RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES FOR CLINICAL TRIAL APPROVAL DURING PUBLICH HEALTH EMERGENCIES

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GUIDELINES DEVELOPMENT HISTORY

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FOREWORD

Rwanda Food and Drugs Authority (Rwanda FDA) is a regulatory body established by the Law N° 003/2018 of 09/02/2018, specifically in article 8, paragraph 7 and 12, the Authority has mandate to regulate and inspect clinical trials for public health protection.

Reference to the provisions of the technical regulation NºCBD/TRG/015 Rev_0 governing the conduct of clinical trials, especially in its article 37, the Authority issues Guidelines Nº DIS/GDL/033 on Clinical Trial Approval during the epidemics, pandemics, or other public health emergencies.

These guidelines provide guidance on conditions and review mechanisms for expedited assessment for clinical trial application and approval of a Clinical Trial Application without compromising ethical principles, safety and efficacy during the Public health emergencies

The Authority acknowledges all the efforts of key stakeholders who participated in the development and validation of these guidelines.

Dr. Charles KARANGWA
Acting Director General

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ACCRONYMES AND ABBREVIATIONS

AVAREF	**:** African Vaccine Regulatory Forum
CRO	**:** Contract Research Organizations
EAC	**:** East African Community
EC	**:** European Commission
EMA	**:** European Medicines Authority
EU	: European Union
GMP/GCP	**:** Good Manufacturing Practices/ Good Clinical Practices
ICH	**:** International Council on Harmonisation of Technical Requirements for
ILAC	**:** International Laboratory Accreditation Cooperation.
ISO/IEC	**:** International Organization for Standardization and the International Electrotechnical Commission
MA	**:** Marketing Authorization**,**
MAGHP	**:** Marketing Authorization for Global Health Products Medical Devices Agency of Japan
MHLW/PMDA	**:** Ministry of Health, Labour and Welfare/ Pharmaceuticals and Medical Devices Agency.
QC	**:** Quality Control
USFDA	**:** United States Food and Drug Administration
WHO PQ	**:** World Health Organization Prequalification

1.0. GLOSSARY

In these guidelines, unless the context states otherwise:

Public Health Emergencies - An outbreak of a disease declared by WHO as an emergency of international concern. It also includes any outbreak of a disease declared as national, subregional, or regional epidemic.

Emergency: An outbreak of a disease with high mortality and which involves significant numbers of individuals and which may have a danger of international transmission.

Epidemic: the occurrence in a community or a region of cases of an illness, specific health-related behavior or other health-related events clearly in excess of normal expectancy.

Fast-track: Fast track is a process designed to facilitate the development, and expedite the review of clinical trial applications for the conduct of clinical trials during emergencies.

Joint review: This process involves a joint assessment of the application by the Authority with the relevant IRBs and other receiving national drug regulatory agencies.

Pandemic: an emergency occurring worldwide or over a wide area crossing international boundaries and affecting a large number of people.

Transparency:

Reliance processes should be transparent regarding standards and processes. In addition, the basis/rationale for relying on a specific entity should be disclosed and understood by all parties.

Well-resourced or reference Regulatory Authority

In this guideline a well-resourced or reference regulatory authority refers to:

a) a member of ICH prior to 23 October 2015, namely: the US Food and Drug Administration, the European Commission and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency of Japan
b) an ICH observer prior to 23 October 2015, namely: the European Free Trade Association, as represented by Swissmedic and Health Canada; or
c) a regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement prior to 23 October 2015

Work-sharing

The work sharing is a process by which the regulatory Authority of two or more jurisdictions share activities to accomplish a specific regulatory task. The opportunities for work-sharing include, but are not limited to, jointly assessing applications for authorization of clinical trials, marketing authorizations or good practices inspections, joint work in the post-marketing surveillance of medical product quality and safety, joint development of technical guidelines or regulatory standards, and collaboration on information platforms and technology

2.0. **INTRODUCTION**

Clinical trials involve the use of predominantly unregistered drugs in human participants. The potential associated risks are often not well known, especially in phase I and II studies. Although efforts are made to control risks to clinical trial participants, some risks may be unavoidable because of the uncertainty inherent in clinical research. Public health emergencies can complicate relating to the conduct of clinical trials. The fear and desperation associated with emergencies, coupled with a heightened sense of urgency, raise challenges for the way in which regulatory requirements for the conduct of clinical trials are interpreted and practically applied.

Although public health and clinical measures are crucial in addressing emergencies and its effects, new interventions to prevent and treat conditions of or relating to emergencies are also desperately needed. In order to establish the safety, efficacy, and effectiveness of such interventions in the emergency context, interventions need to be tested during the emergency.

The aim of these guidelines is to provide general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice (GCP), and minimizing risks to trial integrity during public health emergency.

These guidelines will thus provide an opportunity to carry out ethical, safe and scientifically sound clinical trials of promising new treatments/interventions and vaccines during emergency. The Guideline also seeks to provide better transparency on regulatory procedures to gather evidence based for product safety and effectiveness in a timely manner.

3.0. SCOPE

These Guidelines covers all the steps of review of clinical trial applications, the decision making, including post- decision processes involved, as well as processes for effective communication for the conduct of Phase I, Phase II and Phase III clinical trials during the epidemics, pandemics, or other health emergencies.

The aim is to facilitate to facilitate clinical trials approval, accelerated product development, expedite CTA processing to prevent delays and access to life saving vaccines and medicines during the public health emergencies.

4.0. GENERAL CONSIDERATIONS

The requirements for a clinical trial application (CTA) during public emergency shall be same as described in the module I, section 1.1.2 of Guidelines Nº DIS/GDL/033 for clinical trial applications in Rwanda. However, the timelines for processing Applications during the emergencies are shortened through expedited review, joint review (IRB and Authority) or by adopting reliance procedures. An application to provide of an investigational product being used in a clinical trial under emergency conditions to non-trial participants shall receive prior approval from the Authority.

Conditions for expedited review for Clinical Trial Applications

The Authority shall provide approval of a Clinical Trial when a sufficient clinical evidence is available to provide a reasonable basis for concluding that the investigational drug may be safe and effective without exposing patients to an unreasonable and significant risk of illness or injury. Therefore, conditions for clinical trial expedited review are the following:

a) Clinical trial applications for IMPs to provide treatment to patients with a serious or immediately life-threatening disease or condition where there are no alternative therapy exists according the Standards Treatments Guidelines.
b) Clinical trials conducted in an emergency for example during a disease outbreak.
c) Clinical trial applications that do not explicitly meet the above criteria and are led by the Ministry having Health in its attribution in the interest of a public health intervention.

5.0. ETHICAL CONSIDERATIONS

Reliance pathways are Alternative /Non-Routine Application Approval Pathways used by the authority in its regulatory decisions. The approval of any type of clinical trial, GMP/GCP compliance, quality control procedures, medical product marketing authorization, and vigilance decision, can be accelerated by reliance on prior regulatory decisions from a well-resourced regulatory authority(ies). The reliance aims at reducing timelines compared to standard timelines applied when using normal regulatory practices. However, the authority shall remain responsible and accountable for decisions taken.

This is a risk-based approach and its implementation procedures shall consider factors, such as the type of products, public health needs and priorities, level of resources and expertise available in a well-resourced regulatory authority, and opportunities for reliance in Rwanda (WHO, 2020).

Considering marketing authorization as an example, the following four (4) reliance pathways may involve additional tasks in the assessment process:

1. **Verification of sameness** of the product to ensure that the medical product is the same as the one that has been assessed by the reference regulatory authority.

2. **Confirmation of applicability of the assessment outcomes** of another authority for regulatory decision-making in the national context, for example, in terms of legal and regulatory settings, benefit-risk assessment, co-morbidities, unmet medical needs, risk management plans and any quality-related specificities such as climatic zones for product stability. In case of differences, such as in target population, epidemiology and other features of the disease, concomitantly used medicines and other factors that can substantially affect the benefit–risk profile of a medicine as well as quality parameters, especially in relation to the stability under different climatic conditions, appropriate justification should be provided by the Applicant.

3. **Abridged assessment** of the quality, safety and efficacy/performance data taking into account information in the assessment reports of the reference regulatory authority.

4. **Joint assessment or work-sharing** between two or more regulatory authorities where a primary review by one authority, second review by another authority followed by a joint assessment session to finalize the assessment report and comments.

6.0. REVIEW OF CLINICAL TRIAL APPLICATION

Without compromising patient safety, the Authority may use shortest and realistic timelines to ensure access to vital interventions must be prioritized and ensured. In order to shorten normal review pathway, the authority accepts parallel/simultaneous submission to National ethics Committee/IRB with close collaboration and effective communication for decision-making procedures.

The timeline of 15 working days is suggested for processing CTAs where the product is already registered for other indications, and 30 working days for novel products. These timelines are for the entire review process from receipt of CTA to the final decision and applies to parallel submissions with exception of clock stops.

The assessment of Clinical Trial Application during public health emergencies will be done following a first-in first-out principle. A stop-clock mechanism shall therefore apply each time the Authority requests for additional information of

6.4 Clinical Trials Authorization

The authority

There will be three outcomes from the review of the application submitted;

1. Authorization of the clinical trial and subsequent award of the Clinical Trial Certificate(CTC);
2. Request for additional information to support the application.
3. Rejection of the clinical trial application with reasons

The authority may apply reliance procedures for Clinical Trial Authorization if:

1. The product under investigation has already been evaluated and listed as a WHO Prequalified Product through the WHO PQ collaborative registration procedure between WHO and the Authority.
2. The product under investigation has already been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the European Union Article 58 Procedure or the Swissmedic Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July, 2014)
3. Either trial or the investigational product has been authorized or granted marketing authorization in either an ICH founding regulatory member state or region such as European Commission (EMA), United States (United States Food and Drug Administration), Japan

(MHLW/PMDA) or an ICH standing regulatory member state or region such as Canada (Health Canada), Switzerland (Swissmedic).

4. Further, products registered by WHO listed agencies under investigation may be considered through the reliance pathways on a case-by-case basis.
5. Either the trial or the investigational product has been evaluated and judged satisfactory at a joint review meeting facilitated by the World Health Organization under the African Vaccine Regulatory Forum (AVAREF).

7.0. COMMUNICATIONS DURING EMERGENCIES

7.1 Verification of Documentations

The Authority shall 'verify' that the product intended to be imported and distributed in Rwanda or the Clinical trial to be conducted in Rwanda has been duly registered or authorized respectively by a well-resourced regulatory authority (ies).

In the case of marketing authorization, the product characteristics (use, dosage, precautions) for local registration should conform to that agreed in the authorization by the well-resourced or the reference regulatory authority. In addition, there should be an assurance that the product is either identical or similar to that approved by the well-resourced in terms of quality, safety and efficacy.

In case the reliance is for Clinical trial submissions, the application (protocol, Investigational brochure, nonclinical reports, previous study reports and other relevant documents) should be identical to that submitted, evaluated and approved by the well-resourced or reference regulatory authority.

The authority reserves the right to subject all submissions for approval to an 'abridged' evaluation of a certain part of the application (e.g., relevant to use under local condition) such as product quality data in relation to climatic conditions and distribution infrastructure and a benefit-risk assessment in relation to use in the local ethnic population, medical practice/culture and patterns of disease and nutrition. **Depending on the type of the verification pathway, the regulatory decision will be approved within (30) working days.**

7.2 Reliance Documentations

In addition to the full assessment report from the well-resourced or the reference regulatory authority, the applicant shall be required to submit a full Clinical Trial Application, full Application for Marketing Authorization, Full application for GMP inspection as required by the Authority guidelines towards authorization of the application through the reliance pathway.

7.3 Assessment based on reliance procedures

The assessment or evaluation of the imported assessment report(s) shall be executed in accordance with laid down procedures to ensure appropriateness and completeness of the assessment findings and conclusions

8.0. IMPORTATION OF IMP DURING EMERGENCIES

9.0. POST APPROVAL AUTHORIZATIONS

10.0. REFERENCES

1. FDA. (2019). FDA GHANA RELIANCE POLICY. January, 1–13.
2. WHO. (2020). Good reliance practices in regulatory decision-making: High-level principles and recommendations. WHO Drug Information, 34(2), 201–230.

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