DEPARTMENT OF HEALTH
Republic of South Africa

SAHPRA
South African Health Products Regulatory Authority

POST CLINICAL TRIAL ACCESS (PTA) / CONTINUED ACCESS

This document has been prepared to serve as a guideline to sponsors/applicant and investigators providing investigational product to participants during clinical trials. This is to ensure that participants who derive benefit from the investigational products will be provided with the product as per conditions of this guideline. This guideline represents the South African Health Products Regulatory Authority's (SAHPRA) current thinking on the measures to be taken to ensure that patients gain access to their treatment independently once the trial is over. It is not intended as an exclusive approach. SAHPRA reserves the right to request any additional information and may make amendments in keeping with current knowledge.

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1 BACKGROUND

All research proposals that involve unproven or unregistered medicines should consider making provision for Post-Trial Access (PTA) or Continued Access (CA) to the investigational product, where appropriate. In advance of a clinical trial, sponsors / applicants as well as clinical researchers should make provisions for PTA / CA for all participants who still need an intervention identified as beneficial in the trial. Only those participants who derive benefit from the investigational product will be considered (this excludes participants on standard of care, placebo and registered medicines).

Where appropriate and available, the possibility of PTA / CA should be disclosed to and discussed with potential participants during the initial informed consent process or via a separate consent process. PTA / CA is important for participants on clinical trials who, based on the study endpoints (not on opinion of the investigator), benefit significantly from study investigational product but cannot access the study medicine independently once the trial ends.

2 GUIDELINES

2.1 Protocol

2.1.1 A clinical trial research proposal to test an unproven or unregistered medicine must include discussion of whether post-trial or continued access to the investigational product may be possible in cases where superiority, or non-inferiority based on the study end point is proven especially in case of improved adverse event profile.

2.1.2 If post-trial or continued access is possible, the proposal must include an explanation of how such access will occur, for example:

- in a roll-over study, or
- through an expanded access programme (EAP) of the unregistered investigational product.

2.1.3 If a roll-over study is proposed, the proposal and protocol must be submitted for scientific and ethics review, if this extension study was not part of the original submission. An eligible participant would be enrolled in the roll-over study in the usual way and all the usual clinical trial expectations and standards would apply. The implications for allocation of responsibility for the cost of investigational product and other requirements including monitoring must be evident in the protocol.

2.1.4 If an expanded access plan is proposed, the plan must clearly outline the roles and responsibilities of the key health care personnel to explain whether this programme is a research study or clinical treatment. The plan must be submitted for scientific and ethics review. The implications for allocation of responsibility for the cost of investigational product and other requirements must be evident in the protocol as above.

2.1.5 Where PTA / CA to the study medicine is possible, a smooth transition must occur between the trial and the roll-over protocols or into the expanded access programme so that no harm occurs to the participant or patient respectively.

2.2 Context for Post-Trial Access /Continued Access

2.2.1 PHASE I and II

Post-trial access / Continued Access is not applicable for Phase I and II studies. However, PTA / CA may be necessary for particular diseases such as cancer and other dread or rare diseases for which no other medicines or other standard of care is available.

2.2.2 **PHASE III**

- Post-trial access / Continued Access should be considered for Phase III studies when no registered and marketed standard of care is available in South Africa, provided that data from interim or final analyses shows that post-trial access / continued access is clinically justifiable in light of the study's parameters and endpoints. Benefit must be objective as well as significant to be clinically justifiable, and be based on study endpoints and not only investigator opinion.
- Where the standard of care (SOC) is registered and marketed (as applicable), PTA / CA of the investigational product should be considered only when data from an interim and/or final analysis shows safety and superior efficacy as compared to the standard of care.

2.2.3 **PHASE IV**

PTA / CA is no applicable.

2.3 General

2.3.1 Where appropriate and/or available details of potential PTA / CA should be included in the Clinical Trial Form 1 (CTF1), and Informed Consent Form / Patient Information Leaflet (PIL/ICON).

2.3.2 Where PTA / CA is not planned at the start of the study, but might become applicable, the sponsor / applicant should initiate the discussions about PTA / CA as soon as the outcome of superiority, or non-inferiority has been proven.

2.3.3 PTA / CA will not be applicable in the event of negative study outcomes.

2.3.4 PTA / CA will not be applicable in studies of patients with acute reversible conditions.

2.3.5 PTA must be discontinued immediately if pharmacovigilance demonstrates negative short- or long-term health outcomes.

2.3.6 Labelling of study investigational product accessed post-trial must be in accordance with Regulation 30(9)1 of the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965).

2.3.7 If the study investigator does not wish to or is unable to continue with the PTA / CA programme, arrangements should be made to transfer the participant to another site or to appoint another investigator.

3 GUIDELINE COMPLIANCE

While this PTA / CA guideline aims to improve participant safety and wellbeing, there may be certain instances where, for various reasons, these guidelines cannot be fully adhered to. Justification and motivation would be required in such instances which will be reviewed on a case by case basis to ensure that participant safety and wellbeing is not compromised.

3.1 Period of PTA / CA

A minimum of 4 (four) years after completion of the study is recommended as the acceptable time period to provide PTA / CA to the participants who derived benefit from the investigational product, unless there are compelling reasons for determining otherwise.

During the PTA / CA period, the applicant/sponsor must ensure monitoring and oversight of participants using investigational product.

4 REFERENCES

CIOMS. 2016. International Ethical Guidelines for Health-related Research Involving Humans especially Guideline 6 and its accompanying commentary

National Department of Health. 2015. Ethics in Health Research: principles, processes and structures. 2nd ed.

Medicines and Related Substances Act, 1965 (Act 101 of 1965). Republic of South Africa.

Regulations of the Medicines and Related Substances Act, 1965 (Act 101 of 1965). Republic of South Africa

World Medical Association Declaration of Helsinki. 2013. Ethical Principles for Medical Research Involving Human Subjects.

5 UPDATE HISTORY

Date	Reason for Update	Version & Publication
April 2016	First version for External Stakeholder comment	Version 1, May 2016 for comment
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