

# **National Drug Authority**

## **Guidelines for the conduct of clinical trial**



**NATIONAL DRUG AUTHORITY**



THE REPUBLIC OF UGANDA

**MINISTRY OF HEALTH**



## **Context of the Guideline**

NDA regulates issues related to safety, quality, efficacy, handling and use of pharmaceutical and other medical products in research. Part IV, section 40 of the National Drug Policy and Authority Act 2000 Edition, Chapter 206 states that with respect to clinical trials:

(1) The authority may issue a certificate to any person for the purpose of carrying out clinical trials in respect of a drug that may be specified in the certificate.

(2) No person may carry out any clinical trial in respect of any drug unless he or she is in possession of a certificate issued under subsection (1).

NDA reserves the right to amend any part of the guidelines whenever it deems fit.

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These guidelines were prepared by a Task force set up by National Drug Authority (NDA) Additional Information about the guidelines may be obtained from The Executive Secretary/Registrar National Drug Authority P.O. Box 23096 Kampala Secretariat Office, Plot 46 – 48 Lumumba Avenue Telephone: (+256) 41-255665/347391/347392 Fax: (+256) 41-255758/343921 E-mail: [ndaug@nda.or.ug](mailto:ndaug@nda.or.ug) Website: [www.nda.or.ug](http://www.nda.or.ug)

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## **ABBREVIATIONS**

ADR	:	Adverse Drug Reaction
AE	:	Adverse Event
AIDS	:	Acquired Immune Deficiency Syndrome
CIOMS	:	: Council of International Organization for Medical Science
CoA	:	Certificate of Analysis
CRO	:	Contract Research Organization
CTA	:	Clinical Trial Application
CTC	:	Clinical Trial Committee
CTIL	:	Clinical Trial Import License
DSMB	:	Data Safety and Monitoring Board
EU	:	European Union
GCP	:	Good Clinical Practice
GLP	:	Good laboratory Practice
GMP	:	Good Manufacturing Practice
IB	:	Investigator's Brochure
ICH	:	International Conference on Harmonisation
IRC	:	Institutional Review Committee
ISCTN	:	: International Serial Clinical trial Number
LPLV	:	Last Patient Last Visit
LSO	:	Last Subject Out
NDA	:	National Drug Authority
NRA	:	National Regulatory Authorities
PI	:	Principal Investigators
SAE	:	Serious Adverse Events

TRS : Technical Review Series  
UNCST : Uganda National Council for Science and Technology  
WHO : World Health Organisation



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## **GLOSSARY/DEFINITIONS**

### **Adverse Drug Reaction**

In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase *responses to a medicinal product* means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function. In clinical trials, injuries caused by overdosing, abuse or dependence and interactions with any other product should be considered adverse drug reactions.

### **Adverse Event**

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

An adverse event can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational)

product, whether or not related to the medicinal (investigational) product.

### **Clinical Trial Import License**

A license issued by NDA authorizing the licensee to import any product for purposes of clinical trials, notwithstanding that the product is not a registered product.

### **Clinical Trial**

Any investigation in human and animal subject intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s) and/or to identify any adverse reactions to an investigational product(s) and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

Clinical trials are generally classified into Phases I to IV. It is not possible to draw distinct lines between the phases, and diverging opinions about details and methodology do exist. A brief description of the individual phases, based on their purposes as relate to clinical development of pharmaceutical products is given below:

### **Phase I**

These are the first trials of a new active ingredient or new formulation in humans/animals often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of the safety and the pharmacokinetic, and where possible the pharmacodynamic profile of the active ingredient(s) in humans/animals.

### **Phase II**

These trials are performed in a limited number of subjects and are often, at a later stage, of a comparative (such as placebo controlled) design. Their purpose is to demonstrate therapeutic activity and to assess the short term safety of the active ingredient in patients suffering from a disease or condition for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or regimens and (if possible) clarification of dose-response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

### **Phase III**

Trials in larger (and possibly varied) patient groups, with the purpose of determining the short- and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (clinically relevant medicine interactions, factors leading to differences in effect such as age). These trials should

preferably be of a randomised double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.

#### **Phase IV**

Studies performed after market authorisation of the product. Trials in phase IV are carried out on the basis of the product characteristics for which the marketing authorization was granted and are normally in the form of post-marketing surveillance, or assessment of therapeutic value or treatment strategies. Although methods may differ, these studies should use the same scientific and ethical standards as applied in pre-marketing studies. After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration, new combinations, etc. are normally considered as trials on new pharmaceutical products and are therefore considered to be phase III trials.

#### **Clinical Trial Report**

A written description of a trial/study of any therapeutic, prophylactic, diagnostic agent conducted in human subjects, in which the clinical and statistical description, prescriptions, and analyses are fully integrated into a single report (see the ICH Guideline for structure and content of Clinical Study Reports).

#### **Clinical trial application**

The clinical trial application (CTA) is the dossier that includes all documentation pertaining to the conduct of clinical trial in country

according to the regulation. The dossier includes a cover letter, a protocol, an investigator's brochure or product information, CV's of investigators, etc.

### **Comparator Product**

An investigational or marketed product (i.e. active control) or placebo, used as a reference in a clinical trial

### **Contract**

A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

### **Contract Research Organisation (CRO)**

A person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

### **Good Clinical Practice (GCP)**

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance, that the data and reported results are credible and accurate, and the rights, integrity, and confidentiality of trial subjects are protected.

**Herbal/Animal Medicinal Products**

Plant/Animal-derived materials or products with therapeutic or other human or animal health benefits which contain either raw or processed ingredients from one or more plants/animals.

**Informed Consent**

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

**Inspection**

The act by a regulatory authority (ie s) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

**Medical Institution**

Any public or private entity or agency or medical or dental facility where clinical trials are conducted

**Institutional Review Committee (IRC)**

An independent body constituted of medical, scientific, and non-scientific members whose responsibility is to ensure the protection of the rights,

safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

### **Interim Clinical Trial/Study Report**

A report of intermediate results and their evaluation based on analyses performed during the course of a trial.

### **Investigational Product**

A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a registered product when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication or when used to gain further information about an approved use

### **Investigator**

A person responsible for the conduct of the clinical trial at a trial site.

If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

### **Investigator's Brochure**

A compilation of the available clinical and non-clinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects or animals



**Manufacture**

All operations that include purchase of materials and products production, quality control, release, storage, shipment (from storage related to manufacturing site) of finished products, and related controls.

**Manufacturer**

A company that carries out at least one step of production as well as the final release of the finished product

**Multi-centre Trial**

A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

**Product (synonym: medical product)**

A drug in a pharmaceutical dosage form, a medical device or a cosmetic, having a singular identity, composition, characteristics and origin.

**Protocol**

A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a clinical trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term protocol refers to protocol and protocol amendments.

**Protocol Amendment**

A written description of a change(s) to or formal clarification of a clinical trial protocol

**Registered Product**

Any product approved by NDA

**Serious Adverse Event or serious Adverse Drug Reaction**

Any untoward medical occurrence that at any dose:

- results in death
- is life – threatening
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity, or
- results in a congenital anomaly/birth defect.

**Side effect**

Unintended effect occurring at normal dose related to the pharmacological properties of a drug

**Sponsor**

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial

**Subjects**

In this guideline, subject means animal and/or human participants in a clinical trial.

**Trial Site**

The location(s) where trial-related activities are actually conducted

**Unregistered Product**

Any product that is not registered by NDA

## **INTRODUCTION**

These guidelines as outlined are drawn in conformity with the legal requirements of the National Drug Policy and Authority Act. It is required that all medicines used in Uganda are registered with the National Drug Authority (NDA), and any clinical trial using registered or unregistered medicine must receive written approval from NDA for that purpose.

The guidelines set out the procedures that should be followed by applicants who wish to conduct clinical trials in Uganda and the steps that NDA will take to review, evaluate and permit the conduct of such trials.

The review and approval process in Uganda is expected to take on average 30 working days from the time the completed application is received by the Drug Information Department in NDA.

Approval by NDA for conduct of the clinical trial does not absolve the applicant from compliance with all laws and regulations in Uganda. In particular, other laws may apply to import or use of infectious or genetically modified organisms.

## **SECTION I**

### **GUIDELINES FOR THE SUBMISSION, REVIEW AND EVALUATION OF APPLICATIONS FOR THE CONDUCT OF CLINICAL TRIALS IN UGANDA**

#### **1 PROCEDURES FOR SUBMISSION OF APPLICATIONS**

##### **1.1 Where to Apply**

The application to conduct a clinical trial in Uganda should be submitted to:

The Executive Secretary/Registrar

National Drug Authority

P.O. BOX 23096

KAMPALA

Secretariat Office, Plot 46 – 48 Lumumba Avenue

Telephone: (+256) 41-255665/347391/347392

Hotline: (+256) 41-344052

Fax: (+256) 41-255758/343921

E-mail: [ndaug@nda.or.ug](mailto:ndaug@nda.or.ug)

Application forms and guidelines can be downloaded from the website:

[www.nda.or.ug](http://www.nda.or.ug).

## **1.2 Who can apply**

The Sponsor or the Principal investigator who is to conduct a drug related clinical trial in Uganda shall make the application.

## **1.3 Application Fee**

Every application for conducting a clinical trial shall be accompanied with a non-refundable processing fee. The fee shall be paid in the form of cheques, bank draft electronic transfer in favour of National Drug Authority in US dollars or the equivalent in Uganda currency.

**N.B Fee for approval of conduct of a clinical trial in Uganda shall from time to time be determined by the board**

## **1.4 The Clinical Trials Application Form (CTA)**

- Application for authorisation of the conduct of a clinical trial shall be made on prescribed forms which are available at the NDA Secretariat Head Office or on the NDA website ([www.nda.or.ug](http://www.nda.or.ug))
- Only one copy of completed form shall be submitted for each application.
- The application should be submitted in writing, in the format and numbering set out in the Clinical Trial Application Form [Attachment 5). The text and diagrams must be clear and legible (12 pt Times New Roman font).
- The detail requested in the application form should be completed briefly, but in full, to enable quick review of studies. However each

section should be cross-referenced to the detail in the Trial Protocol, Investigators Brochure, and other appended documentation.

### **1.5 Presentation of the Application**

The application should be bound in a single volume (or series of volumes) and the pages of the CTA numbered sequentially. The appended documents should be bound together with the application, with tabbed sections identifying each appended document.

### **1.6 Supporting documentations**

Complete, legible copies of key (peer reviewed) publications supporting the information in the application should be attached. They should be cross-referenced from within the CTA text. Additional data will be requested as and when necessary. Requests for additional publications may delay the application.

### **1.7 Electronic format**

The Protocol, Investigators Brochure, and Reference publications should also be supplied on appropriate data storage device. Microsoft -word version 7 is an acceptable format, as well as Acrobat PDF files.

### **1.8 Language**

Application for Clinical Trial Import Licence must be in English. All other data, particulars supporting documentations, labels and package inserts must also be in English.

When supporting documentation is not originally in English, a copy of the document in its original language, accompanied by authenticated

translation in English shall be submitted.

### **1.9 Confidentiality**

National Drug Authority commits to maintain the confidentiality of any information submitted as part of a clinical trial application, supporting documents or associated correspondence. A separate, trial-specific, confidentiality agreement with the applicant may be entered into prior to an application, if this is desired by the applicant.

## **2 PROCEDURES FOR REVIEW AND APPROVAL OF APPLICATIONS**

### **2.1 Completeness of application form, document and fee**

On receipt, NDA will screen the application for completeness. Application for conduct of a clinical trial shall essentially be complete in the first instance if it includes all documents and Appendices and one copy of the complete checklist.

Applications which are incomplete will not be received.

Receiving here means acknowledging that the said document is complete and the NDA reference number has been allocated to the document.

### **2.2 Application Reference Number**

When an application is received, an acknowledgement of receipt will be issued with a reference number for each application. This reference number must be stated in all correspondence concerning the application.



## **2.3 Supplementary Information and Updates**

Any new information available for the product such as adverse effects, changes in formulation or manufacturer for the active ingredients or finished products must be reported to NDA. If changes such as protocol amendments, consent form updates and additional trial sites are made, NDA must be immediately informed. The NDA may request for further supplementary data or documentation when appropriate.

In case additional quantity of study medication(s), additional trial site(s), additional new product, additional manufacturing site/re-packer, additional port of entry, and change of applicant, extension of product's shelf life or a new protocol is required. A new CTA must be made where the sponsor/PI will need to fill in the relevant section where changes applied.

## **2.4 Expert review**

2.4.1 The application will be reviewed by experts appointed by NDA.

There is a confidentiality agreement with the reviewers and committee members to ensure that the content of the application remains confidential.

2.4.2 The initial review may result in queries that need to be answered by the applicant. The reviewers will not have direct contact with the applicant and all correspondence should be directed through NDA.

2.4.3 The reviewers will generate a report that will be discussed by the Clinical

Trials Committee (CTC) which will make a recommendation for approval.

## **2.5 Approval**

2.5.1 The NDA will consider the recommendation of the CTC, the approval of the Ethics Committee/s and other relevant information.

2.5.2 NDA may approve the trial application or may reject the application and specify the reasons for rejection.

2.5.3 Approval will be dependent on receipt of approval of the protocol by the local Independent Ethics Committee in consultations with UNCST.

2.5.4 The Approval for importation of trial related medicines will be dependent on the approval of the conduct of the clinical trial.

2.5.5 This decision will be communicated to the applicant in writing.

In case of rejection, the applicant may appeal and provide additional information where applicable.

## **2.6 Post-trial review**

The Final Report from each study conducted in Uganda should be submitted to the NDA. The format of the report should be as specified in Attachment 6.

Following review of all submissions NDA will then pronounce itself on the conduct of that clinical trial.

## **3 THE INSTITUTIONAL REVIEW COMMITTEE (IRC)**

An independent body, constituted by medical professionals and non-medical members, whose responsibility is to verify that the safety, integrity and human rights of the subjects participating in a particular

trial are protected, thereby providing public reassurance. IRCs<sup>1</sup> should be constituted and operated so that the suitability of the investigators, facilities, protocols, the eligibility of trial subject groups, and the adequacy of confidentiality safeguards may be objectively and impartially reviewed independently of the investigator, sponsor, and relevant authorities.

- 3.1 For NDA to approve any clinical trial application, approval from IRC and registration with UNCST are a pre-requisite.

NDA reserves the right to offer final approval for drug related clinical trials. It is acceptable to NDA that parallel submissions are made to the NDA and the UNCST by the applicant. It is important that queries and amendments required by either body are conveyed, for information, to the other.

- 3.2 IRCs should be established and function as in the National Guidelines for Research Involving Humans as Research Participants published in March 2007)

#### **4 AMENDMENTS TO THE TRIAL PROTOCOL.**

- 4.1 If amendment is essential, it is recommended that the application should be withdrawn and the complete amended version re-

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<sup>1</sup> *The Institutional Review Committee (IRC) is synonymous with Institutional Review Board (IRB)*

submitted. If NDA requires amendments, only the revised section may be replaced.

4.2.1 If the amendment is judged (by the DSMB and/or Principal Investigator) as urgently necessary to protect life or well-being of trial participants or the community, the change may be effected immediately, and the investigator must inform the IRC, UNCST and NDA within 48 hours - by telephone followed by a written full explanation and the information in 4.3 below,

4.2.2 If the amendment may affect the safety of the trial participants (e.g. changes to dose, regimen, concomitant medication, monitoring, etc.) the amendment must be submitted in full, and approval from NDA and IRC, UNCST obtained prior to implementation.

4.2.3 If the amendment is unlikely to impact on participant safety (e.g. change of investigator (except Principle Investigator), end point assay, laboratory, statistical analysis, etc.) the full detail of the change must be submitted in writing, and the change may be implemented 14 days after receipt of the amendment by NDA, if no notification to the contrary is received by the applicant within that period.

4.3 Information to be supplied when submitting a protocol amendment

- An amended CTA form should be completed.

- A **Bold Heading** should note that this is an Amendment and the date.
- Each amendment should be BOLD and in a BOX at the relevant position in the text.
- A table in a covering letter should detail all amended parts of the Application Form.
- The reasons for the amendments must be provided.
- The possible consequences for participants already enrolled must be described.
- Where an amended Participant Information Leaflet & Informed Consent form may be required any additional risks or safety issues should be highlighted.
- The amended supporting documents should be appended, including any new relevant publications.

4.4 The NDA will review the application together with supporting approval from the IRC. It will possibly refer it to expert reviewers before making a decision to approve the amendment.

## 5 INSPECTION (AUDIT) BY NATIONAL DRUG AUTHORITY

An inspection or audit of clinical trial site may be conducted by the NDA. The aim is to evaluate the acceptability of clinical data submitted to NDA, and to ensure that legislation, Good Clinical and Laboratory Practice (GCLP) principles and practices as elaborated in the National Guidelines for Research involving Humans as Research Participants, March 2007 and

in this guideline are adhered to. The responsible officer of the regulatory authority may contact the PI or sponsor for the date of inspection when required.

- Such inspections may be before commencement of the trial, or at predetermined intervals, or may be at the request of the Expert Committee, responsible for clinical trial review.
- However, in the case of complaints or reports of unexpected adverse reactions, inspections may take place at short notice and may be unannounced.

5.1 The Inspections will include - but not be limited to:

- The facilities and staff used for the trial: as approved by the NDA
- Compliance with the approved Protocol
- All amendments to the Protocol which may have been approved
- Accurate, complete and current records according to the Protocol
- Verifying that Serious Adverse Events are reported as required by the Protocol
- Verifying that inspections intended to monitor and audit the trial are conducted as required by the Protocol and the reports are available for inspection.

## **6 REPORTS AND FINAL REVIEW**

### **6.1 Reports of Serious Adverse Events**

The PI shall report to IRCs and the sponsor with copies to NDA all serious adverse events (SAEs), both expected or unexpected, as soon as possible

but no later than seven (7) calendar days upon receiving notice of such event.

Additional follow up information should be made available to NDA as soon as possible, but in any case not later than fifteen (15) calendar days.

## ***6.2 Progress and Final Trial Reports***

In the case of trials lasting for more than 6 months, an interim report (refer to Attachment 6) shall be submitted at 6 months' intervals or as may be requested by NDA. The interim report shall include the number of patients so far treated, number and type of Serious Adverse Events (SAEs) reported, number of discontinued patients and the reason for discontinuation.

The PI or sponsor shall submit an End of Study Summary Report pertaining to the sites conducting the trial to NDA, within 3 months from the Last Patient Out (LPO)/ Last Patient Last Visit (LPLV) date (Refer to Attachment 6).

In case of a multi-centre trial within the country, with different end times, a report on each site shall be submitted before the end of the 3<sup>rd</sup> month from the last subject out. SAEs occurring in other countries under the same study should be reported to NDA promptly.

A Final Report on the trial findings (Refer to Attachment 6) shall then be submitted not later than 3 months of completion of the whole trial.

### **6.3 Product Accountability and Disposal**

A product Accountability/Disposal report shall be submitted to NDA within 3 months from the Last Subject Out date. The report should include:

- Date the trial started and ended and the licence/certificate number.
- Clinical Trial Licence/Certificate for the relevant site.
- Date(s) and quantity received for each trial product
- Balance of the study medical product
- Drug Destruction Certificate, and/or written evidence of re-export of the unused drug supplies to country of origin (whichever applicable).

This guideline does not cater for radioactive substances. For such substances, the international guidelines for radioactive substances will be applied.

### **6.4 Archiving**

It is the responsibility of the investigator and the sponsor to archive and ensure the safety of all the documents related to the trial. The licence holder/applicant should inform NDA in writing prior to destroying the documents. Documents shall be retained for a minimum period of 5 years.



## **SECTION II**

### **GUIDELINES FOR APPLICATION FOR THE CLINICAL TRIAL MEDICAL PRODUCT LICENSE**

The approval for importation or manufacture of trial related medical products is dependent on the approval of the clinical trial.

#### **1 PRODUCTS THAT REQUIRE CLINICAL TRIAL LICENCE**

Prior to importation/manufacturing of local product, the Principal Investigator or sponsor is required to apply for Clinical Trial License from NDA.

##### **1.1 Imports**

Products including placebo, which are not registered with NDA and are intended to be imported for purpose of clinical trial must have a Clinical Trial Licence.

A product with a marketing authorization (registered product) when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication or when used to gain further information about an approved use in a clinical trial also requires a Clinical Trial License.

## **1.2 Manufacture**

A local product manufactured for a purpose of a clinical trial requires a Clinical Trial Licence.

## **2 PROCEDURES FOR APPLICATION FOR CLINICAL TRIAL LICENSE**

### **2.1 Who can apply for Clinical Trial Licence?**

2.1.1 Application for Clinical Trial Licence for a particular product shall be made by any Principal Investigator (PI) or an authorized person from a locally incorporated pharmaceutical company (sponsor) with a permanent address in Uganda who intends to import/manufacture the product for the purpose of a clinical trial.

2.1.2 The holder of a Clinical Trial Licence for a particular product need not necessarily conduct the clinical trial himself or herself.

2.1.3 Where a product contains a narcotic or psychotropic substance, applicants must possess the necessary approval under the legislations.

### **2.2 Responsibility of Applicant**

2.2.1 The applicant shall be responsible for the product and all information supplied in support of his/her application for Clinical Trial Licence of his/her product. He shall be responsible for

updating any information relevant to the product/application.

2.2.2 In case where the applicant is not the manufacturer and where secrecy considerations prevent disclosure of certain information to the applicant, such information may be furnished to NDA through the applicant in a sealed envelope marked CONFIDENTIAL.

2.2.3 The sponsor should not supply an investigational medicinal product until all the required documentation has been obtained (e.g. approval from the appropriate ethics committee and regulatory authority(ies)).

2.2.4 The sponsor should ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterised as appropriate to the stage of development of the product(s), is manufactured in accordance with any applicable GMP and is coded and labelled in a manner that protects blinding, if applicable.

2.2.5 The sponsor should state for the investigational medicinal product(s) acceptable storage temperatures, storage conditions (e.g. protection from light), storage times, reconstitution fluids and procedures, and devices for product infusion, if any.

2.2.6 The sponsor should:

- ensure timely delivery of investigational product(s) to the investigator(s);

- Maintain records that document shipment, receipt, disposition, return and destruction of the investigational product(s);
- Maintain a system for retrieving investigational product(s) and documenting this retrieval (e.g. for deficient product recall, reclaim after trial completion, expired product reclaim);
- Maintain a system for the disposal of unused investigational product(s) and document the process.
- Ensure that the investigational product(s) are stable over the period of use. This stability data should be available on request and for inspection purposes. If non-compliance with the specifications becomes evident in the stability studies during the period of use in the clinical trial, the sponsor should notify the investigators and arrange to take appropriate steps;
- Maintain sufficient quantities of the investigational product(s) used in the trial to reconfirm specifications, should this become necessary, and maintain records of batch sample analyses and characteristics. To the extent stability permits, samples should be retained either until the analyses of the trial data are complete or as required by the applicable regulatory requirement(s), whichever represents the longer retention period.

2.2.7 If a sponsor or a PI decides to use a service of Clinical Research Organisation (CRO) for the conduct of a clinical trial, a letter of agreement should be submitted to NDA.

2.2.8 Any person who knowingly supplies any false or misleading

information in connection with his application for Clinical Trial Licence commits an offence under section 60 of the National Drug Policy and Authority Act.

### **3 CONDITIONS FOR THE CLINICAL TRIAL LICENCE**

#### **3.1 Endorsement of Clinical Trial License**

The Licence holder shall submit to NDA a copy of endorsed Clinical Trial License and/or evidence of delivery to the approved investigator(s)/trial centre(s) on importation and supply of each consignment of the product.

- The product shall only be supplied to the investigator(s) at the trial centre(s) named in the application for the Clinical Trial License for the purpose and use as stated in the said application. No change in investigator, trial centre or trial protocol shall be made without notification to NDA.
- The licence holder shall ensure that adequate precautions are taken for all study medication(s), such as storage in a securely locked cabinet, access to which is limited, to prevent theft or illegal distribution.
- The licence holder shall ensure that the study medication(s) be supplied only to subjects involved in the said trial.

#### **3.2 Notification of Change of Information to NDA**

The licence holder shall inform NDA of any change in information, or any information received by him that casts doubt on the continued validity of

the data which was submitted with, or in connection with the application for the Clinical Trial License.

### **3.3 Discontinuation of Trial**

The licence holder shall inform NDA of any decision to discontinue the trial to which the licence relates and shall state the reason for the decision. The licence holder should return the Clinical Trial License to NDA as soon as possible.

## **4 IMPORTATION AND RELEASE OF INVESTIGATIONAL PRODUCT**

Shipping of investigational products should be conducted according to instructions given by or on behalf of the sponsor in the shipping order.

A pre-clearance inspection will be carried out at the port of entry by NDA. This should include the shipping documentation and overall physical condition of the consignment.

If specific storage conditions are essential to ensure the quality of the product, e.g. maintenance of cold chain in the case of vaccines, a device that will confirm that storage temperatures were not exceeded during transport should be included with the shipment.

## **5 DOCUMENTATION FOR INVESTIGATIONAL PRODUCT RELEASE**

Documentation that should accompany each consignment of investigational medicinal product should enable the NDA inspector at the port of entry to release the product to the investigator(s) responsible for conducting the clinical trial in the country.

This documentation should include at least:

- the Certificate of Analysis of each batch of the investigational product(s) as well as comparator(s), if relevant
- a copy of the letter of approval of clinical trial
- a copy of a valid Certificate of Manufacture issued by the competent Regulatory Authority in the country of origin where applicable
- a copy of a valid WHO certificate of a pharmaceutical product issued by the competent Regulatory Authority in the country of origin

The Cover Sheet should be completed by the sponsor and should accompany each consignment of investigational medicinal products. ***See Annex 1***

The Check-list may be used by the sponsor to ensure that the required documents are attached and correct. ***See Annex 2***

## **NOTES ON THE APPENDICES**

This section comprises recommended formats for some of the Appendices.

- Failure to enclose necessary details and supporting documents may result in delay in the processing, or rejection of an application.
- Headings set out for each Appendix are minimum general requirements. These may not be applicable in all circumstances, neither are they exhaustive.
- Interpretation of these guidelines should be flexible and related to the proposed use of the product.
- Where a heading is not applicable or information is not available, indicate clearly in the appropriate section.
- Data in addition to those specified in the guidelines may be submitted to support the application for the clinical trial import licence. Such data must be presented in a well compiled manner as additional appendices, with a summary of the particulars.
- These guidelines do not preclude any other information required by NDA. Such additional information should be supplied to NDA on request.



## **ATTACHMENT 1: FORMAT FOR CLINICAL TRIAL PROTOCOL**

### Note:

The protocol should contain the following particulars, where applicable:

#### **1. Name and Dosage Form of Product**

- a) State the name or code number under which the product will be imported and known during the trial/study. A separate application is required for each trial
- b) State clearly also the pharmaceutical dosage form of the product, e.g. tablet, capsule, injection, etc.

#### **2. Identification of the Trial**

- a) Title of the Trial
- b) ISCTN for the trial

#### **3. Aim of the Trial**

- a) State the specific objective
- b) Rationale of study/trial.

#### **4. Description of the trial design.**

- a) Trial design (randomised controlled trial, open- label parallel group, cross-over technique)
- b) Blinding technique (double blind, Single blind),
- c) Describe procedure of randomisation
- d) Total number required to achieve the trial objective based on statistical consideration (sufficient to allow dropout, variability of effect etc).

5. Description of trial subjects.

- a) Criteria for inclusion and exclusion of potential trial subjects
- b) Process of screening, recruitment and follow up

6. Treatment Profile

- a) Dose – including justification for route of administration, dosage, dosage interval and treatment period for the pharmaceutical product being tested and the product being used as a control.
- b) Previous, any other treatment that may be given or permitted concomitantly or subsequent therapy, if any.
- c) Washout period, where applicable.

7. Study parameters

- a) Indices, variables etc that were selected for measuring parameter under study (effect, reaction etc).

- b) Methods of measurements & assessment of observations including details of measuring techniques, assessment, qualification of response, clinical and laboratory tests, pharmacokinetic analysis, etc.
- c) The rationale for choice of indices, variables and their methods of determination, specificity, sensitivity and the precision of the method selected.

#### 8. Operational aspects

- a) Information on the establishment of the trial code where it will be kept and when, how, by whom it can be broken in the event of an emergency.
- b) Measures to be implemented to ensure the safe handling and storage of pharmaceutical products.

#### 9. Adverse Event

- a) Methods of recording and reporting adverse events/reactions
- b) Provisions for dealing with complications.

#### 10. Evaluation of results.

- a) Data management procedures
- b) Statistical methods and considerations
- c) Participants withdrawn from the trial

11. Name of Principle Investigator & Co- Investigators.

Designation of Principle Investigator & Co- Investigators

## ATTACHMENT 2: INVESTIGATOR'S BROCHURE

### INVESTIGATOR'S BROCHURE

Ø TITLE PAGE (Example)

SPONSOR'S NAME

Product

Name(s)

Chemical, Generic (if approved)

Trade Name

(if legally permissible and desired by the sponsor)

Ø INVESTIGATOR'S BROCHURE

Edition Number

Release Date

Replaces Previous Edition Number

Date

Ø TABLE OF CONTENTS OF INVESTIGATOR'S BROCHURE (Example)

Confidentiality Statement (optional)

Signature Page (optional)

1. Table of Contents
2. Summary

- 3. Introduction
- 4. Physical, Chemical and Pharmaceutical Properties Formulation
- 5. Non clinical Studies
  - 5.1.1 Non clinical Pharmacology
  - 5.1.2 Pharmacokinetics and Product Metabolism in Animals
  - 5.1.3 Toxicology
- 6.0 Effects in Humans
  - 6.1 Pharmacokinetics and Product Metabolism in Humans
  - 6.2 Safety and Efficacy
  - 6.3 Marketing Experience
- 7.0 Summary of Data and Guidance for the Investigator.

N.B: Reference on

- i) Publications
- ii) Reports

These references should be found at the end of each chapter

Appendices *(if any)*

### ATTACHMENT 3: GUIDE FOR LABELLING CLINICAL TRIAL MEDICINES

#### Outer/carton labels & inner labels

*The following information should be presented on the labelling of the product for clinical trial:*

Parameters	Unit Carton/Patient Kit	Inner Labels	Blister/Strips
Study No./Protocol			
Visit	**	**	**
Subjects' No/Subjects' initial		*	
Product Name/Code			NA
Dosage Form	**	**	**
Name of Active Substance(s)	**	**	**
Strength of Active Substance(s)	**	**	**
Instructions for use/take		*	
Batch Number	**	**	**
Manufacturing date/retest Date			
Expiry Date			
For Clinical Trial Use Only		*	

Name and address of manufacturer/final release/Product Owner (corporate address)/sponsor	***	***	***
Route of administration			NA
Storage Condition		*	NA
Pack Sizes (unit/Vol)		*	NA

NA Not Applicable

\* Exempted for small label such as ampoule and vial.

\*\* Where applicable

\*\*\* With letter of authorisation

If the product is supplied without an outer carton, the information that is required on the outer carton should be stated on the inner carton.



**ATTACHMENT 4: LETTER OF AUTHORIZATION FROM  
MANUFACTURER**

Date : .....

(Company's Name)

a company operating under the laws of ....., located in .....,

Local company name and address

Tel No:

Fax No:

E-mail:

To represent us in Uganda for the application of the Clinical Trial Import  
Licence for :

Protocol No : \_\_\_\_\_

Release Date : \_\_\_\_\_

..... (the local company's name and address) is authorized to be

the Clinical Trial Licence Holder and will be responsible for all matters pertaining to the Clinical Trial Licence application for the above mentioned study protocol.

Yours faithfully,

.....

Authorised name & signature

## **ATTACHMENT 5: THE CLINICAL TRIAL APPLICATION FORM (CTA)**

### **THE CLINICAL TRIAL APPLICATION FORM UGANDA NATIONAL DRUG AUTHORITY**

#### **CTA Section 1 Identification of the Clinical Trial**

1.1 Title of the Study

1.2 Protocol number, date, version:

1.3 Contact Person and contact details

1.4 [Space for NDA Reference Number]

1.5 Declaration of Intent signed by the Principal Investigator

We, the undersigned have submitted all the required documentation and have disclosed all the information required for approval of this application.

We have read the Protocol and the Investigators brochure, appended.

We have the authority and responsibility to oversee this clinical trial, and agree to ensure that the trial will be conducted according to the Protocol and all legal, ethical and regulatory requirements in Uganda

Applicant (Local Contact):

NAME: ..... Date: .....

Signature: .....

Designation: .....

## CHECKLIST OF REQUIRED DOCUMENTS

Item	Requirement
Fees	Proof of payment
Materials transfer:	Applications for import and/or export of materials (if required)
CTA	Clinical Trial Application Form
APPENDIX 1:	Trial Protocol
APPENDIX 2:	Investigators Brochure
APPENDIX 3:	Participant Information Leaflet and Informed Consent
APPENDIX 4:	Certificate of GMP manufacture of the trial medicine or other evidence of manufacture quality, safety and consistency <sup>2</sup>
APPENDIX 5:	Package Insert/s for other trial medicines.
APPENDIX 6:	Certificate of GMP manufacture of the placebo - if appropriate.

<sup>2</sup> Note:

*Certificate of Good Manufacturing Practice (GMP) for the investigational product or statement on GMP from the manufacturer/re-packer (whichever is more relevant).*

- *The GMP certificates or other documents must be issued by an authority recognised by NDA i.e. the authorities listed in the WHO certification Scheme On The Quality Of Pharmaceutical Product Moving In International Commerce,*
- *Or the statement on GMP can be issued by the Quality Assurance Department where the product is manufactured.*
- *For local product, the manufacturing licence is required.*
- *For a comparator product, the following is required:*

*i) a GMP certificate*

*ii) If not available one of the following can be submitted:*

- *Approval letter from the regulatory authority*
- *Annual Registration of Drug Establishment*
- *Package insert*

*iii) For a repacked product, a statement of GMP must be submitted by the re-packer.*

<sup>3</sup> *IRC approvals of study protocols should be submitted along with the CTA to NDA and should include:*

- *Details of IRC membership*
- *Statement of compliance with the requirements in the ICH Guide*
- *A relevant minute of the meeting that approved the study protocol*
- *Any amendments to the trial protocol required by the IRC*
- *Any conditions included in the approval*
- *The final decision*

APPENDIX 7:	Evidence of accreditation of the designated Laboratories or other evidence of GLP and assay validation.
APPENDIX 8:	Insurance Certificate specific for the trial in consultation with NDA
APPENDIX 9:	Signed and completed Declarations by all Investigators
APPENDIX 10:	Approval of Ethics Committees for the Protocol <sup>3</sup>
APPENDIX 11:	Full, legible copies of key, peer-reviewed published articles supporting the application.
APPENDIX 12:	Sample of the label for the imported products
APPENDIX 13:	Letter of authorization from the manufacturer/product owner
APPENDIX 14:	Pharmaceutical Data on dosage form
APPENDIX 15:	Other supporting documents

## CTA Section 2                      Basic            Administrative            Data            on            the Application

### 2.1    Name and address of the registered office of the **Applicant**

	Name:	Telephone Number/s:	Fax	E-mail address	Physical Address	Postal address
Applicant						
Sponsor <sup>4</sup>						
Manufacturer						

<sup>4</sup> *If there is no sponsor as in Investigator initiated trials - a statement to*

*this effect.*

### **CTA Section 3 Medicines to be used in the trial**

#### **3.1 Investigational medicine**

3.1.1 Identifier or name of investigational medicine (code if applicable)

3.1.2 Registration number

3.1.3 Manufacturer/s (Include all sites)

3.1.4 Active ingredient, complete composition, potency and presentation

3.1.5 Evidence of manufacture under conditions compliant with current codes of Good Manufacturing Practice

See Attachment 4 for details of the required information.

3.1.6 Release Specifications and tests. Include Certificate of Analysis.

3.1.7 Current approved Package Insert if available.

#### **3.2 Comparator, Concomitant and Rescue medications (and Placebo)**

3.2.1 Proprietary name and INN

3.2.2 Active ingredient/s, composition, and presentation

3.2.3 Registration number/s (country)

3.2.4 Approved Package inserts to be appended to application [Appendix 6]

3.2.5 Evidence that Placebo is manufactured under GMP. [Appendix 7]

#### **3.3 Details of handling Trial medicines**

3.3.1 Shipping, delivery and distribution of trial medicines

3.3.2 Details of storage requirements and arrangements for cold-chain maintenance where necessary and monitoring during distribution.

3.3.3 Details of dispensing trial medicines and Waste disposal procedures.

3.3.4 Packaging and Labelling of the medical products

3.4 Estimates of quantities of each medication (presentation) to be used for the trial, and for which an import permit is needed.

#### **CTA Section 4 Sites & Investigators**

4.1 National Principal Investigator or co-ordinator (Responsible person)

Name:	
Qualifications	
Contact Details	
Physical address	
Declaration of Capacity & Interests [Appendix 10]	

4.2 For each Site list the following:

4.2.1 Site Identifier (Name)

Physical Address: (for rural sites include GPS coordinates)

Telephone & Fax numbers

E-mail address

4.2.2 Description of the site facilities & Staff

- Clinic and counselling rooms
- Emergency facilities
- Facilities for special examinations (if required)
- Capacity to collect, prepare, store and transport clinical samples



- Storage and handling facilities for medicines
- Name and qualifications of person with responsibility for dispensing medicines

#### 4.3 Site Principal Investigator

Name:	
Qualifications	
Contact Details	
Physical address	
Declaration of Capacity & Interests [Appendix 10]	

#### 4.4 Site Sub-investigators and trial-specific support staff

Name:	
Qualifications	
Contact Details	
Physical address	
Declaration of Capacity & Interests [Appendix 10]	

#### 4.5 For Hospital or Public Health Clinic Sites

- Responsible Administrator
- Contact Details
- Append Signed Letter of Agreement for Trial to take place.

#### 4.6 Append Signed Agreement/s between the Investigators and the

Sponsor/s and/or Clinical Research Organization. (Appendix 13)

## **CTA Section 5 PARTICIPANTS**

5.1 Numbers of Participants as stipulated in the table below

5.1.1	Total number to be enrolled, worldwide	
5.1.2	Total number to be enrolled in Uganda	
5.1.3	Number of trial sites in Uganda	
5.1.4	Intended numbers of participants at each site - evidence of availability.	

5.2 Duration

5.2.1 Estimated trial duration: First enrolment to Final Report

5.2.2 Duration for individual Participant

- Screening period
- Intervention period
- Follow-up period

5.3 What is the intended compensation for time and other inconvenience per participant? This should not be confused with compensation in terms of damage.

## **CTA Section 6 History of Previous and in-progress trials**

6.1 List the titles of previous trials with this (or similar) medicines in Uganda

6.2 List the titles of previous trials with this (or similar) medicines in other countries

6.3 Append Interim or Final report-summaries of these trials to this application. (This may be in the Investigators Brochure or

### APPENDIX 3)

- 6.4 Include a letter or certificate from the regulatory authorities in countries where previous trials have been undertaken (including those in-progress) that these trials have been GCP compliant.

### **CTA Section 7 Ethics review**

- 7.1 Provide the local IRC approval of the Protocol for each site [Appendix 11]
- 7.2 What GCP Guidelines have been followed in compiling this protocol?
- 7.3 Will GCP training be provided for local staff and investigators?

### **CTA Section 8 Trial conduct monitoring and reports**

- 8.1 Describe the Safety and Monitoring Plan for each site.
- 8.2 Describe the system to be used to detect, record, assign causality and the actions for adverse events.
- 8.3 Describe the actions to be taken following reports of Serious Adverse Events.
- 8.4 Describe the composition and remit of the Data Safety Monitoring Board or similar body. Include conditions for Pause- or Stop- rules.
- 8.5 When will Interim Reports be submitted?
- 8.6 Final Report - Estimated due-date?

### **CTA Section 9 INSURANCE**

- 9.1 Provide a copy of the current insurance certificate. (APPENDIX 9)
- 9.2 Provide evidence that each member of the Investigator team is covered by relevant Malpractice insurance for this trial

## **CTA Section 10 Description of the Trial**

10.1 Is the Title of the Trial fully descriptive?

10.2 Summarized Rationale for this Clinical Trial, including relevance to Uganda

10.3 BRIEF Background information should include:

- The disease or condition and local epidemiology
- Properties of the medicine - hypothesis for action
- Description of risks of the protocol and the potential harms of the medicine.
- Pre-clinical animal toxicology test results in-animals and in-vitro that establishes probable safety and efficacy in humans <sup>3</sup>\*
- Prior Clinical trial report summaries that establishes probable safety and efficacy in humans \*
- Include evidence that the formulations used in the pre-clinical and previous studies are identical to that in this application. Any variations should be highlighted and justified. \*
- Published reviews or reports relevant to this disease and this type of medicine

---

\* *Cross-reference to detail in the Investigator's Brochure.*

10.4 Objectives of this trial (List as Primary and Secondary objectives and provide justification)

10.5 Trial Design: Describe and justify each component.

10.5.1 Phase

Placebo or comparator

Randomization and blinding

Other detail

10.5.2 Time sequence –

A Table of screening, intervention and follow-up visits will be of assistance.

10.5.3 Participants

Eligibility

Inclusion criteria - list and justify each

Exclusion criteria - list and justify each

10.5.4 Treatment regimens for each group. *The table in 10.5.2 above can be used to set this out*

10.5.5 Follow-up, sampling collection and monitoring plans;

Immediate monitoring - intermediate monitoring - long term monitoring

Diary cards

Telephone access to investigators

10.6 Outcomes Measurements and Analysis

10.6.1 Describe each outcome/variable (including safety) and explain or justify

10.6.2 Describe the samples that will be collected and the analyses to be conducted on each sample

10.6.3 Provide evidence that the Laboratories that will conduct the Safety screening, and the End-point assays are accredited and competent to do the assays. (APPENDIX 8)

10.6.4 Describe the intended statistical analysis to be conducted. Provide evidence that the study is powered to provide the intended outcome.

10.7 Are any Sub-studies intended? Provide full details.

10.8 Are any genetic studies (HLA-typing or gene marker analysis) intended? Provide full details, and justify this.

Is there a separate Informed Consent Form for this?

10.9 Will clinical samples be stored for any period beyond the duration of this trial?

10.9.1 What is the purpose of such archiving?

10.9.2 What controls are to be placed on their confidentiality and possible future use?

10.10 Participant Information Leaflet (PIL) and Informed Consent (ICON)

10.10.1 Append a copy of the PIL & ICON [Appendix 4]

10.10.2 In what languages will this be available?

10.10.3 Append the Parent / guardian consent form, in the case where minor participants will be included.

10.10.4 Are there separate ICON for sub-studies or Genetic studies?

11 Publication Policy

Provide details of the Investigators and Sponsors intentions and freedom to publish the outcomes of this study.

**ATTACHMENT 6: FORMAT FOR CLINICAL STUDY REPORTS**

**ICH TOPIC E3, STRUCTURE & CONTENT OF CLINICAL STUDY REPORTS (CPMP/ICH/137/95)**

1. Title Page
2. Synopsis
3. Table of contents For the Individual Clinical Study Report
4. List of Abbreviations and Definition of Terms
5. Ethics
6. Investigators and Study Administrative Structure
7. Introduction
8. Study Objectives
9. Investigation Plans
10. Study Patients
11. Efficacy Evaluation
12. Safety Evaluation
13. Discussion and Overall Conclusion
14. Tables, Figures and Graphs referred to but not included in the text
15. Reference List
- 16. Appendices**

## **SAMPLE INTERIM/END OF STUDY SUMMARY REPORT**

**< Date>**

**The Executive Secretary**

**National Drug Authority**

**Attention: Head, Drug Information Department**

**Dear < Insert Name>**

INTERIM/END OF STUDY SUMMARY REPORT <Whichever applicable>

< Study Protocol Title and Protocol Number>

<NDA Reference Number>

The following is a summary of the <Study title> trial conducted in  
<insert institution name>:

First Patient In (FPI) : **< insert date>**

Last Patient In (LPI) : **< insert date>**

Last Patient Out (LPO): **<insert date>**

Number of patient screened: **< insert number>**

Number of Patient Randomized: **<insert number>**



Number of Patient discontinued: < **insert number**>

Reasons for discontinued: <**insert number**>

Reason for discontinuation: <**List of individual discontinued patient**

Number of patients completed study: < **insert number**>

Number of Serious Adverse Events SAE's: < insert number>

Number of Endpoints: <insert number if applicable, if not, to be removed>

Last batch of drug supplies collected back from site: < insert date>

Last batch of drug supplies sent back to < originating site> for destruction: <insert date>; if local destruction, attach copy of NDA destruction certificate.

List of any changes in trial personnel – including full CV and Declaration

List of Monitor and Audit reports to date.

**ATTACHMENT 7: FORMAT FOR PHAMACEUTICAL DATA ON DOSAGE FORM.**

**APPLICATION FOR CLINICAL TRIAL LICENCE**

PRODUCT:

REF:

Note: This is the recommended format for Appendix 2 for an individual drug.

Spacing should be adjusted by applicant as and when necessary.

Extension sheets for details and supporting documents should be appropriately numbered and referenced.

**1. FINISHED PRODUCT**

1.1 Description (physical characteristics):

1.2 Composition (Complete Formula)

1.2.1 Active Ingredient

Active Ingredient(s):	<u>Content</u>

1.2.2. Other Ingredients (adjuncts, excipients, preservative, colour, flavour, etc):

<u>Name of Other Ingredient(s)</u>	<u>Content</u>

1.3. Packing/Pack Size (brief):

## 2. MANUFACTURE OF PRODUCT

(Enclose in sealed envelope marked '**CONFIDENTIAL**',

If desired.

If so indicate here, with appropriate reference).

5.2 Complete Batch Manufacturing Master Formula:

<u>Name of Ingredients (Active and</u>	<u>Quantities used per</u>
<u>Otherwise)</u>	<u>batch</u>

5.3 Manufacturing Process:

Brief Description and Principles:

## 6 QUALITY CONTROL

6.1 State whether quality control is done in part or solely by the manufacture's

own quality control department or an external laboratory.

6.2 If quality control tests are done by an external laboratory, state:

- i) name and address of the laboratory;
- ii) tests done by the external laboratory;
- iii) reasons why the tests are not done by the manufacturer;

6.3 Specifications for Ingredients, Active and Otherwise

Name of Ingredient	Specifications	Source (State whether B.P/U.S.P/ Manufacturer's etc).	Manufacturer & Country of Origin

6.4 In- Process Quality Control:

Tests performed during manufacturing process and sampling protocols:

Tests	Stage at which test is done	Frequency of sampling	Quality of sample taken each time

6.5 Finished Product Quality Control:

Tests and Specification Limits (check and Release Specifications):

Test	Acceptance Limits	Release for test method and Limits (B.P./U.S.P./Manufacturers, etc)

The Certificate of Analysis to be certified by Quality Assurance Manager.

Certificate of Analysis of recent batch of product (**minimum 1 batch**) enclosed: [   ]

## 7     **STABILITY OF PRODUCT:**

7.1    Storage condition must be included on the label.

7.2    Proposed shelf life of product:

N.B In the event that the extension of shelf life for clinical trial material is required, industry will provide supportive data to support the extension. Supportive data in the form of retest results will be considered.

7.3    Stability Studies:

7.3.1 Completed    stability    studies/accelerated    stability    studies.  
(Summary of  
                 stability    studies,    characteristics    and    degradation    products

monitoring results and conclusions of completed stability studies).  
Results of studies of at least one batch are required.

#### 7.3.2 On-going/Proposed stability studies.

(Outline of on-going or proposed stability studies).

### **8 CONTAINERS/PACKAGING**

#### 8.1 Description of immediate (primary) containers/packaging:

- a) Type
- b) Material
- c) Capacity (where applicable):
- d) Closure and liner (type and material), (where applicable)

#### 8.2 Description of outer container(s)/packaging(s)

#### 8.3 Dose-measuring device/applicators/administration set/etc, if any:

- a) Description/Type
- b) Material
- c) Capacity (where applicable)

#### 8.4 Packaging inclusions (desiccant, fillers, etc.) if any:

Description and compositions

#### 8.5 Is there any known interaction between the product and packaging

material? (Yes/No); if yes, specify.

**9 LABELLING (Refer to Attachment 3).**

Enclose samples or proposed drafts of the following:

- a) Label(s) for immediate package/container of product
- b) Label(s) for outer package/container of product
- c) Original Package insert(s) for comparator drug

Any changes/amendments must be notified to the regulatory authority.

## **ATTACHMENT 8: FORMAT FOR DECLARATION BY INVESTIGATORS**

### **FORMAT for Declarations by Investigators**

Trial Protocol Number. . . . .

NAME:

Role in Trial

Trial Title:

Site: A current Curriculum Vitae is attached.

1 I am aware of the responsibilities of my role as . . . . .  
in clinical trial number . . . . . as required by the legal, ethical and  
regulatory requirements of Uganda

2 I have read and understand the attached Protocol, Investigators  
Brochure and supporting documentation and I will comply with the  
procedures and requirements included in them.

3 I have read the attached Clinical Trial Application form as submitted  
to the National Drug Authority in Uganda and confirm that the  
information is complete, true and accurate, and conforms to the Protocol  
and supporting documentation.

4 I will not commence with this trial before written authorization has



been received from the Uganda National Drug Authority and the relevant Ethics Committee/s. I will provide the IEC and NDA with reports as required.

5 I will obtain Informed consent from all participants, or if they are not legally competent, from their legal representatives, parents or guardian.

I will ensure that every participant (and other involved person, such as relatives) will be treated in a dignified manner and with respect.

6 I DECLARE: I have no conflict of interest in terms of financial interests or personal relationships that may inappropriately influence my responsibilities and conduct of this trial.

Initials: . . . . .

7 I DECLARE: I have not previously been associated with any clinical study that has been terminated, or study-site that was closed, due to failure to comply with Good Clinical Practice.

Initials: . . . . .

8 I have received suitable, recent training in Good Clinical Practice in the Ugandan context.

9 SIGNED . . . . . DATE . . . . .

WITNESS: . . . . . NAME . . . . .

DATE . . . . .

**ANNEX 1: COVER SHEET (to be completed by the sponsor)**

<b>ANNEX 1: COVER SHEET (to be completed by the sponsor)</b>	
<b>IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS</b>	
Fees (if applicable)	
Study Title and phase of the study	
Protocol Number	
Study Drug	
Unique code number	
NDA approval number of clinical trial	
NDA reference number(s) of comparator drug(s) (if applicable)	
NDA reference number(s) of concomitant drug(s) (if applicable)	
Sponsor	
Applicant	
Trial site(s)	
Sponsor Contact Person: Address Telephone number	

Fax number	
Cell number	
E-mail address	
Batch number(s) and expiry date:	
Study drug	
Comparator drug(s)	
Quantities	
Blinding done or not	
Recommended storage temperature	

**ANNEX 2: CHECK-LIST of required documentation**

*To be supplied by the sponsor for use by the NDA inspector at the port of entry to authorize the importation of the investigational medicinal product.*

<b>IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS</b>			
<b>CHECK-LIST of required documentation</b>			
<b>Are the following documents attached and correct, as indicated:</b>		<b>YES</b>	<b>NO</b>
1	Copy of NDA letter of approval of clinical trial		
2	Certificate(s) of Analysis (CoA) Study drug Comparator (if applicable)		
3	Does the CoA reflect at least the following information:		
	Product name or code		
	Name of company / Sponsor		
	Batch number		
	Expiry date		
	Date of issue		
	Signature, qualification and title of responsible person		
	Results of physical and analytical tests		
4	Copy of valid Certificate of Manufacture issued by the competent Regulatory Authority in the country of origin		

IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS			
CHECK-LIST of required documentation			
Are the following documents attached and correct, as indicated:		YES	NO
5	WHO certificate of a pharmaceutical product issued by the competent Regulatory Authority in the country of origin		
6	Device / Proof of maintenance of cold chain (if applicable)		
7	Labelling: <i>outer packaging, immediate container</i> Does the label clearly indicate		
7.1	That the product is clinical trial material, e.g. "For use in clinical trial only"		
7.2	Product name or unique code (if blinded)		
	<i>Does this concur with the information on the Cover Sheet</i>		
7.3	Storage temperature		
	<i>Does this concur with the information on the Cover Sheet</i>		
7.4	Storage conditions (e.g. protection from light)		
7.5	Batch number		
	<i>Does this concur with the information on the Cover Sheet</i>		
7.6	Date of Manufacture		
7.7	Expiry date		

<b>IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS</b>			
<b>CHECK-LIST of required documentation</b>			
<b>Are the following documents attached and correct, as indicated:</b>		<b>YES</b>	<b>NO</b>
	<i>Does this concur with the information on the Cover Sheet</i>		
7.8	Sponsor contact details		
	<i>Does this concur with the information on the Cover Sheet</i>		
8	Is the physical condition of the consignment acceptable?		

## **REFERENCES**

ICH Guidelines for clinical Trials E6 (R1) CPMP/ICH/135/95, updated in 2002

EU Directive 2005/28/EC

Uganda Guidelines for AIDS Vaccine Research

WHO Guidelines for Clinical Evaluation of Vaccines Technical Report Series -924 (2004)

Guidelines for good clinical practice (GCP) for trials on pharmaceutical products - Annex 3 in the use of essential drugs.6 Report, WHO, 1995 ((WHO Technical Report Series, N°850)