World Health Organization

REGIONAL OFFICE FOR Africa

Joint scientific and ethics reviews of clinical trial applications

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Outline

- Introduction
- African Vaccine Regulatory Forum (AVAREF)
- Joint Review
- Conclusion

Introduction (1)

- Health is a fundamental right and access to medical products is widely recognized
- Ethics and scientific reviews are designed to ensure this right to access to quality, safe and effective products
- Promotion of R&D in Africa has the potential to lead to the identification of appropriate medicines and vaccines to tackle priority diseases
- Growing public health needs require faster availability and access to quality-assured medical products

Introduction (2)

- Variety of systems and regulatory models
- Divergences in regulation often lead to duplication of studies, tests or even conflicting demands
- Lack of efficiency, increased vaccine development costs
- Limited Capacity for reviews and inspections of new vaccines
- Hence the importance of promoting communication, information and experience sharing, exchange of expertise and other resources between regulators and ethics committees.

Introduction (3)

- Thereby, the African Vaccine regulatory Forum (AVAREF) established in 2006 by WHO to serve as a network of National Regulatory Authorities (NRAs) and Ethics Committees (Ecs) to build their capacity, and improve harmonization of practices in support of product development and regulation of clinical trials.
- AVAREF has since played a crucial role in the successful development of several vaccines.

AVAREF History, Progress and Alignment

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

Global, regional standards, strategies and plans

2005 | 2006 | 2007 | 2008... | ...2014 | 2015-16 | 2017 | 2018

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**

2017: Strategy endorsed

Joint Review of Mosquirix®

New Governance & Alignment with AMRH

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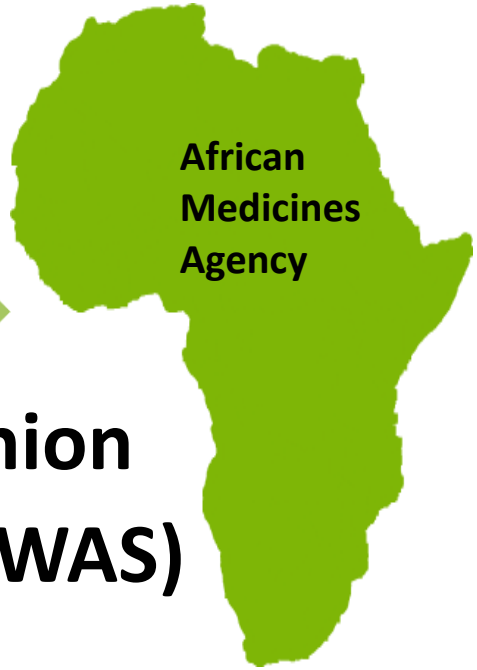
Transformation of AVAREF since 2016 - From 19 countries to 55

55 countries → **5 regions** → **African Medicines Agency**

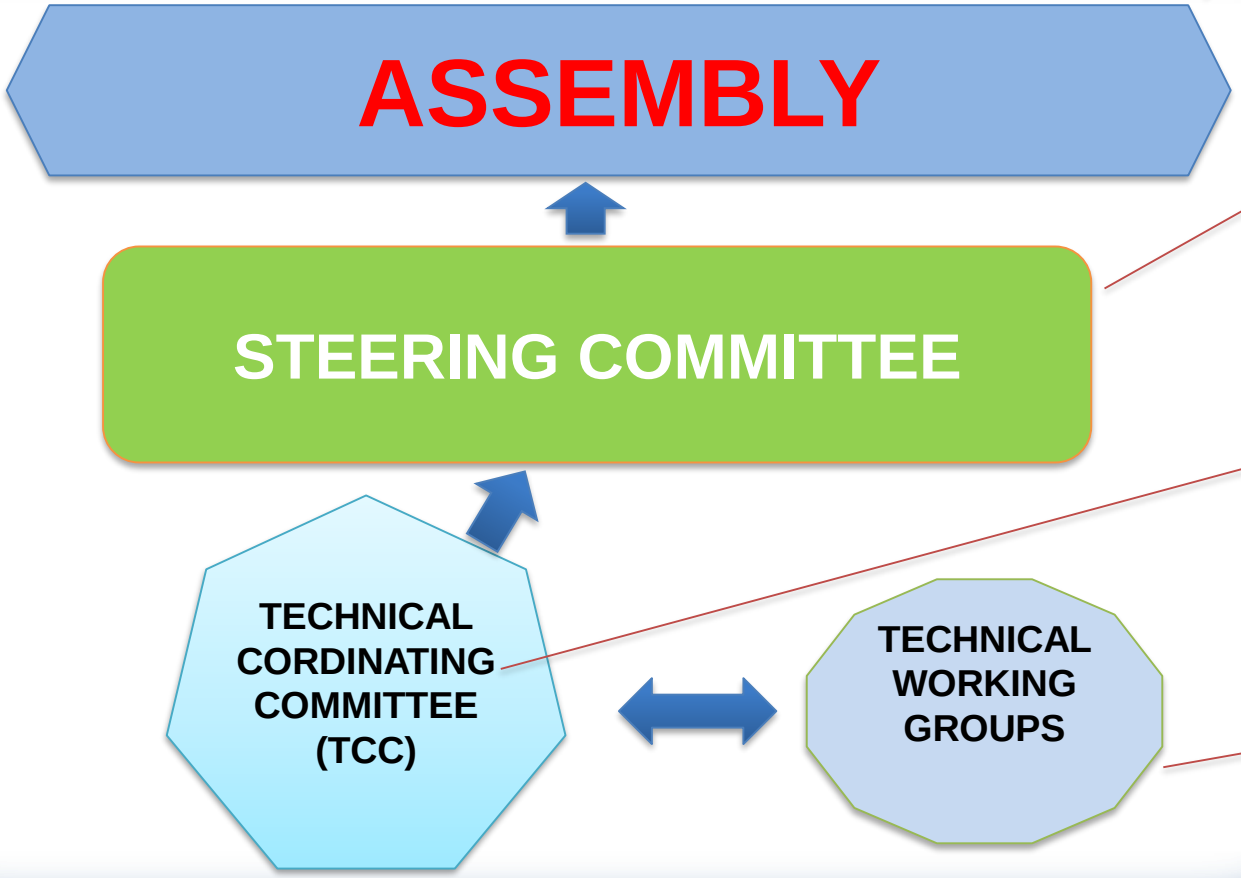


Recognized by the African Union

(EAC, SADC, IGAD, OCEAC ECOWAS)

Only Pan-African ethics and regulatory Harmonization Platform

AVAREF Governance



Meeting of heads NRAs & ECs in Africa

Provides Leadership and Strategic Direction

Identify Technical Needs , Develop Guidelines, make recommendations

Support TCC

What is a joint review?

- An activity in which experts from NRAs and/or ECs of two or more countries review a common application, together with the sponsor, as well as external experts.
- Joint reviews enable NRAs and ECs to validate their findings with peers and experts.
- Joint reviews enable NRAs and ECs to collectively prepare a consolidated list of questions for the applicant and to discuss directly the candidate product, trial design, safety and other aspects of the proposed trial/pilot.

AVAREF Joint review Meeting Objectives

- Convene face to face meeting of NRAs and/or ECs of the concerned countries to review the data package
- Prepare a consolidated list of questions for the applicant and receive responses from the applicant
- Agree on and endorse timelines for the post-review steps (submission of additional information, review of additional information and notification of final outcome)

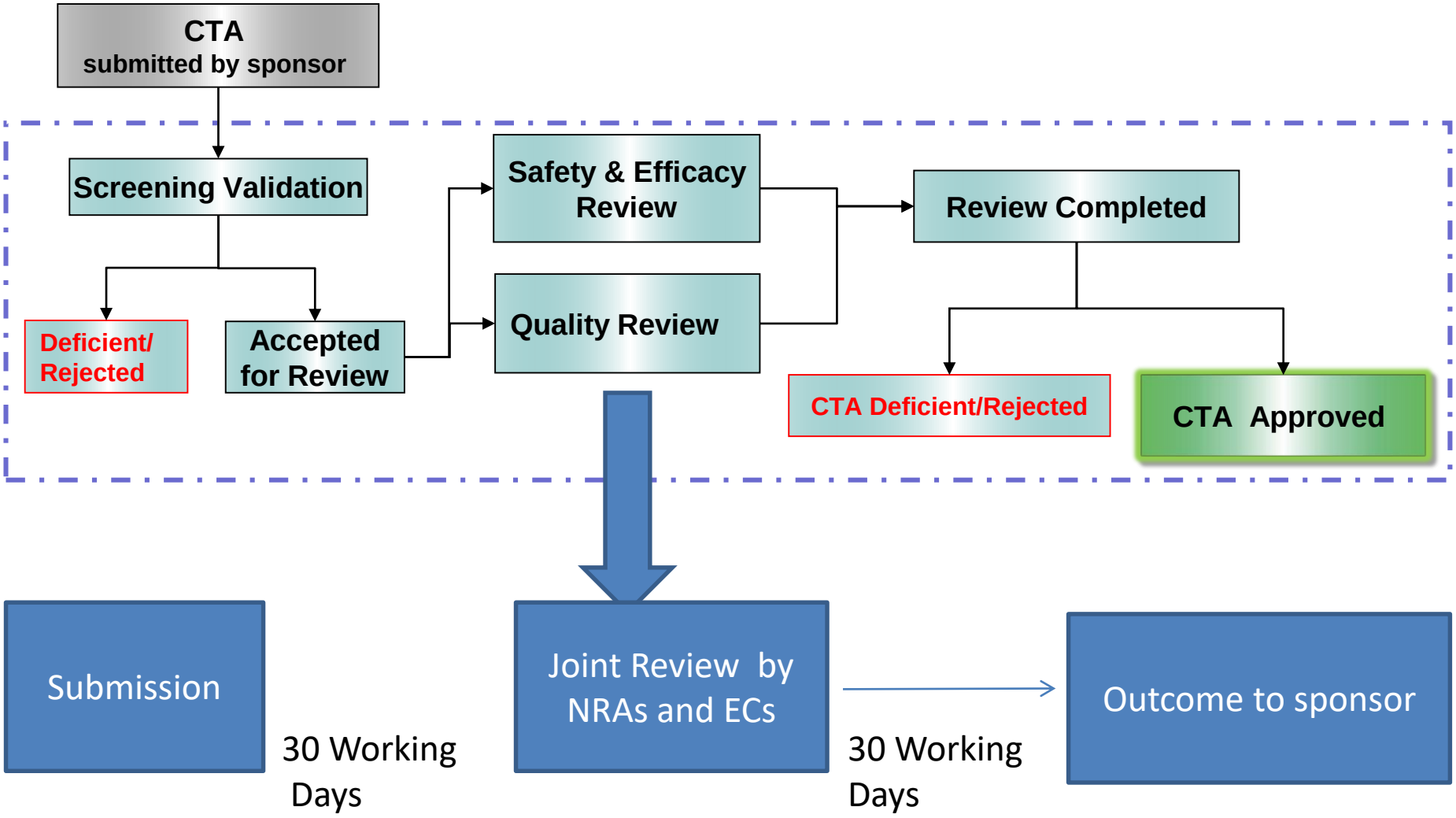
Uses of the Joint Review Model

- Clinical Trial Application Reviews
- Reviews of dossiers for registration or marketing authorizations
- Joint GCP inspections
- Other activities as deemed important (Pilot implementation of vaccine, etc.)

Requirements for a joint review

- Agreement of the manufacturer and/or sponsor
- Neutral facilitator – WHO
- Agreement of the target countries (NRAs and ECs) and nomination of focal points
- Guidelines – AVAREF Guideline available
- Neutral funder – Not for profit product developer- BMGF, PATH, etc.
- External experts – USFDA, EMA, Health Canada

AVAREF Joint Review Model



Participants and Roles

Applicant

Submits proposal according to AVAREF format

Presents proposal and addresses queries

Agrees timelines for addressing outstanding queries

Recipient NRAs and/or ECs:

Review and prepare list of queries for the applicant

Review submissions and provide responses

Agree on timeline for formal response.

Observers:

Observe the process for learning purposes

Facilitating Neutral Broker: WHO

Umbrella Network: AVAREF

Methodology

Step 1 – Roles and Responsibilities, DOIs – Secretariat
Step 2 – Selection of Chair and rapporteurs (EC/NRA)
Step 3 – Presentation of CTA by the applicant
Step 4 – Review of queries and responses posted on platform
Step 5 – Additional Queries
Step 6- Agreement on timelines and next steps
Endorsement of report and timelines prepared by secretariat
Step 7 – Follow up by Secretariat

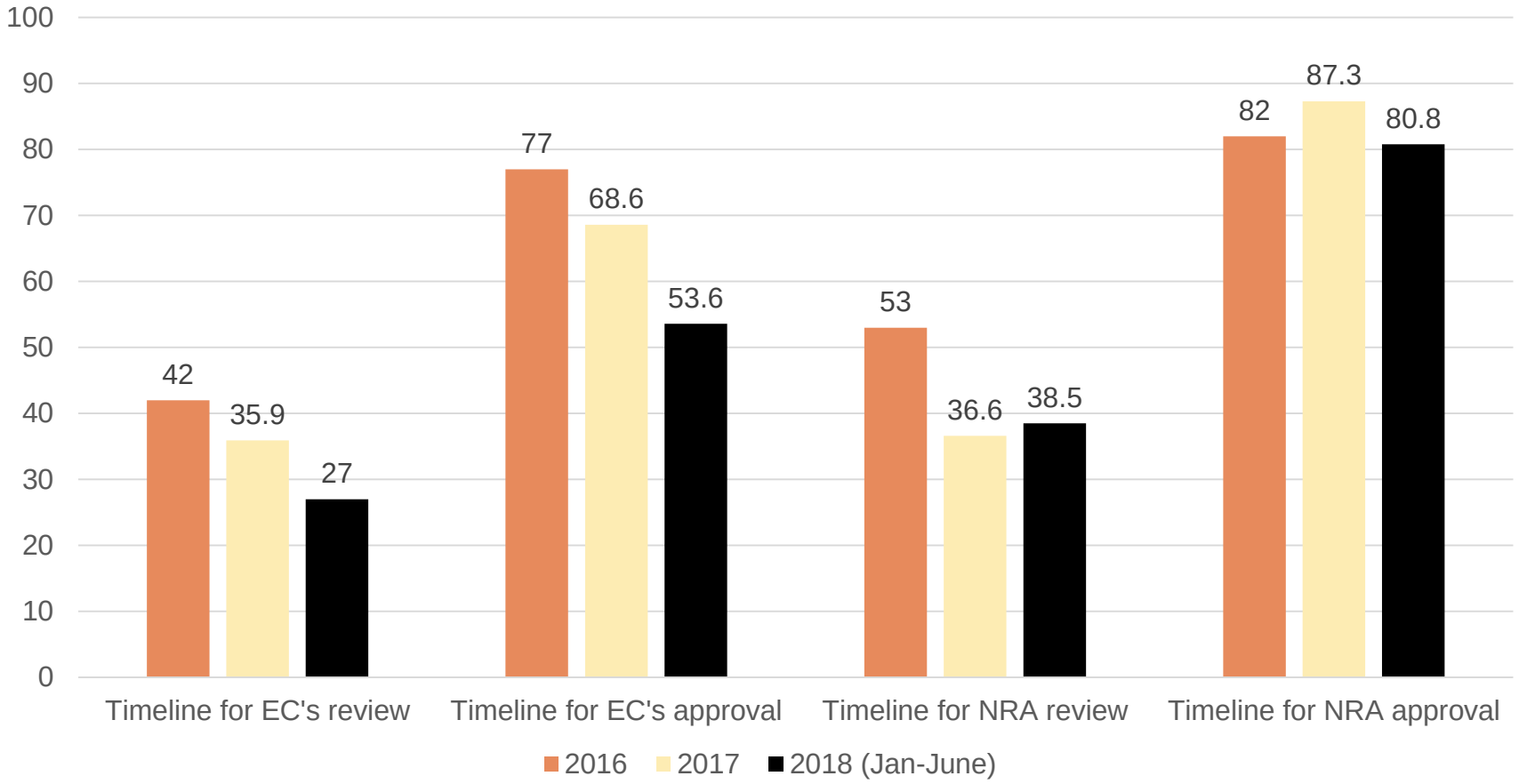
Report and Agreement

- At the end countries endorse timelines to provide final outcome or review additional submissions
- Sponsors endorse timelines to provide additional responses as required
- WHO agrees to follow up with actions

Examples of joint reviews by AVAREF

- Conjugate meningitis A vaccine - 2006
- RTS,S malaria vaccine - 2008
- Expedited review of conjugate men A, 2011
- Expedited review of inactivated polio vaccine – 2012
- Joint reviews of Ebola vaccine clinical trial application in Geneva 2014, Tanzania2015, Sierra Leone, Ghana, 2015
- Assisted review of CTA for medicine against eumycetoma in Sudan
- Medicine against visceral leishmaniasis 2017
- Article 58 scientific opinion and Risk Management Plan (Phase IV) for RTS,S vaccine for use in pilot 2018

National Timelines for review and approval of CTAs from Jan 2016 to June 2018



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Joint Review Timeline

D. Maïga et al. / Vaccine 28 (2010) 571–575

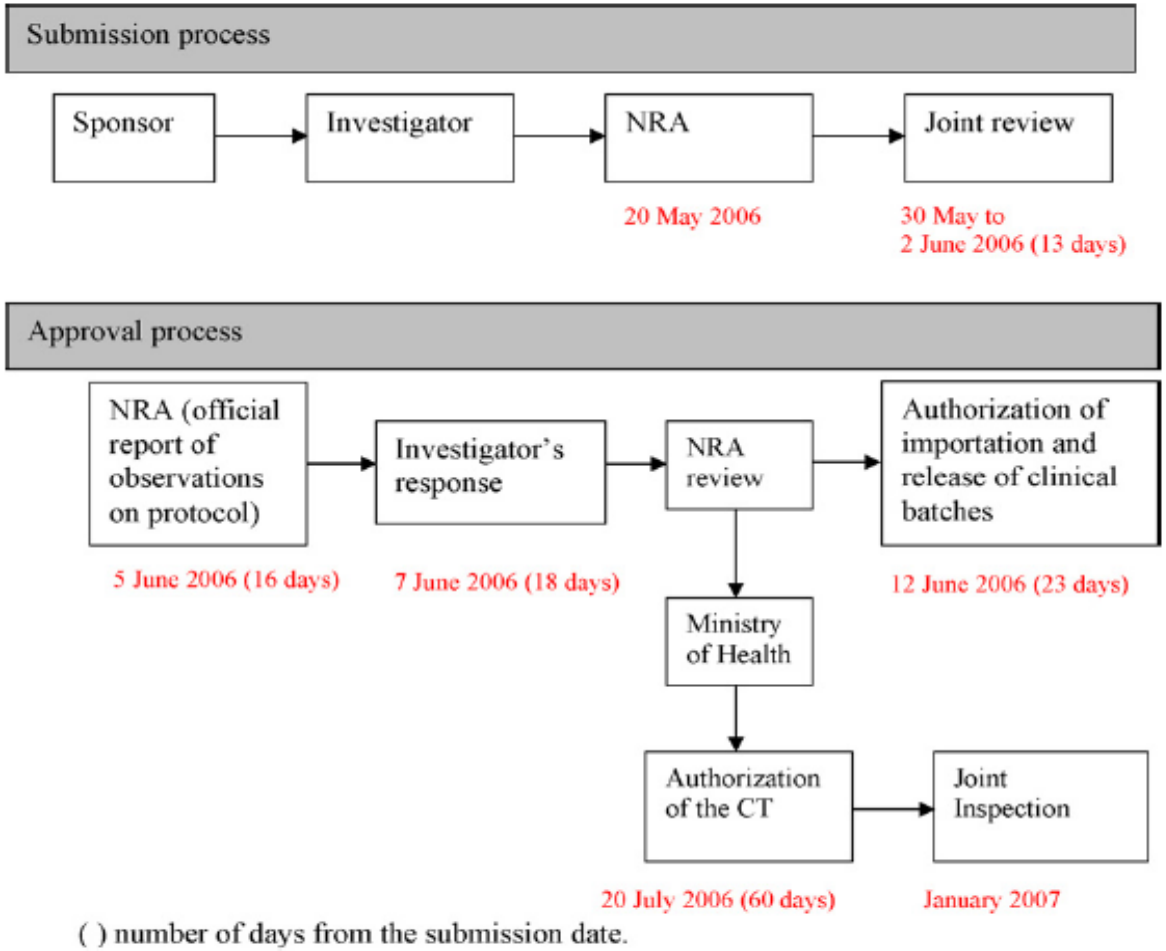

Fig. 1. Submission and approval processes for the conjugate meningitis A vaccine clinical trial: example of Mali. ( ) Number of days from the submission date.

Conclusion

- AVAREF joint reviews have contributed to strengthen:
  - capacity of NRAs and ECs,
  - the regulation clinical trials, their approval and registration.
- Joint reviews have served as vectors of cooperation and harmonization mechanisms and procedures between countries, NRAs and ECs.
- Engaging NRAs and ECs is key to success.
- Country Ownership and decision-making is vital
- Collaboration improves chances of success
- Better within country coordination of ethics committees required.