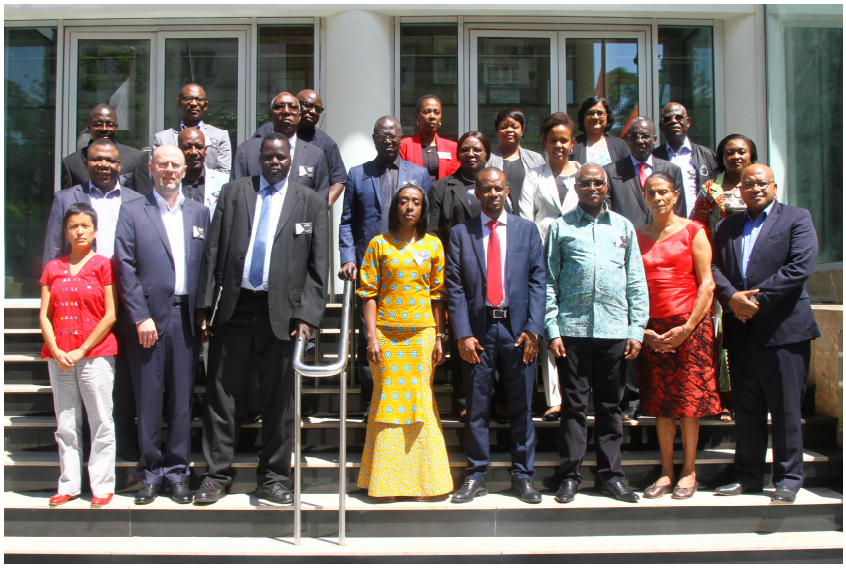
Meeting Report

4th AVAREF Technical Coordinating and Steering Committees Meetings

12 to 16 February 2018, Maputo, Mozambique

World Health Organization
REGIONAL OFFICE FOR Africa

BILL & MELINDA GATES foundation



February 2018

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Executive summary

African Vaccine Regulatory Forum (AVAREF) convened the 4th meetings of its Technical Coordinating and Steering committees in Maputo, Mozambique, from 12 to 16 February 2018. The two meetings took place back to back. The Technical Coordination Committee (TCC) met from 12 to 14 February, and the Steering Committee (SC) met on 15 and 16 February.

The objectives of the meetings were to follow-up the implementation of the endorsed documents and to initiate additional documents, including the following: to discuss implementation of the strategic plan and full domestication of AVAREF key guidelines and documents, to review the AVAREF draft GCP inspection guideline, to plan a GCP inspection, to discuss AVAREF capacity building plan and the leadership development programme.

The above topics were discussed both by the TCC and the SC and the following were agreed:

- Further dissemination by the Secretariat of outcomes and work products of the AVAREF TCC & SC meetings to the heads of NRAs, ECs and RECs secretariats and WHO country offices.
- Members of the TCC and SC should report to their respective RECs the outcomes and work products of AVAREF meetings. They should also report back on the status of implementation of AVAREF decisions during subsequent meetings. Furthermore the ToRs of these committees need to be revised to accommodate these responsibilities.
- Domestication and implementation of AVAREF guidelines and documents through RECs and to leverage AVAREF expertise to facilitate implementation at RECs if needed.
- Implementation of financial sustainability mechanisms identified by the TCC for AVAREF activities, such as countries funding participation of experts in joint assessment and inspections, AVAREF meetings and trainings and hosting meetings at NRAs/ECs facilities.
- To adopt the current ICH-E6 R2 guidelines (as last amended) and have the AVAREF GCP guideline as a reference to RECs.
- Requests the Secretariat to recruit a consultant to assist the working group finalize the GCP guideline and develop GCP inspection tools.
- Urge the TCC working group to revise the proposed tools, including addition of Investigational Medicinal Product dossier for phase I/II studies, drafting of a guidance template for the reviewers i.e. “Reviewers Guide document’ and include relevant guidance document in relevant sections e.g. ICH E6, E8. E9 and E 10, drafting of a template for ECs/IRB reviewers.
- Encourages the Secretariat to continue to seek funding opportunities for a three-day pilot program in September 2018 and for the full program for 2019 and beyond.
- To follow-up and implement proposals made by AVAREF partners as indicated in this report.
- The Secretariat to work with PEI for Implementation of the next steps of their Regulatory capacity strengthening in Africa projects.

1. Background and objectives

Since 2006, WHO has established and maintained the African Vaccine Regulatory Forum (AVAREF), a network of National Regulatory Authorities (NRAs) and Ethics Committees (ECs) of African countries as a platform to build their capacity and to promote harmonization of practices in support of oversight of clinical trials in the region.

AVAREF activities are governed by an Assembly of all Member States, the Steering Committee (SC) representing Regional Economic Communities (RECs), the Technical Coordinating Committee (TCC), also patterned to the RECs and the Secretariat.

The mandate of the SC is to define policies, strategies, and plans for AVAREF, and to oversee implementation by AVAREF members. The TCC is the technical and scientific advisory body of AVAREF, and advises the SC and ultimately the Assembly on all scientific and technical strategies, directions and priorities.

As per the AVAREF terms of reference, the SC and the TCC meet at least twice each year. Therefore the two meetings were convened in Maputo from 12 to 16 February 2018 fulfilling the requirements for two statutory meetings of the year for the two committees.

The previous meetings of the TCC and the SC and the Assembly adopted and endorsed key strategic documents and guidelines including the AVAREF Strategic plan, Guideline for joint review of clinical trial applications, regulatory timelines for review of clinical trial applications.

This 4th meeting was to follow-up the implementation of the endorsed documents and to initiate additional documents, including the following: to discuss implementation of the strategic plan and full domestication of AVAREF key guidelines and documents, to review the AVAREF draft GCP inspection guideline, to plan a GCP inspection, to discuss AVAREF capacity building plan AVAREF leadership programme.

The specific objectives of the meetings were to:

- Provide recent updates to the Members of the TCC and SC.
- Discuss the use of AVAREF documents (strategic plan, guidelines, and recommendations of the table top exercise on regulatory preparedness in case of public health emergency)
- Discuss the AVAREF GCP inspection guideline, a draft GCP inspection guide and planning of a joint GCP inspection in 2018
- Discuss a draft proposal of a pilot version of the Telfer/AVAREF leadership programme.
- Discuss timelines for review of clinical trial applications
- Discuss the AVAREF financial sustainability plan
- Discuss challenges for global registration of vaccines

2. Update from the Avaref Assembly

Dr Diadié Maïga updated the participants on the Assembly held in Accra, Ghana on 29 November 2017. The Assembly is the highest decision-making body of AVAREF. This was the first time an Assembly of all head of national regulatory authorities (NRAs) and national Ethics Committees (ECs) are meeting since a new governance structure has been adopted in 2016.

In addition to the heads of NRAs and chairs of national ECs from ECOWAS, EAC, SADC and ECCAS the Assembly 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.

Participants have been also updated on the new appointments made by the Assembly to the statutory bodies (TCC, SC and Chair of the Assembly) and key decisions, namely the endorsement of the AVAREF Strategic plan 2018-2020 together with a sustainability plan and an annual work-plan for 2018; endorsement of a 60 working days timeline for the review and decision on clinical trial applications (CTAs), promotion of parallel submissions of the CTAs to the ECs and NRAs for all countries to reduce the timelines, and specific recommendations on the report of the AVAREF Tabletop Exercise to test the AVAREF Guideline for Joint and Assisted Reviews of Clinical Trial Applications in case of public health emergency.

Participants welcomed the great achievements made with the endorsement of the documents and decisions made at the Assembly. They pointed the need for further country ownership, calling members of the TCC and SC to disseminate information within RECs after the AVAREF meeting since they represent their RECs at the meetings. Discussions also brought suggestions to have joint reviews by the ECs and NRAs where possible to address the problem of the turnaround time of 60 working days; and to consider signature of memorandum of understanding regarding sharing information between NRA and ECs within countries as well as among member countries.

3. Implementation and domestication of AVAREF documents

The objective of this session was to facilitate the use of AVAREF documents (strategic plan, guidelines, and recommendations of the table top exercise on regulatory preparedness in case of public health emergency) by NRAs and Ethics Committees. The session was introduced by the chair of a working group established for this end composed by the following as members: Dr. Beno Yakubu Nyam, NAFDAC, Nigeria, Chair of the TCC of AVAREF, Priscilla P Nyambayo, Medicines Control Authority of Zimbabwe, Dr Maminata Traoré, Institut de recherche en sciences de la santé, Burkina Faso and Prof. Ambrose Rachier, Chairperson KEMRI Ethics Committee, Kenya. The session aimed to produce a draft detailed activity plan for the domestication of AVAREF guidelines in countries and RECs as well as implementation plan of the recommendations made on the report of the table top exercise on regulatory preparedness in case of emergency.

According to the working group members the AVAREF guidelines and documents are important tools to facilitate the work of NRAs and ECs and therefore should be considered for domestication and implementation at both RECs and country levels as that will help in harmonising clinical trial activities within Africa.

The guidelines and documents that should be considered include, among others, AVAREF GCP Guideline, Joint and assisted review guidelines for CTAs, the strategic plan.

Participants agreed on the need to have RECs responsible for the implementation of the AVAREF guidelines, documents, tools, where there are challenges members of the TCC and SC as well as the Secretariat should provide assistance.

It was also highlighted that, in domesticating these important guidelines and documents, the TCC, SC, and the Secretariat must make sure the documents are made available to all the RECs and Heads of ECs and NRAs. Representatives of countries in the forum should seek the approval of their respective Governments in adopting and domesticating AVAREF's guidelines and documents within their countries. To further ensure the documents' domestication they must be robust and easy to use (as long and its scientific relevance is maintained) by all members. Also, publishing AVAREF activities, guidelines and other documents on the member countries websites should be encouraged to improve awareness and use in countries and RECs.

To put in place a monitoring scheme to guide countries on the use of some of these guidelines and documents.

Countries should be encouraged to document their experiences, comments and suggestions in the use of the documents as that will help during the revision of the documents.

The working group is encouraged to further develop strategies for full domestication of AVAREF documents in all RECs and countries.

4. Good Clinical Practice Guidelines

A working group constituted by Mrs Portia Nkambule, Medicines Control Council, South Africa (Chair of the WG), Prof. Lesly Burgess, Medicines Control Council, South Africa, Damson Kathyola, Director, MOH, Malawi, Elhadji Ibrahima Touré, Direction de la Pharmacie et du Médicament, Senegal and Mr. Kayode Isiaka Amuda, NAFDAC, Nigeria shared the summary of their discussion on the AVAREF GCP Guideline and for the development of an Inspection guide.

The objective of the session was to discuss the review of the harmonized Good Clinical Practice (GCP) Guideline for AVAREF countries based on the current WHO and ICH guidelines and other relevant documents. The second objective was to discuss drafting of a GCP inspection guide. This regulatory tool, when finalized and adopted, will become AVAREF harmonized standard for use by NRAs and Ethics Committees for conducting inspections, including joint inspection of clinical trials.

The previous AVAREF GCP guideline is dated August 2009. Since then, there have been a number of important updates to international declarations and guidelines, including Declaration of Helsinki (October 2013), Council for International Organizations of Medical Sciences (CIOMS 2016), ICH-GCP R2 guidelines (2016).

Many of these guidelines deal with crucial issues pertaining to developing countries, such as post trial access, use of placebo, ethical inclusion of potentially vulnerable participants and clinical trial insurance.

According to the working group and discussions held by the TCC and SC, the ICH-GCP remains the authoritative document. Therefore, a possible approach to revise the AVAREF GCP guidelines is to base them on ICH GCP R2 guidelines and add in additional required guidelines (those particularly relevant to developing countries with vulnerable populations). Thus investigators and sponsors only have to refer to a single set of guidelines to conduct GCP inspection.

The proposed format for the GCP Guideline is as follow:

1. ***Introduction***

Purpose and scope of guidelines

2. ***Protection of participants***

Expand on concept of vulnerable participants in the setting of a developing country – additional ethics oversight, community involvement, informed consent issues, insurance, post-trial access

3. ***Research ethics committees***

Responsibilities, composition, procedures – NB role and scope of local ethics committee in international research

4. ***Investigator***

Principal investigators in multinational clinical trials – especially when using international sponsors from first world countries

5. ***Sponsor***

International sponsors and CROs and need to conform to local requirements, trial management, reporting to local regulatory authority; management and reporting of safety information; role of registries and publication of results; return of results to participants

6. ***Clinical trial protocol and protocol amendments***
7. ***Investigators Brochure***
8. ***Essential documents***
9. ***Conflict of interest***

Appendices

I. Glossary of terms

II. Checklist

Decision was made by the participants to adopt the current ICH-E6 R2 guidelines and have the AVAREF GCP guideline that makes reference to the differences in the RECs plus including a clause that whenever these revisions changes the new guidelines have to be adopted;

Participants expressed the need to hire a consultant to assist the working group finalize the GCP Guideline and develop GCP Inspection tools (guideline, checklist).

The meeting also agreed on the following:

- GCP guidance should include the requirement of electronic records system generation e.g. CRF and they should provide access to verifiable source documents.
- For the proposed AVAREF GCP training in 2018, there was need to assess the GCP country capacity of AVAREF members and include those countries that required GCP

inspection. There was also need to include at least two GCP inspections if possible to target Anglophone and Francophone countries.

- To consider the various GCP inspection models e.g. Ghana GCP training pilot project by NEPAD, US-FDA –WHO GCP inspection train the trainer (TOT), SADC trainings etc.

5. Clinical trial working Tools

The objective of this session was to develop harmonized key tools to support clinical trial oversight by NRAs and ECs in countries, particularly countries that do not have enough capacity, resources or expertise. Members of the working group are comprised of Edward Abwao, Pharmacy and Poisons Board, Kenya (Chair of the WG), Eric Karikari-Boateng, Food & Drugs Authority, Ghana, Winfred Badanga, National Council For Science & Technology, Uganda, Dr Dorah Diale, Medicines Control Council, South Africa and Rassul Nalá, Executive Secretariat of a national Bioethics committee, Mozambique.

Drafts of the following clinical trial working tools have been proposed by the working group and reviewed by the TCC and SC (see annexes):

- Clinical Trial Application Form
- Clinical Trial Application Reviewer's document

It was agreed to revise the documents to include several things as follows:

- Add Investigation Medicinal Product (IMP) dossier for phase I/II studies should be included as a separate requirement 4.2 and current 4.2 numbering changed to 4.3 e.
- There was a need to draft a Guidance template for the reviewer i.e. "Reviewers Guide document' and include relevant guidance document in relevant sections e.g. ICH E6, E8. E9 and E 10 etc.
- Under checklist for completeness of application submission, to consider criteria on a "major", "critical" or "non-critical" requirements as per the EMA/ICH E6 definitions versus use of percentages.
- To draft a template for ECs/IRB reviewers and compare notes on the WHO/ European EC template.

6. AVAREF leadership development program: proposal for a Pilot Version of the Program

The purpose of this session was to discuss a draft proposal for a pilot version of the AVAREF leadership program. The full version of the leadership program was approved by the AVAREF Assembly held in Accra in November 2019. Considering financial constraints for implementation of the full version this pilot was tabled at the TCC and SC for discussion during this session.

The program is intended to meet the needs of Heads of the National Regulatory Authorities (NRAs) and Ethics Committees (ECs) who interact at the political level, as well as members of the Steering and Technical Coordinating committees, and key AVAREF partners.

It was presented by Glen Bailey from the Telfer School of Management, University of Ottawa.

Despite the progress made by the WG and the unanimous endorsement of the proposed program, source of funds has not yet been secured to enable the delivery of the full leadership program as it was proposed and endorsed by the AVAREF Assembly.

To enable continued progress towards the proposed vision for the program, it is proposed that a preliminary first step be considered for 2018. This first step would entail the design and delivery of a smaller-scale pilot version of the program. The funding required for a smaller pilot program would be significantly reduced relative to the funding that will be required for the full program and may enable AVAREF to bring on a funding partner on a progressive basis.

Accordingly, it was recommended to develop a pilot version of the program that can be delivered as a 'proof of concept' for both AVAREF committee members and possible funding agencies.

The draft outline of the proposed three day program is as follow:

Day 1: Collaboration Context

a. Drivers and barriers,
b. Implications,
c. Collaborative problem-solving and decision-making

Day 2: Personal Leadership

d. Self-awareness and capacity for reflection
e. inter-personal dynamics and managing conflict
f. capacity for reflection

Day 3: Leading Organizational Change

g. Building alignment around the vision
h. Mobilizing/motivating partners and teams
i. Developing influence

Upon deliberation, the TCC and SC made recommendations for the running of the project (see recommendations section).

7. Challenges for global registration of vaccines presented

This was presented via Skype by Dr Nora Dellepiane on behalf of Developing Countries Vaccine Manufacturers Network (DCVMN). She presented on the variations in the Common Technical Document (CTD) formats and impact on the timelines for registration of vaccines global study.

The preliminary results indicated some differences in the tool in terms of the content and format. However, only one country from Africa, Tanzania, was included in the study.

During the discussion, it was noted that although the study was a great welcome initiative, it only included one country from Africa, Tanzania hence there was not adequate data for Africa. It was reported and agreed that AMRH had already done some work in drafting a template for harmonized CTD template for Africa through RECs and that African countries should adopt that CTD format. It was noted however that Module 1 to Module 5 based on the ICH CTD format was the standard format to be adopted by AVAREF and AMRH although module 1 could be different based on the country administrative differences.

8. Timelines for review of clinical trials

Dr Diadié Maïga from WHO AFRO presented current timelines for clinical trials review based on data collected from participating countries (NRAs and ECs). All clinical trial applications of medicines and vaccines from January to December 2017 were included in the survey. Twenty one countries contributed to the data.

In summary, the calculated timelines (median times) from the data received are as follow:

- 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).

There was some improvement in the timelines for 2017 compared with 2016 although the NRA timelines were higher than ECs timelines. The presentation and analysis did not however account for the timelines to responses by researchers to queries raised by NRAs /ECs although the template had provision for such information. From the discussion it was recommended to consider all key factors that affect timelines for approval including the time researchers take to respond to queries raised by NRAs/ECs since it affects timelines for approvals and that there was already provision for inclusion of such data on the WHO clinical trial approval timeline template.

9. Financial sustainability of AVAREF

Mr. Hiiti Sillo from WHO HQ presented the AVAREF sustainability plan.

It was emphasized that there was serious need to consider practical funding options for AVAREF as recommended under funding models for the establishment of African Medicines Agency (AMA) for sustainability since donor and development partners funding will come to an end one day!

From the discussion, it was agreed that there was need to do country assessment for NRA & ECs funding mechanisms and assess what works and what doesn't and lessons to be learnt. There is also need to present proposal to all the development partners e.g. DFID, BMGF, UNICEF, WHO, EDCTP, Global Health PEI, etc.

It was noted that under the AVAREF terms of reference, roles and responsibilities of Head of agencies "…vii Include a budget line to support AVAREF activities at agency level, including travel to meetings." It was therefore agreed to make that recommendation to the SC of AVAREF. There is also need for NEPAD Agency to play the advocacy role to AU Heads of States to persuade them to invest and fund the AVAREF and AMRH/AMA activities.

10. FDA/CBER Perspective and Support for Regulatory Systems Strengthening

Dr Gopa Raychaudhuri on behalf of US FDA Center for Biologics Evaluation and Research (CBER) updated participants on their support to AVAREF, including considerations and approach to support RSS activities in Africa.

CBER activities supporting RSS in African Countries through CBER-WHO Cooperative Agreement (2016-2018) include benchmarking of NRAs develop IDPs and supporting its implementation; follow-up activities to address gaps, developing and piloting AVAREF guideline on joint GCP inspection, supporting development of guidance document (TCC Working Group; consultant), Pilot guideline by performing two joint GCP inspections in two African countries; and trainings to address gaps identified in benchmarking (including self-assessments).

Other activities supported via the cooperative agreement include pilot implementation of the "Coalition of Interested Partners" framework in IGAD countries and development of WHO guideline on Good Reliance Practices, support for RTS,S study in Ghana, Kenya and Malawi, support participation of regulators from LMICs in regional and global committees and networks, meetings, and workshops.

11. Paul-Ehrlich-Institut Partnership for Capacity building - Global Health Program of the German Ministry of Health

Dr Christoph Conrad and Juárez Hernández Marcela from Paul-Ehrlich-Institute (PEI) updated participants on the support of the Institut for the African region. This support includes contribution to the WHO NRA assessment, participation in the ECOWAS NRA self-assessment,

PEI-NEPAD-WHO joint workshop in regulatory capacity strengthening needs for Africa hosted at the Paul-Ehrlich-Institut, Langen Germany from 6 to 7 December 2017; a call for pilot partner countries for Regulatory capacity strengthening in Africa.

The PEI-NEPAD-WHO joint workshop was attended by representatives from African NRAs, NEPAD AMRH, WHO AFRO, WHO HQ, AVAREF, CBER FDA, Health Canada, and European Institutions.

African NRAs interested in strengthening their capacity with regards to the regulatory oversight of clinical trials for vaccines and biologicals, and the regulation of blood, blood components, and blood products responded to the call and submitted their application to the pilot regulatory capacity strengthening in Africa. Applications received are from ECOWAS, SADC, EAC, IGAD, COMESA and CENSAD. No application received from Central Africa but PEI is still hoping to get support from EDCTP to do training in Lambarene.

PEI is designing their program so that they can address all applications and finalizing selection with NEPAD and WHO by end of March 2018. To work under the paradigm of a system of reliance PEI is thinking about starting with ECOWAS or EAC. In the ECOWAS, having FDA Ghana established as an RCORE for registration and clinical trials, provides an opportunity to strengthen cooperation in the region by twinning an established NRA with younger NRAs (Liberia, Gambia, Sierra Leone). The other twinning possibility stems from the EAC region between Tanzania and Burundi.

Other planned and ongoing activities by PEI include merging of Blood Indicators into the WHO Global Benchmarking Tool (GBT); work with WHO RSS to bring the blood indicators into the merged GBT; Benchmarking of Blood Regulatory Systems in selected African countries; 10 countries (Ethiopia, Kenya, Liberia, Malawi, Nigeria, Uganda, Rwanda, South Africa, Tanzania and Zimbabwe), selected from *Call for Pilot Partner Countries,* benchmarking to start in 02/2018; WHO/AFRO Regional Training Workshop in Blood Regulation Douala, Cameroon (21^{st} – 23^{rd} March 2018) for African NRAs and National Blood Service (NBS) staff – Promoting the concept of a *Forum for Blood Regulator.*

12. Update from EDTCP

Dr Thomas Nyirenda updated the participants on European and Developing Countries Clinical Trials Partnership (EDTCP) activities.

The EDCTP2 Programme (2014-2024) was presented which includes call for proposal covering, among others, clinical trials in Africa on PRDs and capacity building for clinical trials in Africa.

Key activities supported by EDCTP grants to strengthen ethical and regulatory oversight include the following:

- Pan African Clinical Trial Registry
- Mapping of ethics review and trial regulatory capacity in sub-Saharan Africa (MARC, www.researchethicsweb.org): 166 African HRECs identified, 23 countries with NRA mapped
- National Ethics Committees/NRAs capacity development
- Pharmacovigilance capacity development,

- EDCTP ethics workshop (AVAREF strategic work plan): training to combine GCP-GCLP-ethics workshop, Plan was to invite some members of NRAs and ECs to participate, to discuss interactions.
- Reviving Pan-African Clinical Trials Alliance (PACTA): workshops to facilitate interaction between NRAs, national ethics committees, PACTR African systematic reviewers' network, cofounded by Cochrane collaboration.

13. Update from the BMGF

Dr. David Mukanga on behalf of the BMGF updated participants on regulatory affairs in the context of the AVAREF work, highlighting processes and infrastructures around discovery and clinical development; registration & licensure; and delivery and surveillance. He also presented the current status and needs in terms of vaccine development and new therapies, mainly for the following diseases: HIV/AIDS, TB, Malaria, Pneumonia, Dengue, Dengue, Lassa Fever, Zika.

He presented the perspectives on areas for focus in 2018, as follow:

- Intensify joint reviews and engagements with PDPs/sponsors. Continue to demonstrate the value proposition – pre-submission meetings with sponsors.
- Domestication of AVAREF guidelines and standards with prioritization of countries with high volume CT applications. Leverage REC Secretariats, TCC members
- Engagement and alignment with CEPI and other regulatory networks
- Complete process for assessing quality of reviews – QMS or specific indicators. Capacity and quality improvement.
- Visibility on CTs in Africa. Where is the volume? Typology? Review timelines? Improvement needs?

He congratulated AVAREF statutory bodies as well as the secretariat for the good work done. He encouraged countries to have a provision for pre-submission meetings for CTAs and the secretariat to document information on countries implementing AVAREF guidelines and report in the AVAREF website. He reiterated the need for AVAREF and NEPAD to align strategies and promote alignment.

14. Update from NEPAD: Brief Overview of 3rd Biennial Scientific Conference on Medical Products Regulation in Africa

Dr Hudu Mogtari on behalf of NREPAD updated participants on the 3rd biennial scientific conference on medical products regulation held in Accra from 27 to 28 November 2018.

The Conference was attended by two hundred ninety five (295) participants representing AU Member States, RECs, UN, Development Agencies, Civil society Organizations, Academia, Private sector, and NGO's.

There were the following sessions:

- First High-Level Plenary: Putting patients first – reforming access to medicines in Africa
- Second High-Level Plenary: Accelerating access to medicines – perspectives of industry, Civil Society and Patient Organizations
- Plenary Session I: Harmonization of regulation of medical products in Africa, where are we?
- Parallel Session I: Investing in Africa's Pharmaceutical Industry: The role of regulation
- Parallel Session II: Post Marketing Surveillance and Pharmacovigilance Initiatives
- Plenary Session III: Expanding the scope for regulatory harmonization in Africa & sustaining the momentum after 10 years of harmonization efforts – opportunities and challenges

The conference recommendations were categorized into three sections namely:

- Sustaining momentum for harmonization,
- NMRAs strengthening and,
- Local production of pharmaceuticals.

Conclusions and next steps are:

- Increased commitment from key stakeholders on regulatory systems strengthening and harmonization as exemplified by the number of participants who funded their participation and diligently listened to the discussions throughout the two conference days.
- Actions for sustaining the momentum on regulatory harmonization in Africa were identified and agreed as part of conference recommendations.
- Increased knowledge on regulation of medical products and harmonization efforts in Africa.
- Stakeholder awareness on the progress made in medical products regulatory systems in Africa through the various presentations made.
- Agreed framework for collaboration and networking among regulators, researchers and industry in advancing research and development and subsequent commercialization of products for diseases disproportionately affecting Africa.

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

Hiti Sillo presented a summary of the table top exercise organized by WHO and the NEPAD with the support of the Coalition for Epidemic Preparedness Innovations (CEPI) and involvement of other partners including the EDCTP, the BMGF, CBER FDA, and the Paul-Ehrlich-Institut.

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. 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. The TCC and the SC were informed that the AVAREF joint review guideline was validated by the Assembly as fit for purpose as a result of the exercise, and 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.

16. Recommendations of the Technical Coordinating Committee of AVAREF for approval by Steering Committee

Outcomes and actions from the first AVAREF Assembly

The TCC discussed the outcomes and actions from the AVAREF Assembly held in Accra in November 2017. The TCC recommends the following:

R1. Further dissemination of the Assembly report and endorsed documents, including the strategic plan, guidelines and resolutions to Regional Economic Communities Secretariats, Heads of NRAs and national ethics committees.

R2. Communication by the Secretariat of outcomes and work products of the AVAREF TCC & SC meetings to the heads of NRAs, ECs and RECs secretariat and WHO country offices.

R3. Invites WHO Secretariat to find out and document the pathways for approval of clinical trials in the member countries to identify and adopt best practices.

Implementation and domestication of AVAREF documents

R4. Members of the TCC and SC should report to their respective RECs the outcomes and work products of AVAREF meetings. They should also report back on the status of implementation of AVAREF decisions during subsequent meetings.

R5. Requests the SC to endorse domestication and implementation of AVAREF guidelines and documents through RECs and to leverage AVAREF expertise to facilitate implementation at RECs if needed.

R6. Invites RECs to develop TORs of their expert working groups on clinical trial oversight which should be in compliance with AVAREF platform.

R7. Exploring training opportunities for ethics committees and regulators on roles and responsibilities during CTA reviews and clinical trial legislation to meet the 60 days timeline.

Table top exercise on regulatory preparedness for public health emergencies

The TCC recommends the following

R8. Recommendations from the table top exercise should be implemented by the TCC through the established working group with support from WHO secretariat.

R9. Previous annual AVAREF scientific session should be brought back in order to build capacity of NRAs, ECs and RECs to keep abreast of latest scientific development.

Financial sustainability

It was noted that under the AVAREF terms of reference, roles and responsibilities of Head of agencies include a budget line to support AVAREF activities at agency level, including travel to meetings. Therefore the TCC recommends the following:

R10. The SC to consider implementation of financial sustainability mechanisms identified by the TCC for AVAREF activities, such as countries funding participation of experts in joint assessment and inspections, AVAREF meetings and trainings, and hosting meetings at NRAs/ECs facilities.

R11. Inviting NEPAD Agency (as a secretariat of AMRH) to play advocacy role in all member states to persuade them to invest and fund AVAREF.

GCP Guideline and Inspection Guide

The TCC recommends:

R12. To adopt the current ICH-E6 R2 guidelines (as last amended) and have the AVAREF GCP guideline that makes reference to the differences in the RECs.

R13. Need for the Secretariat to hire a consultant to assist the working group finalize the GCP guideline and develop GCP inspection tools.

Clinical trial regulation working tools

The TCC recommends:

R14. Inviting the established working group to revise the proposed tools, including addition of Investigation Medicinal Product dossier for phase I/II studies, drafting of a guidance template for the reviewer i.e. “Reviewers Guide document’ and include relevant guidance document in relevant sections e.g. ICH E6, E8. E9 and E 10, drafting of a template for ECs/IRB reviewers and compare notes on the WHO/ European EC template.

Proposal for a pilot version of the AVAREF leadership development program

R15. Requests the secretariat to seek funding for the pilot version of the AVAREF/Telfer leadership program and invites the SC to approve it for implementation in 2018.

17. Decisions and Recommendations of the AVAREF Steering Committee

The Steering Committee carefully reviewed the report of the TCC together with the attached documents and made the following recommendations:

Outcomes and actions from the first AVAREF Assembly

The SC discussed the outcomes and actions from the AVAREF Assembly held in Accra in November 2017. The SC endorsed the following:

R1. Further dissemination of the Assembly report and endorsed documents, including the strategic plan, guidelines and resolutions to Regional Economic Communities Secretariats, Heads of NRAs and national ethics committees.

R2. Dissemination by the Secretariat of outcomes and work products of the AVAREF TCC & SC meetings to the heads of NRAs, ECs and RECs secretariat and WHO country offices.

R3. Identification by the Secretariat of the pathways for approval of clinical trials in the member countries in order to adopt best practices.

Membership of the Steering Committee

The SC endorsed:

R4. Appointment of Agnes S. Kijo, Acting Director General of TFDA, to the Steering Committee to replace Mr. Hiiti Sillo, former member of the SC who joined the WHO.

Implementation and domestication of AVAREF documents

The SC endorsed the proposed recommendations made by the TCC as follow:

R5. Members of the TCC and SC should report to their respective RECs the outcomes and work products of AVAREF meetings. They should also report back on the status of implementation of AVAREF decisions during subsequent meetings. Furthermore the ToRs of these committees need to be revised to accommodate these responsibilities.

R6. Domestication and implementation of AVAREF guidelines and documents through RECs and to leverage AVAREF expertise to facilitate implementation at RECs if needed.

R7. Encourages RECs to develop TORs of their expert working groups on clinical trial oversight which should be in compliance with AVAREF guidelines and practices.

R8. Exploring training opportunities for ethics committees and regulators on regulation of CT.

R9. Reintroducing the annual AVAREF scientific session to address the need for in-country capacity building for NRAs, ECs and RECs to keep abreast of latest scientific development.

Table top exercise on regulatory preparedness for public health emergencies

The SC was updated on a tabletop exercise which was held in Accra, Ghana on 26 November 2017 preceding the AVAREF Assembly; and endorsed the following recommendation:

R10. Implementation of the recommendations from the table top exercise by the WHO Secretariat in consultation with TCC through the established working group.

Financial sustainability

It was noted that under the AVAREF terms of reference, roles and responsibilities of NRAs and ECs include a budget line to support AVAREF activities, including travel to meetings. Therefore the SC endorsed the following:

R11. Implementation of financial sustainability mechanisms identified by the TCC for AVAREF activities, such as countries funding participation of experts in joint assessment and inspections, AVAREF meetings and trainings and hosting meetings at NRAs/ECs facilities.

R12. Inviting NEPAD Agency (as a secretariat of AMRH) to play an advocacy role in member states to persuade them to invest and fund AVAREF.

R13. Agreed to establish a Working Group on Financial sustainability to further explore strategies and implementation plans.

GCP Guideline and Inspection Guide

The SC endorsed the following:

R14. To adopt the current ICH-E6 R2 guidelines (as last amended) and have the AVAREF GCP guideline as a reference to RECs.

R15. Requests the Secretariat to recruit a consultant to assist the working group finalize the GCP guideline and develop GCP inspection tools.

Clinical trial regulation working tools

The SC recommends the following:

R16. Urge the working group to revise the proposed tools, including addition of Investigational Medicinal Product dossier for phase I/II studies, drafting of a guidance template for the reviewers i.e. "Reviewers Guide document' and include relevant guidance document in relevant sections e.g. ICH E6, E8. E9 and E 10, drafting of a template for ECs/IRB reviewers.

Proposal for a pilot version of the AVAREF leadership development program

The SC discussed the pilot version of joint AVAREF/Telfer leadership development program. The SC is supporting the pilot program and made the following recommendations:

R17. Encourages the Secretariat continue to seek funding opportunities for a three-day pilot program in September 2018 and for the full program for 2019 and beyond.

R18. Encourages NRAs, ECs and RECs to include funding requests for leadership development as part of their submissions for funding to EDCTP and other donors

Other Recommendations and endorsements

R19. The SC encourages Member States to provide for pre-submission meetings with applicants/sponsors to discuss issues related to application process and requirements.

R20. The Secretariat to post all approved AVAREF guidelines and documents to the website

R21. Translate all approved documents and guidelines into the African Union official Languages.

R22. The Secretariat to work with PEI for Implementation of the next steps of their Regulatory capacity strengthening in Africa projects.

Annex 1: List of participants to the 4th Meeting of the Technical Coordinating Committee of the African Vaccine Regulatory Forum (AVAREF), 12 - 14 February 2018, Maputo, Mozambique.

Name	Institution	Country
Edward Abwao	Kenya Pharmacy and Poison Board	Kenya
Damson Kathyola	Director of Research, Ministry of Health, Malawi	Malawi
Beno Nyam Yakubu	National Agency for Food and Drug Administration and Control	Nigeria
Priscilla Nyambayo	Head of Pharmacovigilance, Medicines Control Authority of Zimbabwe	Zimbabwe
Marie Claire Okomo Assoumou	National Ethics Committee	Cameroon
Winfred Badanga	Head of Research Quality Assurance, UNCST	Uganda
Eric Karikari -Boateng	Ghana FDA	Ghana
Carine Mbadinga Mbadinga	Direction du médicament et de la Pharmacie	Gabon
Hudu Mogtari	NEPAD	Ghana
Gopa Raychaudhuri	Senior Scientist and CBER Liaison to WHO	USA
Juárez Hernández Marcela	International Cooperation / Regulatory Service, Paul-Ehrlich-Institut	Germany
Hiiti Sillo	Secretariat, WHO HQ	Geneva
Diadié Maïga	Secretariat, WHO AFRO	Congo Republic

Annex 2: List of participants to the 4th Meeting of the Steering Committee of the African Vaccine Regulatory Forum (AVAREF), 15 – 16 February 2018, Maputo, Mozambique.

Names	Title	Country of Residence
Delese Mimi Darko	CEO Ghana Food and Drug Authority	Ghana
Wiltshire Johnson	Registrar/CEO Pharmacy Board of Sierra Leone	Sierra Leone
Heran Gerba	Deputy Director General Food, Medicine, and Health care Administration and Control Authority	Ethiopia
Nalá Rassul	National Bioethics Committee	Mozambique
Portia Nkambule	Clinical Evaluation and Clinical Trials, MCC	South Africa
Agnes Kijo	Acting Director General, Tanzania Food and Drugs Authority	Tanzania
Simon Langat	Chief Science Secretary National Council for Science and Technology	Kenya
Beno Nyam Yakubu	National Agency for Food and Drug Administration and Control	Nigeria
Thomas Nyirenda	South Networking and Capacity Development Manager	South Africa
Bernice Mwale	Director General, Zambia Medicines Regulatory Authority	Zambia
Samba Cor Sarr	Comité National d'Ethique pour la recherche en Santé	Sénégal
Consuelo Ondotfua Mangue	Directrice Générale de la Pharmacie de l'approvisionnement des médicaments et de la médecine Traditionnelle	Equatorial Guinea
Peter Aguek Kon Baak	Chair of South Sudan Ethics Committee	South Sudan
Yaya Coulibaly	Directeur de la Pharmacie et du Médicament	Mali
Felicien Munday	National Ethics Committee	DRC
Hudu Mogtari	NEPAD	Ghana
P.Tarpowah Kear, Jr.	Professional Officer for Pharmacy Programme, WAHO	Burkina Faso
Gopa Raychaudhuri	Senior Scientist and CBER Liaison to WHO	USA
David Mukanga	Senior Program Officer, BMGF	USA

Christoph Conrad	Head DZIF Office for Scientific and Regulatory Advice, Paul-Ehrlich-Institute	Germany
Juárez Hernández Marcela	International Cooperation / Regulatory Service, Paul-Ehrlich-Institut	Germany
Hiiti Sillo	Secretariat, WHO HQ	Geneva
Diadié Maïga	Secretariat, WHO AFRO	Congo Republic