South African Health Products
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GUIDELINE FOR CLINICAL TRIAL INVESTIGATORS

This document has been prepared to serve as a guideline for applicants/investigators who wish to submit the application to conduct a clinical trial, application for additional sites and add additional investigators to an approved trial. It represents the South African Health Product Regulatory Authority's (SAHPRA) current thinking on the investigators provision of oversight during the conduct of clinical trial. This guideline intends to provide clarity on conditions applicable to Co-Principal Investigators. SAHPRA reserves the right to request any additional information and may make amendments in keeping with the knowledge which is current.

Document History

Final Version	Reason for Amendment	Effective Date
1	First version published for implementation	May 2017
2	Administrative changes	May 2019
3	Administrative changes, document number change from 9.84 to SAHPGL-CEM-CT-09	October 2022

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1. INTRODUCTION

The South African Health Products Regulatory Authority (SAHPRA) recognises the importance of good oversight of clinical trials. SAHPRA 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, SAHPRA has reviewed the oversight of clinical trials and is recommending that new categories of investigators for trial leadership will be recognised and approved. Currently, SAHPRA's guidelines define the roles of principal investigators and sub-investigators. In addition to the aforementioned, SAHPRA 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.

1.1 Purpose

This document intends to serve as a guideline for applicants/investigators who wish to submit the application to conduct a clinical trial, apply for additional investigators to an approved trial or submit the application for additional/change in site. The guideline provides the conditions for investigators and in particular the Co-Principal Investigators. This guideline should be read in conjunction with the SA GCP guidelines.

2. LEGAL PROVISION

This guideline is established in terms of Regulation 30 of the medicines and related substances act, 101 of 1965, conduct of clinical trials.

3. PRICINCIPAL INVESTIGATORS

According to the current ICH-GCP Guidelines, 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-I)** 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.

SAHPRA resolved that at least one of the **Sub-Investigators** 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 Good Clinical Practice Guidelines 2020, 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.

4. CO-PRINCIPAL INVESTIGATORS

SAHPRA 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.

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

For these reasons SAHPRA 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 each **Co-Principal Investigator** should be described for the study, and their complementary responsibilities carefully detailed, so that all the responsibilities 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 and separate 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 the clinical field of the study and must be responsible for the application to SAHPRA 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 SAHPRA as necessary.

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**.
3. At least one Co-Principal Investigator must be a clinician, registered with the appropriate statutory body, qualified to provide medical oversight within his/her scope of practice, and provide professional indemnity insurance.
4. The non-clinical **Co-Principal Investigator** must be registered with the statutory body for his/her profession, where appropriate. In addition, indemnity insurance must be provided regardless of clinical qualification.
5. Both Co-Principal Investigators must be based in South Africa.0

5. REFERENCES

South African Good Clinical Practice Guideline.2020. 3rd ed. South Africa

6. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the communication on Clinical Trial Investigators, document number 9.84. It will be reviewed in this timeframe or as and when required.