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HEALTH RESEARCH ETHICS COMMITTEE

STANDARD OPERATING PROCEDURE FOR THE NECESSITY OF INFORMATION LEAFLET AND INFORMED CONSENT

1. DOCUMENT HISTORY

Date	Version No	Reason for revision
11 July 2018	1	Newly formulated
31 January 2022	2	Updated

2. ABBREVIATIONS AND/OR DEFINITIONS

Abbreviation/Definition	Description
IC	Informed Consent
Informed consent	The process of making a free and informed decision (such as participating in the research). Individuals who provide informed consent must be legally competent and have enough decision-making capacity to consent to research.
Minimal risk	A risk that is not greater than routine medical or psychological tests or examinations or a risk ordinarily encountered in daily life activities.
Informed consent waiver	In human participant research, the decision by HREC (or set aside) some all of the informed consent requirements. Usually, waivers are not granted unless necessary to conduct the research and pose minimal risks to participants.
Informed consent, blanket(general)	A provision in an informed consent document that gives general permission to researchers to use participants' data or samples for various purposes and share them with other researchers.
Informed consent, documentation	A record (such as a form) is used to document the process of consent. Research regulations require the consent to be documented, however, a departmental research ethics committee may decide to waive documentation of consent if research carries

Informed consent, specific	A provision in an informed consent document requires researchers to obtain specific permission from the participant prior to using samples or data for purposes other than those that are part of the study or sharing them with other researchers.
Informed consent, tiered	Provisions in an informed consent document that give the participant various options concerning the use and sharing of samples or data. Options may include blanket consent, specific consent, and other choices.

3. POLICY

The ethical principle of respect for persons entails that participants are provided with the opportunity to choose what may or may not happen to them. In research parlance, informed consent is the primary mechanism for securing a participant's consent and involves a process between the researcher and the potential participant. For the informed consent process to be valid, participants must receive sufficient and relevant information about, the research, and voluntarily choose to participate. The informed consent process for adults (persons over 18 years) allows them to make independent decisions. Consent for participants with diminished or no decision-making capacity (factually incapacitated) for minors (legally incapacitated) is described in a separate standard operating procedure: Research Involving Adults with Decisional Impairment and Children in Research.

Consent documentation must be written in layperson's language. The consent process is ongoing throughout a study, and consent documentation should be revised when new information becomes available.

4. PURPOSE OF THIS POLICY

To provide ethical and regulatory guidance on the informed consent process and the format and content of informed consent documents.

5. SCOPE

This document covers the process to be followed in providing the necessary information and engaging with the person before a decision is reached, known as the informed consent process. Informed consent is a necessary and important element of ethical research. The fact that a person chooses to participate voluntarily does not mean that the research process is ethical. All other elements should also stand up to ethical scrutiny. An important element of making an informed choice is the nature and quality of information available to the potential participant.

6. PROCESS AND DOCUMENTATION

6.1 Informed consent as an ongoing conversation

Informed consent is not simply a signature on a form but a process of interactive communication between the researcher and the potential participant. Depending on the nature and duration of the research, ongoing discussion with and education of participants may continue long after the signed consent document. Questions may arise well into the research experience; for example, a discussion of confidentiality may not be meaningful until participants are asked sensitive

questions. They must feel free to raise further concerns.

Informed consent involves educating potential participants, not merely disclosing information. Researchers need to distinguish comprehension (understanding the factual components of the information) from appreciation (what the information means for individual participants). Written informed consent document emphasizes factual information, and interactive communication is able to focus on what the factual information means for a particular participant; for instance, how an individual participant interprets 'risk' or 'benefit' is likely to depend on that participant's specific circumstances. Informed consent should indicate effective communication with adequate opportunity to ask questions, achieve clarity and understanding, and make reasoned decisions. Apart from the written consent form, other creative methods of conveying information to the participants include:

- Videotapes, photographs or diagrams of research procedures.
- Pre-visits to the research site to see equipment, such as MRIs.
- Group discussions.
- Web sites.
- Comics that explain the nature of the research.
- Distribution of participant-oriented material about clinical and other research, for example, cancer trial pamphlets, brochures and guidance on participants' rights in research.

7. SETTING

- Conduct the discussion in a private and quiet place, although this will be a challenge in busy outpatient clinics and community health centers.
- Researchers may need to delay the consent process if potential participants' privacy and confidentiality cannot be protected.
- Be prepared to accommodate potential participants with disabilities. For example, visually-impaired people may benefit from the large font and high-contrast documentation. Hearing-impaired people may need sign language interpreters.

8. WHO SHOULD OBTAIN CONSENT?

The principal investigator ensures that participants understand what it means to engage in a study. The principal investigator can delegate this task to suitably qualified team members. The protocol must list the names, positions, and experiences of those who will obtain informed consent.

The decision will depend on the following:

- The technical details of the protocol and who can best explain them.
- Who is most capable of answering participants' questions? This function could be shared between the principal investigator and another staff member such as a research nurse, social worker or counsellor.
- Multilingualism – is a well-trained interpreter needed to facilitate the consent process?
- Minimizing the possibility of undue influence and ensuring the person obtaining the consent is appropriately trained, independent, and bias-free. For instance, if the investigator is also the treating doctor, is the participant able to distinguish the different roles, and will

the participant not feel he or she must agree to take part in order to 'please' the doctor and guarantee continued treatment?
Other settings where authority figures may influence a potential participant's voluntary decision include prisons, schools, or work environments.

9. WRITTEN CONSENT WAIVER

In line with the National Health Act of 2003[1], the UFH HREC has limited latitude to waive the legal requirement for written (signed) informed consent in prospective research with human participants, including research with no/or minimal risk. However, in some circumstances, for example, where a signed consent form is the only link between the participant and the research and the main risk is potential harm to privacy, the investigator may request and justify a waiver of written consent. The Committee will consider such requests on a case-by-case basis.

10. SIGNATURES ON CONSENT FORMS, INCLUDING WITNESSES

- The signature of the participant or legally authorized representative on the informed consent form indicates that the study has been explained to the person, and he/she agrees to participate.
- The signature of a witness is not required if the participant can read and understand the consent document.
- The signature and the date of the witness of the participant who is unable to read and write, indicates that another, preferably impartial, a person has observed the consenting of the participant and attests to the accuracy and apparent understanding of the participant.

11. TRANSLATION OF INFORMED CONSENT DOCUMENTS

The informed consent document must be in a language the participant understands. When a study intends to enroll participants, who are unlikely to understand English or who might prefer to be interviewed in their home language, the UFH HREC expects the informed consent document to be translated into participants' first language.

The English version of the informed consent documents and any other written/audio/video materials should be submitted and approved by the UFH HREC before translation. Unless required by funders or sponsors, the Committee does not expect researchers to use certified translation services to translate informed consent documents. However, if not formally certified, translators should have extensive experience in research and medical terminology. In addition, a second person should back translate the consent document into English to verify accuracy and ensure all information from the English version is included.

The Committee will approve only the English version and acknowledge receipt of other language versions and certificates of translation.

Other points to consider include:

- To protect the privacy and prevent pressure or bias, the Committee prefers interpreters not to be related to potential participants.

- If the research team obtaining informed consent is not fluent in the participant's home language, an interpreter fluent in English and the participant's language should be available to address the participant's questions and assess their comprehension.
- How transparent and authentic will the interpreted conversation be? With three people communicating (participant, researcher and interpreter), will everything said by each person be translated?
- How will the interpreter incorporate cultural considerations into the consent information?
- Informed consent is an ongoing process. Will an interpreter be present at future meetings to ensure participants understand ongoing study-related communication and address ongoing questions?

12. ALLOW ENOUGH TIME FOR DECISION-MAKING

Discussions with potential participants should take place with enough time to think carefully about participation. Participants may want to take the consent document home to discuss participation with their family, friends, religious advisors, or community elders. According to national research ethics guidelines: 'No person should be *required* to make an immediate decision.'[4]

13. ENSURING READABILITY

The consent document should be written in non-technical terms at a level that potential participants will understand, taking into consideration that:

- Written in no higher than a 6th to 8th-grade reading level.
- Check the Flesch-Kincaid Reading Level using Microsoft Word. Many formulas are available for determining rough estimates of reading levels, but they must be interpreted with caution, and researchers are urged to keep in mind their shortcomings which are well-described in freely downloadable literature.
- Use simple and short sentences.
- Avoid technical language, medical jargon, and acronyms.
- Use common, everyday words instead of jargon, for example, 'medical check-up' instead of 'clinical examination'.
- Be careful of common words used in uncommon ways; for example, health workers may refer to 'positive' test results which may not be good news in the customary sense of the word, whereas 'negative' results may be good news.
- Be careful of homonyms which are words with different meanings that sound alike. The words may or may not be spelt in the same way. For instance, participants may misinterpret homonyms such as 'stool', 'gait', 'dressing', 'tissue', and 'shots' (injections). During the consent process, make clarify what words mean in the research context.
- Avoid large blocks of printed text. Break the text into short sections.
- Use reader-friendly headings to format consent documents:
    - Why is this study being done?
    - Why are you being asked to take part?
    - How many people will take part in the study?
    - How long will the study last?
    - What do we do to decide if you are eligible to take part?

    - What will happen if you decide to take part in the study?
    - What are the risks and discomforts of this study?
    - Are there any benefits to you for being in the study?
    - What other choices do you have?
    - What will happen when the study is over?
    - Will your test results be shared with you?
    - Will the results of the research be shared with you?
    - Will any of your blood, tissue or other samples be stored and used for research in the future?
    - Will you receive any reward (money or food vouchers) for participating in this study?
    - Who will see the information which is collected about you during the study?
    - Whom do I speak to (or contact) if I have any questions about the study?
- Use the second person (you), not the third person (the participant), to enhance personal identification.
- Use active rather than passive verbs, for example, 'We will need to collect a blood sample from your child rather than 'A blood sample will be needed from your child'; 'We will ask you questions about your health rather than 'You will be asked questions about your health.
- Give fluid volumes in equivalent teaspoons or tablespoons rather than in mls.
- Avoid words that do not add value to your text, such as 'very', 'actually, and 'really'.
- Break up dense chunks of content. Convert long lists embedded in sentences into bulleted lists with one point per line (for example, eligibility criteria for enrolment). Use numbered lists if the order of items is important.
- A useful rule of thumb is to tailor the amount of information in the consent form to the level of risk involved in a study.

14. INFORMED CONSENT FORM SUMMARY

Consider including a simple written one-page summary titled 'This is a summary only'. Participants can refer to the main consent document for complete, more –detailed information. The summary must include, in lay language (i.e. understandable to the people being asked to participate) the following elements:

- What is the rationale or justification of the research?
- Why are you being invited to take part?
- How long will you take part in this research – how much of your time will be needed – will you need to take time off work?
- What procedures, drugs, or other treatments are involved in this research?
- What are the risks and discomforts of taking part in this research?
- Are there any benefits to you if you take part in this research?
- What other choices do you have?
- What happens if you do not want to take part in this research?
- What happens at the end of this research?

15. ANSWERING PARTICIPANTS' QUESTIONS

Before reaching a decision, participants must have an opportunity to ask questions about the

research (See also Assessing Understanding).

Some questions participants should consider before taking part in research are:

- Who is doing this study
- What is the study about?
- Will this research help in understanding my condition? If so, how?
- What could happen to me, good or bad, if I take part?
- What will I be asked to do?
- What tests or procedures will be done during the study?
- How will my treatment be decided?
- Is it possible I'll receive a placebo?
- Could my condition get worse during the research?
- What will happen if it does?
- Could I stay on my ordinary treatment?
- What other choices do I have if I decide not to be in this study?
- What happens if I say no?
- If I'm hurt or get sick during the research, who will pay the costs that may result?
- If this is a new medicine, will I be insured if things go wrong?
- Who will pay for extra costs related to the research?
- Will I be charged anything or be paid for being in the study?
- If I decide to take part in the research, how will it affect my daily life?
- Will I have to visit the hospital/clinic more often? If so, how much more often?
- Who will be in charge of my care? Will I still be able to see my own doctor?
- How long will the study last?
- What will happen if I change my mind and want to leave the study?
- What must I do if I want to stop being in this study?
- Will I be told the results of the study?
- What will happen to my personal information?
- Who will see my study results and medical records?
- If I have any questions, who should I call?
- Who reviewed or approved this study?
- What is a Research Ethics Committee?

The inclusion of this or a similar list of questions at the end of the informed consent document might encourage participants to raise issues they do not fully understand or are hesitant to ask.

16. ASSESSING UNDERSTANDING

Teach-Back is a way to confirm that you have explained what a potential participant needs to know. It is not a test of the participant but rather how well you explained a concept.

Investigators should ask questions throughout the consent process to sure potential participants understand what they are consenting to. For example:

- 'It's my job to explain things clearly. I'd like to hear what you understand about this research to make sure I did this properly.
- Please tell me about this study in your own words?'

- Make sure potential participants have understood all the important elements of the study:
- Purpose of the Study
    - Could you explain to me what we will ask you to do in this study? This will help me understand the research instead of do you understand the research and what will happen?
    - Why are we doing this study – tell me in your own words?
    - How would you explain this research to your husband/wife/friend?
    - Tell me in your own words what will happen to you if you agree to be in this study?
    - What is required of participants?
    - What are you expected to do if you decide to be in this study?
    - How long will this research last?
- Risks
    - Can you tell me the possible good and bad things which may happen to you if you take the experimental drug?
    - What worries you most about choosing to be in this study?
    - What is the worst thing that could happen to you if you participate in this research?
    - Tell me about some of the side effects we talked about.
    - What are some of the side effects that you need to watch and report to your doctor/ the investigator/ the research nurse?
- Benefits
    - What chance do you think your condition will get better if you take part in this research?
    - What do you expect to gain by being in the study?
- Voluntariness
    - Will anything happen to you if you refuse to be in the study?
- Stopping Participation
    - What happens if you say you don't want to participate in the study?
    - What should you do if you agree to be in this research but later change your mind?
    - What options do you have if you choose not to be in this research?
- Privacy
    - Who will be able to see the information you give us?
- No-Fault Insurance
    - What happens if you get sick or hurt during this study?
- Compensation
    - What about the costs of being in this research?
    - Will you be paid to take part in the study?
- Contact Information
    - Who should you contact if you have a problem or a question about the research /your rights/ or a complaint?
    - When participants' answers are unclear, the researcher should ask follow-up questions to determine if participants' understanding is correct. The idea is not to quiz potential participants but to foster an open exchange of information and encourage them to ask questions, including some they might not have thought of. Tell participants that the need to ask these questions is due to the complexity of the

content rather than the 'fault' of potential participants. Ask potential participants if they have any further questions.

- The best questions are non-directive and open-ended. Avoid questions that require a 'yes' or 'no' answer:
- 'What more do you want to know?' instead of 'Do you have any questions?'
- 'What else would you like to know?'

Remember that participants may say they don't have any questions simply because they don't know what to ask.

17.'WRITTEN TESTS'

Researchers may also 'test' participants' understanding using a written test, especially when technically complex studies involve difficult scientific concepts. Written tests usually include multiple-choice or true/false questions or questions that can be answered in one or two words. Although written tests provide a permanent record of participants' understanding, they are less flexible than oral questioning.

Researchers must also ensure that participants receive the correct answers, with verbal explanations if necessary, after completing a written test. Unwittingly, tests and quizzes tend to put the responsibility for understanding on the participants. What distinguishes teach-back from a test or quiz is that it puts the onus on us, the investigator or study coordinator, and not the participant. If the participant cannot teach back the information correctly, then it is because we did not do a good enough job of explaining it.

18. PARTICIPANTS HIGHLY DEPENDENT ON MEDICAL CARE

Participants who are highly dependent on medical care deserve special attention when considering research participation. The gravity of their medical condition may require invasive measures that carry an increased risk of harm. The quality of informed consent may be compromised by the effect the medical condition has on the participant's decision-making or communication abilities. A participant may be reluctant to refuse consent, fearing this may compromise medical treatment. Characteristic features of intensive care research include difficulties in communicating with participants receiving ventilation assistance and impairment of cognition in heavily sedated individuals. For planned intensive care research, if possible, researchers should obtain informed consent from potential participants before admission to that care.

19. DELAYED CONSENT

There are circumstances where the UFH HREC may approve delayed consent. The UFH HREC should ensure that the researcher provides a clear and full justification for the proposed delay. The UFH HREC may approve a delay in obtaining informed consent for research participation of participants highly dependent on medical care if:

- The research is based on valid scientific hypotheses that support a reasonable possibility of more benefit than that offered by standard care.
- Participation is not contrary to the medical interests of participants.

- Care is taken not to violate participants' personal or cultural values.
- The research interventions pose no more risk of harm than that inherent in the participant's condition or alternative methods of treatment.
- The participant and his/her relatives or legal representatives will be informed of the participant's inclusion in the research as soon as reasonably possible and advised of his/her right to withdraw from the research without any reduction in quality of care.

Note: This does not mean that informed consent is waived.

20. CONTEXT-SPECIFIC, REQUIRED INFORMATION IN INFORMED CONSENT FORMS

Contact details for the UFH Health Research Ethics Committee

Informed consent forms must include the following statement (required wording):

'The UFH Health Research Ethics Committee can be contacted on 043 704 7585 in case you have any ethical concerns or questions about your rights or welfare as a participant on this research study.'

21. CARE AFTER RESEARCH (ALSO KNOWN AS POST-TRIAL ACCESS)

The Declaration of Helsinki[9] ensures that researchers have an ethical responsibility to research participants and provides the following interpretation of post-trial provisions:

> *"In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process."* (Paragraph 34, Declaration of Helsinki 2013).

This interpretation of post-trial provisions emphasizes the importance of post-trial access to proven interventions and access to other care or benefits. Investigators should aim to secure the provision of care after the research package including the investigational product where appropriate, before the trial initiation. The lack of such arrangements should be justified to the UFH HREC. The proposed care after research package must be described in the informed consent document.

If a sponsor does not intend to provide post-trial access, the informed consent document must explain the following in **large, bolded text**:

- Even if a participant's condition improves on the study drug, the sponsor will not provide it after the end of the study.
- .
- How participants will be managed at the end of a clinical trial; for example, will they resume their previous treatment regimen?

22. INSURANCE COVER IN INTERVENTIONAL STUDIES

In interventional clinical research and trials, the consent form must include a simply-worded statement that the sponsor's insurer will pay for reasonable medical expenses imposed by research-related injuries according to the Department of Health's Good Clinical Practice Guidelines6. In the case of interventional research that is not sponsored by a commercial entity, the University has no-fault insurance cover.

23. EXCULPATORY LANGUAGE

Written and oral informed consent must not include any exculpatory language which implies that a participant will waive their legal rights or releases or appears to release the investigator, the sponsor or the institution from liability or negligence. 'The Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA) consider exculpatory language to be a language which has the general effect of freeing or appearing to free an individual or an entity from malpractice or negligence, or blame, fault or guilt. Therefore, a waiver in an informed consent document of any legal right a subject may be permissible so long as that waiver does not have the general effect of freeing or appearing to free an individual or entity from responsibility for malpractice or negligence, blame, fault, or guilt.

Exculpatory statements are statements in which a participant is asked to agree to or accept something, usually unfavourable to the participant. However, a statement that provides simple facts is unlikely to be viewed as exculpatory. Please consider these two examples:

23.1. Permissible

'The investigators will remove some cells from the blood you donated as part of the research. The University may commercialise some of these cells. The university will not share any profits with you. Tissue donated by you in this study may be used to establish a cell line that could later be patented. There are no plans to provide financial compensation to you should this happen'.

23.2. Exculpatory

'I understand that the institution will not share any profits received from the sale or commercialisation of any cells developed in this study. By consenting to participate, I authorise the use of my bodily fluids and tissue samples for the research described above."

'I understand that I will not sue the sponsor or investigator for any negligence'.
In short, simply state the factual situation and avoid any statement which requires prospective participants' agreement.

24. MANDATORY REPORTING AND DISEASE NOTIFICATION

If an investigator is planning a study that is designed or likely to produce information that may generate mandatory reporting obligations (such as physical abuse of a child or elder), the permission/assent/consent form(s) must disclose mandatory reporting requirements and how finding such information will be handled. If the investigator is planning a study that requires home visits, the permission/assent form(s) must disclose the obligations of the investigator if such information is discovered unexpectedly (i.e., not anticipated given the study design or subject population) and how the discovery of such information will be handled.

Consent form: The researcher(s) may not be able to maintain confidential information about known or reasonably suspected incidents of abuse or neglect of a child, dependent adult or elder, including, but not limited to, physical, sexual, emotional, and financial abuse or neglect. If the researcher is given such information, he or she may report it to the authorities.

Likewise, where indicated, researchers must inform participants about mandatory reporting of

notifiable conditions (e.g. tuberculosis) (http://www.sastm.org.za/Home/DiseaseNotification).

25. FOCUS GROUPS AND PARTICIPANT OBSERVATION

In the context of focus groups, the informed consent document must include a statement indicating that the researcher cannot guarantee that participants' confidentiality will be maintained as other participants in the group may disclose what was discussed with persons outside the group. The researcher can request that focus group members respect each other's confidentiality by not speaking to others about matters raised in the group.

In the context of participant observation, the researcher should:

- Ensure that participants are aware of the researcher's identity and purpose in the group.
- Disclose and disseminate the researcher's purpose, research topic, and data-gathering methods as broadly as possible through general announcements or other informal means. Participants should be aware that any of their interactions with the researcher may constitute some form of data gathering.
- Obtain permission from group leaders or spokespersons, where appropriate, but especially if they can help communicate the researcher's identity, purpose, and methods to a community. At the same time, researchers must be careful to avoid situations where such public endorsements or announcements to the community create pressure to participate. Participants must remain free to avoid all interaction with the researcher
- To the extent possible, the researcher must obtain informed consent from each participant with whom the researcher interacts.

26. RECOMMENDED WORDING FOR CONSENT FORMS IN CLINICAL TRIALS

There are sections of consent forms for clinical trials which are often too legalistic or include excessive medical terminology. To address this problem, the UFH HREC has formulated sample text for clinical trials, specifically, for sections on Study Procedures, Possible Side-Effects of the Study Medicines and Confidentiality (Similar recommendations for Sample Storage and Future Use, and Insurance Clauses are provided in the relevant SOPs). In this regard, researchers are referred to national guiding documents for clinical trials.[1]

26 .1 Study procedures/schedule

Many consent forms for clinical trials describe the study procedures in detail over numerous pages, and procedures repeated in the study during different visits are described repetitively. The UFH HREC proposes that such detailed descriptions, if necessary, be provided in an appendix to the main consent form.

The main consent form procedures can be summarised, for example:

"If you agree to participate in this study, you will then have certain tests and procedures. These include:

[1] Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa - http://www.kznhealth.gov.za/research/guideline2.pdf

[1] Registration of Clinical Trials Undertaken in South Africa - http://www.sanctr.gov.za/

[1] Medical Research Council: Guidelines on Ethics for Medical Research - http://www.samrc.ac.za/sites/default/files/attachments/2018-06-27/ResponsibleConductResearchGuidelines.pdf

- Recording your personal information, including, for example, your name, age, gender, ethnicity;
- Physical examination including your height, weight, blood pressure and heart rate;
- **Blood tests**. Blood will be taken from a vein in your arm to test your general health and medical condition/disease. We will take XXX ml from your arm XXX times in the course of this study. This is the same as XXX table/teaspoons. The most we will ever take at once is XXX ml (XXX table/teaspoons);
- **CT Scan**. This means that a picture is taken of your internal organs. You will need to lie on a bed, and the bed will be moved into the scanning machine. The procedure is painless but you could feel a bit anxious about being inside the machine;
- **Questionnaires**: you will be asked to answer questions about how you have been feeling, about how your condition/disease has affected your daily activities, your diet and any worries that you have had about your health.
- The following details should be given on each of these procedures and when they will happen in the section called 'Study Procedures' (Appendix 1). In this section, you will be provided with an information leaflet on what purpose of the study and what is expected of you in the study. For example, information will be provided on:
    - How often do you have to come and see the doctor/study nurse;
    - How long each visit will take;
    - Which tests and procedures will be performed at each visit;
    - What samples are being collected, and how they will be used?

26.2 Possible side-effects of the study medicines

The participants should be told in clear, plain language that:

> *"All medicines can cause unwanted effects. We call these 'side-effects' of the medicine. Because this is research, we do not yet know all the side effects of the medicine that we will ask you to take. Part of the reason for doing this study is to find out if it is safe. It is possible that some of the side effects of the medicine in this study will be harmful to your health – now or in the future. There is also a small chance that you may experience a serious or permanent side effect from the study medicines. This is why it is important that you tell your study doctor or nurse about any side effects. Please tell them all your symptoms, even when you do not think they are related to the medicine you are taking for this study. We are careful to monitor your health during this study because we do not yet know all the side effects of the medicines you are taking. This is why we take so many blood samples. For this reason, it is also very important that you come to all the study visits."*

The most common side effects that we know about so far are:

- Provide a short list of the drug's known side effects in plain language. Examples are 'headache', 'diarrhoea', 'skin rash ', 'vomiting, and general body weaknesses. Please do not use any medical terms for symptoms.
- Also, indicate the relative severity of these side effects and the known incidence, e.g., these types of side effects occur in one in 5 people (There is considerable variation about what constitutes 'common' side effects vs rarer side effects. 'Common' varies between 5% and 20%, 'rare' side effects can occur in 1%-5% of people who take the drug).

- The most severe side effects that we know so far about are:
  Give severe side effects even if they are uncommon. Examples are severe blistering, organ failure, bone marrow suppression, and death. Again, please use a common language to describe these effects.
- Also, indicate the known incidence, including whether serious side effects are rare or common for the drug or drug class.
- A detailed description of all the possible side effects of the medicines in this study is given in Appendix 2 of this form."

26.3 Confidentiality

Confidentiality of information is important and should be highly respected. This should be clearly spelled out in the study.

> *"The sponsor will use the information collected about you for the purposes of this study and for scientific research such as the study of your disease. The sponsor may also use this information to apply for permission to sell the drug in some countries. The information will be stored both on paper and on a computer. However, to protect your privacy, the information will be labelled in a way that will not identify you. The study doctor will give a code to you, and your information and samples will be known only by that code. If the results of this study are published, your identity is kept confidential. The information collected may be sent to other sponsor companies' members, contractors working for them, and regulatory authorities. By signing this form, you are allowing the use of the study information. Your study doctor will keep your medical records and a list that links each participant's name to their code number for at least XXX years in a secure place. Regulatory authorities, members of the research ethics committee, employees at the study site, and the sponsor will have access to this list. These persons can compare and check the study information collected about you with information on your medical records. They will do this to check that the study has been done properly. Your medical records will not be made public as far as the law allows. You can arrange with your study doctor to see the information collected about you, and you can ask for any mistakes to be corrected.*
>
> *The sponsor may delay your access to this information if the study is not yet complete. If you decide to leave the study at any time, the sponsor may still use your information collected up to that point.*
>
> *You will find information about this trial at (give web address), e.g., www.clinicaltrials.gov. This website will not include any information that can identify you."*

27. REGULATORY FRAMEWORKS FOR INFORMED CONSENT

South African Department of Health (DoH)[1]

Adults, i.e. persons over 18 years, may make independent decisions about research participation. The DoH requires the HREC to assess the adequacy and readability of the following elements of information in consent documentation:

- Seek consent of the participants to participate in research.
- Voluntary participation.
- That refusal to participate will not be penalised.

- That choosing to participate can be reversed, i.e. the person may decide to terminate participation at any time without explanation or prejudice.
- The purpose and nature of the research procedures and components are explained to the participants.
- The participant is being asked to consent to the research-related activities and procedures.
- The expected duration of participation.
- The nature of the participant's responsibilities.
- The nature of the researcher's responsibilities.
- The anticipated risks of harm or discomfort.
- The measures to minimise the risk of harm.
- The extent to which confidentiality is possible.
- Whether reimbursement for expenses is available. Additionally, the informed consent document should indicate whether reimbursements are pro-rata if the participant does not complete the study; i.e. whether only some of the offered reimbursement is available if participation is stopped before the anticipated end of the study.
- That sponsors of the research and regulatory authorities may inspect research records.
- Who the researchers are and the nature of their expertise.
- The potential benefits, if any, for participants both during and after the research.
- That the research may be terminated early in particular circumstances.
- That the research has been approved by a registered REC (include identifying details).

The DoH guidelines also require researchers to assess potential participants' level of understanding of the information, particularly when 'very vulnerable' participants will be recruited.

South African Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants 2006 (SA GCP Guidelines)

NOTE: SA GCP Guidelines state that the informed consent procedure must be 'tailored to local conditions. This implies that, at a minimum, the documentation must be appropriately translated and adapted to meet the levels of comprehension and language needs of local participants. Therefore, it is incumbent on the Human Research Ethics Committee to ensure that investigators comply with these standards in clinical trials.

SA GCP Guidelines require the following information/explanations in consent documents to be used in clinical trials:

- That the trial involves research.
- The purpose of the trial.
- The trial treatment(s) and the probability for random assignment to each treatment, where appropriate.
- The trial procedures to be followed, including all invasive procedures.
- The participant's responsibilities.
- Participation in the trial is voluntary and refusal to participate or withdraw from the trial will not prejudice the ongoing care of the person in any way.
- Those aspects of the trial that are not experimental.
- The foreseeable risks of harm or inconveniences to the participant and, when applicable, to an embryo, foetus, or nursing infant.

- The expected benefits. When there is no clinical benefit to the participant, the participant must be made aware of this.
- The alternative procedure(s) or course(s) of treatment that may be available to the participant and their potential benefits and risks.
- The compensation and/or treatment available to the participant in the event of trial-related injury.
- The anticipated payment, if any, to the participant in the trial.
- The anticipated expenses, if any, to the participant for taking part in the trial.
- Allow access of sponsor, SAHPRA, National Health Research Ethics Council, relevant research ethics committees and/or other regulatory authority to participant records.
- Provide a contact name and number for the principal investigator and directly responsible investigator.
- The identity of the sponsor and any potential conflict of interests.
- The requirement to preserve the participant's confidentiality.
- Expected duration of subject's participation.
- Foreseeable circumstances and/or other reasons under which the subject's participation in the trial may be terminated.
- Approximate number of subjects in the trial.
- Once consent is obtained, the investigator must:
- Place a copy of the signed consent form and a source document identifying the study and recording the dates of participation in the participant's medical record.
- Keep the original signed consent form with the trial records.
- Offer a copy of the signed consent form to the participant (Researchers should remind participants that the consent form includes important contact details, especially phone numbers if they have questions or concerns during the study).

28. REFERENCE DOCUMENTS

The UFH HREC adopts as its guiding reference documents the following:

- The National Health Act, No 61 of 2003.
- Regulations Relating to Research with Human Participants, 11 July 2018.
- Ethics in Health Research: Principles, Processes and Structures (Department of Health, 2015)
- The Rules for the Management of Research Ethics at the University of Fort Hare, 2011
- University of South Africa, SOP for SOPs
- North -West University, SOP for SOPs

29. ADDENDA

No	Document name
1	Informed consent checklist
2	Study Procedures