Meeting Report

AVAREF Assembly, 29 November 2017, Accra, Ghana

November 2017

Contents

Executive summary

The Assembly of the African Vaccine Regulatory Forum (AVAREF) was held in Accra, Ghana on 29 November 2017. It brought together heads of National Regulatory Authorities, from ECOWAS, EAC, SADC and ECCAS and chairs of national ethics committees of countries of the African region. The meeting was also attended by key stakeholders from NEPAD Agency and partners from BMGF, USFDA, EDCTP, Paul-Ehrlich-Institut, and Telfer School of Management of University of Ottawa. The meeting was officially opened by Dr. Afisah Zakaria, Chief Director at the Ministry of Health of Ghana after welcome remarks by Dr. Owen Kaluwa, the World Health Organization Resident Representative for Ghana.

The AVAREF Assembly, which is the highest decision-making body of AVAREF endorsed several important documents, made key appointments to the two statutory bodies, the Steering Committee (SC) and the Technical Coordinating Committee (TCC) and made key decisions. The AVAREF Strategic plan 2018-2020 was endorsed together with a sustainability plan and an annual work-plan for 2018. The heads of NRAs and chairs of national ethics committees (EC)/directors of research of MoHs, also endorsed a timeline of 60 working days for the review and clearance of clinical trials, will publish the timeline and aim to achieve this target. The Assembly also unanimously elected its chair in the person of Wiltshire Johnson, head of the regulatory agency of Sierra Leone and endorsed its new chair of the Steering Committee, Ms. Mimi Darko, CEO of the Ghana Food and Drugs Authority. The Assembly also discussed the report of the AVAREF Tabletop Exercise on emergency preparedness for ethics and regulatory approvals of clinical trials during emergencies and made specific recommendations. In addition the Telfer School of Management of the University of Ottawa, Canada also presented a proposal developed with AVAREF for training of senior regulators. Finally the Assembly accorded the heads of NRAs and ECs the opportunity to review the status of timelines for review and clearance of CTAs in their countries and to consider how to improve of their performance.

While remarkably successful in convening to approve important guidelines and documents, there is an urgent need to fully domesticate the model for joint reviews, and timelines for clinical trial reviews and to work towards attainment of the targets that were set. Rigorous follow-up by the WHO secretariat, NEPAD Agency, the RECs as well as all stakeholders and partners will be needed to ensure that the countries meet these targets.

1. Background and objectives

Health is a fundamental right and access to medical products remains a centerpiece. To ensure access to products and to meet regional health priorities, product development will have to improve and the current slow pace of introduction of new products and poor access in Africa dealt with. Regulators and ethics committees have an important role to play in offering independent decisions which ensure this right to access is to products which meet quality, safety and efficacy requirements. In emergencies or disease outbreaks an additional burden is placed on them to accelerate product development and to access to products with potential benefit.

Recognition of the challenges confronting ethics and regulatory authorities and the need to utilize a network approach to strengthening ethics and regulatory oversight of clinical trials led to the establishment of AVAREF in 2006. The work of AVAREF is based on strengthening capacity through reliance and cooperation, while recognizing national ownership, leadership and transparency.

Working collectively and with the support of regulators from other regions and the WHO secretariat, the countries reviewed and approved clinical trials of a conjugate vaccine against epidemic meningococcal meningitis, which has played an important role in the elimination of epidemics of meningococcal A meningitis from the meningitis belt of Africa. Over the years AVAREF has played an unappalled role in addressing the needs of countries in clinical trial oversight, while evolving from an initial informal network to a formal one and later to a new AVAREF, with a renewed governance structure and modelled on the Regional Economic Communities (RECs) concept of the African Medicines Regulatory Harmonization (AMRH).

The new governance structure comprises a Steering Committee, a Technical Coordinating Committee, with Working Groups and an Assembly. As the strategic and policy decision-making body, the Steering Committee (SC) will develop through its Technical Coordinating Committee (TCC) and Working Groups, the key guidelines and documents required by AVAREF, review them and present them to the Assembly for endorsement and domestication. It was in this light and in fulfillment of the new AVAREF Terms of Reference that the AVAREF Assembly was held on 29th November 2017, in Accra, Ghana.

The objectives of the AVAREF Assembly were:

- To elect members of the statutory bodies, Assembly, SC and TCC.
- To adopt decisions related to AVAREF policy documents, strategies and plans, namely:
  (a) The Strategic plan for AVAREF, 2018-2020, and annual work-plan for 2018
  (b) Guideline for joint and assisted reviews of clinical trial applications;
  (c) Regulatory timelines for review of clinical trial applications;
  (d) Make recommendations on the AVAREF/Telfer School of Management proposal for training in leadership.
- Review the summary report of the AVREF tabletop exercise on ethics and regulatory readiness for R&D in emergencies and disease outbreaks, which was organized a day earlier.

2. Election of the chairs of the Assembly and the SC, and members of SC and TCC

It was noted that there are vacancies for the TCC and SC memberships from CENSAD, ECCAS, IGAD and UMA as per the AVAREF terms of reference. It was also noted that the former chair for the Steering Committee, Hudu Mogtari, was no longer the CEO of Ghana FDA, hence the need to appoint a new chair to replace him.

After closed discussions among the members in their respective RECs, followed by discussions in plenary the Assembly elected the following:

Chair of the Assembly

- Wiltshire Johnson, Registrar/CEO, Pharmacy Board of Sierra Leone

Steering Committee Members

COMESA

- Bernice Mwale, Director General , Zambia Medicines Regulatory Authority

CENSAD

- Yaya Coulibaly, Directeur, Direction de la Pharmacie et du Médicament, Mali

EAC

- Silo Hiiti, Director General, Tanzania Food and Drugs Authority (TFDA), Tanzania
- Simon Langat, EC, Director, MOH, Kenya

ECOWAS

- Mimi Darko, CEO, Ghana Food and Drugs Authority (Chair of the Steering Committee)
- Samba Cor Sarr, Comité National d'Ethique pour la Recherche en Santé (CNERS), Direction de la Planification, de la Recherche et des Statistiques/ Division de la Recherche

ECCAS

- Consuelo Ondotfua Mangue, Equatorial Guinea NRA
- Félicien Munday, Democratic Republic of Congo Ethics Committee (Vice Chair of the Steering Committee)

IGAD

- Denekew Yehulu Alemneh, Director General, ENHACA, Ethiopia
- Peter Aguek Kon Bak, Chair of South Sudan Ethics Committee

SADC

- Rassul Nala, Executive Secretariat of a national Bioethic committee, Mozambique (Vice Chair of the Assembly)
- Portia Nkambule, Medicines Control Council, South Africa

Technical Coordinating Committee Members

- Beno Yakubu Nyam, NAFDAC, Nigeria (Chair)
- Maminata Traore, Comité d'éthique, Burkina Faso;
- Eric Karikari-Boateng, Food & Drugs Authority, Ghana;
- Priscilla Nyambayo, Medicines Control Authority of Zimbabwe (MCAZ), Zimbabwe
- Damson Kathyola, Director, MOH, Malawi
- Edward Abwao, KPPB, Kenya;
- Winfred Badanga, NCS&T, Uganda
- Marie Claire Okomo Assoumou, Ethics Committee Cameroon
- Okouyi Ndakissa, NRA Gabon

3. Endorsement of the AVAREF Strategic plan 2018-2020

The strategic plan was developed by the SC through a working group and the TCC. The plan was reviewed by the TCC and SC in February 2017 and again in September 2017 at the two meetings of the two committees. It received the inputs of all stakeholders, CBER USFDA, PEI, EDCTP, NEPAD Agency and BMGF in between meetings and was revised by the secretariat on account of the comments and suggestions received. It was presented by the Assembly chair who traced its development and review process. He also highlighted the contents of the document and the value it adds to the work of AVAREF by charting the way towards achievement of the goals of the network. The document was discussed and endorsed by the Assembly.

The document was accompanied by a resolution, which was also endorsed. The strategic plan has seven directions, namely: i) Improve the efficiency of reviews, inspections and timelines for regulatory and ethics decisions for better outcomes and access to priority medical products; ii) Promote the safety of patients and products; iii) Accelerate the alignment with the AMRH initiative; iv) Stimulate innovation in ethics and regulatory work in Africa to improve access; v) Enhance emergency preparedness; vi) Strengthen AVAREF's capacity building role; vii) Promote awareness; build sustainability and institute monitoring and evaluation of the implementation of the strategic plan of AVAREF.

The strategic plan was accompanied by a work plan for 2018. It includes the following activities under seven components:

Establishment of a system for countries to report their CTA and EC review timelines:

- Undertake a baseline survey on NRA and EC review timelines in the African region;
- Submission of Data on clinical trial review times for 2018, and root cause analysis of the current CT review timelines by using qualitative data
- Track progress on CTA and EC review timelines

Promoting joint activities on clinical trials in the African region

- Implement the AVAREF joint review of CTAs Guideline
- Select products for joint review
- Convene at least two joint review meetings

Strengthening capacity of countries to align with AVAREF standards for CTA and EC review

- Revise guidelines and SOPs in RECs and countries to align with AVAREF standards

Strengthening Medical Products Safety and Vigilance in the African Region

- Strengthen capacity of the region in collecting, analysing and reporting safety and vigilance data for decision making and enforcement

Joint Good Clinical Practices Inspection

- Implement the AVAREF Guideline on Good Clinical Practices Inspection
- Convene at least one joint inspection of clinical trial

Continuation of the capacity building effort for the NRAs and ECs

- Develop and Implement joint Telfer School of Management AVAREF leadership program (ALP)

Convening AVAREF statutory meetings

- Convening the fourth meetings of the TCC and SC.

4. Endorsement of the Guideline for joint and assisted reviews of clinical trial applications

The Guideline for joint review has been used for several years now, starting with the joint review of the clinical trial application of MenAfrivac in 2006. The guideline was also used during the outbreak of Ebola virus disease for clinical trial applications of vaccines against the disease, proving very effective in expediting review and clearance of clinical trial applications. Subsequently it was piloted on two other occasions in joint reviews, involving two RECs, EAC and IGAD. The comments and suggestions from these joint reviews were incorporated into the document and final version with the addendums was presented to the Assembly. Consequently, members of the Assembly unanimously endorsed the guideline.

There were discussions on how to ensure the full domestication of the guidelines. In this regard, the guidelines will also require revisions as they are used in different settings by different countries, RECs and across RECs. The adaptation will ensure that the guidelines conform to the existing arrangements within different RECs.

The guideline covers:

- Purpose
- Scope
- Definitions
- Pre-requisites for Joint Review
- Criteria for joint review
- Joint review process
- Process Steps
- Post-approval collaboration by participating countries

- Amendments
- Implementation of joint review

The document provides guidance to NRAs, ECs, trial sponsors and their investigators on a joint review model for submission and review of CTAs in Africa. It addresses the criteria for triggering a joint review using the AVAREF platform, the key participants and their respective roles, as well as the steps and expected outcomes from the joint review process. The model for joint review has a potential for adoption and use by other regions of the world.

The guideline was accompanied by a resolution, which has been also endorsed.

5. Endorsement of 60 working days ethics and regulatory timelines for review of clinical trial applications

Data on clinical trial review timelines was presented by the secretariat of AVAREF.

Recognizing that comprehensive information is needed about the CT reviews and approval from both the NRAs and ECs, the Assembly encourages and advocates for parallel submissions of the CT applications to the ECs and NRAs for all countries, to reduce the timelines. The Assembly endorsed 60 working days timeline for completing reviews and communicating of outcomes of clinical trial applications. The timeline should be published by all countries and adhered to.

6. AVAREF leadership development program

At the Health Canada Regulatory Forum co-organized with the Paul Ehrlich-Institut, the federal vaccine and biomedicine institute of Germany, in 2016, a side-meeting was held with selected heads of agencies and chairs of national ethics committees from the African region who were at the meeting. Discussions were held on how to improve management at the highest level of these institutions, mould the values and excellence of AVAREF into the institutions and ensure that quality of work and efficiency improves. A recommendation was made by the SC at its meeting in February to constitute a SC/TCC/Telfer Working Group to develop a proposal to this effect. The working group discussed over several teleconferences convened by the secretariat and came up with a proposal. The proposal was reviewed by the TCC and endorsed by the SC, to be presented to the Assembly.

The Assembly deliberated on the proposal and is supportive of its implementation and encourages the secretariat to look for funding and running of the project, initially as a pilot.

The design of the leadership development program envisages a short online orientation followed by three in-class modules of 4-5 days' duration, interspersed with online group learning sessions and post-program self-coaching opportunities, also online. It would be delivered over a 10-month period, just before or after regular meetings of the SC, TCC or Assembly to minimize travel costs and other logistics.

Options for identifying the funding possibilities for the leadership program were discussed since WHO does not have funding for this and will also be looking for possible sponsors. These options include the following: (i) Invite NRAs, ECs and Regional Economic Communities

(RECs) to use funds already approved for various programs or projects to fund their participation. This is particularly appropriate for those who have identified training as part of their project plan. (ii) Invite NRAs, ECs and RECs to request both tuition fees and travel expenses for the leadership program in any new project requests being submitted. This could be supported and coordinated with the AVAREF Secretariat.

7. AVAREF table top exercise on regulatory preparedness for public health emergencies

On 26 November 2017, a day prior to the commencement of the regulators scientific conference, an AVAREF table top exercise on regulatory preparedness for public health emergencies was held with national regulatory authorities and ethics committees from 10 countries.

The exercise was organized by WHO and the African Union's New Partnership for Africa's Development (NEPAD) with the support of the Coalition for Epidemic Preparedness Innovations (CEPI) and involvement of other partners including the European and Developing Countries Clinical Trials Partnership (EDCTP), the Bill and Melinda Gates Foundation (BMGF), CBER FDA, and the Paul-Ehrlich-Institut. Summary of the table top exercise was presented to the Assembly by member of the SC, Portia Nkambule of SADC.

The exercise consisted of a case study using MERSCoV as a pathogen against which a vaccine and a diagnostic are being developed and for which clinical trials need to be accelerated and requiring expedited review, using the AVAREF joint review guideline. Working in two groups the participants pressure-tested the joint review model by addressing a set of key questions. One set of questions focused on the use of the joint review model, while the second set of questions addressed broader issues associated with ethics and regulatory preparedness for a public health emergency, including post-review authorizations for importation and use of the candidate product, community engagement, communication and other considerations. The discussions were very good bringing in the experiences of Guinea, Liberia and Sierra Leone, countries which were affected by Ebola and undertook clinical trials of vaccines, therapies and diagnostics. Several recommendations were made on how to make the AVAREF joint review fit for purpose in emergencies and how to address other related issues to support product development in outbreak situations. Led by a consultant, Dr. David Wood, former head of Technology, Standards and Norms at WHO HQ, Members of the Assembly discussed the report. They recognized the importance of AVAREF and the joint review guideline in accelerating clinical trial approvals in outbreaks and emergency.

The AVAREF joint review guideline was validated as fit for purpose as a result of the exercise.

A series of recommendations were made to AVAREF on further improvements to the Guideline and the broader issues identified by the group to make it better suited for use in emergencies and outbreak situations.

8. Resolutions of the AVAREF Assembly

The Assembly carefully reviewed the documents developed by the TCC and the SC and adopted the following resolutions:

Resolution 1 of the AVAREF Assembly

THE ASSEMBLY OF THE AFRICAN VACCINE REGULATORY FORUM (AVAREF) ASSEMBLY

AVAREF 1/R1

29 November 2017, Accra, Ghana

RESOLUTION

THE AVAREF STRATEGIC PLAN FOR NATIONAL REGULATORY AUTHORITIES (NRAs) AND NATIONAL ETHICS COMMITTEES (ECs), 2018 - 2020

(Document AVAREF/1/1)

The AVAREF Assembly,

Recalling that the regulatory and product development landscape in Africa has evolved substantially since the launch of AVAREF in 2006;

Recognizing that the past decade has also witnessed an increase in the sophistication of trials and the number and complexity of products undergoing clinical trials for diseases endemic to Africa for which no prior knowledge and evidence base exist in high income countries;

Having identified the urgent need for a regulatory platform for promoting human resource capacity, best practices, common technical requirements and the efficiency and transparency of the regulatory process, especially in acute times or crisis;

Recalling also the launch of the East Africa Community Medicines Regulatory Harmonization (EAC MRH) Project in March 2012 as an important initiative predicated on the principles of regional harmonization, work-sharing and reliance;

Acknowledging the endorsement by all Member States of the WHO Region of the document on status of reviews and authorization of clinical trial applications in the African region at the 67th Regional Committee meeting;

Having reviewed the progress they have made and identified their needs;

Concerned that the timelines for reviews and approvals of clinical trials and registration of medical products still remain too long;

1. APPROVES the AVAREF Strategic Plan 2018 -2020;

2. URGES NRAs and ECs to:

(a) increase the efficiency and quality of reviews and inspections and the timeliness and transparency of regulatory decisions for all interventional trials conducted in Africa;

(b) promote the safety of patients, through pharmacovigilance systems and regular reporting, investigations and communication;

(c) enhance emergency preparedness on the continent, in RECs and in individual countries

(d) stimulate innovation in ethics and regulatory work in Africa to improve access

3. REQUESTS the WHO AVAREF Secretariat, the AVAREF members and partners to:

(a) strengthen AVAREF's capacity building role;

(b) advocate for and promote awareness, sustainability and monitoring of AVAREF;

(c) foster continued collaboration between international and multilateral agencies, donor organizations and national Ethics Committees and NRAs;

(d) enhance the capacity of Member States to ensure the safety and timely conduct of clinical trials, report on timelines;

(e) continue monitoring the implementation of the strategic plan;

(f) report to the Assembly on the progress made.

Resolution 2 of the AVAREF Assembly

THE ASSEMBLY OF THE AFRICAN VACCINE REGULATORY FORUM (AVAREF)

AVAREF 2/R2/2017

29 November 2017, Accra, Ghana

RESOLUTION

THE AVAREF GUIDELINE FOR JOINT AND ASSISTED REVIEWS OF CLINICAL TRIAL APPLICATIONS FOR NATIONAL REGULATORY AUTHORITIES (NRAs) AND ETHICS COMMITTEES (ECs)

(Document AVAREF/3/3/2017)

The AVAREF Assembly,

Recalling that the regulatory and product development landscape in Africa has evolved substantially since the launch of AVAREF in 2006;

Recognizing also that clinical trial applications are often submitted to more than one country and across more than one Regional Economic Community (RECs);

Acknowledging that over the years clinical trials have become sophisticated and the number and complexity of products have increased;

Having also identified the need to promote the sharing of best practices, joint reviews by ECs and NRAs, to optimize timelines for regulatory and ethics processes related to clinical trials and to accelerate R&D;

Concerned that the different processes and timelines of individual countries and RECs for approval of clinical trials may impact negatively on access;

1. APPROVES the AVAREF format, timelines for clinical trial reviews and approvals and Guideline for joint and assisted reviews of clinical trial applications;

2. URGES ECs and NRAs to:

(a) participate in joint or assisted reviews according to the AVAREF joint and assisted review guideline when criteria for such reviews are met.

(b) ensure that agreed upon timelines for completing the scientific review of outstanding questions are respected and that timely decisions are made on the authorization of the trial.

(c) share information about submissions of CTAs and to increase the efficiency in the screening of clinical trial applications, scheduling of review meetings and communication of outcomes with timeliness and transparency;

(d) adopt and use the common format for clinical trial applications,;

(e) aim at completing reviews and communicating of outcomes for clinical trial applications within 60 working days;

(f) adopt a parallel review system of CTAs by NRAs and ECs, while at the same time promoting collaboration between the NRAs and ECs;

(g) publish timelines for clinical trial application processing on their websites;

(h) provide quarterly updates on the progress of implementation of the above to the WHO AVAREF secretariat.

3. REQUESTS the WHO AVAREF Secretariat, AVAREF members and partners to:

(a) strengthen the capacity of the AVAREF network and NRAs and ECs to review and authorize clinical trials;

(b) advocate for resources to support AVAREF to strengthen the capacities of the ECs and NRAs to realize the goal of meeting the 60 working days timeline;

(c) continue monitoring the implementation of the processes and CTA timelines;

(d) foster continued collaboration between international and regional agencies; donor organizations and ethics committees and NRAs;

(e) report to the Assembly on the progress made.

9. Conclusion

The chair reiterated that the good work done in developing guidelines and documents and making recommendations should be translated into the use of these documents to improve reviews and approvals and to meet the agreed timelines. He also thanked all Member States for their contributions.

The secretariat presented the proposed dates for the two SC committee meetings and the AVAREF Assembly for 2018. Member states were given one month to submit bids to host the

Assembly. Based on the most competitive in terms of meeting some local costs, a decision will be made and the venue and dates shared with Assembly.

The agreed next meetings are scheduled as follow:

- First Meetings of TCC and SC
    - TCC: 12 to 13 February 2018
    - SC: 15 to 16 February 2018
    - Venue: Maputo, Mozambique
- Second meetings of TCC and SC
    - TCC: 10 to 11 September 2018
    - SC: 13 to 14 September 2018
    - Venue: Brazzaville, Congo
- AVAREF Annual Assembly
    - 15 to 16 November 2018
    - Venue: TBD