safety of patients. (databases of valuable AEs from CT ➔ post market)

• The need to strengthen PV systems and data sharing post approval especially during public health emergencies and post approval of novel products

• Ensure follow up on ‘missing data’

• Data available to share valuable that is being collected during trials
Status of safety monitoring in the African Region

• Within the African Region an AEFI/national safety committees exist in some countries

• Many countries have made good progress. The % of countries reporting AEFI's has increased from 75% in 2012 to 86% in 2016 and is likely to sustain and improve in future

• Although its mandate doesn’t focus on monitoring of product safety AVAREF can play key role in this area given the importance of the safety considerations in almost all CT applications submitted to the platform
Proposed AVAREF Reporting System

- Focal points for safety in all 54 countries and in all RECs
- All AEs will be reported through the AVAREF system (To be set up)
- AVAREF Safety reporting system to be linked to the AMA system for all adverse events
- NRAs will have access through the AVAREF Clinical Trial Portal (yet to be set up)
- The TCC and SC will review safety data and advice NRAs
Conclusion

• Regulators have a role to play to scientifically fast-track drug development and make potential diagnostics, treatments and vaccines available

• AVAREF as a regional network has the structures and ideal linkages with partners that encourage collaboration and convergence, capacity strengthening and trust building among these Regulators in the Region

• This network can form the building blocks for introduction of new entities like vector control products

• There is the need to leverage this platform towards achieving Universal Health Coverage and the ultimate realisation of an AMA for the region
THANK YOU