Presentation of AVAREF and its emergency joint-review process

29 July 2020
Opening remarks:

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Regional Advisor Vaccine Regulation, WHO AFRO
Objectives of today's webinar

- Introduce the AVAREF platform and service offering
- Present the emergency review process including a developer testimony
- Conduct open discussion with developers
### Presentation of AVAREF

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Overview of AVAREF and joint review platform 15 min.
Development of the emergency joint review process 15 min.
Developer testimony 15 min.
Poll 10 min.
Q&A 30 min.
The African Vaccine Regulatory Forum (AVAREF) was established by the World Health Organization in 2006.

AVAREF serves as a capacity-building platform aimed at improving the regulatory and ethics oversight of interventional clinical trials conducted in Africa.
Since its creation, AVAREF connects regulators, ethics committees and developers to expedite access to treatment & prevention of major illnesses in Africa.

To date, AVAREF network connects regulators and ethics committees from 55 member states in Africa.

The AVAREF platform has supported in tackling diseases such as COVID-19, Ebola, Malaria, Tuberculosis and others.
AVAREF offers a one-stop process for clinical trial application and helps improve the regulatory landscape in Africa

**Joint reviews**
Providing a standardized regulatory and ethics process involving authorities from multiple countries to increase efficiency of CTA review process

**Harmonisation**
Working toward standardisation of the regulatory processes to enhance efficiency and improve transparency

**Collaboration**
Ensuring ethics committees and regulatory authorities of all member states collaborate and develop strong relationships

**Support**
Providing support to all member states with a focus on building institutional/technical capacity to meet demand in Africa
3 ways in which developers can benefit from AVAREF platform

Scientific advice tailored to specific platforms, vaccines and medical products

Orchestration of meetings with developers and national authorities from each target country for Clinical trial applications

Alignment of deadlines and support to countries to enable streamlined review processes and timelines
AVAREF's joint review platform is a collaborative process with multiple stakeholders involved.

Experts from NRAs and/or ECs of two or more countries **review a common application**. This process includes the sponsor, investigators, external experts, and other observers.

This process allows NRAs and ECs to **collectively engage the developer** by discussing aspects of the candidate product and proposed trial.

Through collaboration, NRAs and ECs can **validate findings** with peers and external experts, **improve the quality** of the review, and optimize the timeline of the process.
Three types of joint review exist within AVAREF

Regular
Expected timeline: +60 days

Expedited
Expected timeline: +30 days

Emergency
Expected timeline: 10 or 15 days

Authorization process can take up to 6m-1y when conducted at the national level

For more information on Regular and expedited reviews, please refer to AVAREF guidelines

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Due to the COVID-19 crisis, clinical studies are coming at an unprecedented rate around the world.

More than 480 candidates in development...
Global count of vaccines and treatments in development for COVID-19

- Vaccines: 198
- Other treatments: 123
- Anti-viral: 86
- Antibodies: 77

...And more than 3,000 clinical trials initiated to fight COVID-19 around the world
Global count of new COVID-related clinical trials per month (Jan-Apr 2020)

- Jan-20: 34
- Feb-20: 243
- Mar-20: 586
- Apr-20: 1,014
- May-20: 607
- Jun-20: 447
- Jul-20: 84
- Total: 3,015

Note: Data as 22/05/2020
Source: Milken Institute, COVID-19 Clinical Trial Tracker, BCG analysis
More clinical trials might be conducted in Africa while no treatment nor vaccine is available yet

Declining transmission in Europe, N. America and Asia...

Confirmed deaths due to COVID-19, from 21st March to 27th July 2020 (log scale)

...while cases are escalating in many African countries...

Confirmed deaths due to COVID-19, from 21st March to 27th July 2020

...might lead developers to conduct Clinical Trial in Africa

1. While declining transmission rates will complicate conduct of CT, developers might turn to Africa where the disease transmission rates are still high

2. AVAREF and African countries need to be prepared to conduct more joint-review and to accelerate review timeline to face the current challenge

1. Clinical Trial

Source: European Centre for Disease Prevention and Control (ECDC), BCG study and analysis
COVID-19 Crisis Highlights Need For Coordinated Emergency CTA Review Process

Conventional approach to clinical trial review may be sequential and could result in ineffectiveness and delays resulting from repeated steps and duplication of work.

Better coordination is needed for accelerating CTA reviews in emergency situations in order to minimize delays and increase the potential to reduce morbidity and mortality.

During the Ebola crisis of 2014-2015, AVAREF applied a Joint and Assisted Review for CTAs. A Table-Top exercise was used to formalize and improve the approach for emergencies, resulting in the newly endorsed AVAREF Strategy and Guidance for Emergency Preparedness.
In light of this, AVAREF has committed to release emergency CTA joint-review in 10 or 15 days on 1 April 2020¹

¹ Decision communicated on 20 April 2020
**Intention to submit**

At least 2 weeks prior to submission, applicant informs AVAREF of its intention to submit.

AVAREF notifies national stakeholders (NRA and EC) about potential application to ensure readiness for joint-review.

**Application**

Applicant submits application for emergency joint-review to AVAREF.

AVAREF notifies the applicant about submission requirements for national authorities of potential target countries.

All stakeholders are notified about successful screening, national stakeholders are prompted to indicate their willingness to participate.

**Pre-submission meeting**

Countries confirm their participation in the joint-review.

AVAREF promptly screens application the same day.

During the pre-submission meeting, applicants share application key info, stakeholders agree on responsibilities and on submission requirements and the joint-review timeline is finalised.

Applicant submits application for emergency joint-review to AVAREF.

Countries confirm their participation in the joint-review.
Emergency Joint-Review process of clinical trial application (2/2)

Country screening and review (4 days)

Day 0: Applicant submits application to national stakeholders following country-specific guidelines – clock starts once the application is submitted to every target country.

Day 1-3: After screening application to ensure completeness (1 day)...

Day 4: Applicant reviews the list of questions and prepare responses for the joint-review meeting (clock stop).

Joint review (2 days)

Day 5-6: During the joint-review meeting, national authorities and applicant discuss the application...

Day 7: Should some questions remain unanswered, the clock stops and applicant indicates time required to provide answers...

Resolution of questions (1 day)

Day 8-10: ...And all national stakeholders review the application and upload their questions to the applicant on the platform (2 days).

National Authorization (3 days)

National authorities review responses to questions and identify queries that should be further discussed in joint review (1 day).

National authorities take decision regarding application...

...and communicate decision within emergency timeline (3 days).

And all national stakeholders participate a review finalisation meeting (1 day).

...with appointed Discussants presenting LoQs for allocated section and applicant sharing its responses.

Country screening and review, joint review, resolution of questions, national authorization.

1.353 KB / 6.052 KB
Allocation of the 10-day timeline for products approved for other indications

Note: Timeline for products approved for other indications. Additional details on emergency procedure can be found at the link below https://www.afro.who.int/sites/default/files/2020-05/AVAREF_Guidance_Emergency_Preparedness_May2020.pdf
Steps taken by AVAREF to meet revised timelines

- **Early scheduling** of meetings and deadlines
- **Expedited response and availability** of all stakeholders along the process steps
- **Efficient communication** through digital tools (i.e., video conferencing)
- **Strengthened collaboration** and cooperation to allow each stakeholder to meet the deadlines
- **Adaptation of Process** to the emergency and remote working context
  - Electronic submission and electronic completion of administrative requirements
  - Remote online meetings
Presentation of AVAREF

Overview of AVAREF and joint review platform 15 min.
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Developer testimony: Dr. Nathalie Strub-Wourgaft

Dr. Strub-Wourgaft joined Drugs for Neglected Diseases initiative (DNDi) in 2009 and is the Director of Neglected Tropical Diseases.

She has over 20 years of Clinical development experience with companies such as Pfizer and Lundbeck.

With DNDi, she has been involved in 3 joint reviews including an emergency joint review that took place in July 2020.
DNDi has conducted 3 joint-reviews with AVAREF

**Disease:** Eumycetoma  
**Product:** Fosravuconazole  
**Year:** 2016  
**Countries:** 3

**Disease:** Visceral Leishmaniasis  
**Product:** Miltefosine / Paromomycin  
**Year:** 2017  
**Countries:** 4

**Disease:** COVID-19  
**Product:** Hydroxychloroquine / Lopinavir / Paracetamol  
**Year:** 2020  
**Countries:** 14

Streamlining and accelerating reviews
Providing a parallel review process with face to face discussions between developer and national authorities (regulatory authorities and ethics committees) enables a lean, efficient and faster review.

Facilitation and coordination
Defining and communicating timelines early with consistent follow up and multiple meetings to ensure all stakeholders are able to meet timelines and adequately prepare. Provision of a web platform accessible to all stakeholders, which enables queries to be posted by national authorities and answered by developers, avoiding duplication of queries.

Collaboration of authorities
Encouraging NRAs and ECs to collaborate in reviewing applications facilitates less experienced national authorities in meeting deadlines.

3 main sources of value provided to developers by joint reviews

~17 KB / 6.052 KB
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- Poll: 10 min.
- Q&A: 30 min.
We would greatly appreciate your input via the upcoming polls
Question 1: Do you plan on coming to Africa? If so, when?

- Yes, 2\textsuperscript{nd} half of 2020
- Yes, 1\textsuperscript{st} half of 2021
- Yes, 2\textsuperscript{nd} half of 2021
- Yes, after 2021
- No, I do not plan on coming to Africa
Question 2: How many African countries are you interested in conducting clinical trials in?

• 1
• 2-3
• 4+
• Don't know
• N/A
Question 3: What are your key criteria when selecting countries to conduct clinical trials

Please select your top 3

- Efficient regulatory processes
- Short application review timeline
- Clear submission requirements
- Clear guidelines
- Site availability
- Low variability in clinical practice
- Recruitment potential
- Costs
- Sales potential of product in target country
- Other (please specify in the chat)
Question 4: How can AVAREF best support you with clinical trial applications

Please select your top 2

- Identifying submission and administrative requirements for African authorities
- Facilitating face to face conversations with African authorities
- Accelerating application review processes with defined timelines
- Providing scientific advice
- Other (please specify in the chat)
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Any questions?