Regional experience on the vaccines regulation harmonisation process: **African Vaccines Regulatory Forum (AVAREF)**

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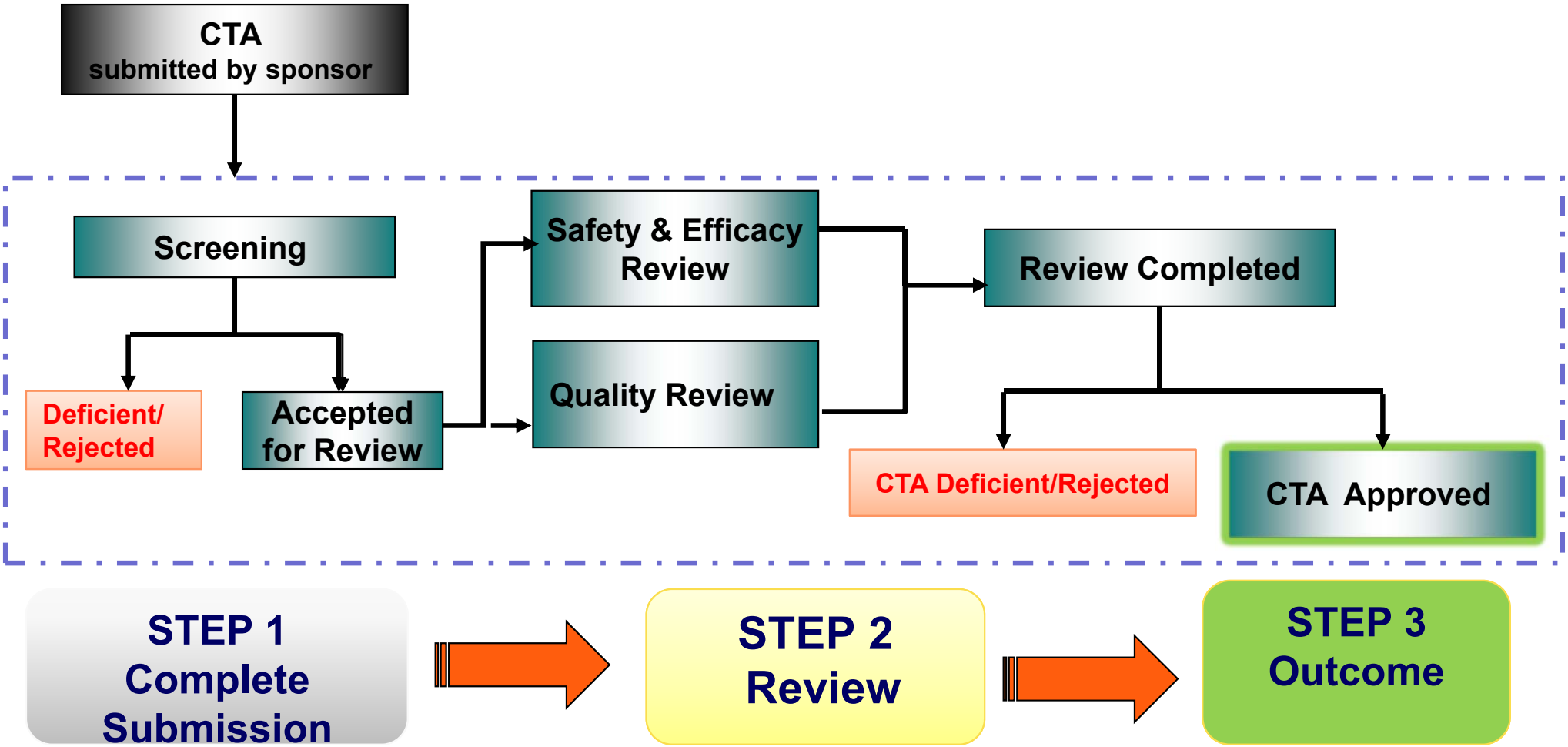
INTRODUCTION- Global Product Development challenges

- **Growing public health needs and limited resources**
- **Mosaic of regulations govern product development and oversight**
- **Duplication due to overlapping reviews and inspections.**
- **Significant and rising portion of R&D budgets is spent on differing regulatory requirements**
- **Harmonization of procedures** and processes is too slow.
- **Enhanced collaboration** would ensure that the best possible science, standards, and practice drive the regulatory process, resulting in improved safety, innovation, and access.

Regulatory Challenges

- Timelines for clinical trials and product registration in Africa are too long e.g. 4-7 years for product registration
- When safe and efficacious interventions are held back from those who need them:
  - ↑ morbidity and mortality → negative socio-econ dev't
- Challenges precipitating this scenario

Authorizations of Clinical Trials Should Be Simple!



Takes 6 months to several years!

GLOBAL EFFORTS TO TACKLE GAPS IN CLINICAL TRIALS

Initiative	Main Accomplishments/Activities
WHO - African Vaccine Regulatory Forum (AVAREF)	▪ Accelerated & quality review and approval of Clinical Trial Applications by NRAs and Ethics Committees (e.g. MenAfriVac, RTS,S, AERAS TB)
BMGF - Global Health Regulatory Team	▪ Coordination of activities of non-profit Global Health product developers (e.g., PATH, DNDi, IAVI, MMV) ▪ Database of requirements for clinical trial reviews
African Medicines Regulatory Harmonization	▪ Regional guidelines and process for joint market authorization.e.g SADC & EAC. Joint reviews of products by regional initiatives such as Zazibona

EAC = East African Community; SADC = Southern African Development Community

AVAREF HISTORY & 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** | **2007** | **2008...** | **...2014** | **2015** | **2016...**

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

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

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

2014/15: Joint reviews of CTAs for Ebola interventions

2015: New AVAREF strategy developed

Nov. 16: New AVAREF strategy launched

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Examples of Joint Reviews/inspections by AVAREF

- Conjugate meningitis A vaccine phase II trial: The Gambia – June 2006 and GCP inspection in Mali in 2007
- Conjugate meningitis A vaccine phase III trial: Senegal – June 2007 and GCP inspection in Senegal
- RTS,S malaria vaccine Phase III trial - 2008
- Expedited review of MenAfricaVac dossier- 2009
- Expedited review of inactivated polio vaccine dossiers – 2012
- Joint reviews of ebola vaccine clinical trial application in Geneva – December 2014
- Joint review of ebola vaccine clinical trial February 2015, in Arusha, Tanzania
- Assisted review for ebola clinical trial application for Sierra Leone, Ghana, 2015
- Assisted review of clinical trial application for medicine against eumycetoma in Sudan

Success, Benefits, Advantages

- Provides single platform for review of documents by experts with different technical backgrounds and competence
- Evaluation in a timely manner without compromise in the quality of the review
- Experts augments the capacity building platform
- Promotes collaboration and information sharing between NRAs and ECs
- Encourages harmonization of procedures and decision criteria

Challenges of Joint Reviews So Far

- When used in emergency, pressure on NRA's resources due to fast track mechanism used
- Capacity building primarily limited to the few NRA staff participating in actual review.
- Conflict of joint review processes with some established local review processes (Expert Committees)
- Post-review final decisions are not uniform

A New Vision and Blue Print for AVAREF

Developments leading to the creation of the Blue print for AVAREF

- Creating a new vision while building on past achievements

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The launch of the new AVAREF strategy

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Changes

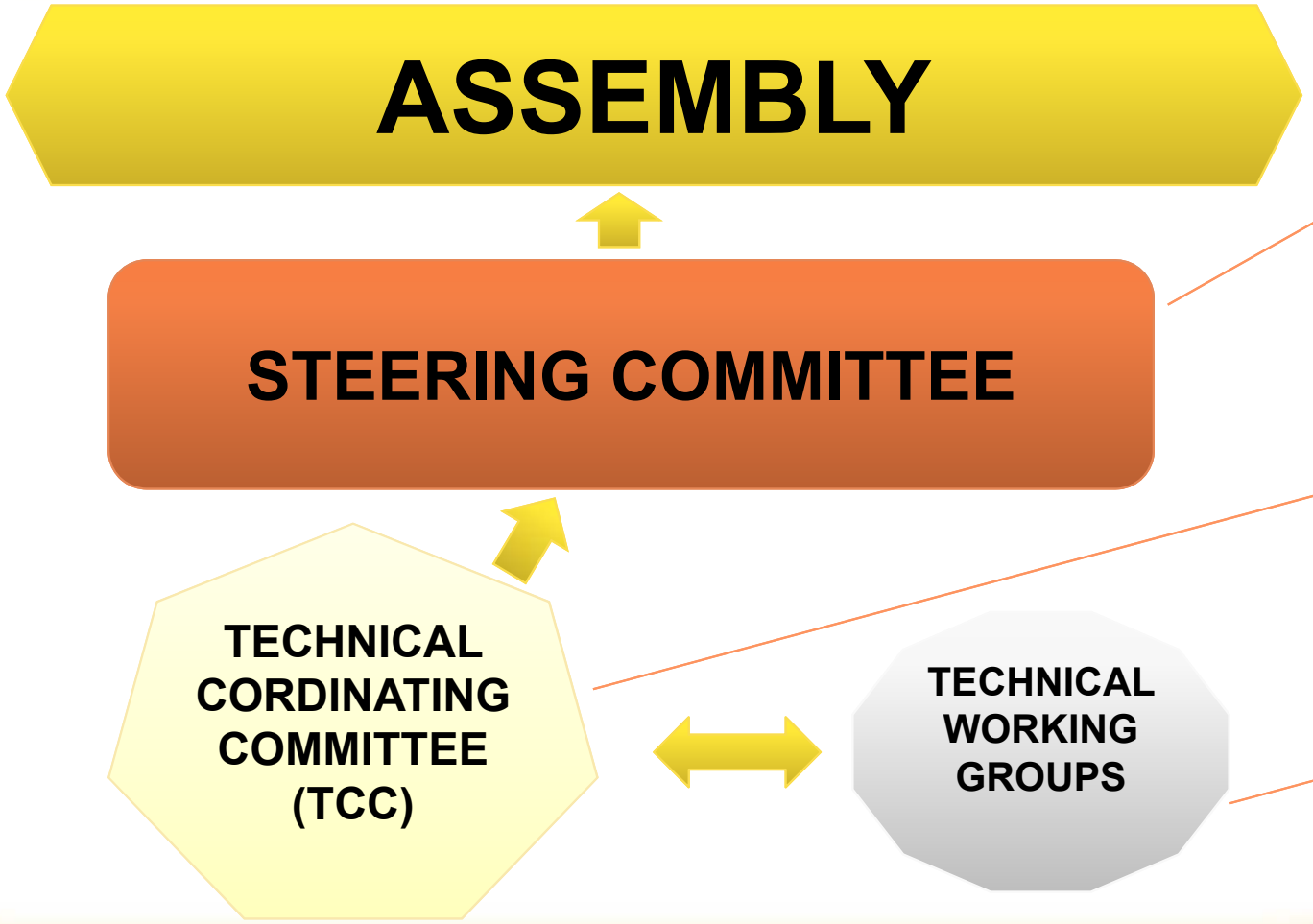
AVAREF

- Governance structure
  - Decision by NRAs & ECs
- Membership/Representation
  - NRAs and ECs of countries
- Alignment
  - No formal linkages with AMRH
- Minimal accountability
- No sustainability plan

New AVAREF

- Governance structure
  - Decision by Steering Committee
- Membership/representation
  - Representatives of RECs
- Alignment
  - Formal alignment with AMRH
- Full accountability
- Sustainability plan and ownership

New AVAREF Governance Model



Meeting of All NRAs & Reps of ECs in Africa

Provides Leadership and Strategic Direction

Identify Technical Needs , Develop Guidelines , make recommendations

Support TCC

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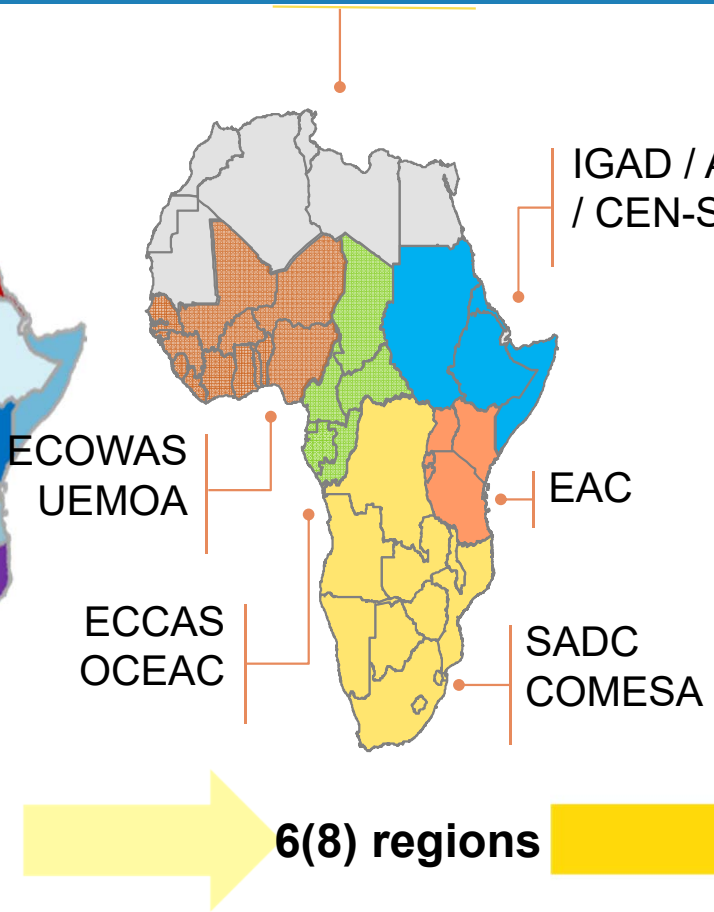
NEW

African Vaccine Regulatory Forum (AVAREF)

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



54 countries → **6(8) regions** → **1 continent**

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Steering Committee and Technical Coordination Committee Members

- *Steering Committee*

- Bernice Mwale, Director General - Zambia Medicines Regulatory Authority
- Nala Rassul, Chair -- National Ethics Committee, Mozambique
- Samba Cor -- Head of Research Division of the DPRS/MOH, Senegal
- Simon Langat -- Director, MOH, Kenya
- Denekew Yehulu Alemneh -- Director General, ENHACA, Ethiopia
- Silo Hiiti (Chair) -- Director General, TFDA, Tanzania
- Portia Nkambule -- Director: Clinical Evaluations and Trials, MOH,MCC, South Africa

Each Meets Twice a year
Second meeting just before AVAREF Assembly Meeting

- *Technical Coordinating Committee (TCC)*

- Mimi Darko, Food & Drugs Authority, Ghana;
- Priscilla Nyambayo, MCAZ, Zimbabwe;
- Edward Abwao, KPPB, Kenya;
- Damson Kathyola, Director, MOH, Malawi;
- Maminata Traore, NEC, Burkina Faso;
- Julius Ecuru, NCS&T, Uganda
- Beno Yakubu Nyam, NAFDAC, Nigeria (Chair).

KEY ELEMENTS OF NEW AVAREF STRATEGY

Goal
To strengthen clinical trials regulatory authorization and oversight in Africa by increasing system's efficiency and building an optimal clinical trial infrastructure

Key objectives

- Develop/update harmonized requirements for clinical trial regulatory authorization and ethics committee approval
- Develop and implement guidelines for joint review of clinical trial applications at regional or multi-country level for vaccines and drugs candidates

Key principles of new AVAREF vision

- Development of benchmark data on baseline review / approval timelines and annual improvement targets
- Expansion of scope to medicines (in addition to vaccines)
- Adoption of a regional approach (vs. country-focused engagement), aligning with and leveraging AMRH platform
- Practical capacity building for work sharing and promotion of joint activities

New AVAREF

Where are we?

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Updates

- TCC and SC Met twice, back-to-back in Kigali, Rwanda, Sept. 2016 & Zanzibar 20-24 Feb 2017
- Endorsed Common AVAREF process and timelines for approval of CTAs
  - Working on setting timelines based on existing realistic timelines
  - Clear steps, each with specified timeline
  - Roles and responsibilities of EC and NRA defined
  - Proposes parallel submission
  - Collaboration between NRA & Ethics and avoidance of duplication
  - Use of electronic submission for efficiency
- Endorsed AVAREF communication strategy
  - Newsletter, website, brochure, etc.
- Joint review for special authorization of new vaccines –RTS,S (malaria), and PQed vaccine cholera vaccine

Coming Soon.....

- Harmonised, competitive clinical trial review timelines to be published by all countries.
- This might accelerate product development for priority diseases, and promote timely access to safe and efficacious medical products of assured quality.
- Working alongside the African Union and Regional Economic Communities, AVAREF is also likely to affect the quality and efficiency of regulatory systems and processes for product licensing and post-market surveillance.

Conclusion - New AVAREF

- New and better governance and operating model
- Efficient, transparent & flexible - Better quality and shorter review and approval timelines for CTAs
- Reaches out to stakeholders; rapidly responds to R&D in emergencies
- Alignment - Strategy, members, resources, work in common with AMRH, AMA and other initiatives.
- Harmonization of common requirements and procedures
- Country ownership, accountability and sustainability

Acknowledgements

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US FDA
EMA
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PEI

Thank You!