Global Vaccine and Immunization Research Forum15-17 March 2016, Johannesburg, South Africa

African Vaccine Regulatory Forum (AVAREF): ***New Vision and Blueprint for Ethics and Regulatory Capacity Strengthening in Africa***

Dicky Akanmori

World Health Organization

REGIONAL OFFICE FOR Africa

REGULATORY CHALLENGES IN LMICs

Clinical development

- Weak capacity and unclear regulatory and ethics processes e.g.
  - No clarity of roles for regulatory authorities and ethics committees
  - Lack-of / disparate application requirements
  - overall weak capacity and no transparency

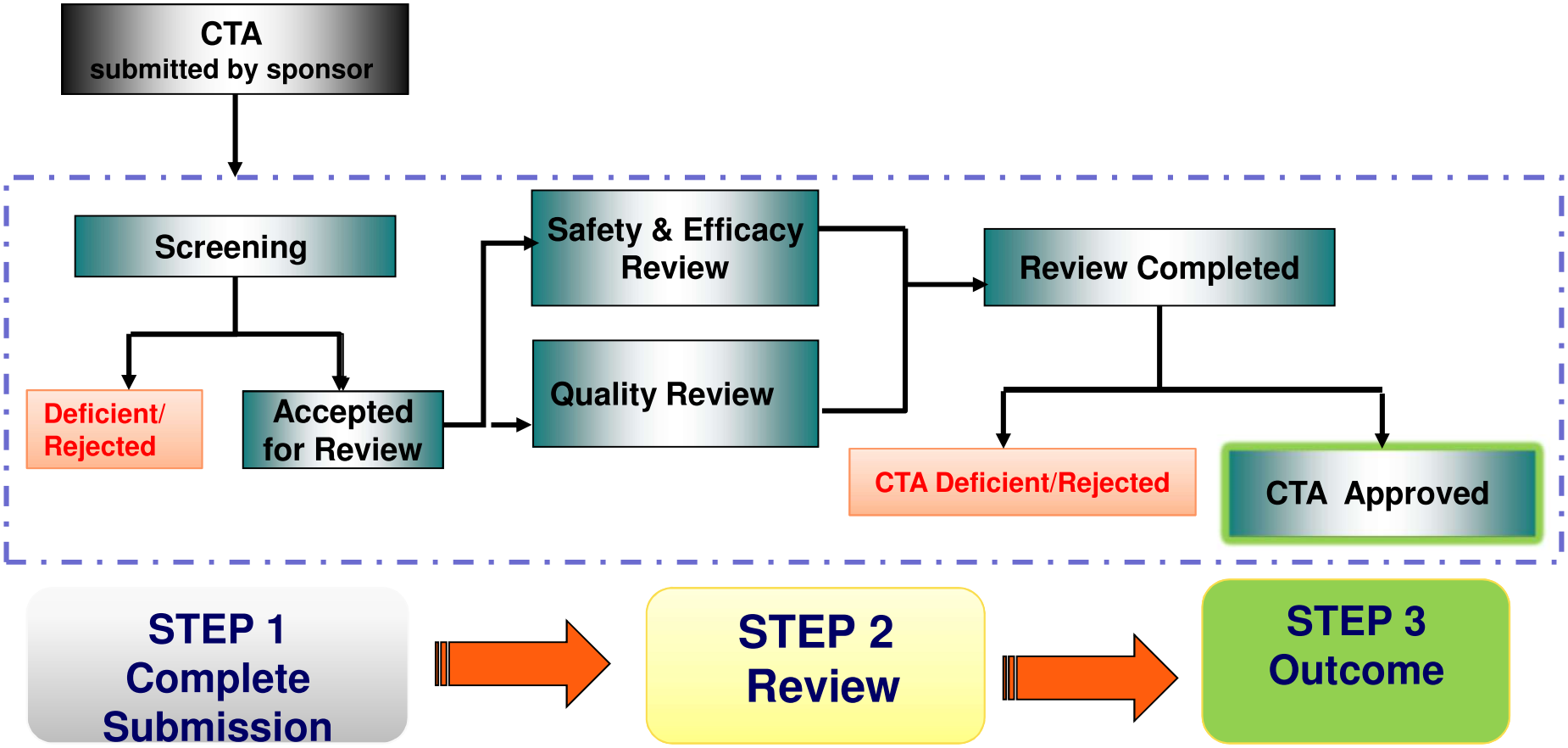
Registration & Licensure

- **Rx/Vx: well established "3-step" process, but slow and redundant** retarding timely country introduction of needed global health products
- **Dx: unpredictable processes** with lack of agreed-upon standards, multiple quality assurance mechanisms, and slow registration and uptake of novel technologies

Post-licensure / surveillance

- **Limited pharmacovigilance capacity** in a context of increasing number of vaccines and drugs for focus country introduction
- **Increased inflow of counterfeit and substandard products** due to poor surveillance

Authorizations of Clinical Trials Should Be Simple!



Takes 6 months to several years!

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Common Causes of Delays

- Different timelines for reviews by Ethics and NRAs
- Validation/screening of submissions
- Communication of screening/acknowledgement
- Additional requirements often not listed/forgotten
- Scheduling reviews/no timetables
- Communicating decisions to sponsors
- Attempts to re-write CTAs (A change in design alone cannot significantly alter the safety of a test product!)

CHALLENGES IN CLINICAL TRIAL OVERSIGHT, THE WHO RESPONSE THROUGH AFRICAN VACCINE REGULATORY FORUM (AVAREF)

- **Non-streamlined steps** in reviews by all ECs/NRAs – *Communication, collaboration and pre-defined steps – ECs and NRAs in AVAREF.
- **Lack of clarity in roles of ECs and NRAs –** *Dialogue among NRAs and ECs; common guidelines, better understanding and separation of responsibilities - Annual AVAREF Meetings and Joint Reviews
- **Disparate application requirements and processes –*A**doption of common application documents/formats, approval guidelines and timelines
- **Weak technical expertise and capacity within some individual NRAs and Ethics Committees** – *Exploit technical expertise and perspectives of stringent Regulatory Authorities (SRAs) in joint & assisted reviews
- **Lack of data on review / approval timelines for CTAs and Ethics Reviews** – *Generate and display reliable performance data

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	▪ EAC guidelines and process for joint market authorization. Joint reviews of products by 2 companies. Expansion to ECOWAS and to clinical trials in progress

EAC = East African Community; ECOWAS = Economic Community of West African States

AVAREF HISTORY

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

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

2015: New AVAREF strategy developed

Nov. 16: New AVAREF strategy launched

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

2014/15: Joint reviews of CTAs for Ebola interventions

Joint/Assisted Reviews and GCP Inspections

"Process has been widely viewed as successful, improving the capacity and coordination and encouraging the use of defined review timelines and common documentation" -

Source: *Safer, Faster, Cheaper Improving Clinical Trials and Regulatory Pathways to Fight Neglected Diseases - Report of the Center for Global Development's Working Group on Clinical Trials and Regulatory Pathways*

ELEMENTS OF NEW AVAREF STRATEGY

Target
Botswana, Burkina Faso, Cameroun, Ethiopia, Gabon, Gabon, Ghana, Kenya, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, South Africa, Tanzania, Uganda, Zambia & Zimbabwe

Goal
strengthen clinical trials regulatory authorization and oversight by increasing efficiency and building optimal clinical infrastructure

Key objectives

- Develop/update harmonized requirements for regulatory authorization and ethics approval
- Implement guidelines for joint review of CTAs (regional /multi-country levels)

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, not just country-focused, aligning with and leveraging AMRH initiative
- Practical capacity building for work sharing and promotion of joint activities

KEY OUTCOMES PLANNED FOR 2016

Key outcomes	By Q2 2016	By Q4 2016
1 AVAREF strengthened and operating model in synergy with AMRH	▪ **Governance structure and operating model** established ▪ Draft **strategic plan**, and expansion to **medicines**,	▪ **Baseline of CTA approval and ECs review timelines** established ▪ **Harmonized** NRA / EC tech guidelines and requirements for CTAs
2 % of African countries meet internationally competitive AVAREF target review timeline for 90% of CTA review decisions	▪ Model for **joint/assisted review** endorsed and implemented ▪ **Formal mechanism** for AVAREF to quickly **respond to emergencies** established ▪ Plan to **promote awareness and transparency**, using the AMRH communication and advocacy platform under NEPAD	▪ AVAREF establishes **internationally competitive CTA review target** ▪ **Forecasting of pipeline** of candidate products ▪ **25%** RECs and Member States **reporting review times** ▪ **25%** of RECs and Member States have **coordinated NRA and EC processes** ▪ **10%** of AVAREF operational **costs funded directly** by members

New AVAREF

- New governance and operating model
- Efficient, transparent & flexible - Better quality and shorter review and approval timelines for CTAs
- Reaches out to stakeholders; rapid response 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

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