UCT Sponsorship and Insurance of Clinical Research Studies

1. Introduction

Clinical research (sometimes also called biomedical research) involves study of human participants with some aspect of clinical interaction, including, but not limited to, biological samples/tests, electrocardiograms (ECGs), medical questionnaires, medical imaging, medical devices, etc. All research involving human participants is governed by South African Good Clinical Practice (GCP) guidelines[1]; which provides that all clinical research studies must have a study sponsor – that is, a person or organisation responsible for initiation, management **and/or** financing of the clinical study. The sponsor can be a pharmaceutical company, an institution, a funding body, or an individual or organisation designated by the funding body or academic institution[1]. Note: Student research falls under a named Principal Investigator/Supervisor and as such is governed by the same rules that hold for other researchers.

2. Who should be the sponsor?

2.1. Where a commercial organisation (such as a pharmaceutical company) funds a study for which it retains ownership of the intellectual property and publishing rights, the company invariably acts as the sponsor.

2.2. Where a study is funded by a research council, medical charity or other non-commercial body, the funder may be willing to act as the sponsor, particularly where it also employs members of the research team or retains an interest in any intellectual property that is generated. It is important to note that funders do not automatically accept the role of regulatory sponsor and where this is the case, the grant application will need to confirm details of sponsorship arrangements, as per GCP.

2.3. Where an investigator undertakes a study on behalf of his/her employing institution and the funding body is unwilling to act as the sponsor, the employing institution may act as the sponsor.

2.4. The sponsor may also be the institution conducting the research (e.g., a university), particularly where it is funding the study, an external funder of the study is unwilling or unable to do so, such as a charity (e.g. CANSA) or a national funding body (e.g. NRF, MRC, NIH). If a commercial company is unwilling or unable (e.g., due to size) to take on the full sponsor roles and responsibilities for a study (e.g., some medical device companies), then the institution conducting the research will need to act as sponsor (after first assessing the project risk as well as intellectual property and publishing rights).

2.5. Where an investigator undertakes a study in which the participants are owed a duty of care by the hospital rather than the investigator's employing institution, the host institution may act as the sponsor. However, the duty of care remains the responsibility of the hospital, irrespective of whether they are the sponsor.

2.6. If no one is willing to take on the sponsor role for a clinical study that requires a sponsor, the study **may not** proceed.

3. **Responsibilities of sponsor**

3.1. The legal responsibilities of a sponsor are outlined in SA GCP Guidelines. Some of the main responsibilities of a sponsor include, but are not limited to:

3.1.1. Quality control and management oversight

3.1.2. Assigning a monitor who will develop a risk-based monitoring plan

3.1.3. Providing necessary indemnity (insurance) for the study.

4. UCT as sponsor

4.1. The University of Cape Town (UCT) may be required to act as sponsor in the case of 2.2, 2.3, 2.4 and 2.5 above. If UCT should be the designated sponsor, then a formal ***sponsorship agreement*** will need to be obtained from the Faculty of Health Sciences (FHS). In the case where UCT is required to act as sponsor, the Principal Investigator (PI) needs to ensure that all costs related to sponsor responsibilities (e.g., appointment of a monitor, payment for members of the Data Safety Monitoring Board, etc.) are accounted for in the study budget up front. One exception to this, is the cost of no-fault insurance, which is discussed in Section 5.1.1 (see details for studies involving minors, pregnant women, or participants outside South Africa).

4.2. <u>To apply for UCT sponsorship:</u>

4.2.1. The PI completes FHS026 form.

4.2.2. The PI (or designee) submits the study protocol, Funder Contract and the FHS026 form via email to the Research Governance Officer (RGO), (fhs.sponsorship@uct.ac.za) with the subject line: *new application for UCT sponsorship.*

4.2.3. The RGO will then review the application, in consultation with the UCT Risk Management Office, and reply to the email to indicate whether UCT will act as the study sponsor. If so, they will attach a sponsorship agreement for the PI to sign.

4.2.4. PI (or designee) returns the signed sponsorship agreement via email to the RGO.

4.3. If in doubt as to whether or not a particular study requires UCT to act as its sponsor, please contact the RGO (fhs.sponsorship@uct.ac.za).

5. UCT as insurance provider

UCT has a range of insurance of which 'no-fault insurance' for study participants is one type. It is for claims made by research participants who may be injured or suffer side effects or death (where there is no negligence from the study staff) as a direct result of their participation in the study.

Unless a study has an external regulatory sponsor and is covered by that sponsor's no-fault insurance, the UCT FHS PI must apply to UCT to act as regulatory sponsor for the project and to provide insurance cover.

For studies that require approval from both the FHS Human Research Ethics Committee (HREC) and the South African Health Products Regulatory Authority (SAHPRA), submissions to these two authorities should be done in parallel with each other. No-fault insurance confirmation for a study is granted prior to ethics approval (and SAHPRA approval where relevant), but its validity is **conditional** on the ethics approval subsequently being granted (i.e., the insurance will not respond without ethics approval being in place).

5.1. UCT provides 3 types of insurance for clinical research studies (also see the UCT INSURANCE COVER GUIDELINE [FG008]):

5.1.1. **No-fault insurance** (also see UCT No-fault Insurance Policy, updated annually, and Figures 1-4 below):

- No-fault insurance cover is for human participants in UCT FHS research studies who may be injured or suffer side effects or death as a direct result of their participation in the study. Any injury to the participants not linked to the study is not covered under this insurance policy. To be covered, all relevant studies must have study-specific insurance confirmation from the UCT Risk Management Office and the appropriate regulatory approvals prior to commencement. Annual renewal of approvals is also required.
- It is important that PIs provide the relevant information on study participant numbers when requested, as UCT's no-fault insurance has an annual cap on numbers of participants covered.
- UCT no-fault insurance cover is applicable to all FHS studies involving human participants where these are not covered by no-fault insurance external to UCT (e.g., by the external sponsor). This includes observational or interventional studies, and studies that are deemed low risk, moderate risk, or high risk (according to risk assessment).
- UCT no-fault insurance provides cover for one year at a time (March-February) and the premium is based on the number of human participants in FHS studies in that upcoming insurance year plus a buffer number of participants (typically a few thousand overage). The buffer is to accommodate new studies that may commence

during the course of the year, while acknowledging other studies may conclude during the course of the year.

- To gain initial UCT no-fault insurance, studies must be declared via the RGO (fhs.sponsorship@uct.ac.za) (per section 4.2) as part of the sponsorship agreement process, to the UCT Risk Management Office, who will provide a study-specific certificate indicating cover – on receipt of this studies will be covered until the date indicated on the certificate – the PI has a responsibility to request a new/valid certificate annually.
- NB: Per requirements from the insurers, studies involving minors, pregnant women or participants outside South Africa will undergo additional review and *may* be required to pay an additional insurance premium.
- For ongoing studies to remain covered in subsequent no-fault insurance years (March-February), they must be on the annual list provided by HREC to the UCT Risk Management Office in February each year. PIs must provide relevant information to HREC when requested to do so (specifically regarding the number of participants involved in the upcoming insurance year for each ongoing study).
- A 6-month check is performed (via list submission of ongoing studies from HREC to the UCT Risk Management Office in August every year) to assess if the number of participants in that insurance year is still adequately within the number for whom cover has been purchased.

5.1.2. **Professional indemnity cover** (also see UCT Professional Indemnity Policy, updated annually):

- Professional indemnity cover is for sums which a UCT staff member may become legally liable to pay arising out of breach of professional duty by reason of any neglect, error, or omission. Cover is worldwide but excluding North America. It applies to all staff working on the clinical research study. (If members of the study team are not UCT employees (i.e., do not have a UCT staff number) and require cover, this must be declared and discussed with the RGO (fhs.sponsorship@uct.ac.za) up front.

5.1.3. **Public liability cover**:

- Public liability insurance is for damages which UCT shall become legally liable to pay consequent upon accidental death of, or bodily injury to, or illness of any persons, or accidental loss, or physical damage to tangible property of others (e.g., visitors).

5.2. To obtain insurance certificates, once the PI has returned the signed sponsorship agreement (see 4.2.4 above):

5.2.1. The RGO obtains countersignature on the sponsorship agreement as well as obtains a no-fault insurance certificate for the study (valid for 1 year) and confirmation of professional indemnity cover for the named investigators as requested from the UCT Risk Management Office and returns these via email to the PI/designee.

5.2.2. The no-fault insurance certificate must then be included in the FHS013 submission to HREC per the FHS013 checklist.

5.3. Ongoing insurance & sponsorship cover:

5.3.1. The PI will provide FHS016 annual progress reports to HREC, noting recruitment progress.

5.3.2. In addition, the PI will be prompted by HREC on an annual basis to confirm whether ongoing no-fault insurance is required (i.e., whether any participants are still being recruited onto the study or are still in follow-up on the study).

5.3.3. The PI has a responsibility to request renewed no fault certificate(s) annually from Debbie Erasmus (debbie.erasmus@uct.ac.za) in the UCT Risk Management Office.

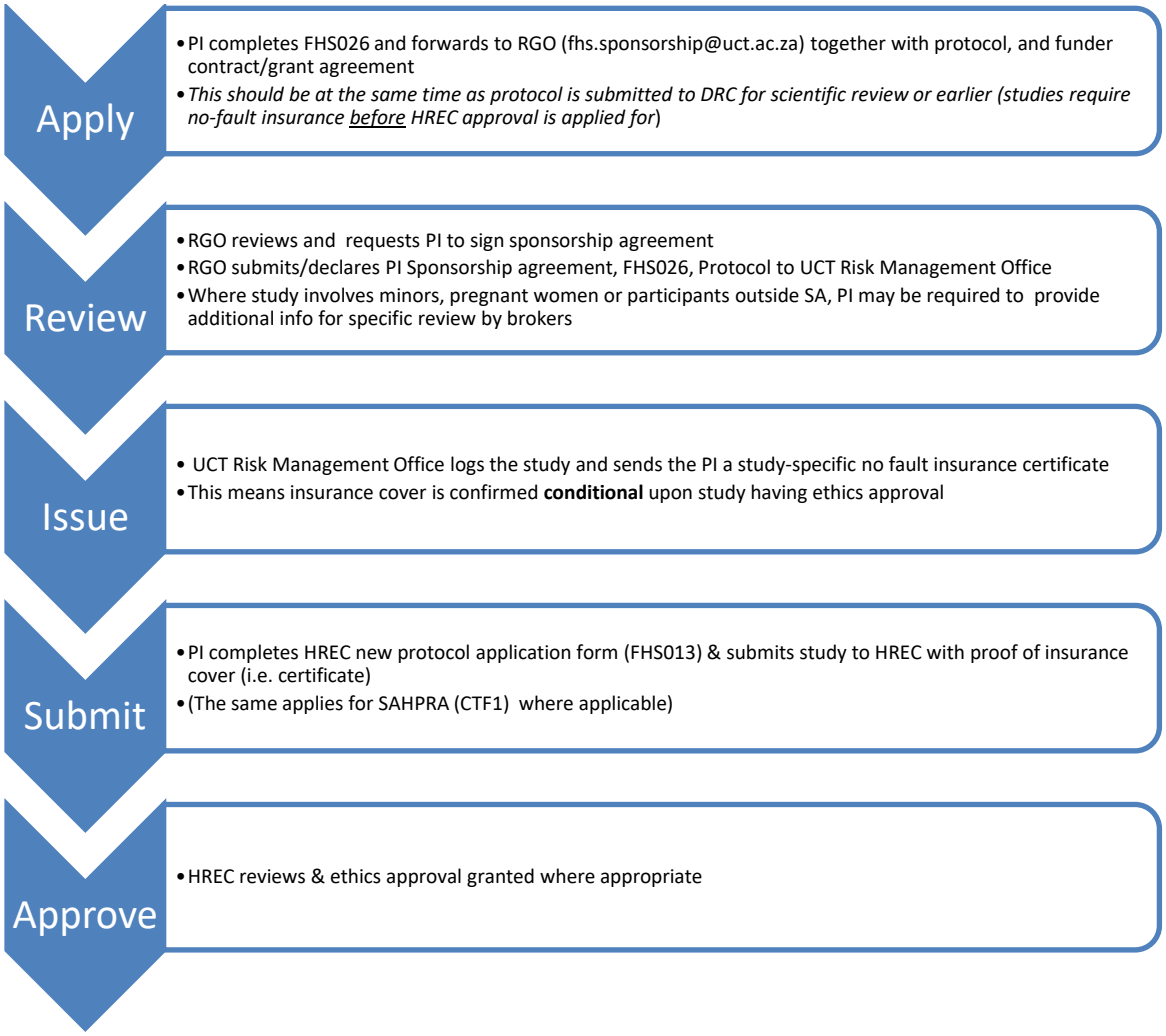
5.3.4. Insurance certificates (and the updated insurance certificates) must be filed in Investigator Site Files (ISF) for the entire duration that the study is ongoing.

5.3.5. At the end of the study the PI submits an FHS010 study closure report to HREC and to the RGO (fhs.sponsorship@uct.ac.za) so that the end of the sponsorship agreement may be noted.

5.4. All insurance claims must be referred by the PI to:

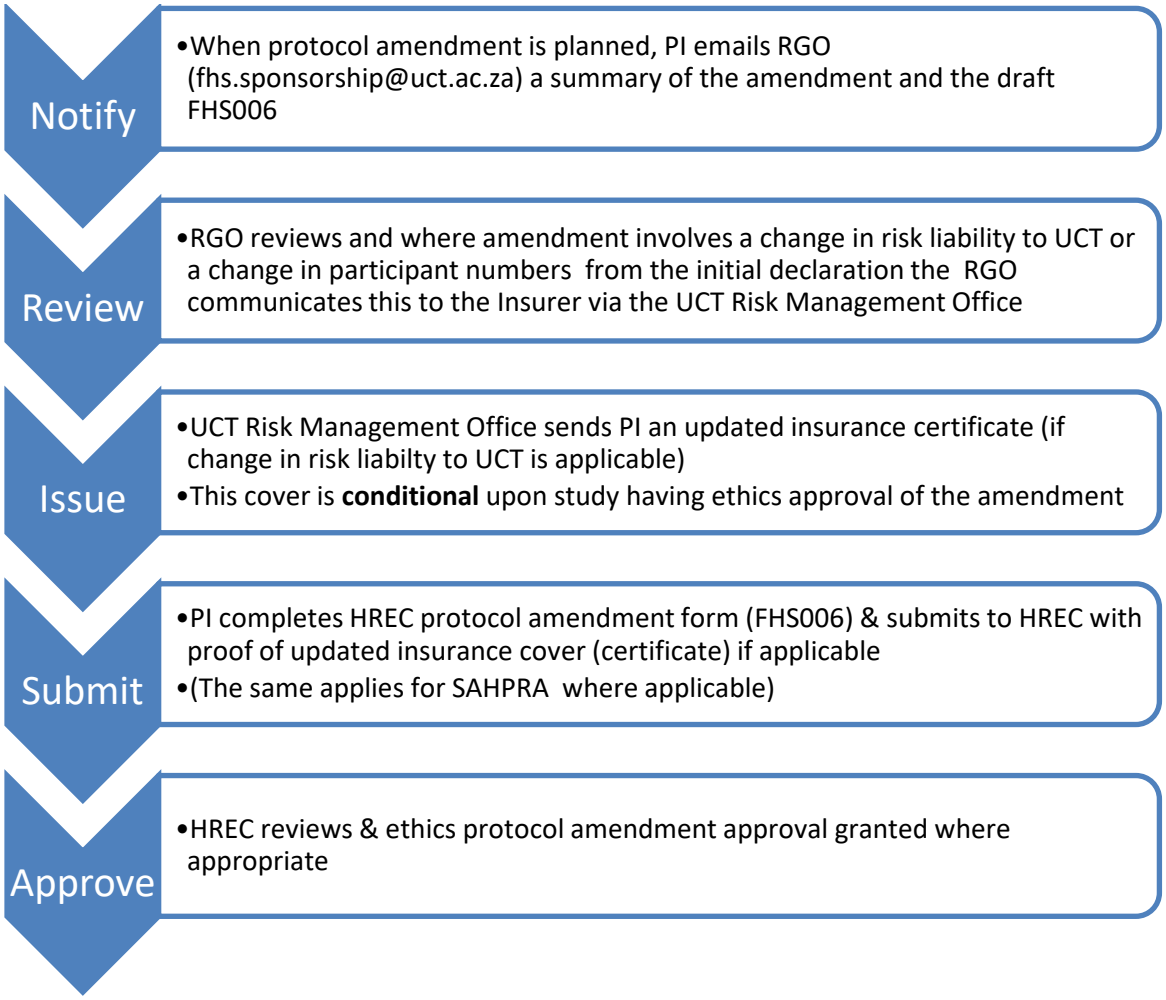
UCT Risk Management Office
Finance Department
Room 240, Bremner Building, Lovers Walk, Rondebosch
Phone: 021 650 2204
Email: debbie.erasmus@uct.ac.za

Figure 1 Process flow for: new applications (initial submissions) for no-fault insurance



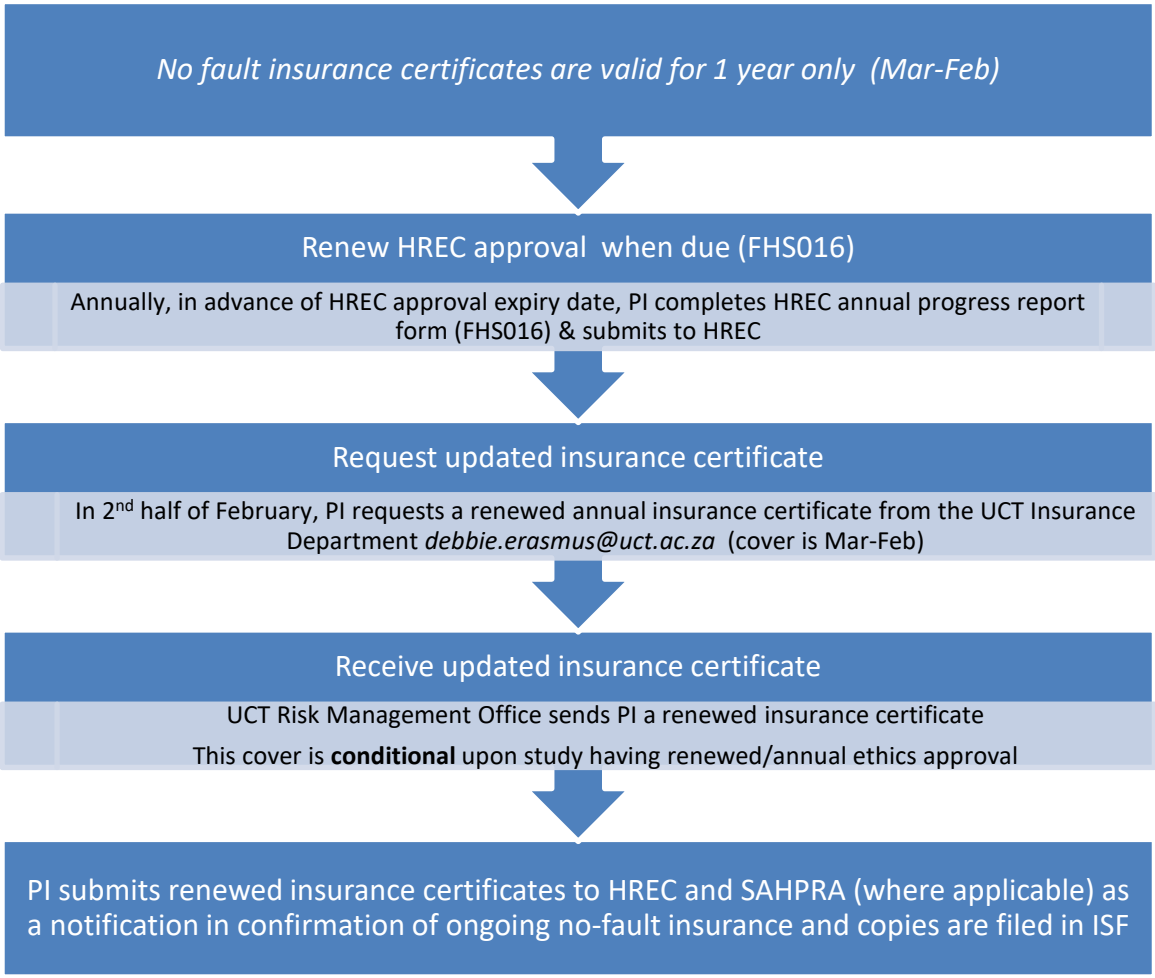
Notes:
RGO: Research Governance Officer (fhs.sponsorship@uct.ac.za)
CTF1: Clinical Trial Form 1 – initial application to SAHPRA
DRC: Departmental Research Committee
HREC: FHS Human Research Ethics Committee
PI: Principal Investigator
SA: South Africa
SAHPRA: South African Health Products Regulatory Authority

Figure 2 Process flow for protocol amendments for no-fault insurance: By study



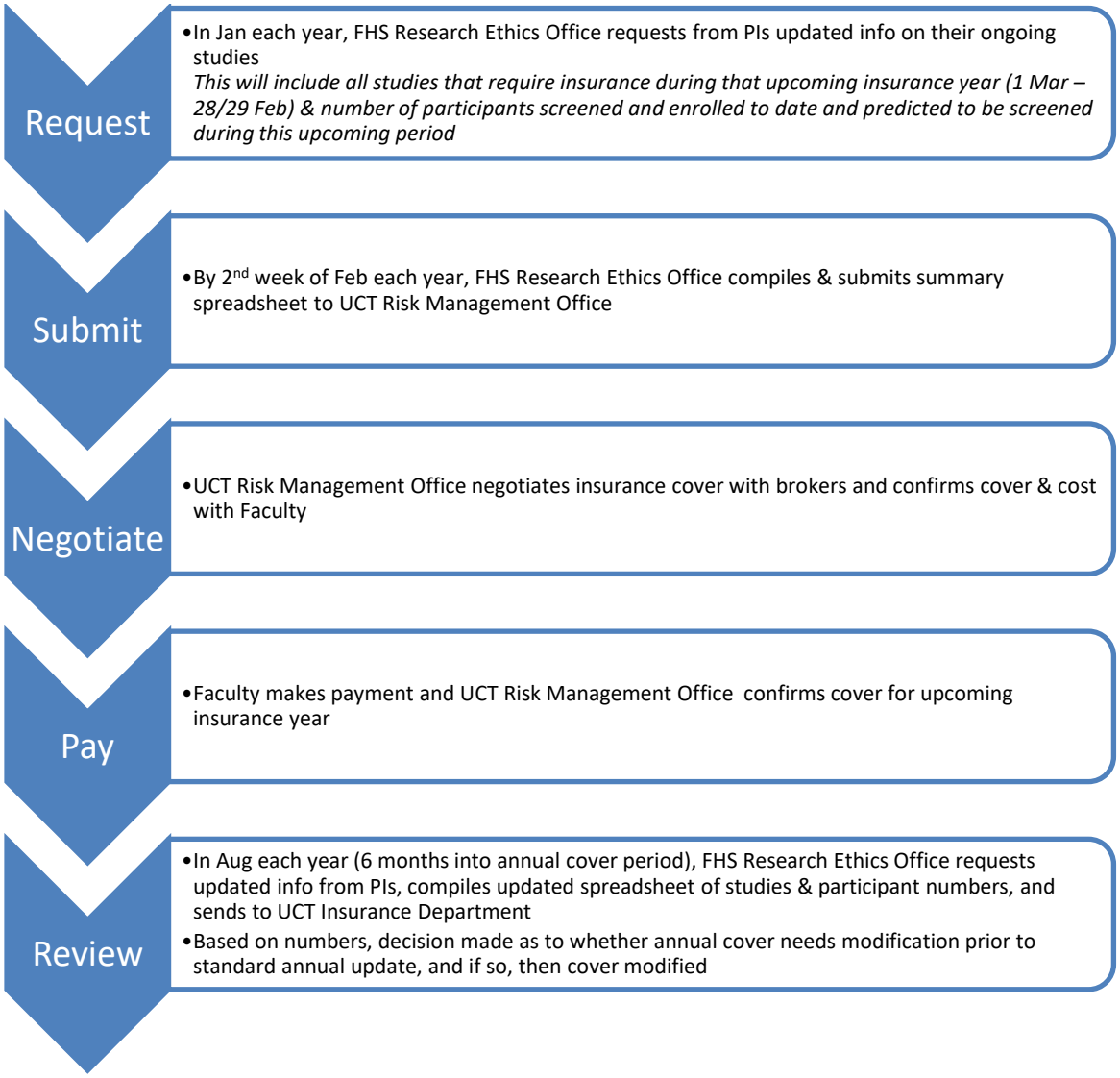
Notes:
RGO: Research Governance Officer (fhs.sponsorship@uct.ac.za)
HREC: FHS Human Research Ethics Committee
PI: Principal investigator
SAHPRA: South African Health Products Regulatory Authority

Figure 3 Process flow for annual renewals for no-fault insurance: By study



Notes:
RGO: Research Governance Officer (fhs.sponsorship@uct.ac.za)
HREC: FHS Human Research Ethics Committee
PI: Principal investigator
SAHPRA: South African Health Products Regulatory Authority
ISF: Investigator Site File

Figure 4 Process flow for annual and 6-month grouped no-fault insurance submission from FHS



Notes:
HREC: FHS Human Research Ethics Committee
PI: Principal investigator

6. Responsibilities of the Principal Investigator (PI) of a UCT-sponsored study

Key PI responsibilities include:

6.1. Obtain HREC approval and SAHPRA approval (if applicable) for the study protocol.

6.2. Obtain facility/provincial approval(s) as necessary depending on the physical site where the study will be conducted.

6.3. Conduct the study according to the approved study protocol and SA GCP. Failure to comply with the approved protocol and SA GCP will void the insurance cover.

6.4. Report study progress regularly as required by HREC and SAHPRA (if applicable).

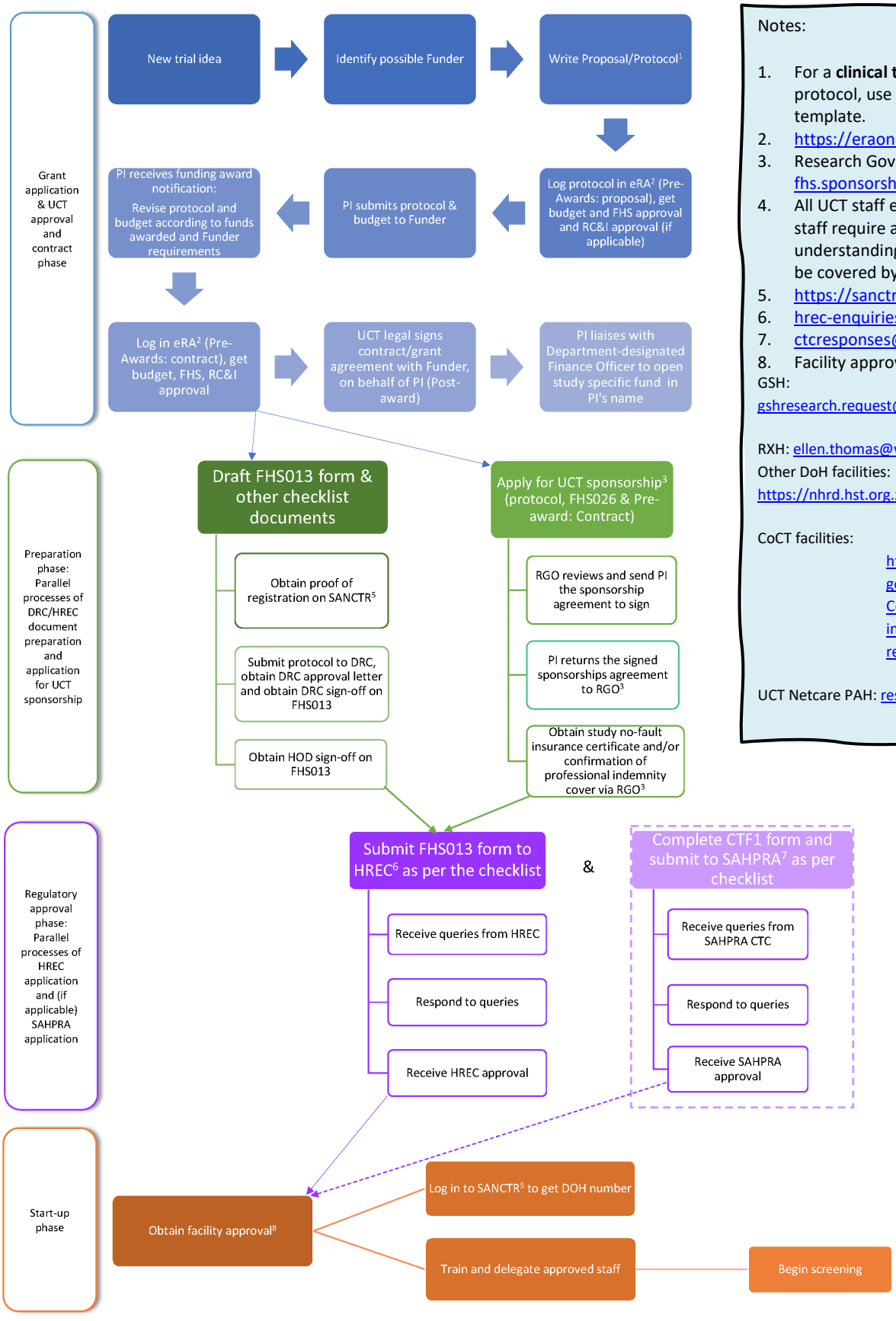
6.5. Report Serious Adverse Events (SAEs) and major protocol deviations to HREC and SAHPRA (if applicable).

6.6. Relay auditing and study monitoring reports to HREC and SAHPRA (if applicable).

6.7. Submit updated versions of the protocol to HREC and SAHPRA (if applicable) for approval before implementing changes.

6.8. Maintain an updated Investigator Site File (ISF).

Figure 5 Process flow for new investigator-led clinical trial



Notes:

1. For a **clinical trial** proposal or protocol, use the HREC FHS015 template.
2. https://eraonline.uct.ac.za
3. Research Governance Officer: fhs.sponsorship@uct.ac.za
4. All UCT staff eligible; non-UCT staff require a memorandum of understanding (MOU) in order to be covered by UCT as well.
5. https://sanctr.samrc.ac.za
6. hrec-enquiries@uct.ac.za
7. ctcresponses@sahpra.org.za
8. Facility approvals:

GSH: gshresearch.request@westerncape.gov.za

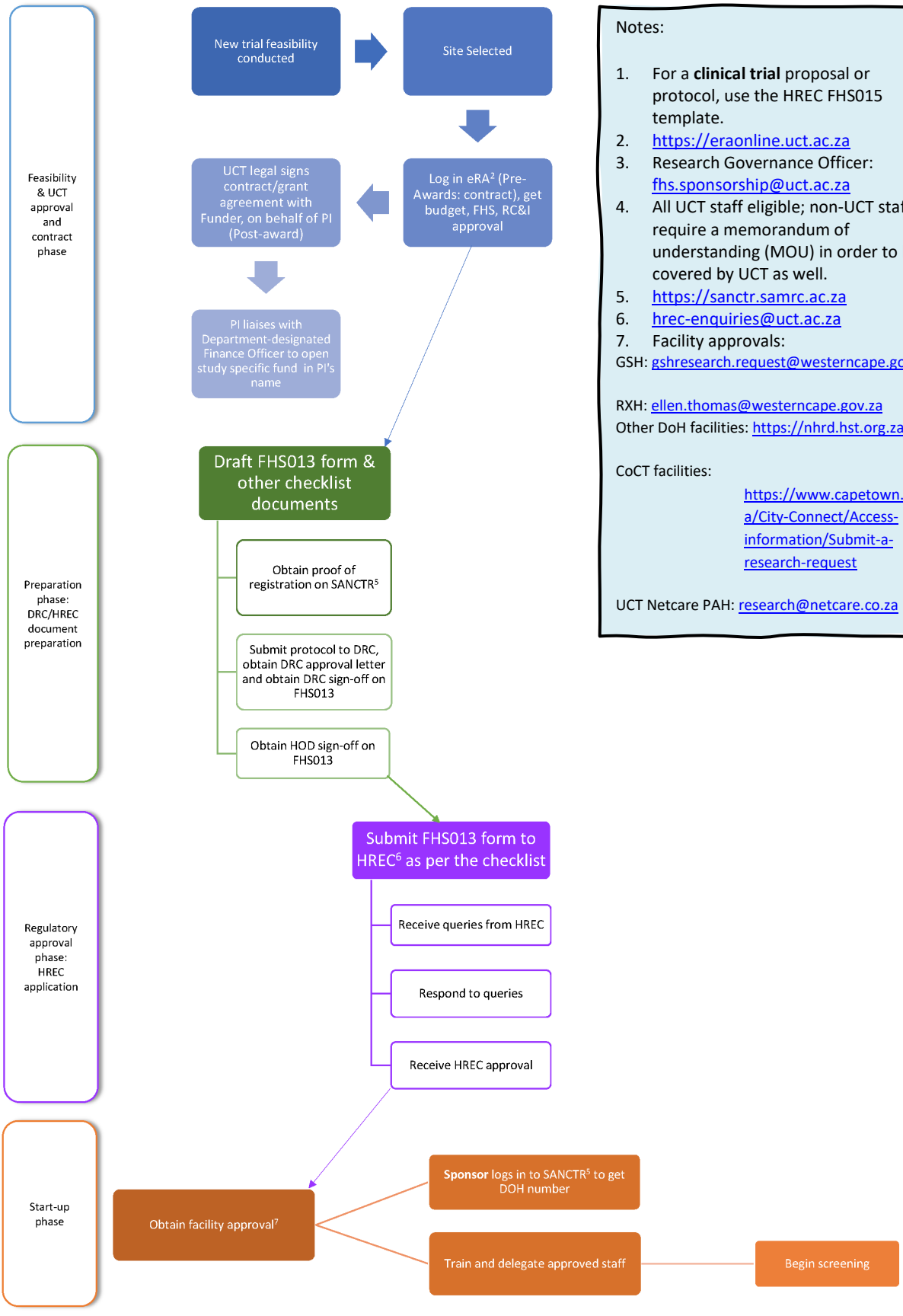
RXH: ellen.thomas@westerncape.gov.za

Other DoH facilities: https://nhrd.hst.org.za/

CoCT facilities: https://www.capetown.gov.za/City-Connect/Access-information/Submit-a-research-request

UCT Netcare PAH: research@netcare.co.za

Figure 6 Process flow for new industry-led clinical trial



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CoCT facilities:
https://www.capetown.gov.za/City-Connect/Access-information/Submit-a-research-request

UCT Netcare PAH: research@netcare.co.za

7. Frequently Asked Questions and answers relating to sponsorship of publicly funded studies

7.1. *Can there be more than one sponsor for a trial?*

- Where two or more organisations share a significant interest in a study, for example, one as employer of the chief investigator and another as the principal host institution, they may elect to act as co-sponsors or joint sponsors. Co-sponsors divide amongst themselves both the responsibilities and the liabilities associated with sponsorship per GCP. Joint sponsors are partner organisations who accept joint liability for all the sponsor's responsibilities. They are jointly and severally responsible for all the duties of the sponsor, such that all are responsible in the event of a failure of any one of the partner organisations to discharge their responsibilities. The clinical trial agreement (CTA)/Grant must clearly define the set of sponsorship responsibilities taken on by each party.
- N.B. Most institutions that sponsor drug trials have chosen to adopt sole sponsorship or co-sponsorship arrangements as they offer the greatest degree of clarity and transparency in the allocation of roles and responsibilities.

7.2. What are the risks attached to an organisation taking on the role of sponsor?

A sponsor organisation is exposed to potential risks in several areas:

- Financial – e.g., claims for damages from individuals who participated in clinical trials.
- Legal – e.g., prosecution by SAHPRA or other regulatory authority for a breach of Clinical Trials Regulations, such as failure to comply with the conditions of ethical approval or contravention of pharmacovigilance requirements.
- Reputation – e.g., adverse publicity arising from failure of the study, failure to meet required standards of GCP identified at SAHPRA inspection, or from prosecution as outlined above.

7.3. How can a sponsor mitigate risk?

The following principles underpin successful risk mitigation:

- Risk assessment prior to commencement of trial and careful consideration when deciding to undertake high-risk activities (the sponsor must be confident that the appropriate systems, capacity, and expertise are in place and any risks are mitigated and are substantially outweighed by the benefits).
- Ensuring oversight of any delegated functions.
- Ensuring the competence of the chief/principal investigator (and the research team) and host organisation(s) to oversee, manage and conduct the study.

- Implementing appropriate training in research methods and GCP for members of the research team and for multi-site studies, ensuring site staff have the necessary training and resources to successfully conduct the study.
- Undertaking monitoring and audit of studies to detect and rectify poor compliance.

7.4. What are the implications for indemnity with respect to sponsorship?

- A sponsor is responsible for ensuring that provision has been made for the insurance and indemnity to cover the liability of the investigator and sponsor which may arise in relation to the study.
- For each study, the sponsors should check that the insurance policies that are used to provide cover contain no exclusions that could impact on the cover for research participants or the investigators.

8. References

1. Department of Health , 2020 . *South African Good Clinical Practice.Clinical Trial Guidelines*.

Acknowledgments

The editorial team relied on their experience and knowledge, on expert advice sought through consultation with industry, research ethics office and various other interested parties as well as accepted standards and guidelines.

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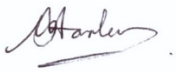
pp 

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