MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

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CLINICAL TRIAL INVESTIGATORS

This document has been prepared to supplement the guideline on Oversight and Monitoring in Clinical Trials, to clarify and define the roles of investigators in investigational studies of medical products, including human medicine and biological products, medical devices, and combinations thereof. Council reserves the right to request any additional information and may make amendments in keeping with the knowledge which is current at the time of consideration.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website

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1 INTRODUCTION

The Medicines Control Council (MCC) recognises the importance of good oversight of clinical trials.[1] The MCC also recognises that over the past twenty years the complexity of clinical trials has changed, requiring combination teams of either differently-skilled clinicians and/or suitably qualified clinical research scientists to lead the team.

Noting these changing requirements, the MCC has reviewed the oversight of clinical trials and is recommending that new categories of investigators for trial leadership will be recognised and approved. Currently, the MCC's guidelines define the roles of principal investigators and sub-investigators. In addition to the aforementioned, the MCC resolved to define a new category of a Co-Principal Investigator. This category will allow both clinician and non-clinician scientists to assume the role of Co-Principal Investigator for approved clinical trials. This will enhance trial leadership and has the potential to build capacity to undertake clinical trials in the country.

2 CATEGORIES OF INVESTIGATORS

2.1 Principal Investigator and Sub-investigators

According to the ICH-GCP Guidelines 1996, an investigator in a clinical trial is a suitably qualified person responsible for the conduct of the clinical trial at a trial site or with oversight of several trial sites. If a trial is conducted by a team of individuals at a trial site, the investigator who is the responsible leader of the team is called the Principal Investigator (PI).

A **Sub-Investigator (Sub-PI)** is any individual member of the clinical trial team who is designated and/or supervised by the **Principal Investigator** at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions.

MCC resolved that at least one of the **Sub-Principal Investigator** at any trial site must be a clinician, registered with the appropriate statutory body and qualified to provide clinical oversight within his/her scope of practice.

According to the South African Department of Health Good Clinical Practice Guidelines 2006, the **Principal Investigator** must be a South Africa-based scientist who has a sole or joint responsibility for the design, conduct, delegation of trial responsibilities, analysis and reporting of the trial. The **Principal Investigator** is accountable to the Sponsor/Applicant and to the regulatory authorities, as required by these Guidelines. The **Principal Investigator** should be knowledgeable and have an understanding of the study medicine(s), including toxicology and safety.

In the case of a multi-centre trial there must be a local **Principal Investigator** responsible for each study site. It is unacceptable to have an "absentee" **Principal Investigator** who is based in another city or country. If there are multiple sites in South Africa it is recommended that a **National Principal Investigator** be appointed, who will take overall responsibility for the conduct of the study.

2.2 Co-Principal Investigator

MCC recognises that there may be instances where the **Principal Investigator** for a trial may be a suitably qualified non-clinician scientist. This type of investigator may be a laboratory scientist, pharmacist, or other appropriately qualified and experienced person, who is able to provide critical trial oversight and management and can lead a study team.

[1] *2.43 Oversight and Monitoring in Clinical Trials*

In this instance the MCC currently requires that an adequately qualified research clinician is also part of the leadership team. There may be instances where more than one clinical speciality is required for the clinical management of participants in a study, therefore requiring more than one clinical investigators' core skills to ensure proper management of trial procedures and participants.

For these reasons the MCC has introduced a category of **Co-Principal Investigator (Co-PI)**, which allows for a team consisting of two **Co-Principal Investigators** to lead a study at a site. The role of the each **Co-Principal Investigator** should be described for the study, and their complementary responsibilities carefully detailed, so that all the responsibilites of a PI as defined are covered. At least one of the **Co-Principal Investigators** must be a clinician registered with the appropriate statutory body and qualified to provide clinical oversight within his/her scope of practice. While the co-PIs will have defined roles and functions in relation to the conduct of the trial, in terms of legal responsibility they will be jointly and severally liable.

For multi-centred studies there must be a **National Principal Investigator** appointed, who may or may not be a site **Principal Investigator**. The **National Principal Investigator** must have appropriate experience and expertise in that field and must be responsible for the application to the MCC to conduct the study. The **National Principal Investigator** must meet all other requirements to be a **Principal Investigator** and must sign a declaration accepting the responsibility as **National Principal Investigator** and sign off the Clinical Trial Form (CTF) application. The **National Principal Investigator** must coordinate concerns of investigators regarding the conduct of the trial and communicate these with sponsor, applicant, ethics committees and MCC as necessary. [~~**National Co-Principal Investigators** may also be apponted~~.]

~~**Co-Principal Investigators**~~

Where **Co-Principal Investigators** are appointed, the following conditions apply:

1. Appropriate and acceptable reasons must be provided for the appointment of two **Co-Principal Investigators**. Such applications will be considered and approval granted on a case-by-case basis.
2. Both **Co-Principal Investigators** must meet all the requirements of being a **Principal Investigator**.

~~2 [In the case of a **Co-Principal Investigator** appointment, all the existing requirements for a **Principal Investigator** must be met with the exception of the requirement that each person be a clinician.]~~

3. At least one **Co-Principal Investigator** must be a clinician, registered with the appropriate statutory body, [~~and~~] qualified to provide medical oversight within his/her scope of practice, and provide professional indemnity insurance. [~~He/she must, however, meet all the other requirements of being a **Principal Investigator.**~~]
4. The non-clinical **Co-Prinicpal Investigator** must be registered with the statutory body for his/her profession, where appropriate. In addition, indemnity insurance must be provided.
5. Both **Co-Principal Investigators** must be based in South Africa.

3 UPDATE HISTORY

Date	Reason for Update	Version & Publication
November 2016	First version published as Communication to Industry 9.84	v1, Nov 2016
April 2017	Revised for clarity and published as guideline 2.47	v2, May 2017