RWANDA FOOD AND DRUGS AUTHORITY	Department/Division/ Directorate	Food and Drugs Inspection and Safety Monitoring Department
Document Type: **Standard Operating Procedure**		Doc. Number : DIS/SOP/….
RWANDA FDA Rwanda Food and Drugs Authority	Title: **REVIEW/ASSESSMENT OF CLINICAL TRIAL APPLICATIONS (CTA)**	Revision Number : 0 Revision Date: : 23 February 2021 Effective Date : 01 March 2021 Review Due Date : 01 March 2023

RWANDA FOOD AND DRUGS AUTHORITY STANDARD OPERATING PROCEDURE (SOP) ON ASSESSMENT OF CLINICAL TRIAL APPLICATIONS (CTA)

	Author	Checked by			Authorized by	
Title	**Clinical Trial Specialist**	**Division Manager PV-SM**	**Head od Department of FDISM**	**Quality Management Systems**	Director General	Page 1 of 18
Signature & Date						

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1.0 Purpose

1.1 This standard operating procedures(SOPs) describe the procedures for review of Clinical Trial Application (CTA) submitted to Rwanda FDA including end reporting to the Competent

1.2 Ensure the overall consistency in the norms and standards applied throughout the review of Clinical Trial Application

1.3 Ensure that the information in CTA is consistent with the provisions of Rwanda FDA regulations and requirements.

2.0 Scope

The SOP is applicable to new applications, additional data provided in response to deficiency letters for **Clinical Trial Applications**

4.0 Definitions and Abbreviations

CTA: Clinical Trial Application

FIFO: First in First Out

SOPs: Standards Operating Procedures

Rwanda FDA: Rwanda Food and Drugs Authority

5.0 Responsibility

5.1 The Director General is responsible for the overall approval or rejection it specifying of Clinical Trials

5.2 Head of department of Food & Drugs Inspection and Safety Monitoring are responsible for:

a) Ensuring that this SOP is correctly and consistently implemented during the process of review of Clinical Trial Application and related additional information

b) Reviewing and providing regulatory guidance on draft feedbacks (additional data requests, approval letters) according to the outcome of the assessment

c) Monitoring and evaluation of Clinical Trial Oversight

d) Ensuring that this SOP is regularly updated.

5.3 Clinical Trial Analyst and Clinical Trial Specialists are responsible for:

a) Becoming familiar with procedures of assessment/review of clinical trial

b) Complying with this SOP whenever carrying out assessment of Clinical Trial Application (CTA) and related additional information

c) Singing the declaration of interest (DOI) and Confidentiality Agreement (COA)

d) review of the submitted Clinical Trial Applications according to the first in First out (FIFO) rules

e) Writing assessment report of Clinical Trial Application

f) Preparing draft feedbacks (additional data requests, approval letters) according to the outcome of the assessment

g) Ensuring that this SOP is regularly updated.

6.0 Distribution

6.1 Director General

6.2 Heads of Department of Food and Drugs Inspection and Safety Monitoring

6.3 Division Manager of Pharmacovigilance & Safety Monitoring,

6.4 Clinical Trial Analyst

6.5 Clinical Trial specialists

6.6 In charge of Quality Management System

7.0 Reference

NA

8.0 Safety Precautions

NA

9.0 Materials and equipment

9.1 An electronic copy of the Clinical Trial Application

9.2 Guidelines No DIS/GDL/033 Rev Nº 0 for Clinical Trial Application and its annexes

9.3 Rwanda FDA regulations No CBD/TRG/015 Rev 0 governing Clinical Trials in Rwanda

9.4 Regulations No CBD/TRG/004 Rev No 1: Related to the regulatory services tariff/fees and fines

9.5 Clinical Trial Approval No DIS/FMT/050 Rev No: 0

9.6 Screening and Assessment templates

10.0 PROCEDURES

10.1. FIRST REVIEW/ASSESSMENT OF CLINICAL TRIAL APPLICATION

10.1.1 Access the screened Clinical Trial Application (CTA) and Screening Report

10.1.2 Open a folder on your PC and give it a name corresponding to the CTA file number, e.g. for **XX-CTA-2021-RwandaFDA.**

10.1.3 Copy the Screening Report, rename and save as **R1**. **e.g.XX-CTA-2021-RwandaFDA-R1**

10.1.4 **.**Copy the Protocol from the CTA and paste it at the end of the Screening Report

10.1.5 Perform your assessment in line with Rwanda FDA regulations and requirements in clear unambiguous language referring to deficiencies or lack of data submitted

10.1.6 In the assessment report, the comments should be typed with "Times New Roman 12" fonts and the 1st assessor's (R1) comments should be introduced in RED font.

10.1.7 The proposed points to be communicated with the applicant shall be highlighted in YELLOW.

10.1.8 Ensure that all points to be communicated to the applicant (questions) are properly phrased so as to be easily understood to facilitate proper responses.

10.1.9 A good communication to the applicant shall have three components:

a) State the problem that you have identified;

b) Identify the section of the relevant guideline that has not been complied with; and

c) State what information the applicant shall submit to the Rwanda FDA

10.1.10 Save the final Clinical Trial Assessment Report as modified in 3, 4 and 5 above in the folder in 2 above

10.2 SECOND REVIEW/ASSESSMENT OF CLINICAL TRIAL APPLICATION

10.2.1 The second reviewer shall obtain a folder containing the first assessor's report. N° **XX-CTA-2021-RwandaFDA-R1**

10.2.2 Rename the first assessor's report as **R2** e.g.: **XX-CTA-2021-RwandaFDA-R2**

10.2.3 Review the first assessor's report and enter your comment notes as second reviewer notes in the report using 2nd assessor's (R2) comments should be written in **BLUE**.

10.2.4 Deficiencies confirmed by the second assessor/reviewer should be highlighted in YELLOW or BLUE (in either RED or BLUE text depending) in the body of the report.

10.2.5 The second assessor (R2) should not delete the comments and questions raised by the first assessor (R1). They may instead strikethrough the text accompanied by the second assessor's comments.

10.2.6 Discuss with the first assessor any areas of contention and arrive at a common position. The analyst or Division Manager may be contacted if necessary for resolution of contentious matters and further guidance

10.2.7 At end the end of second Assessment report (R2), take all agreed points to be communicated with the Clinical Trial Applicant to the appropriate section'' **point to be communicated with the applicant"** CTA assessment template

10.2.8 List issues identified during the assessment for the follow up assessment, such as information to be confirmed, to be verified under the section ''**General remarks to next assessors"** of the CTA assessment template.

10.2.9 List all issues identified during the CT assessment that require verification during a GCP inspection under section' **Recommendations to GCP Inspectors"** of the CTA assessment template

10.2.10 Save the final Clinical Trial Assessment Report (R2) as modified in 10.2.2

10.3 COMMUNICATION OF LIST OF CLINICAL TRIAL DEFICIENCIES /QUERIES

10.3.1 After consolidation of the deficiencies queries to be communicated to the applicant in assessment report, draft the letter to the applicant, specifying a request for any representations within 30days of receipt of the letter. Unless the applicant requested for extension

10.3.2 Submit the draft letter with second assessment report to the Division Manager of Pharmacovigilance and Safety Monitoring for review and further action.

10.3.3 If it is a deficiency letter, dispatch the queries via email, to the local national Principal investigator with copy to sponsor and official of Rwanda FDA hierarchy

10.4 ASSESSMENT OF REPONSES ON DEFICIENCIES /QUERIES

10.4.1 Access the Clinical Trial Application query responses and Assessment template Report

10.4.2 Rename and save the assessment template as **R1**. **e.g.XX-CTA-2021-RwandaFDA-QR1**

10.4.3 Copy the question raised by previous assessors from assessment report (**R2**) and paste in the additional data assessment report template under section of **''QUESTION FROM PREVIOUS ASSESSOR''**

10.4.4 Copy or take snapshot of the proposed applicant response to the raised query responses and paste in the additional data assessment report template under section of **''REPONSE FROM APPLICANT''**

10.4.5 Perform your assessment in line with Rwanda FDA regulations and requirements in clear unambiguous language referring to deficiencies or lack of data submitted in the additional data assessment report template under section of **''COMMENT FROM ASSESSOR"**

10.4.6 In the assessment report, the comments should be typed with "Times New Roman 12" fonts and the 1st assessor's (R1) comments should be introduced in RED font.

10.4.7 If the responses are unsatisfactory or partially responded to, the query may be raised again or clarifications are needed. The proposed points to be communicated with the applicant shall be highlighted in YELLOW.

10.4.8 Save the final additional data assessment report as above modified in section 10.4.2

10.4.9 In case the applicant repeatedly provides unsatisfactorily query responses, a face to face meeting shall be convened and final decisions will be taken according to the provisions of the regulation governing clinical trial in Rwanda.

10.5 APPROVAL OF CLINICAL TRIAL APPLICATION

10.5.1 After completion of the Clinical trial Application review (first or second) without outstanding issues, invite the Principal investigator for face to face or virtual presentation to Rwanda FDA Team as part of approval process.

10.5.2 Submit the folder containing Draft Clinical Trial Certificate (CTC), Second assessment report (R2), Application letter, Copy of Protocol, Approval from National Ethics Committee and evidence of Payment of non-refundable fees to Rwanda FDA as a zipped folder to the Division Manager of Pharmacovigilance and Safety Monitoring for further action.

11.0 Document Revision History

Date of revision	Revision number	Author(s)	Changes made and/or reasons for revision
16/11/2020	0	Clinical trial Specialist	First issue

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Annexes

TEMPLATE FOR ASSESSMENT OF CLINICAL TRIAL APPLICATIONS

Date of the submission (covering letter)	
Date of receipt (Rwanda FDA stamp)	
Application Reference Number	**XX**/CTA/2021RwandaFDA.
Date of Application Screening	
Date of 1st assessment	
Date of 2nd assessment	
Type CT Application	☐ New Application ☐ Amendment Application ☐ Additional Information
Title of Clinical Trial Application	
Protocol Reference Number	
Protocol Version Number (where applicable)	
Name and complete address of CT Applicant	

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Names of Principal Investigator		
Names of Co-Investigator		
Names of Sponsor (If applicable)		
Name and address of the Contract research Organisation (s) (CRO) where the clinical studies proving efficacy and safety of the product were conducted.		
Phase of Trial (if applicable)		
Number of Participants (Trial subjects)		
Number of Clinical Trial Site.		
List of Clinical Trial Sites		
Duration of Clinical Trial		
First assessor	Name	Signature
Second assessor	Name	Signature
Name of Investigational Product (IP) Proprietary Product Name (if relevant)		
International Non-proprietary Name (INN) of the Active Pharmaceutical Ingredient (API), strength, pharmaceutical form.		

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Name (s) and complete address (es) of the manufacturer (s) of the Investigational product (s), including the final product release if different from the manufacturer.	
IP Therapeutic Classification	
IP Route of Administration	
IP storage Information	
Conclusion of the CT Assessment	☐ **ACCEPTED** ☐ **ADDITIONAL DATA REQUESTED** ☐ **REJECTED**
Points to be communicated with the Clinical Trial Applicant: *Please copy all relevant information to be communicated to the CT applicant in the corresponding letter and save it accordingly*	
Clinical Trial Commitments (if any)	
General remarks to next assessors: *List issues identified during the assessment for the follow up assessment, such as information to be confirmed, to be verified, etc.*	
Recommendations to GCP Inspectors:	

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List issues identified during the CT assessment phase that require verification during a GCP inspection	

The Clinical trial assessment report should be written in clear unambiguous language referring to deficiencies or lack of data submitted, as communication with the manufacturer may result from the assessment.

- The assessment report should be typed with "Times New Roman 12" fonts. The format of tables must not be changed.
- The 1st assessor's (R1) comments should be introduced in **red**.
- The 2nd assessor's (R2) comments should be written in **blue**.
- Deficiencies should be highlighted in yellow (in either red or blue text depending) in the body of the report. The assessor should write the deficiencies in the form of a question to the applicant. The question should be written such that it can be understood without reading the assessment report.
- The R2s should not delete the comments and questions raised by the R1s. They may instead strikethrough the text. In case of a disagreement, this should be clearly indicated and a justification for the disagreement should be provided by the R2.
- At end the end of R2 reports, take all agreed points to be communicated with the Clinical Trial Applicant to the appropriate section'' point to be communicated with the applicant''.

CLINICAL TRIAL APPLICATION (CTA) SCREENING REPORT FORM

	Clinical Trial Application Number (CTA number):	
	Clinical Trial Application (CTA) Title	
#	**CTA CHECKLIST OF REQUIRED DOCUMENTS**	
a.	**Cover letter addressed to Director General of the Authority**	☐ **Provided** ☐ **Not Provided**
	Comments:	
b.	**A duly filled and signed clinical trial application form obtained from Rwanda FDA**	☐ **Provided** ☐ **Not Provided**
	Comments:	
c.	**General investigational plan**	☐ **Provided** ☐ **Not Provided**
	Comments:	
d.	**Clinical trial Protocol (detailed content Annex 2)**	☐ **Provided** ☐ **Not Provided**
	Comments:	

e.	**Investigators' brochures**	☐ **Provided** ☐ **Not Provided**
	Comments:	
f.	**Capacity building plans including training and updating of staff involved in the trial**	☐ **Provided** ☐ **Not Provided**
	Comments:	
g.	**Clinical study reports (accomplished Clinical trial phases):**	☐ **Provided** ☐ **Not Provided**
	Comments:	
h.	**National Ethics Committee Clearance**	☐ **Provided** ☐ **Not Provided**
	Comments:	
i.	**Participant Information Leaflet (PIL).**	☐ **Provided** ☐ **Not Provided**

	Comments:	
j.	**Informed Consent Forms (English, French and Kinyarwanda)**	☐ **Provided** ☐ **Not Provided**
	Comments:	
k.	**Curriculum vitae (CVs) of Principal investigator and Co-investigators**	☐ **Provided** ☐ **Not Provided**
	Comments:	
l.	**Joint declaration by Sponsor (or representative) and National Principal Investigator in prescribed format (Annex 3)**	☐ **Provided** ☐ **Not Provided**
	Comments:	
m.	**Evidence of accreditation of the designated Laboratories or other evidence of Good Laboratory Practice (GLP) and assay validation**	☐ **Provided** ☐ **Not Provided**
	Comments:	

n.	**Letters of Access (if applicable) authorizing the Authority to access related files (Drug master, Site Reference Files) must be submitted.**	☐ **Provided** ☐ **Not Provided**
	Comments:	
o.	**Filled in Quality Overall Summary – Chemical Entities Template. (Annex 4)**	☐ **Provided** ☐ **Not Provided**
	Comments:	
p.	**Declarations by Principal investigator and Co-investigators (Annex 5)**	☐ **Provided** ☐ **Not Provided**
	Comments:	
q.	**Evidence of agreement between the Sponsor and the Investigator.**	☐ **Provided** ☐ **Not Provided**
	Comments:	
r.	**Case Report Forms (CRFs)**	☐ **Provided** ☐ **Not Provided**
	Comments:	
s.	**Serious Adverse Events reporting form (Annex 6)**	☐ **Provided** ☐ **Not Provided**

	Comments:	
t.	**Valid insurance policy cover of study participants**	☐ **Provided** ☐ **Not Provided**
	Comments:	
u.	**Certificate of Good Manufacturing Practice (GMP) for manufacture of the trial product and/or placebo**	☐ **Provided** ☐ **Not Provided**
	Comments:	
v.	**Trial product labels and package Insert/s for other trial medicines.**	☐ **Provided** ☐ **Not Provided**
	Comments:	
w.	**Mock up labels for the Investigational products.**	☐ **Provided** ☐ **Not Provided**
	Comments:	

x.	**List and Charter of the Data Safety Monitoring Board/Committee (DSMB).**	☐ **Provided** ☐ **Not Provided**
	Comments:	
y	**Declaration of Conflict of Interest, Financial Disclosure by the investigator**	☐ **Provided** ☐ **Not Provided**
	Comments:	
z	**Evidence of payment of prescribed fees for CTA or CTA**	☐ **Provided** ☐ **Not Provided**
	Comments:	

Note:

1. Certificate of Good Manufacturing Practice (GMP) for the investigational product or statement on GMP from the manufacturer/re-packer (whichever is more relevant) is required.
2. For local product, the manufacturing license is required.
3. For a comparator product, a valid GMP/ISO certificate is required. If not available, Approval letter from the competent regulatory authority or Package insert is required

4. EC approvals of study protocols should be submitted along with the CTA to the Authority