Ambition Trial Coordinating Centre
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Trial Management
Work Practice Document 1
Site Selection

Title of study	High Dose AMBISOME© on a Fluconazole Backbone for Cryptococcal Meningitis Induction Therapy in sub-Saharan Africa: A Phase III Randomized Controlled Non-inferiority Trial		
Acronym	Ambition-cm – AMBIsome Therapy Induction OptimizatioN		
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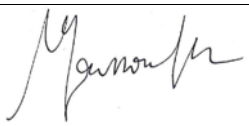
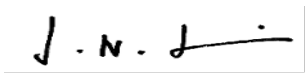
Author(s)	Nabila Youssouf Study Manager		20/07/2017
Reviewer(s)	Sile Molloy Study Manager		20/07/2017
Approved by	Joseph Jarvis CI		20/07/2017

Revision History:		
Version Number	Effective Date	Reason for Change
1.0	20/07/2017	First version

Working Practice Document
Site Selection

Purpose

The purpose of this Working Practice Document (WPD) is to describe the process for evaluation and selection of investigators and sites to conduct the Ambition trial.

This WPD applies to the Ambition trial conducted by the Ambition Trial Coordinating Centre and will be carried out according to applicable aspects of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) standards.

References

Ambition Phase III Trial Protocol
ICH Harmonised Tripartite Guideline for Good Clinical Practice (1996), accessible at:
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf
Peto, Baigent, BMJ 1998; 317(7167):1170
MacPherson, Complementary Therapies in Medicine (2004) 12, 13 6–140
http://ec.europa.eu/health/files/eudralex/vol1/dir_2001_83_cons/dir2001_83_cons_20081230_en.pdf

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Appendix

Site Feasibility Assessment template
Pharmacy Feasibility Assessment template

Procedures

The overall responsibility for tasks related to trial site identification and selection resides with the Trial Manager (TM) / Chief Investigator (CI).

Upon receipt of an expression of interest, the following points should be considered to make a decision as to whether to progress the site:

a) Site Recruitment Capabilities

- The pragmatic nature of this trial will allow for the recruitment of patients from a wide variety of health care facilities. Participating hospitals may be selected from middle and low income countries. There is a limit to the maximum number of patients to be recruited at each site and this must be considered carefully before selecting the site for progression.
- Number of cases of CM in the last 12 months should allow for a predicted recruitment rate of a minimum of at least 3 randomisations per month.
- The TM may conduct a Site Feasibility Visit to assess the site and its facilities (Pharmacy, Laboratories etc); if this occurs, a Site Feasibility Report will be prepared to document findings.

b) Principal Investigator's Qualifications

- ICH GCP Section 4.1 states that the suitability of the investigator should be assessed in three respects. He or she must be qualified in terms of education, training and experience. The evidence of these three elements should be present in the investigator's CV:
- The PI should be a doctor of medicine
- The PI should be a senior member of the hospital department e.g. they should have overall responsibility for the doctors and nurses who will be part of the trial team.

If the hospital fails on one of the above criteria, an email should be sent requesting more information, or requesting an alternative PI be sought for that site, or declining their participation.

c) Manpower

A strong trial team at each hospital will be crucial to the success of the trial there. For example the PI should have named members of staff who are suitably qualified to carry out tasks such as:

- Taking consent and recruiting patients
- Collecting data and sending it to the Coordinating Centre
- Management of the Investigational Medicinal Product (IMP)

The Emergency Department must be on board and supportive of the study to ensure that all eligible patients who present to the hospital are screened and recruited as soon as possible.

The above criteria are for guidance only and exceptions may be allowed at the discretion of the Chief Investigator.

Progressing with Regulatory Submissions a Site

Applying for local ethics approval

In most cases English documents will be submitted to the Local Ethics Committee (LEC) for their approval. Subsequent translation of the patient information sheet and consent forms following approval should be submitted to the LEC for their information.

Where translated documents are available (i.e. received approval by the National Ethics Committee (NEC)), these should also be submitted to the LEC.

For Investigator

- Covering letter to PI
- Protocol or Country specific Protocol for PI (in the appropriate language if translated)
- Investigator Brochure
- IMP Management Risk Assessment form

For Chair of Ethics Committee

Envelope labelled "For the Attention of the Chairman of the Ethics Committee" which includes:

- Covering letter to the Chairman

- Protocol or Country specific Protocol for PI (in the appropriate language if translated)
- Investigator Brochure and applicable annual review document
- LSHTM ethics approval
- LSHTM sponsorship letter and confirmation of indemnity
- LSHTM or Country specific insurance certificate
- Country Specific National Regulatory Approval Letter, if already granted
- Country Specific National Ethics Approval Letter, if already granted
- Country Specific Ministry of Health Approval (if applicable)

Arranging GCP training

Site personnel are directed to the LSHTM Online Course portal to complete the GCP course and obtain a certificate, which may be used for 3 years.

Further GCP training will be delivered during the Site Initiation Visit (SIV) [See TM WPD 2 Site Training].

Applying for Regulatory Authority and National Ethics Committee Approval

This process is handled as per the Sponsor's SOPs.

Ready to start

Before the trial can start at a site that has all relevant approvals, a study file must be sent to the PI. The TM is responsible for ensuring that all essential documents listed below, have been received before sending the study file and the trial drugs:

- NEC approval (if required)
- National Regulatory approval (if required)
- Local ethics approval (if required)
- PI GCP training completed
- Patient documents (including translations as appropriate) have been personalised to site
- IMP Management Risk Assessment has been completed, and assessed by the TM.

Once all of the above is in place, the SIV will be booked.

The site will be issued with authorisation to recruit at the end of the SIV, following completion of training sessions and all necessary paperwork.

Training

Each staff member receives or has direct access to applicable Working Practice Documents (WPDs).

Each staff member reviews the applicable WPDs once a year.

All WPD training is documented and tracked in the training log located in the Investigator Site File (ISF)

New staff is trained on applicable WPDs within 30 days of employment and all WPDs within 90 days of employment.

Staff members whose duties fall within this WPD scope are retrained within 14 days of the approval of each WPD revision.

Staff signatures: (signing below indicate that you have read this SOP and understand the material contained in it)

Date	Name (Please print)	Signature