

MEDICINES CONTROL COUNCIL



GUIDELINE ON COMPLETING CLINICAL TRIAL APPLICATIONS

This document has been prepared to serve as a recommendation and guideline to applicants wishing to submit applications for the conduct of clinical trials. It represents the Medicines Control Council's current thinking on the safety, quality and efficacy of medicines. It is not intended as an exclusive approach. Council reserves the right to request for any additional information to establish the safety, quality and efficacy of a medicine and may make amendments in keeping with the knowledge which is current at the time of consideration of data accompanying applications for the conduct of clinical trials. The MCC is committed to ensure that all medicines available that are used in clinical trials are of the required quality, safety and efficacy. It is important for applicants to adhere to these requirements.

First publication released for implementation and comment	May 2003
Update to include new contact details	August 2010
Date of implementation	29 April 2003

REGISTRAR OF MEDICINES
MS M. HELA

GUIDE TO COMPLETING CLINICAL TRIALS APPLICATION FORMS

The following attached documents should be used to assist Applicants in completing clinical trials application forms.

1. A Guide to completing clinical trials application (CTA).
2. B Declaration by Principal Investigator.
3. C Provisional Declaration by Co- and Sub-Investigators and other staff involved in a clinical trial.
4. D Declaration by Regional Monitor.
5. E Joint Declaration by Sponsor (or representative) and Principal Investigator (or National Principal Investigator (concerning sufficient funds to complete the study.
6. F Standardized wording to be added to PILs
7. G MCC Format for CVs of Individuals Participating in the Conduct of Clinical Trials in South Africa.

A. CLINICAL TRIALS APPLICATION

Guide to completing Clinical Trials Application (CTA) [*Version MCC/2003/1*]

The purpose of the CTA is to assist members of the Clinical Trials Committee to determine the answers to the following questions:

- Does this proposed trial contribute to new knowledge in a scientific way?
- Are all aspects of this proposed trial ethical?
- Can patient safety be assured?
- Should this trial be done in SA?

The application is divided into three sections.

Section 1: A checklist of required documentation. (If the documentation is incomplete, the application will not be further processed.)

Section 2: Administrative and Supplementary Details.

Section 3: Applicant's Report / Presentation

Section 1: Use the checklist to ensure that all the necessary documentation has been collated.

The ethics approval can be submitted later – but a copy of the letter of application for an ethics committee to assess the proposed clinical trial must be included.

If the insurance certificate is not specific to the particular protocol, ensure that there is an accompanying letter stating that the insurance does cover this particular protocol.

List the files submitted electronically and their format(s). Ensure that all required documentation is available electronically. This does not include electronic copies of insurance certificate, CVs, declarations, certificates of analysis, ethics approval, recruitment advertisements, etc. Ensure that it is possible for the reviewer to 'copy and paste' from the electronic documents should this be necessary. [Note: If complete information is provided in Section 3 without any inconsistencies or discrepancies between it and the information in the protocol, the investigator's brochure or other documentation, this should not be necessary.]

Section 2: Should be self-explanatory.

Section 3: Applicants are advised to complete this as a report / presentation as if they were reviewing the proposed trial. Apart from the required information about the trial itself, the question 'why' should be asked constantly and the answers provided in the form of a rationale or justification. The reviewers will read all the documentation provided, will double-check the accuracy of the information provided in this section, and will raise unsatisfactorily addressed issues or unanswered questions. Their recommendation to the CTC / MCC will be based on their ability to answer the four questions above after reading all the documentation and the applicant's report / presentation.

- Item 1 Check that the title is accurate and specific (e.g. if a drug being tested is actually an adjuvant treatment, this should be stated in the title). Make sure that no component is left out of the title – e.g. ‘phase’.
- Item 3 . Make sure that the rationale for doing the study is clear. It could be the next logical component in a series of studies (e.g. phase III following phase I or II trial). It could be to test different delivery mechanisms. It could be a ‘marketing study’. Try to make sure the answer to the question ‘Why should this study be done at all?’ is clear and logical.
- Item 4. Should be self-explanatory – the important thing is to be brief without losing essential data.
- Item 5 . State objectives and give rationale for each of them. Ensure that these are scientifically credible. Double check that each objective will in fact be ‘analysed’ in the statistics section – or else questions must be asked of sponsor / other about why the objective is included without analysis.
- Item 6. Summarise study design in one (to two) sentences then justify each component. Show that this study design is the correct scientific one to answer the stated objectives.
- Item 7. Provide details of numbers of participants required and why. Justify, using data from section 2, the ability to recruit the required numbers within a certain time period.
- Item 8. List the inclusion and exclusion criteria – and justify each of them in a sentence or a half sentence. Pay particular attention to how these criteria may or may not confound or invalidate the objectives of the trial. Ensure that no discrimination against certain groups takes place – or that particular criteria are well justified. (E.g. HIV patients who have developed resistance to all available treatments.)
- Item 9. A brief summary of the actual administration of medications. If participants take certain medications at home, or use a patient-diary, ensure that these are described and are not confusing. Ensure that dosage regimens are consistent with recommendations in the investigator’s brochure – e.g. dose modifications in cytotoxic therapy.
- Item 10. Clear descriptions of outcome measures. If surrogate markers are being used when the drug is intended to decrease mortality, etc., they should be justified. Ensure that all intended measurements necessary. Ensure that no intended measurements are likely to be of more risk to participants, than they are likely to provide useful information.
- Item 11. Indicate how known or likely adverse events will be dealt with. Clearly describe components requested in Section 3.
- Item 12. Ensure that all components are adequately addressed. Answer the question, ‘Is this the best statistical approach / method for the outcome measures / objectives?’ Clearly indicate reasons for doing an interim analysis or for not doing one.
- Item 13. Comment on the adequacy of each of the ethics components requested in terms of the proposed trial. Pay special attention to the Patient Information Leaflet and the Informed Consent process / form. Have they been properly modified for SA? Ensure that if any blood specimens are to be archived or kept for genetics research, that this is appropriately addressed in a separate consent form, and that it makes the various ethical aspects of this clear.
- Item 14. Any other comments on the proposed trial – including the quality of the protocol, (e.g. well or poorly written / structured; or does it look like it was simply downloaded from a website?); the extent to which the four questions (which the reviewer must answer) can be satisfactorily answered; any other relevant information which the reviewer could take into account in making a recommendation to the CTC / MCC.

B. DECLARATION BY PRINCIPAL INVESTIGATORS

Name:

Title of Trial:

Protocol:

Site:

1. I have read and understood Item 1.5.5 on page 5 and Section 3 (pages 14 – 20) ‘Responsibility of The Principal Investigator (PI) and Participating Investigators’ of the *Clinical Trials Guidelines of the Department of Health:2000*.
2. I have notified the South African regulatory authority of any aspects of the above guidelines with which I do not / am unable to, comply. (If applicable, this may be attached to this declaration.)
3. I have thoroughly read, understood, and critically analysed (in terms of the South African context) the protocol and all applicable accompanying documentation, including the investigator’s brochure, patient information leaflet(s) and informed consent form(s).
4. I will conduct the trial as specified in the protocol.
5. To the best of my knowledge, I have the potential at the site(s) I am responsible for, to recruit the required number of suitable participants within the stipulated time period.
6. I will not commence with the trial before written authorisations from the relevant ethics committee(s) as well as the South African Medicines Control Council (MCC) have been obtained.
7. I will obtain informed consent from all participants or if they are not legally competent, from their legal representatives.
8. I will ensure that every participant (or other involved persons, such as relatives), shall at all times be treated in a dignified manner and with respect.
9. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial.
[*Conflict of interest exists when an investigator (or the investigator’s institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.*]*
*Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)
10. I have* / have not (delete as applicable) previously been the principal investigator at a site which has been closed due to failure to comply with Good Clinical Practice. (*Attach details.)
11. I have* / have not (delete as applicable) previously been involved in a trial which has been closed as a result of unethical practices. (*Attach details)
12. I will submit all required reports within the stipulated time-frames.

Signature:

Date:

Witness:

Date:

C. PROVISIONAL DECLARATION BY CO- AND SUB- INVESTIGATORS AND OTHER STAFF INVOLVED IN A CLINICAL TRIAL

Name:

Title of Trial:

Protocol:

Principal Investigator's Name:

Site:

Designation:

1. I will carry out my role in the trial as specified in the protocol.
2. I will not commence with my role in the trial before written authorisations from the relevant ethics committee(s) as well as the South African Medicines Control Council (MCC) have been obtained.
3. If applicable to my role in the trial, I will ensure that informed consent has been obtained from all participants or if they are not legally competent, from their legal representatives.
4. I will ensure that every participant (or other involved persons, such as relatives), shall at all times be treated in a dignified manner and with respect.
5. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial. [*Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.*]**Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)
6. I have not previously been involved in a trial which has been closed due to failure to comply with Good Clinical Practice.
7. I will submit all required reports within the stipulated time-frames.

Signature:

Date:

Witness:

Date:

D. DECLARATION BY REGIONAL MONITOR

Name:

Title of Trial:

Protocol:

Site:

1. I have read and understood Item 1.5.7 (p5) and Section 5.1 (p30-33) 'The Monitor' of the *Clinical Trials Guidelines of the Department of Health:2000*.
2. I have notified the South African regulatory authority of any aspects of the above guidelines with which I do not / am unable to, comply. (If applicable, this may be attached to this declaration.)
3. I will carry out my responsibilities as specified in the trial protocol and according to the *Clinical Trials Guidelines of the Department of Health:2000*.
4. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial. [*Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.*]**Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)
5. I have* / have not (delete as applicable) previously been the monitor at a site which has been closed due to failure to comply with Good Clinical Practice. (*Attach details.)
6. I have* / have not (delete as applicable) previously been involved in a trial which has been closed as a result of unethical practices. (*Attach details)
7. I will submit all required reports within the stipulated time-frames.

Signature:

Date:

Witness:

Date:

E. JOINT DECLARATION BY SPONSOR (OR REPRESENTATIVE) AND PRINCIPAL INVESTIGATOR (OR NATIONAL PRINCIPAL INVESTIGATOR) CONCERNING SUFFICIENT FUNDS TO COMPLETE STUDY*

Title:

Protocol:

I, <full name>, representing <sponsor or representative>

And

I, <full name>, Principal Investigator/National Principal Investigator

Hereby declare that sufficient funds have been made available to complete the above-identified study.

Signed

Date

SPONSOR (or alternative)

Name
Address
Contact details

Signed

Date

PRINCIPAL INVESTIGATOR (or National PI)

Name
Address
Contact details

*Section 4.13, page 26: Clinical Trials Guidelines 2000, Department of Health, South Africa.

F. STANDARDISED WORDING TO BE ADDED TO PATIENT INFORMATION LEAFLET (PILS).

If you have questions about this trial you should first discuss them with your doctor or the ethics committee (contact details as provided on this form). After you have consulted your doctor or the ethics committee and if they have not provided you with answers to your satisfaction, you should write to the South African Medicines Control Council (MCC) at:

The Registrar of Medicines
Medicines Control Council
Department of Health
Private Bag X828
PRETORIA
0001

Fax: (012) 395 9201

e-mail: mogobm@health.gov.za

G. MCC FORMAT FOR CVS OF INDIVIDUALS PARTICIPATING IN THE CONDUCT OF CLINICAL TRIALS IN SOUTH AFRICA.

Trial:

Protocol:

Designation: (e.g. National Principal Investigator, Investigator (Principal, Co- or sub-), Study Co-ordinator, Regional Monitor, Local Monitor, Contract Research Affiliate)

1. Personal Details

Name:
Work Address:
Telephone Number:
Fax Number:
Cell-phone Number:
e-mail address:

2. Academic and Professional Qualifications

3. Health Professions Council of South Africa (HPCSA) registration number if applicable (or other health professions body registration particulars if applicable – e.g. Nursing Council)
4. Current personal medical malpractice insurance details [medical and dental practitioners]
5. Relevant related work experience (brief) and current position
6. Participation in clinical trials research in the last three years (title, protocol number, designation) [If multiple trials, only list those with relevance to this application, or in the last year.]
7. Peer-reviewed publications in the past 3 years
8. Date of last GCP training (as a participant or presenter)
9. Any additional relevant information supporting abilities to participate in conducting this trial. [briefly]

Signature:

Date: