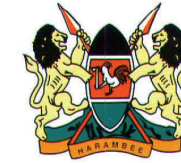


This detailed guidance should be followed unless it is otherwise justified in an application to the PPB.

References

- Pharmacy and Poisons Act, CAP 244 Laws of Kenya.
Operation guidance: Information needed to support clinical trials of herbal products. *UNICEF/UNDP/World Bank/ WHO special Programme and Training in Tropical Diseases (TDR)*.
Guideline for regulating the conduct of clinical trials in human participants. *SADC April 2004*
Guidelines for Application to Conduct Clinical Trials in Tanzania Second Edition. *TFDA February 2009*
Guidelines for Application to Conduct Drug Related Clinical Trials in Malaysia

Pharmacy & Poisons Board House
Lenana Road, Next to Lenana Conference Centre
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0733884411
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www.pharmacyboardkenya.org



REPUBLIC OF KENYA

PHARMACY AND POISONS BOARD

GUIDELINES FOR APPLICATIONS TO CONDUCT

CLINICAL TRIALS IN KENYA



PREPARED BY

EXPERT COMMITTEE ON CLINICAL TRIALS

ECCT JUNE 2010

16.0 GENDER	
Female	<input type="radio"/>
Male	<input type="radio"/>

17.0 GROUP OF TRIAL SUBJECTS	
Healthy volunteers	yes <input type="radio"/> no <input type="radio"/>
Patients	yes <input type="radio"/> no <input type="radio"/>
Specific vulnerable populations	yes <input type="radio"/> no <input type="radio"/>
Women of child bearing potential	yes <input type="radio"/> no <input type="radio"/>
Women of child bearing potential using contraception	yes <input type="radio"/> no <input type="radio"/>
Pregnant women	yes <input type="radio"/> no <input type="radio"/>
Nursing women	yes <input type="radio"/> no <input type="radio"/>
Emergency situation	yes <input type="radio"/> no <input type="radio"/>
Subjects incapable of giving consent personally	yes <input type="radio"/> no <input type="radio"/>
If yes, specify :	
Others :	yes <input type="radio"/> no <input type="radio"/>
If yes, specify	

18.0 PLANNED NUMBER OF SUBJECTS TO BE INCLUDED :	
In Kenya	()
For a multinational trial:	
In the Community	()
In the whole clinical trial	()

19.0 PLANS FOR TREATMENT OR CARE AFTER A SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL. If it is different from the expected normal treatment of that condition, please specify (free text):
--

CLINICAL TRIAL SITES/INVESTIGATORS CONCERNED BY THIS REQUEST
--

20.0 CO-ORDINATING INVESTIGATOR (for multicentre trial) and principal investigator (for single centre trial)
Given name
Middle name, if applicable
Family name
Qualification (MD.....)
Professional address:

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14.0 DESIGN OF THE TRIAL			
Controlled		yes	o no o
If yes, specify:			
Randomised		yes	o no o
Open :		yes	o no o
Single blind :		yes	o no o
Double blind:		yes	o no o
Parallel group:		yes	o no o
Cross over :		yes	o no o
Other :		yes	o no o
If yes to other specify:			
If controlled, specify the comparator:			
Other medicinal product(s)		yes	o no o
Placebo		yes	o no o
Other		yes	o no o
If yes to other, specify :			
Single site in Kenya :		yes	o no o
Multiple sites in Kenya :		yes	o no o
Number of sites anticipated in Member State concerned ()			
Multiple States:		yes	o no o
Number of sites anticipated in the Community ()			
Does this trial involve countries outside the EAC?		yes	o no o
Does this trial have a data monitoring committee?		yes	o no o
Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial :			
Initial estimate of the duration of the trial (years ,months and days):			
In Kenya	years	months	days
In all countries concerned by the trial	years	months	days
15.0 AGE SPAN			
Less than 18 years		yes	o no olf yes specify:
In Utero		yes	o no o
Preterm Newborn Infants (up to gestational age < 37 weeks)		yes	o no o
Newborn (0-27 days)		yes	o no o
Infant and toddler (28 days - 23 months)		yes	o no o
Children (2-11 years)		yes	o no o
Adolescent (12-17 years)		yes	o no o
Adult (18-65 years)		yes	o no o
Elderly (> 65 years)		yes	o no o

ABBREVIATIONS AND DEFINITION OF TERMS

The meaning of the following words used in these guidelines are as defined herein.

9.0 PRINCIPAL INCLUSION CRITERIA (list the most important)

10.0 PRINCIPAL EXCLUSION CRITERIA (list the most important)

11.0 PRIMARY END POINT(S) :

12.0 SCOPE OF THE TRIAL – Tick all boxes where applicable																											
<table style="width: 100%; border-collapse: collapse;"> <tr><td style="padding: 2px;">Diagnosis</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Prophylaxis</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Therapy</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Safety</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Efficacy</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Pharmacokinetic</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Pharmacodynamic</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Bioequivalence</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Dose Response</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Pharmacogenetic</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Pharmacogenomic</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Pharmacoeconomic</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Others</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> </table>	Diagnosis	<input type="checkbox"/>	Prophylaxis	<input type="checkbox"/>	Therapy	<input type="checkbox"/>	Safety	<input type="checkbox"/>	Efficacy	<input type="checkbox"/>	Pharmacokinetic	<input type="checkbox"/>	Pharmacodynamic	<input type="checkbox"/>	Bioequivalence	<input type="checkbox"/>	Dose Response	<input type="checkbox"/>	Pharmacogenetic	<input type="checkbox"/>	Pharmacogenomic	<input type="checkbox"/>	Pharmacoeconomic	<input type="checkbox"/>	Others	<input type="checkbox"/>	
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Efficacy	<input type="checkbox"/>																										
Pharmacokinetic	<input type="checkbox"/>																										
Pharmacodynamic	<input type="checkbox"/>																										
Bioequivalence	<input type="checkbox"/>																										
Dose Response	<input type="checkbox"/>																										
Pharmacogenetic	<input type="checkbox"/>																										
Pharmacogenomic	<input type="checkbox"/>																										
Pharmacoeconomic	<input type="checkbox"/>																										
Others	<input type="checkbox"/>																										
If others, specify:																											

13.0 TRIAL TYPE AND PHASE																			
<table style="width: 100%; border-collapse: collapse;"> <tr><td style="padding: 2px;">Human pharmacology (Phase I)</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Is it:</td><td></td></tr> <tr><td style="padding: 2px;">First administration to humans</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Bioequivalence study</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Other :</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">If other, please specify</td><td></td></tr> <tr><td style="padding: 2px;">Therapeutic exploratory (Phase II)</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Therapeutic confirmatory (Phase III)</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> <tr><td style="padding: 2px;">Therapeutic use (Phase IV)</td><td style="text-align: right; padding: 2px;"><input type="checkbox"/></td></tr> </table>	Human pharmacology (Phase I)	<input type="checkbox"/>	Is it:		First administration to humans	<input type="checkbox"/>	Bioequivalence study	<input type="checkbox"/>	Other :	<input type="checkbox"/>	If other, please specify		Therapeutic exploratory (Phase II)	<input type="checkbox"/>	Therapeutic confirmatory (Phase III)	<input type="checkbox"/>	Therapeutic use (Phase IV)	<input type="checkbox"/>	
Human pharmacology (Phase I)	<input type="checkbox"/>																		
Is it:																			
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Other :	<input type="checkbox"/>																		
If other, please specify																			
Therapeutic exploratory (Phase II)	<input type="checkbox"/>																		
Therapeutic confirmatory (Phase III)	<input type="checkbox"/>																		
Therapeutic use (Phase IV)	<input type="checkbox"/>																		

ADR	Adverse Drug Reactions	All noxious and unintended responses to a clinical trial medicinal product related to any dose or all unintended noxious responses to a registered medicinal product which occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.
AE	Adverse Event	Any untoward medical occurrence in a patient or clinical investigation study participant administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of an investigational medicinal product (IMP), whether or not related to the IMP.
	Applicant	A person applying to conduct a clinical trial – the Principal Investigator (PI) or a representative of the sponsor, a clinical research organization (CRO) or research institution.
	Audit Certificate	A declaration of confirmation by the auditor that an audit has taken place.
	Audit Report	A written evaluation by the sponsor's auditor of the results of the audit.
	Blinding/Masking	A procedure in which study participants, investigators or data analysts are kept unaware of the treatment assignment(s). Single-blinding usually refers to the study participant(s) being unaware and double-blinding usually refers to the study participant(s), investigator(s) and data analyst(s) being unaware of the treatment assignment(s).

1.0 BIOLOGICAL / BIOTECHNOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS INCLUDING VACCINES	
Type of product	
Extractive	yes <input type="radio"/> no <input type="radio"/>
Recombinant	yes <input type="radio"/> no <input type="radio"/>
Vaccine	yes <input type="radio"/> no <input type="radio"/>
GMO	yes <input type="radio"/> no <input type="radio"/>
Plasma derived products	yes <input type="radio"/> no <input type="radio"/>
Others	yes <input type="radio"/> no <input type="radio"/>
If others, specify :	
2.0 SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)	
Origin of cells	
Autologous	yes <input type="radio"/> no <input type="radio"/>
Allogeneic	yes <input type="radio"/> no <input type="radio"/>
Xenogeneic	yes <input type="radio"/> no <input type="radio"/>
If yes, specify species of origin :	
Type of cells	
2.4 Stem cells	yes <input type="radio"/> no <input type="radio"/>
2.5 In vivo gene therapy:	yes <input type="radio"/> no <input type="radio"/>
2.6 Ex vivo gene therapy:	yes <input type="radio"/> no <input type="radio"/>
Type of gene transfer product	
2.7 Differentiated cells	yes <input type="radio"/> no <input type="radio"/>
If yes, specify the type (e.g. keratinocytes, fibroblasts, chondrocytes) :	
Others :	yes <input type="radio"/> no <input type="radio"/>
If others, specify :	
3.0 GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS	
Gene(s) of interest :	
3.1 Nucleic acid (e.g. plasmid) :	yes <input type="radio"/> no <input type="radio"/>
If yes, specify if:	
Naked:	yes <input type="radio"/> no <input type="radio"/>
Complexed	yes <input type="radio"/> no <input type="radio"/>
3.4 Viral vector:	yes <input type="radio"/> no <input type="radio"/>
If yes, specify the type: adenovirus, retrovirus, AAV,	
3.6 Others :	yes <input type="radio"/> no <input type="radio"/>
If others, specify :	
4.0 Genetically modified cells :	yes <input type="radio"/> no <input type="radio"/>
If yes, specify - origin of the cells :	
4.1 Autologous :	yes <input type="radio"/> no <input type="radio"/>
4.2 Allogeneic :	yes <input type="radio"/> no <input type="radio"/>
4.3 Xenogeneic :	yes <input type="radio"/> no <input type="radio"/>

DSMB	Data and Safety Monitoring Board	An independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data and the critical efficacy endpoints and to recommend to the sponsor whether to continue, modify, or stop a trial.
DPG	Department of Pharmacovigilance	The department at the PPB at the time being responsible for the issues of pharmacovigilance and clinical trials.
	Documentation	All records, in any form, that describes the methods, conduct, and/or results of a clinical trial, the factors affecting a trial, and the actions taken.
	Drug/Medicine	Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient. The term drug/ medicinal product is used in a wider sense to include the whole formulated and registered product, including the presentation and packaging, and accompanying information.
	Essential Documents	Documents which individually and collectively permit evaluation of the conduct of a clinical trial and the quality of the data produced.
	Ethical Clearance	An authorization issued by an NCST accredited ethics committee to conduct a clinical trial in Kenya.

GCP	Good Clinical Practice	A standard for the design, conduct, performance, and monitoring, auditing, recording, analyses and reporting of clinical trials that provide assurance that the data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial study participants are protected.
GMP	Good Manufacturing Practice	An assurance that investigational products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.
	Impartial Witness	A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the study participant or the study participant's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the study participant.
IEC	Independent Ethics Committee	An independent body accredited by the National Council for Science and Technology (NCST) and constituted of medical and non-medical members, whose responsibility is to verify that the safety, integrity and human rights of participants in a particular trial are protected and to consider the general ethics of the trial, thereby providing public reassurance.

Comment on monitors and monitoring plan
Indicate how additional staff (monitors, pharmacists, nursing staff, etc.) will maintain patient confidentiality, follow the protocol, and abide by ethical and regulatory requirements
Comment on insurance and indemnity measures
Comment on Patient Information Leaflet and Informed Consent (NB: inclusion of ABPI guidelines; appropriate level of education/English; possible benefits / risks clear; ensuring patient rights; contact names and numbers, as well as MCC details, included)
Comment on availability and completeness of separate PILs and informed consent forms for any proposed archiving of blood specimens for later research or for genetics research.
Comment on ethics of the publication policy
Comment on treatment and/or management of participants and their disease condition (s) after completion of trial
Comment on ethics committee capacity to monitor site if not a local ethics committee
Provide an explanation if minimum recommended compensation for participants is not being provided.

ECCT Reviewer's comment:

14. Other relevant information not included above

E.g. Are references adequate and dates of references current?

Are there discrepancies between protocol and IB or package inserts? Are there specific explanation(s) for these discrepancies?

Are the explanations for not following the 'GCP guidelines' acceptable?

Other comments on this trial.

ECCT Reviewer's comment:

For office use:

ECCT Reviewer's questions and concerns to be considered and/or forwarded to applicant:

ECCT Reviewer's recommendation:

ECCT recommendation (date): 1A, 1B, 2A, 2B, 3, 4, 5

8. Eligibility and enrolment: (Inclusion and exclusion criteria listed and justified)

ECCT Reviewer's comment:

9. Treatment modalities and regimens, drug accountability [clearly explained and justified for all participant groups/arms e.g. in terms of route of administration, dose, etc. Drug accountability clearly described.]

ECCT Reviewer's comment:

10. Outcome measurements/variables (each clearly stated and justified)

ECCT Reviewer's comment:

11. Adverse events (prevention, definitions – including causality assignment, recording, reporting, time-lines, action to be taken, all clearly described)

ECCT Reviewer's comment:

12. Statistical measures:

Determination of sample size correct, clear and justified (with and/or without stratification)

Statistical method(s) and analysis of quantitative measures appropriate, clear and justified

Statistical method(s) and analysis of qualitative measures appropriate, clear and justified

Data processing (how, where, when, who) clearly described and justified. If a SA person will be involved in data processing, please identify that person

Interim analysis envisaged or not (justify) and stopping rules if applicable (explain)

ECCT Reviewer's comment:

13. Ethical Issues: justification of 'Section 2 part 6' including:

Explanation of which GCP guidelines are or are not being followed

Comment on choice of investigators ()

Comment on need for, appropriateness of, and relevance of GCP training / updating / for staff involved in this trial

Comment on capacity building element of trial

Comment on resources of sites and sponsor

	<i>Informed Consent</i>	A participant's documented voluntary confirmation of willingness to participate in a specific trial after all appropriate information about the trial including a clear statement of it being a research, its objectives, potential benefits, risks and inconveniences, alternative treatment that may be available, and of the subject's rights and responsibilities in accordance with the current revision of the Declaration of Helsinki.
	<i>Inspection</i>	The act of conducting an official review of documents, facilities, records, and any other resources deemed to be related to the clinical trial and that may be located at the trial site, at the sponsor's and/or CRO's facilities.
	<i>Interim Clinical Trial/Study Report</i>	A report of intermediate results and their evaluation based on analyses performed during the course of a trial.
<i>IMP</i>	<i>Investigational medicinal Product</i>	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization 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.
	<i>Investigator</i>	A person appropriately qualified to conduct a clinical trial at a trial site. See also Sub-investigator.
<i>IB</i> <i>IMP</i>	<i>Investigator's Brochure</i> <i>Investigational Medicinal Product</i>	A compilation of the clinical and non-clinical data on the investigational product(s) relevant to the study of the investigational product(s) in human study participants.

MTA	Material Transfer Agreement	A written agreement entered into by a <i>provider</i> and a <i>recipient</i> of research material, aimed at protecting the intellectual and other property rights of the provider while permitting research with the material to proceed.
	Monitor	A person appointed by, and responsible to the sponsor or Contract Research Organization (CRO) for the monitoring and reporting of progress of the trial and for verification of data.
	Monitoring Report	A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's SOPs.
	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.
	Participant	
	Phase I Clinical Trial	The purpose of these trials is to obtain preliminary data on safety of investigational products such as medicines or vaccines, or devices. These studies are carried out in a small number of healthy volunteers.

SECTION 3 – APPLICANT’S REPORT / PRESENTATION

1. Title:

ECCT Reviewer’s comment:

2. Protocol Number/identification:

3. Rationale for study summarised: (Why should this trial be done at all?) Include statement about Kenyan contribution, if any, to the development of this protocol.

ECCT Reviewer’s comment:

4. Background information (**summarised** – **essential** points that apply to this trial) [1-2 sentences max for each point]:

Disease / problem

Kenyan context (e.g. local epidemiology)

Properties of Drug / Entity; hypotheses about mechanism of action, etc.

Pre-clinical findings: (e.g. laboratory / animal / toxicity / mutagenicity)

Clinical findings (e.g. phases; PK; PD; dose-finding; ADRs, NNT/NNH, other)

Systematic review(s) and/or citations per year-group on a Medline search

ECCT Reviewer’s comment:

5. Objectives of study (clearly listed and justified)

ECCT Reviewer’s comment:

6. Study design (clearly described and each component justified)

[includes phase, use of placebo, dosages, randomisation, blinding, duration, etc.]

ECCT Reviewer’s comment:

7. Participants: (number of participants; ability to enroll required number within stated time)

ECCT Reviewer’s comment:

5.7 Details if this trial is being undertaken in EAC, any other country in Africa, or any country where there is no regulatory control of clinical trials:

5.8 Previous studies using this agent which have been approved by ECCT:

ECCT approval number:

Study title:

Protocol number:

Date of approval:

National PI / Principal Investigator:

Date(s) Progress report(s):

Date Final report:

5.9 If any substudies are proposed as part of this protocol, indicate whether or not they will also be done in Kenya. If not, please explain.

Part 6: ETHICS

6.1 Ethics Committee responsible for each site, date of approval or date of application:

6.2 Attach copy of response(s) made by, and/or conditions required by ethics committee(s) if available. Ensure that date of EC response is legible.

6.3 State which Good Clinical Practice (GCP) guidelines are being followed.

6.4 Details of capacity building component of the trial, if any:

6.5 Details of the training of investigators, monitors, study co-ordinators in terms of carrying out this trial and in terms of GCP:

6.6 Detailed safety and monitoring plan for each site: [May be attached]

6.7 Details of trial insurance certificate: (e.g. title, protocol, dates, policy #, amount)

6.8 Details of possible conflict of interest of any person(s)/organisation(s) who/which will be involved in the trial:

6.9 Remuneration to be received in Kenya Shillings: (Investigators) (Trial participants) (Others) Indicate broad breakdown of costs to be covered by this amount – if applicable.

Reviewer's comments:

	Phase II Clinical Trial	The purpose of these trials is to demonstrate therapeutic activity of medicines, or immunogenicity of vaccines, and to determine appropriate dose ranges or regimens. In addition, these trials obtain additional safety data. These studies are carried out in a small number of healthy volunteers.
	Phase III Clinical Trial	These are large trials aimed at determining efficacy of the investigational product. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use. The information obtained in this phase of the trials is used for licensure of the investigational product.
	Phase IV Clinical Trial	These are studies performed after registration of the medicinal product for use by the general public. Phase IV trials are normally in the form of post-marketing surveillance, or assessment of therapeutic value or treatment strategies.
	Pre-clinical Studies	Biomedical studies not performed on human study participants.
PPB	Pharmacy and Poisons Board	The organisation as established by the Cap 244 laws of Kenya being responsible for the ensuring the quality of medicines administered in the country and the practice of the Pharmacy profession.
PSUR	Periodic Safety Update Report	

PI	Principle Investigator	An appropriately qualified person responsible for the conduct of the clinical trial at a trial site and resident in Kenya. If a trial is conducted by a team of individuals at a trial site, the Principle Investigator is the leader of the team. See also Sub-investigator.
	Protocol	A document which states the background, rationale and objectives of the trial and describes its design, methodology and organization, including statistical considerations, and the conditions under which it is to be performed and managed. The protocol should be dated and signed by the investigator, the institution involved and the sponsor.
	Protocol Amendment	A written description of change(s) in the study protocol.
QA	Quality Assurance	All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with good clinical laboratory practice (GCLP) requirement(s).
QC	Quality Control	The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.
	Randomization	The process of assigning trial study participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

	Lectures / tutorials		
<u>Writing up</u> work for publication / presentation			
<u>Reading</u> / sourcing information (e.g. internet searches)			
<u>Other</u> (specify)			

3.3 Details of Site(s) (Name of site, physical address, contact details, contact person, etc.)

3.4 Capacity of Site(s): (Number of staff, names, qualifications, experience -- including study co-ordinators, site facilities, emergency facilities, other relevant infrastructure)

Part 4: PARTICIPANTS (SUBJECTS)

4.1 Number of participants in Kenya:

4.2 Total worldwide:

4.3 Total enrolment in each Kenyan centre: (if competitive enrolment, state minimum and maximum number per site.)

4.4 Retrospective data indicating potential of each site to recruit required number of patients within envisaged duration of trial.

Part 5: OTHER DETAILS

5.1 If the trial is to be conducted in Kenya and not in the host country of the applicant / sponsor, provide an explanation:

5.2 Estimated duration of trial:

5.3 Name other Regulatory Authorities to which applications to do this trial have been submitted, but approval has not yet been granted. Include date(s) of application:

5.4 Name other Regulatory Authorities which have approved this trial, date(s) of approval and number of sites per country:

5.5 If applicable, name other Regulatory Authorities or Ethics Committees which have rejected this trial and give reasons for rejection:

5.6 If applicable, details of and reasons for this trial having been halted at any stage by other Regulatory Authorities:

2.7 Date PPB registrations applied for – or envisaged date of application for trial medication. Explain if registration is **not** envisaged:

2.8 Registration status of entity, for the indication to be tested in this trial, in other countries: (i.e. Country: date registered / date applied for / date registration refused / date registration withdrawn by applicant / date registration cancelled by regulatory authority) [Attach as an appendix if necessary.]

Part 3: DETAILS OF TRIALIST(S) AND SITE(S)

3.1 Details of Investigator(s): [designation, title: (i.e. principal investigators / investigators) Include Name/Address/Tel/Cell/Fax/E-Mail]

3.2 Current work-load of Investigator(s): (Number of studies currently undertaken by trialist(s) as principal and/or co- or sub-investigator, and the total number of patients represented by these studies. Time-commitments of researcher(s) in relation to clinical trial work *and* non-trial work.)

Recommended format for response:

Investigator (Name and designation):			
Total number of current studies (all stages) on specified date	Number	Date	
Total number of patients / participants for which responsible on specified date	Number	Date	
ESTIMATED TIME PER WEEK [168 hours denominator]	Hours	%	
Clinical trials	Clinical work (patient contact)		
	Administrative work		
Organisation (Practice / university / employer)	Clinical work		
	Administrative work		
Teaching	Preparation / evaluation		

SAE/SADR	Serious Adverse Event or Serious Adverse Drug Reactions	Any untoward medical occurrence that at any dose: - Results in death, - Is life threatening, - Requires hospitalization or prolongation of existing hospitalization, - Results in persistent or significant disability/incapacity, or - Is a congenital anomaly/birth defect.
	Source Data	All information in original records and certified copies of original records of clinical findings, observations or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).
	Source Documents	Original documents, data and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, study participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, study participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).
	Sponsor	An individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of a clinical trial.

SOPs	Study Participant Identification Code	A unique identifier assigned by the investigator to each trial participant to protect their identity and used in lieu of the study participant's name when the investigator reports adverse events and/or other trial related data.
SUSARS	Sub-Investigator	Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or make important trial-related decisions.
	Trial Audit	A systematic examination, carried out independently of those directly involved in the trial, to determine whether the conduct of a trial complies with the agreed study protocol and whether data reported are consistent with those on records at the site.
	Trial Participant	An individual who takes part in a clinical trial as a recipient of either the investigational medicinal product(s) or comparator.
	Trial Site	The location(s) where trial-related activities are actually conducted.

Annex 5

ADMINISTRATIVE AND SUPPLEMENTARY DETAILS

Title:

Protocol Number/identification:

Date of protocol (initial/final):

Part 1: CONTACT DETAILS (NAME/ADDRESS/TEL/CELL/FAX/E-MAIL)

1.1 Applicant:

1.2 Sponsor:

1.3 If no sponsor – person or organization initiating, managing, and / or funding the clinical trial:

1.4 Local Contact Person for correspondence:

1.5 National Principal Investigator/Coordinator: (or equivalent person)

1.6 International Principal Investigator: (if applicable)

1.7 Regional Monitor:

Part 2: DETAILS OF INVESTIGATIONAL PRODUCT(S)

2.1 Name(s) and details of investigational product(s) to be used in trial: [Formulation (s) and strength(s) (e.g. 10 mg/ml–10ml amp.)] Include PPB registration number and date of registration if applicable.

2.2 Name(s) and details (as above) of comparator product(s) and PPB registration number(s) and date(s) of registration if applicable: [Ensure package inserts or complete pharmacological information been included.]

2.3 Name(s) and details (as above) of concomitant medication(s) including rescue medications which are required in the protocol, and PPB registration number(s) if applicable: [Ensure package inserts or complete pharmacological information has been included with application.]

2.4 Estimated Quantity of Trial Material (each drug detailed separately) for which exemption will be required:

2.5 If any of the above drugs are available in Kenya, give an explanation for not using what is available in Kenya:

2.6 Details of receiving of drugs from supplier, storage, dispensing, packaging of drugs:

Annex 4

Declaration by applicant:

We, the undersigned have submitted all requested and required documentation, and have disclosed all information which may influence the approval of this application.

We, the undersigned, agree to ensure that if the above-said clinical trial is approved, it will be conducted according to the submitted protocol and Kenyan legal, ethical, PPB requirements and principles of good clinical practice;
 It is reasonable for the proposed clinical trial to be undertaken;
 I will submit reports of suspected unexpected serious adverse reactions and safety reports according to applicable guidance;
 I will submit a summary of the final study report to the PPB and the ethics committee concerned within a maximum 1 year deadline after the end of the study in all countries.

Applicant (local contact)	Date
National Principal Investigator / National Co-ordinator / Other (state designation)	Date

UADR	Unexpected Adverse Drug Reaction	<p>An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product).</p>
	Vulnerable Study Participants	<p>Individuals whose decision to participate in a clinical trial may be unduly influenced by the expectation of benefits associated with participation, or by coercion. This includes but is not limited to medical students, members of the uniformed forces, prisoners, minors, orphans, homeless, unemployed, refugees and the mentally challenged.</p>

INTRODUCTION

Clinical trials are systematic studies aimed at determining the safety and efficacy of drugs or devices.

The Pharmacy and Poisons Board is the national drug regulatory authority in Kenya established under Cap 244 Laws of Kenya. The importance of Research and Development in the attainment of national health, social and economic goals is well recognized. The Pharmacy and Poisons Board as the national drug regulatory authority has the mandate to ensure that clinical trials involving the use of new investigational drugs and older drugs for new conditions or diseases or investigational devices in human subjects are in compliance with national regulations including procedures to protect the safety of all participants.

As part of Board's continuing process of improving its efforts to facilitate clinical research, ECCT has developed this guidelines to assist clinicians, researchers and scientists be familiar with the procedures required for the conduct of drug-related clinical trials in the country. This will enhance and expand research activities and capabilities in the country. The guidelines provide the pharmaceutical industry, sponsors and investigators with the specific procedures required in the application for permission to conduct clinical trials in Kenya.

These guidelines have been developed to provide information for researchers on the current minimum requirements for authorization to conduct clinical trials involving investigational drugs, medical devices or herbal drugs in Kenya. The guidelines stipulate, among other things, application procedures for obtaining approval to conduct clinical trials (including clinical trials application form), procedures for approval of protocol amendments, requirements for reporting serious adverse events (SAEs)/ suspected unexpected serious adverse events (SUSARs), requirements concerning data and safety monitoring board (DSMB), submission of progress reports, procedures for termination of clinical trials, and information on inspection of trial sites.

Where necessary, appropriate forms have been attached as appendices at the end of the guidelines in order to aid in the application process. These should be filled in and submitted together with the required documents as specified in the guidelines.

Annex 3

CHECKLIST

Applicant's

PPB

Check list	double-check
COVERING LETTER	
FULLY COMPLETED APPLICATION	
PROTOCOL (INCLUDING RELEVANT QUESTIONNAIRES ETC.)	
PATIENT INFORMATION LEAFLET(S) <u>AND</u> INFORMED CONSENT(S)	
INVESTIGATORS BROCHURE AND/OR ALL PACKAGE INSERT(s)	
PRINCIPAL INVESTIGATOR'S CV(s)	
SIGNED DECLARATION(s) BY INVESTIGATOR(s)	
INSURANCE CERTIFICATE	
AND IF NECESSARY:	
LETTER ENDORSING GENERIC INSURANCE CERTIFICATE	
ETHICS APPROVAL	
COPY/IES OF RECRUITMENT ADVERTISEMENT(s) (IF APPLICABLE)	
FINANCIAL DECLARATION (SPONSOR AND NATIONAL PI)	
<u>Electronic versions of the application form, the protocol, the investigator's brochure and/or other relevant documents:</u>	
LABELLED CD-ROM/FLASH DISK (MSWORD OR PDF FORMAT)	
<u>List of files submitted on CD-ROM/ FLASH DISK:</u>	
<u>NB: DO NOT SUBMIT THE APPLICATION IF DOCUMENTATION IS INCOMPLETE: IT WILL NOT BE PROCESSED</u>	

Annex 2
 KENYA: CLINICAL TRIAL APPLICATION
SECTION 1 – CHECK-LIST OF REQUIRED DOCUMENTATION
 To be completed by Applicants for all Clinical Trials
COVER SHEET

Study Title:	
Protocol No:	
Version No:	Date of Protocol:
Study Drug:	
ECCT Ref number (if applicable):	
Date(s) ECCT approval of previous protocol(s):	
Sponsor:	
Applicant:	
Contact Person:	
Address:	
Telephone Number:	Fax Number:
Cell Number:	E-mail address:

To be completed by PPB

Date original application received:

Tracking No:

Proposed Clinical Trials Committee Meeting Date if applicable:

Signature: _____ **Date:** _____

ACKNOWLEDGEMENT OF RECEIPT OF CTA. (Contact details to be completed by the applicant). Whole cover sheet to be faxed to applicant once details in block above are completed.

Contact Details: Name:	Fax No.:
Receipt of new application is hereby acknowledged.	Date:
Signature (of PPB recipient):	Name:

SECTION ONE

APPLICATION REQUIREMENTS

1.1 An application to conduct a clinical trial is required for any study that intends to use human subjects for the testing of:

1. Unregistered medicines, vaccines or medical devices
2. Registered medicines where the proposed clinical trials are outside the conditions of approval for registration. These may include changes to:
 1. Indications and clinical use
 2. Target patient population(s)
 3. Routes of administration
 4. Dosage

Post-marketing clinical trials (Phase IV) of a registered medicine is provided for within the approved conditions of registration of such a medicine and approval is not required from the ECCT.

1.2 An application to conduct a clinical trial may be made by a sponsor, CRO on behalf of the sponsor, or Principal Investigator.

1.3 An application must be made by completing the appropriate application form (**Appendix 1**) and submitting this together with the required supporting documents and an application fee as prescribed below. Application forms and application guidelines can be downloaded from the PPB website: www.pharmacyboardkenya.org

1.4 An application to conduct a clinical trial shall include:

1. Covering letter
2. Duly filled and signed application form
3. Study Protocol in latest version which is dated
4. Investigator's Brochure
5. Declarations by Sponsor or Investigators
6. Financial declaration by Sponsor and/or PI
7. Certified copy of insurance for participants (if applicable)
8. Copy of the approval letter from the local IRB
9. Copy of the approval letter from a nationally accredited ERC
10. Curriculum vitae (CV) of Principal Investigator(s) co investigators
11. Copy of approval letter(s) from collaborating institutions or other regulatory authorities, if applicable
12. A signed statement by the applicant indicating that all information contained in, or referenced by, the application is complete and accurate and is not false or misleading.

13. Where the trial is part of an international study, sufficient information regarding the other participating countries and the scope of the study in these countries.
14. For multicentre/multi-site studies, all details of each centre/site should be provided upon initial application.
15. Payment of application fee as prescribed below

A non-refundable application fee of US\$ 2,000.00 (or equivalent in Kenya Shillings) per protocol, is to be paid in the form of at a Banker's Cheque drawn in favour of "Pharmacy and Poisons Board" at the PPB's accounts office on submission of the application wherein a receipt will be issued. Payment can also be made by electronic fund transfer (EFT) if required. All bank charges for EFT shall be borne by the applicant. Details for EFT payment should be obtained from PPB prior to such a transaction.

1.5 The application shall be submitted in both paper (4 copies) and electronic format (One copy in PDF format) via re-writable CD/Flash Disk.

1.6 Applications are to be submitted to the following address:

Attention: Department of Pharmacovigilance/ECCT

The Registrar

Pharmacy and Poisons Board

Lenana Road

P.O. Box: 27663-00506

Nairobi, Kenya

Tel: (020) – 3562107, 2716905/6, 0720608811, 0733884411

Fax: (020) - 2713431/2713409

E-mail: pv@pharmacyboardkenya.org

Any application that does not meet the above listed requirements will not be accepted. (SEE CHECKLIST TO TICK OFF)

Annex 1

TO ALL APPLICANTS

APPLICATION TO CONDUCT A CLINICAL TRIAL

The following are the requirements when submitting a clinical trial application.

Covering letter.

Cover sheet.

Checklist.

Completed Application form.

All documents to be submitted in with electronic copies.

Additional four copies of the application form itself must be submitted.

Protocol

Patient Information leaflet and Informed consent form

Investigators Brochure/Package inserts.

Signed investigator(s) CV(s).

Signed Declaration by Principal investigator(s).

Signed joint declaration by Sponsor/National Principal investigator.

Signed Provisional declaration by Co- or Sub-investigator

Indemnity and Insurance Certificate and/or

Proof of Malpractice insurance of trialist(s).

Ethics committee(s) approval

2.1 PROCEDURES FOR ACCEPTANCE, REVIEW AND APPROVAL OF APPLICATIONS

All applications to conduct a clinical trial will be received at the Department of Pharmacovigilance at the Pharmacy and Poisons Board.

20.3. | Information needed to support phase 3 trials

Safety data. If the population has broader entrance characteristics compared to the populations of prior trials, the favourable safety profile shown for constricted populations in prior trials may or may not convey to the broader populations in the phase 3 trials. Arguments that the product is likely to be safe in the broader population should be stated, and the phase 3 protocol should include re-testing of the safety parameters. Another reason to re-test safety parameters in phase 3 trials is the greater chance of identifying rare adverse events with the large number of patients used in phase 3.

- Preliminary efficacy data from phase 2 trials.
- Evidence from dose-ranging trials that the chosen dosing regimen is likely to be the optimum regimen with respect to safety and efficacy.

All of the fundamental ethical principles of human participation in research apply equally to herbal remedies and research involving these compounds. Consent must be obtained, subject selection must be equitable, risks and benefits must be weighed and must be favourable to the potential participant, and experimental design must be sound. Concerns that particularly apply to clinical trials with herbal products include:

Product adulteration (has it been documented?)

Interactions between herbal remedies and other entities (rarely understood)

Reproductive and organ toxicity data (may be minimal)

Prior dose finding (likely to be incomplete).

On receipt, the Department of Pharmacovigilance will screen the application for completeness.

If the application dossier is complete, PPB will assign a unique PPB Application Reference Number and file and acknowledgement of receipt will be issued to the applicant. Thereafter all correspondence with PPB on the application must bear the PPB Application Reference Number.

The application will then be scheduled for review according to its receipt date and the meeting and review calendar of the ECCT

All applications will be reviewed by the ECCT according to its Standard Operating Procedures (SOPs).

The ECCT may, where necessary, utilize the services of external experts to review the protocols.

Reviewers are required to declare any conflict of interest as regards the application before being assigned its review.

Strict confidentiality is maintained at all times during the review.

After review of the application, ECCT may either approve the trial application defer approval or rejection pending satisfactory responses from the applicant for additional information, explanations/ clarifications and/or responses to specific questions or reject the application giving reasons for the rejection.

This decision will be communicated to the applicant in writing.

In the case of rejection, the applicant may appeal and provide additional information to satisfy the ECCT expectations. In such cases, ECCT will decide whether or not to refer the matter to external experts for a recommendation.

Applications that are approved are also issued with license for importation of trial related medicines at the time of approval.

The “application for license to import trial related medicines and devices” must be on the prescribed form and submitted as part of the application dossier. Only under exceptional circumstances will such an application be considered post approval of the application. At any rate it is unlikely that an application missing the “application for license to import trial related medicines and devices” would be accepted.

3. | INFORMATION ON ONGOING TRIALS

3.1 The sponsor and/or PI must submit progress reports to PPB on a six monthly basis from the date of initiation of the clinical trial. The progress report should contain:

1. SAE Log
2. DSMB report
3. Number of patients recruited

3.2 Supplementary Data/New Information 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 PPB. If changes such as protocol amendments, consent form updates and additional trial sites, etc are made, PPB must be immediately informed along with informing the nationally certified IECs.

3.3 A new CTA is required for certain changes. The sponsor/PI will need to fill in the relevant section where changes are applied for, such as: application of additional quantity of study medication(s), additional trial site(s), additional new product, additional manufacturing site/re-packer, additional port of entry, change of applicant, extension of product's shelf life and new protocol.

4. | POST TRIAL INFORMATION

4.1 A Final Report is required to be submitted to the ECCT at the end of the trial. The PPB shall conduct a review that shall include scrutiny of Interim Reports, Study Monitor Reports and any PPB Inspection Reports. If all the requirements of GCP and local requirements are met, the PPB will provide a statement certifying that the Clinical Study has been conducted within the legal, ethical and regulatory requirements of Kenya.

4.2 It is a requirement that copies of all publications resulting from a clinical trial conducted in Kenya are submitted to the PPB.

5. | QUALIFICATIONS AND RESPONSIBILITIES OF INVESTIGATORS, SPONSORS AND MONITORS

5.1 The principal investigator engaged in clinical trials must be appropriately qualified to conduct the study, with relevant practical experience within the professional area, and must be a resident of Kenya.

5.2 In case of multi-centre studies where the PI is not a resident of Kenya, the appointed local principal investigator must be a resident of Kenya and should assume full responsibilities for all local clinical trial sites.

5.3 All investigators in a clinical trial as well as the trial monitor must have had formal training in Good Clinical and Laboratory Practices (GCLP) within the last three years. Evidence of attending GCLP course should also be submitted.

if the particular tested dose of the intervention was ineffective, the community may conclude that all doses of the intervention are ineffective, and patients will be denied possible benefits from the intervention. The inappropriate rejection of an intervention, “because phase 2 studies did not precede a phase 3 trial, and a suboptimal dose was used in the phase 3 trial”, is common for herbal medicines. For some herbal products, there may exist previous research that has determined the optimum dose for a treatment. For others, dose-ranging phase 2 studies will need to be performed prior to beginning more extensive phase 3 studies. Therefore, if the scientific literature does not contain scientifically valid dose-ranging data, the investigator should first perform phase 2 trials to generate these data.

For dose-ranging studies, clinical investigators should consult biostatisticians for examples of dose-ranging schemes, and decide which scheme best fits the needs of the particular clinical problem.

20.2. | Information needed to support phase 2 trials

Although data from prior human experience may suggest confidence in the clinical safety of the product, it is important to verify tolerance in phase 2 trial patients. Both the literature review and the provisions in the protocol to be performed should focus on complete review of the clinical safety parameters.

Examples of safety parameters are:

Organ system	Safety parameter
Neurological:	lack of neurologic symptoms
Skin:	clinical evidence of lack of allergic reactions
Musculoskeletal:	lack of arthritis or myalgias, normal values of CPK
Gastrointestinal:	clinical evidence of tolerability
Liver:	normal values of SGOT or SGPT, alkaline phosphatase, Total bilirubin,
Kidney:	normal values of BUN or creatinine
Endocrine system	normal values of albumin or total protein, uric acid, glucose, cholesterol, amylase or lipase, sodium/potassium, calcium
Cardiovascular:	normal EKG and blood pressure
Hematopoietic:	normal values of complete blood count
Additionally:	more intensive investigation of any organ system likely to be particularly effected by the product

protocol development team, where those traditional practitioners exist. For all clinical trials, biostatisticians should be consulted to ensure that the sample size is sufficient to satisfy the primary endpoint/objective.

20.1. | Introduction: Information needed for a standard intervention

Phase 1 studies are designed to determine safety associated with increasing doses in normal volunteers, as a precursor to phase 2 and phase 3 trials. In addition, phase 1 studies investigate toxicity and drug levels in states in which drug levels might be altered: the fed vs. the fasted state, in renal or hepatic impairment. Mechanisms of action are also investigated in phase 1.

Phase 2 studies evaluate the efficacy of a range of dosages in individuals with disease. Phase 2 studies typically start by evaluating the maximum tolerated dose determined in the prior phase 1 normal-volunteer studies. If this dose is effective, dose-ranging downwards would be investigated. If the phase 1 dose is ineffective, it is possible that higher doses will demonstrate efficacy and only mild intolerance, so dose-ranging upwards may be performed. Phase 2 dose-ranging studies utilize a relatively small number of patients per dosage group. Placebo and standard intervention groups may be included. If surrogate markers rather than disease endpoints are used in the phase 2 studies, it may be necessary to repeat dose-ranging in phase 3 trials with more valid disease endpoints. Phase 3 studies are expanded trials of safety and efficacy. They are performed after preliminary evidence suggesting efficacy for the intervention has been obtained, and are intended to gather the additional information about efficacy and safety that is needed to evaluate the overall benefit-risk ratio of the intervention and to provide an adequate basis for general clinical use. Phase 3 studies usually include large numbers (several hundred to several thousand) of subjects, may involve human populations with broader entrance characteristics than were used in the phase 2 trials, and involve statistical comparison of the intervention to standard and/or placebo interventions.

20.1.1. Important note on phase 1, phase 2, and phase 3 trials

Development of safe and effective herbal products requires subjecting all such product to the different phases of clinical investigation of a new investigational product. The purpose of a clinical trial is to evaluate an intervention for a clinical condition. Positive (or negative) data can lead to a recommendation to use (or not to use) the treatment. Use of a suboptimal dose that is safe but ineffective does not serve the needs of the community. Although the trial indicates only

5.4 Investigators, sponsors and monitors should assume responsibilities as provided in the ICH – GCP guidelines.

6. | STUDY PROTOCOL

The clinical trial study protocol must contain at least the following:

6.1 General Information

- Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).
- Name and address of the sponsor and monitor (if other than the sponsor).
- Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor.
- Name, title, address, and telephone number(s) of the sponsor's medical expert for the trial.
- Name and title of the investigator(s) who is (are) responsible for conducting the trial, their address and telephone number(s) including updated mobile numbers.
- Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable), who is responsible for all trial-site related medical (or dental) decisions (if other than investigator).
- Name(s) and address (es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

6.2 Background Information

- Justification and need for the study
- Name and description of the investigational product(s).
- A summary of findings from non-clinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.

Summary of the known and potential risks and benefits, if any, to human subjects.

Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).

A statement that the trial will be conducted in compliance with the protocol, GCP and PPB requirement(s).

Description of the population to be studied.

References to literature and data that are relevant to the trial and that provide background for the trial.

6.3 Trial Objectives and Purpose

A detailed description of the objectives and the purpose of the trial.

6.4 Trial Design

A description of the clinical trial design should include:

A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.

A description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.

A description of the measures taken to minimize/avoid bias, including Randomization and Blinding.

A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of packaging, and labelling of the investigational product(s).

The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.

A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

Determination of the "No Adverse Effect Level (NOAEL) following administration to animals (rats) via the same route to be used in clinical studies.

19.2. | Information needed to support a clinical trial for a herbal product

19.2.1. Efficacy

It is recommended that the appropriate literature sources be searched for all available evidence on efficacy. Examples of such sources are medical and scientific journals, pharmacopeia, and articles on traditional medicines. Only if there are obvious gaps in the information or the total amount of data is insubstantial should it be necessary to perform new efficacy experiments.

19.2.2. Toxicology

It is imperative that the appropriate literature sources (as above) be reviewed for the toxicities of the herbal products in prior human experiences or existing animal data. The need for additional non-clinical studies prior to clinical trials depends on the following considerations:

Similarities between the new and old preparations, in terms of product characteristics, and usages in clinical settings.

Scale and exposure (dosage/duration) of the proposed new clinical studies.

Frequency and severity of any known toxicity.

Thus, in general, requirements for pre-clinical studies may range from none for early phase, small, studies using the same preparations that have been used extensively and without known safety problems, to a complete set of conventional toxicology studies for relatively new products in large phase 3 trials. For many herbal products, certain non-clinical studies may be necessary but can be conducted concurrently with the proposed clinical trials.

19.2.3. Pharmacokinetics

It is important that the active ingredient (s) is identified, and the pharmacokinetic profile of the active ingredients and their metabolites described.

20. | CLINICAL CONSIDERATIONS FOR HERBAL PRODUCTS

Good Clinical Practice should be applied in all stages of clinical trials to ensure that quality and ethical requirements for clinical studies are met. It is expected that a traditional practitioner familiar with the product proposed for investigation be an integral member of the

performing generally the same procedures as for phase 1/2 trials, but more extensively and with more stringent oversight.

HERBAL SUBSTANCE:

As above for phase 1/2 trials.

In addition:

ii. Statement that the plant is cultivated according to Good Agricultural Practices or harvested according to Good Wildcrafting Practices

Reference batch.

HERBAL PRODUCT:

As above for phase 1/2 trials.

In addition:

Environmental impact statement.

19. | PRE-CLINICAL CONSIDERATIONS FOR HERBAL PRODUCTS

19.1. | Introduction: Information needed for a conventional drug

Pre-clinical information generally needed to support a clinical investigation of a conventional drug consists of data on efficacy, toxicity, and pharmacokinetics.

Efficacy is demonstrated in enzyme/receptor assays, in vitro, and in animal models.

Toxicity is investigated:

in vitro and in mice to assess genotoxicity

in vitro to assess cytotoxicity

in rodents to assess single-dose acute toxicity and maximum tolerated dose

in one rodent model and one non-rodent model to investigate repeat dose (1, 3, 6, 9 months) toxicological effects

in a rodent model and in the rabbit to assess reproductive toxicity

in the rat to assess carcinogenicity.

Pharmacokinetic analyses relate to:

absorption of the drug from the gut after e.g. oral dosing, or mobilization from the injection site after injection

distribution of the API around the body

rate of drug metabolism, the metabolic enzyme involved, and the nature of the metabolites produced.

A description of unblinding and breaking of the blind (for safety reasons).

Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.

Maintenance of trial treatment randomization codes and procedures for breaking codes.

The identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data.

6.5 Selection and withdrawal of study participants

Inclusion criteria.

Exclusion criteria.

Withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) and procedures specifying:

1. When and how to withdraw participants from the trial/ investigational product treatment.
2. The type and timing of the data to be collected for withdrawn participants.
3. Whether and how participants are to be replaced.
4. The follow-up for participants withdrawn from investigational product treatment/ trial treatment.

6.6 Treatment of study participants

The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for participants for each investigational product treatment/trial treatment group/arm of the trial.

Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

Procedures for monitoring participant's compliance.

content from batch to batch may be an issue, and several analytical procedures may be needed to adequately quantify their constituents.

18.1.5. Because herbal products are sourced from plants, levels of contaminating herbicides and pesticides as well as toxic contaminations must particularly be addressed. The presence of adulterants should also be considered.

18.1.6. Many herbal medicines are in fact polyherbal. Plants may either be mixed before extraction or the extracts may be combined. In either case, information on each individual plant species used must be collected.

18.1.7. Herbal products intended for administration to humans are clinical trial materials, and they should therefore be made following the principles of GMP. The production facility should have a current certificate of GMP.

18.2. | Information needed to support a clinical trial for a herbal product

18.2.1. Information on the herbal product proposed for phase 1/2 studies

HERBAL SUBSTANCE:

Description of the plant: genus, species (cultivar where appropriate); region(s) and country(ies) of origin; time of harvest; parts to be harvested
Plant processing: drying, mechanical disruption, solvent extraction (aqueous or organic solvents, others)
Isolation, identification and purification of active ingredients
Analytical procedures
Specification
Storage conditions/shelf life.

HERBAL PRODUCT:

amount of active ingredient
list of excipients
type of product (tablet, capsule, etc.) and its method of manufacture
analysis of putative active ingredient(s) via chemical or biological parameters
analysis of a sizeable chemical constituent (analytical marker compound)

18.3. | Information on the herbal product proposed for phase 3 studies

Phase 3 trials are performed on large number of patients and are often carried out prior to registration and general use. Therefore, GMP standards are needed prior to phase 3 trials. In practice, this means

SECTION TWO

HERBAL PRODUCTS

18. | CHEMISTRY- MANUFACTURING- CONTROL (CMC) CONSIDERATIONS FOR HERBAL PRODUCTS

For conventional, chemically-defined drug products, general considerations are synthesis and/or purification of the active pharmaceutical ingredient (API), manufacturing of the product that is administered to the patient and control of these processes so that the API and product are made reproducibly. Since herbal products are manufactured from plant material, these considerations have to be translated into terms appropriate to this plant source.

18.1. | Overview of CMC evidence needed to support clinical trials for herbal products

18.1.1. Unlike standard chemically-defined drugs, herbal products have often had substantial human use prior to clinical trial evaluation. To capitalize on the use of this information in protocols to evaluate these products, it is important that the chemistry, manufacturing, and control of the product to be used mimic that for the traditionally-used formulation.

18.1.2. Also unlike conventional drugs, herbal products are mixtures of at least partially uncharacterized constituents. It is postulated that being a mixture provides a therapeutic advantage, in that unknown constituents may combine in an additive or synergistic fashion with known constituents to provide more efficacy than would be provided by the known constituent alone. Thus, evaluation of herbal products does not require attempts to purify the medicines down to known or otherwise single chemical constituents.

18.1.3. For herbal products, “analysis of the active pharmaceutical ingredient(s)” may be best approached by analysis of one or more hypothesized active ingredient(s), analysis of a chemical constituent that constitutes a sizable percentage of the total ingredients, and a chemical fingerprint of the total ingredients. The latter two analyses are surrogates for analysis of the unknown constituents that contribute to efficacy.

18.1.4. Specifications for acceptable values of analytic data should reflect the best available standards. For herbal products, variation of

6.7 Assessment of Efficacy

Specification of the efficacy parameters.

Methods and timing for assessing, recording, and analyzing of efficacy parameters.

6.8 Assessment of Safety

Specification of safety parameters.

The methods and timing for assessing, recording, and analyzing safety parameters.

Procedures for eliciting reports of and for recording and reporting adverse events and intercurrent illnesses.

The type and duration of the follow-up of subjects after adverse events.

6.9 Statistics

A description of the statistical methods to be employed, including timing of any planned interim analysis(es).

The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.

The level of significance to be used.

Criteria for the termination of the trial.

Procedure for accounting for missing, unused, and spurious data.

Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).

Procedures for reporting any protocol violations.

The selection of study participants to be included in the analyses (e.g. all randomized participants, all dosed participants, all eligible participants, evaluable participants).

6.10 Direct Access to Source Data/Documents

The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit PPB inspection(s), providing direct access to source data/documents.

6.11 Quality Control and Quality Assurance

The protocol should contain a description on how to maintain quality control and quality assurance of the study.

6.12 Ethics

Description of ethical considerations relating to the trial should include the following issues:

1. Choice of investigators
2. Monitors and monitoring plan
3. Indicate how additional staff (monitors, pharmacists, nursing staff, etc.) will-maintain
4. patient confidentiality, follow the protocol, and abide by ethical and PPB requirements
5. Insurance and indemnity measures
6. Patient Information leaflets and Informed Consent forms for any proposed archiving
7. of biological specimens for later research or for genetics research.
8. Treatment and/or management of participants and their disease condition (s) after
9. completion of trial
10. Institutional ethics committee capacity to monitor site and conduct of trial
11. Provide an explanation if minimum recommended compensation for a participant is
12. not being provided.
13. Follow-up of trial study participants after the conclusion of the trial

In case of transfer of materials, provide Material Transfer Agreement (MTA) highlighting among other things, the following:

17.2 Change of Information

The sponsor shall inform PPB 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 Import Licence.

17.3 Discontinuation of Trial

The sponsor shall inform PPB of any decision to discontinue the trial to which the licence relates and shall state the reason for the decision. The sponsor should return the Clinical Trial Import License to within two weeks.

Post trial review:

The Final Report from each trial conducted in Kenya should be submitted to the ECCT. The review shall include scrutiny of Interim Reports, Study Monitor Reports and any PPB Inspection Reports. If all the requirements of GCP and local requirements are met, the PPB will provide a statement certifying that the Clinical Study has been conducted within the legal, ethical and regulatory requirements of Kenya.

16. ARCHIVING

16.1 It is the responsibility of the investigator and the sponsor to archive safely all the documents related to the trial. All archiving shall be done within the country and not exported. The sponsor/applicant should inform ECCT in writing prior to destroying the trial documents. It should include the protocol number, date started and ended and the licence number.

PPB will also archive all documents and maintain a database of all submissions made to PPB.

17. CONDITIONS FOR CLINICAL TRIAL IMPORT LICENCE**17.1 Endorsement of Clinical Trial Import License**

The Sponsor shall submit to PPB a copy of endorsed Clinical Trial Import 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 Import Licence/Clinical Trial Exemption 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 PPB.

The sponsor 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 sponsor shall ensure that the study medication(s) be supplied only to subjects involved in the said trial.

1. Identification of the provider and recipient
2. Identification of the material and the volume of material
3. Definition of the trial and how the material will and will not be used
4. Maintenance of confidentiality of background or supporting data or information, if any
5. Indemnification and warranties (where applicable)

6.13 Data Handling and Record Keeping**6.14 Publication Policy**

Publication policy, if not addressed in a separate agreement.

7. THE INVESTIGATOR'S BROCHURE

The investigator's brochure must contain at least the following information in respect to the investigational medicinal product:

The physical, chemical and pharmaceutical properties

The pharmacological aspects including its metabolites in all animal species tested

The pharmacokinetics and metabolism including its biological transformation in all animal species tested

Toxicological effects in any animal species tested under a single dose study, a repeated dose study or a special study

Results of clinical pharmacokinetic studies

Information regarding safety, pharmacodynamics, efficacy and dose responses that were obtained from previous clinical trials in humans.

More details are provided in ICH-GCP guidelines and may be followed when compiling information on this part.

For registered products being investigated for new conditions, latest PSUR, certifi c certificate of analysis, GMP should also be submitted.

8. | REQUIREMENTS CONCERNING INFORMED CONSENT

8.1 In obtaining and documenting informed consent, the investigator should comply with National Ethics Committee (NEC) requirement(s) and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki (Appendix 6). Prior to the beginning of the trial, the investigator should obtain Ethical Clearance from NEC followed by PPB approval.

8.2 Informed consent to study participants shall be administered in either English or Kiswahili and local spoken language of the area, where applicable. The same information will be given to participants in a written format.

8.3 The written informed consent form and any other written information to be provided to participants should be revised whenever important new information becomes available that may be relevant to the participant's consent. Any revised written informed consent form, and written information should receive ethics and PPB approval in advance of use.

8.4 Neither the investigator, nor the trial staff, should coerce or unduly influence a participant to participate or to continue to participate in a trial.

8.5 None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the participant or the participant's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.

8.6 The investigator, or a person designated by the investigator, should fully inform the participant or, if the participant is unable to provide informed consent, the participant's legally acceptable representative, of all pertinent aspects of the trial including the written information and ethics and PPB approval.

8.7 The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the participant or the participant's legally acceptable representative and the impartial witness, where applicable.

15.11 Supplementary Data/New Information 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 PPB. If changes such as protocol amendments, consent form updates and additional trial sites, etc are made, PPB must be immediately informed along with informing the nationally certified IECs.

15.12 A new CTA is required for certain changes. The sponsor/PI will need to fill in the relevant section where changes are applied for, such as: application of additional quantity of study medication(s), additional trial site(s), additional new product, additional manufacturing site/re-packer, additional port of entry, change of applicant, extension of product's shelf life and new protocol.

15.13 All applications will be reviewed according to Standard Operating Procedures (SOPs) of ECCT. Conflict of interest will be declared by each member prior to reviewing the application. Confidentiality will be maintained at all times during the review. The Committee may, when necessary, utilize the services of external experts to review the protocols.

15.14 ECCT may approve the trial application or may reject the application and specify the reasons for rejection. Approval will be dependent on receipt of approval of the protocol by the nationally certified Independent Ethics Committee. Approval for importation of trial related medicines will be dependent on the approval of the clinical trial.

15.15 This decision will be communicated to the applicant in writing stating whether the trial has been approved as it is, or if it requires certain corrections or if it has been rejected.

15.16 In the case of rejection, the applicant may appeal and provide additional information to satisfy the ECCT expectations. In such cases, ECCT will decide whether or not to refer the matter to external experts for a recommendation.

15.17 Import of IMP will be using the prescribed format. All application should be received either at the point of applying for approval of protocol or once protocol is approved. The Pharmacovigilance department shall process the same and respond to the applicant once import permit is signed.

15.18 The review by ECCT will take 21 working days.

15| PROCEDURES FOR REVIEW AND APPROVAL OF APPLICATIONS

15.1 All applications for conduct of clinical trials will be reviewed according to Standard Operating Procedures of ECCT.

15.2 Conflict of interest will be declared by each member of ECCT prior to reviewing the application.

15.3 Confidentiality will be maintained at all times during review. ECCT may, when necessary utilize the services of external experts to review the protocols.

15.4 ECCT may approve the trial application or reject it specifying reasons for rejection.

15.5 The decision made by ECCT will be communicate to the applicant in writing stating whether the trial has been approved as it is, or requires corrections or has been rejected.

15.6 Approval for importation of investigational products and comparator will be dependent on approval to conduct the clinical trial.

15.7 In the case of rejection, the applicant may appeal and provide additional information to satisfy ECCT expectations. In such cases ECCT may decide to refer the matter to external experts for recommendation.

15.8 All applications for carrying out clinical trials in Kenya will be received at the Department of Pharmacovigilance at Pharmacy and Poisons Board.

15.9 On receipt, the Department of Pharmacovigilance will screen the application for completeness.

15.10 Application Reference Number:

When an application for a Clinical Trial is accepted, an acknowledgement of receipt will be issued with a reference number for each application. This PPB/ECCT reference number must be quoted in all correspondence concerning the application in the future.

8.8 Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the participant or the participant's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the participant or the participant's legally acceptable representative.

8.9 Prior to participation in the trial, the written informed consent form should be signed and personally dated by the participant or by the participant's legally acceptable representative, and by the person who conducted the informed consent discussion.

8.10 If a participant is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to participant, is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the participant's legally acceptable representative has orally consented to participate in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form.

8.11 By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally acceptable representative, and that informed consent was freely given by the participant or the participant's legally acceptable representative.

8.12 Both the informed consent discussion and the written informed consent form and any other written information to be provided to participants should include explanations of the following:

1. That the trial involves research.
2. The purpose of the trial.
3. The trial treatment(s) and the probability for random assignment to each treatment.
4. The trial procedures to be followed, including all invasive procedures.
5. The participant's responsibilities.
6. Those aspects of the trial that are experimental.
7. The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, foetus, or nursing infant.

The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.

The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks.

The compensation and/or treatment available to the participant in the event of trial-related injury.

The anticipated prorated payment, if any, to the participant for participating in the trial.

The anticipated expenses, if any, to the participant for participating in the trial.

That the participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.

That the PPB will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, to the extent permitted by PPB and that, by signing a written informed consent form, the participant or the participant's legally acceptable representative is authorizing such access.

That records identifying the participant will be kept confidential and will not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential.

That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participating in the trial.

The person(s) to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial-related injury.

The foreseeable circumstances and/or reasons under which the participation in the trial may be terminated.

The expected duration of participating in the trial.

The approximate number of participants involved in the trial.

8.13 Prior to participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated (same day as that signed for approval to participants) written informed consent form and any other written information provided to the participants. During participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to participants.

13.2 End of trial (Study closeout):

After the trial has been conducted and closed, the sponsor and/or principal investigator shall submit a closing report within 60 days. This should be followed by a final study report within six months after trial closure unless otherwise justified. The structure and content of the final study report should be as provided in the ICH guidelines. Any unexpected safety issue that changes the risks-benefit analysis and is likely to have an impact on trial participants should be reported together with proposed actions to be taken.

14. INSPECTION OF CLINICAL TRIAL SITES

14.1 The Board may inspect clinical trial (investigator) sites, sponsor's office, data management centre, contract research organization (CRO) or any other establishment related to the trial as it will be deemed appropriate by the Board to ensure that the generally accepted principles and/or requirements of GCP, ICH and PPB are met. The authorized officer of the board may contact the PI or sponsor for the date of inspection when required.

14.2 Such inspections may be before commencement of the trial, or at predetermined intervals, or may be at the request of the Expert Committee on Clinical Trials.

14.3 However, in the case of complaints or reports of unexpected adverse reactions, inspections may take place at short notice and may be unannounced.

14.4 The objectives of inspection will be to ensure that participants are not subjected to undue risks, to validate the quality of data generated and/or to investigate complaints.

14.5 The Board may use the information collected as a result of inspections to ensure compliance with regulatory requirements and may take enforcement action where necessary.

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

1. The facilities and staff used for the trial: as approved by the PPB.
2. Compliance with the approved Protocol
3. All amendments to the Protocol have been approved.
4. Accurate, complete and current records according to the Protocol.
5. Serious Adverse Events are reported as required by the Protocol
6. Monitor and Audit inspections are conducted as required by the Protocol and the reports are available for inspection.

1. A broad statement of the aims and objectives of the DSMB
2. Terms of Reference
3. Composition of DSMB
4. Qualification of the DSMB members
5. Specific roles including responsibilities of statisticians
6. The role of statistical stopping rules
7. Relationship with the principal investigators and trial management team
8. Clarification of the decision-making powers
9. How DSMB meetings will be organized
10. Whether the DSMB will be blinded to treatment
11. What option a DSMB can recommend
12. In what form and to whom decisions will be conveyed
13. The role of the DSMB in publication of results
14. Disclosure of competing interests of DSMB members

12.2 Submission of Progress Reports

The sponsor and/or PI must submit progress reports to PPB on a quarterly basis from the date of initiation of the clinical trial. The progress report should contain

1. SAE Log
2. DSMB report
3. Number of patients recruited

13. TERMINATION OF CLINICAL TRIAL

13.1 Premature termination:

If a clinical trial is terminated by the principal investigator or sponsor in its entirety, the principal investigator or sponsor must inform PPB not later than 15 days after the date of the termination; and must

As soon as possible, inform all co-investigators of the termination and of the reasons for the termination and advise them in writing of potential risks to the health of clinical study participants or other persons including ensuring that patients continue to receive medical care.

Provide PPB with the reason(s) for the termination and its impact on the proposed or ongoing clinical trials in respect of the investigational medicinal product including issues related to accountability and disposal of investigational products as well as maintenance of records.

13.1 Withdrawal of PPB approval:

PPB may withdraw the authorization to conduct a clinical trial if the Authority is of the opinion that the safety of the study participants in the trial is compromised or that the scientific reasons for conducting the trial have changed.

8.14 When a clinical trial includes participants who can only be enrolled in the trial with the consent of the participant's legally acceptable representative (e.g., minors, or patients with severe dementia), the participant should be informed about the trial to the extent compatible with the participant's understanding and, if capable, the participant should sign and personally date the written informed consent.

8.15 In emergency situations, when prior consent of the participant is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the participant is not possible, and the participant's legally acceptable representative is not available, enrolment of the participant should require measures described in the protocol and/or elsewhere, with documented PPB approval to protect the rights, safety and well-being of the participant and to ensure compliance with NEC and PPB requirements. The participant or the participant's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

9. INVESTIGATIONAL MEDICINAL PRODUCT (IMP) DOSSIER

9.1 Clinical trial investigational medicinal products must be manufactured in accordance with Good Manufacturing Practices (GMP). This implies that the manufacture of the investigational product may be subject to control and inspection in the same way as in the case of marketed medicinal products.

9.2 Chemistry and manufacturing information for IMP(s) which have not been registered by PPB should be presented in a concise manner and should include the following:

Required details on Active Pharmaceutical Ingredient (API)

1. Nomenclature
2. Name and address of the manufacturer
3. Physicochemical properties
4. Route of synthesis and manufacturing process
5. Documented evidence of structure and stereochemistry
6. Characterization of impurities
7. Specifications and their justifications
8. Batch analyses
9. Validation of analytical procedures
10. Container closure system
11. Stability studies

Required details on Investigational Medicinal Product (IMP)

1. Name, strength and dosage form
2. Description and composition
3. Name and address of the manufacturer
4. Pharmaceutical development
5. Description of manufacturing process including flow diagram and process validation.
6. Manufacturing information for novel excipients.
7. Specifications and their justifications (including excipients)
8. Batch analyses
9. Validation of analytical procedures
10. Characterization of impurities
11. Certificates of analysis (CoAs) and Bovine Spongiform Encephalopathy (BSE)/
12. Transmissible Spongiform Encephalopathy (TSE) certificates for excipients of human
13. or animal origin
14. Stability studies
15. Container closure system

9.3 If the pharmaceutical or chemical properties of the IMP have been altered compared to those in use during animal testing or previous clinical trials, such alterations must be described and justified.

9.4 Pharmaceutical and/or chemical alterations in the IMP that are used in an ongoing clinical trial and that may affect the quality, safety and/or efficacy of the IMP must immediately be reported and justified to PPB.

9.5 In cases where an extension of shelf life for the IMP is desired, an application for this must be submitted to PPB. In such cases stability data and certificates of analysis (CoAs) from reanalysis of the relevant batches must be submitted.

9.6 In case of IMP(s) which have been registered by PPB, a cross reference to the part of the dossier containing chemistry and manufacturing information should be declared.

9.7 Information on preclinical pharmacology and toxicology studies done must be submitted as prescribed in ICH guidelines. In case

3. Changes that affect patient discontinuation
4. Addition/deletion of an investigational site
5. Change of principal investigator
6. Changes that result in the extension of duration of a trial
7. Changes that relate to the chemistry and manufacturing information that may affect drug safety and quality (For example: specifications for the IMP where limits of the test are relaxed or deleted; where a new impurity or degradation product has been identified; and addition of new raw materials, solvents, reagents, catalysts or any other materials used in the manufacture of the API).

10.6 The application for amendment(s) shall be accompanied by Ethical Clearance or authorization from the IEC.

11. REPORTING OF SERIOUS ADVERSE EVENTS (SAES)/ SUSPECTED UNEXPECTED SERIOUS ADVERSE REACTIONS (SUSARS)

11.1 All serious adverse events (SAEs) including suspected unexpected serious adverse reactions (SUSARs) should be reported to PPB within 14 days and for fatal ones within 24 hours of their occurrence.

11.2 Form attached as Appendix 7 should be used when reporting followed by detailed written reports. When completing the form, the application number and/or protocol number should be included.

11.3 Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should also be reported.

11.4 For reported deaths, additional information (e.g., autopsy reports and terminal medical reports) should be submitted.

11.5 The relationship between SAE(s)/SUSARs and the IMP must be established, evaluated, clarified and submitted to PPB for further assessment.

12. REQUIREMENTS CONCERNING DATA AND SAFETY MONITORING BOARD (DSMB)/DATA MONITORING COMMITTEE (DMC)

12.1 For trials that will involve Data and Safety Monitoring Board (DSMB) to monitor trials, the following issues related to DSMB must be submitted:

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.

9.12 Product Accountability and Disposal:

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

Clinical Trial Import Licence for the relevant site.
Date(s) and quantity received for each product
Balance of the study medication(s)
Drug Destruction Certificate, and/or written evidence return to the used/unused drug supplies to country of origin (whichever applicable).

PPB shall be informed in writing of any possible delay in submission of the report where the delay is unavoidable.

10. CLINICAL TRIAL AMENDMENTS

10.1 Application for amendment(s) to a previously authorized clinical trial shall be made in forms (Appendices 7 and 8), whichever is applicable.

10.2 The applicant must submit the description of the proposed amendment including reasons thereof.

10.3 Original wording, revised wording and rationale for the change(s) including a copy of complete protocol incorporating all amendments should also be submitted, where applicable.

10.4 The applicant must also submit supporting data for the amendment, including as possible;

Updated overall risk-benefit assessment
Possible consequences for participants already in the trial
Possible consequences for the assessment of trial results
Summaries of data

10.5 PPB approval must be obtained for the following amendments:

1. Changes that affect patient selection and monitoring
2. Changes that affect clinical efficacy and safety requirements (e.g. dosage adjustments, study procedures, etc)

information on preclinical studies was submitted in phase I study application, a summary of preclinical studies for late phase trials (i.e. phase II and III) should be submitted.

9.8 Information on human experience data and previous clinical studies done must be submitted as prescribed in ICH guidelines and in accordance with applicable GCP guidelines.

Labelling:

Investigational medicinal products (including registered products) used in clinical trials must be properly labelled. A final copy/version of the labelling must be submitted for approval and should contain the following minimum information:

1. Statement indicating that the product is for “*clinical trial purpose only*”
2. Name, number or identifying mark
3. Recommended storage conditions
4. Name and address of the sponsor
5. Protocol code or identification

Re-labelling

Any remaining IMP from previously manufactured batches must be performed in accordance with established written procedures and GMP principles.

Sponsor responsibilities:

The following responsibilities are expected of the sponsor as regards the IMP:

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 products and documenting this retrieval (e.g. for deficient product recall, reclaim after trial completion, expired product reclaim).
Maintain a system for the disposition of unused investigational product(s) and for the documentation of this disposition.
Take steps to ensure that the investigational product(s) are stable over the period of use.
Maintain sufficient quantities of the investigational product(s) used in the trials to re-confirm specifications, should this become necessary, and maintain records of batch sample analyses and characteristics. To the extent stability permits,