HREC GUIDANCE ON CLINICAL TRIAL (CT) REGISTRATION AND SAHPRA APPROVAL

This document provides guidance only and complex applications may require careful reflection by the researcher(s) and HREC and could be discussed during consultation prior to submission of an ethics application. HREC acknowledges that not all clinical trials or randomized clinical trials/studies (RCTs) involve the use of a medicinal or health product or device and thus may need careful consideration in terms of the specific planning and registration of such studies that fall outside of the ambit of SAHPRA.

- HREC cannot take responsibility for the interpretation of directives and decisions as made by an independent body such as SAHPRA.
- Four critical questions are highlighted, followed by the relevant or probable HREC expectation/ guidance and further remarks.

Critical question	If yes, HREC expectation	Further remarks
1 Is the study a clinical study?	The study will either be a clinical trial or an observational study	Study makes use of human volunteers (participants)
2 Is the study a clinical trial? *Affirmative on all the following:* a. The study involves human participants b. The participants are prospectively assigned to an intervention c. The study is designed to evaluate the effect of an intervention on the participants d. The effect being evaluated has a health-related biomedical or behavioural outcome? (NIH, 2017)	Register as a clinical trial – may focus on intervention(s) such as "*prevention, health promotion, screening, diagnosis, treatment, rehabilitation, or organization and financing of care*" (DoH (2015:77)	**Provide evidence of** 1. GCP training is required by HREC and 2. Clinical trial registration with a. SANCTR and b. PACTR (The Pan African Trials Register - WHO approved, hosted by the SAMRC: https://pactr.samrc.ac.za/ or contact pactradmin@mrc.ac.za
3 Is the health intervention a health product [1] (orthodox or complementary)?	Register as a clinical trial [2] – Reflect on 4 below for guidance on considering SAHPRA[3] approval	**Provide evidence of** 1. Clinical trial registration (SANCTR) is essential and registration with PCTR is advised 2. SAHPRA notification of a CT
4 Is the health product a. *Unregistered* OR b. *Registered*, but used differently from original registration, for example	Register as a clinical trial Obtain SAHPRA approval	**Provide evidence of:** 1. Clinical trial registration with a. SANCTR and b. SAHPRA

[1] Orthodox and complementary medicine. Include medical device, prosthesis, pharmaceutical product, medical product, biological product (including vaccines), diagnostic medicine, radiational product, ionising and non-ionising radiation emitting device, radioactive nuclides.

[2] CT: "*…any investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy".* (DoH GCP, 2020:66)

[3] SAHPRA responsible for regulation (monitor, evaluate, investigate, inspect and register) of all health products, inclusive of *"clinical trials, complementary medicines, medical devices and in vitro diagnostics (IVDs)*". (https://www.sahpra.org.za/who-we-are/ accessed 2021/08/06.

Critical question	If yes, HREC expectation	Further remarks
• Different dose *or* • Different mode of administration *or* • Different indication/purpose		c. PACTR (The Pan African Trials Register (is advised) Reflect on so-called off-label use 2. GCP Training certificate

Please note

1. The table above provides broad guidance for the researcher in terms of determining if a clinical study requires registration and SAHPRA approval.
2. The discipline radioactive pharmaceuticals are particularly complex and may require further reflection
3. If uncertain, the Researcher Is advised to study/ consult the
   a. Medicines and Related Substances Act 101 of 1965
   b. HREC Standard Operating Procedures (2019)
   c. SAHPRA Website, documentation and/or advisors
   d. The Health Research Ethics Office
4. **Clinical trials not studying "health products" as an intervention**

   These may include for example health, educational, behavioural, management and policy interventions in the medical and health sciences:
   a. If such a CT is relates to the health of the participant and/or is conducted in the health care setting and/or is explicitly related to or imbedded in clinical/ health care provision, then GCP training of the primary investigator would be advisable and HREC may require such.
   b. Such studies is advised to also register with the SANCTR or PACTR. Evidence of such a registration are often required in the publication of findings.

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