

AVAREF GUIDELINES – Tools for Processing Clinical Trial Applications by Ethics Committees and National Regulatory Authorities in Africa

Introduction: The Work of AVAREF

The African Vaccine Regulatory Forum (AVAREF), a Pan African network of National Regulatory Authorities (NRAs) and Ethics Committees (ECs) was established by the WHO in 2006 as a platform for building ethics and regulatory capacity for clinical trials, while promoting harmonization of ethics and regulatory processes in the continent. Recognizing the pressing health needs on the continent, AVAREF's governance and scope was extended during an extraordinary meeting in 2016 in Addis Ababa. AVAREF became one of the Continental Technical Committees of the African Medicines Regulatory Harmonization Initiative. The new mandate covers vaccines, medical products, and medical devices in line with the AVAREF strategic plan 2018-2020.

As an effort to improve clinical trial review practices, AVAREF member states agreed to a maximum 60 calendar day timeline for processing and clearance of clinical trial applications. The AVAREF Assembly, comprising of heads of NRAs and Ethics Committees, met in Accra, Ghana in November 2017 and endorsed this timeline. The Secretariat, which monitors these timelines has established that not all Member States are consistently meeting them due to their different capabilities for assessing clinical trial applications, stressing the need for further harmonization. Through the monitoring of the timelines, member states realized the importance of harmonization of regulatory and ethical review practices to address gaps in the capacities and processes.

Development of Tools

To facilitate the review and monitoring of clinical trials on the continent, the AVAREF technical working group on inspection of good clinical practices (GCP) and clinical trials working group (CTWG). The CTWG was selected from experts from AVAREF's Technical Coordinating Committee representing NRAs and ECs from Burkina Faso, Ghana, Kenya, Malawi, Nigeria, Uganda and Zimbabwe on voluntary basis. The group was technically supported by experts from other regulatory agencies (Paul Ehrlich Institute). Other partners (CEPI, BMGF, USFDA,) also provided inputs into the development of these documents. The CTWG developed standardized templates and guides for GCP Inspection, the submission and assessment of clinical trial applications, as well as the checklist and guides for monitoring of clinical trials on the continent.

Based on existing templates used by African NRAs and other international NRAs, these tools (assessment templates for quality; non-clinical; clinical data, and clinical trial application forms) were compiled and reviewed for the assessment of clinical trial applications. A draft was presented at AVAREF's biannual meeting in Maputo, Mozambique in February 2018, and later to the Steering Committee who endorsed it at their September 2018 meeting in Entebbe, Uganda.

The tools are divided into 3 processes and categories:

1. Process- Screening and validation of clinical trial applications: Tool- Clinical trial application form and checklist
2. Process -Assessment of clinical trial applications: Tool-Joint review guidelines, templates for clinical, nonclinical, quality, and biostatistics assessment
3. Process: Monitoring of clinical trials: Tool- Good clinical practice inspection checklist and good clinical practice inspection guide

Adoption and Use of the Tools

To ensure full adoption, domestication, and use of the tools, in February and May 2019 they were presented to members of Economic Community of West African States (ECOWAS), the East African Community (EAC), and the Southern Africa Development Community (SADAC), who reviewed and revised them. These tools were unanimously adopted by the AVAREF Assembly in Victoria Falls, Zimbabwe, in October 2019. Some countries already adopted the tools in their regulatory system and some regions have developed the regional version through group review and minor changes for adoption. All 55 African member states are encouraged to incorporate these tools posted here into their battery of tools for the evaluation of clinical trial applications, including in epidemics and pandemics such as the current COVID-19.

Use of these tools is further example of the shift to standardized clinical trial applications and assessments, and proof of ongoing harmonization initiatives on the continent, which will ultimately lead to shorter timelines for product development.

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