Faculty of Health Sciences **Research Ethics Committee**

Standard Operating Procedure: Research involving minors and vulnerable persons.

1. Purpose

The purpose of the SOP is to define the circumstances and the conditions that need to be applied for research involving vulnerable research participants. This SOP was approved by resolution of the Faculty of Health Sciences Research Ethics Committee on 27 September 2023 and replaces all previous SOPs in this regard. It should be reviewed within 3 years after this date of approval.

_____Date: 27 September 2023

Signed by the Chairperson

2. Scope

The SOP is intended to inform and guide all researchers, members of the Research Ethics Committee, the Executive Management Committee, the Preliminary Subcommittee of the REC, and the REC in its deliberations. It should be interpreted alongside the Ethics Guidelines of the Department of Health (2015), guidelines 3.21 – 3.2.9. This SOP should also be interpreted with reference to the Terms of Reference of the REC and other SOPs that may be relevant.

3. Definitions and criteria (See DOH Guidelines, 2015)

a. "Vulnerable persons" means those persons at increased risk of research-related harm, or who are limited in their freedom to make choices, or relatively incapable of protecting their own interests. (Regulations related to Research with Human Participants)
b. A vulnerable research participant is someone who, because of some characteristic or prevailing set of circumstances, is at risk of being exploited or harmed in the course of biomedical research.
c. Vulnerable groups and individuals are defined by the Declaration of Helsinki as those who are vulnerable because of a reduced ability to provide informed consent and as such they require special protection. These include individuals who cannot give or refuse informed consent as well as those "who may be vulnerable to coercion or undue influence" (Gordon, 2020).
d. Child**:** Is defined as someone younger than 18 years in the Bill of Rights of the Constitution of SA.
e. Child headed households**:** Means a household per s 137 Children's Act 38 0f 2005.
f. Guardian: Means a person appointed by a court to look after the financial and welfare interests of a minor, or a person appointed by the parents with sole responsibility for the minor in terms of the parents Will.
g. Harm: Means physical, emotional, psychological, social or legal harm.
h. Minor: Means a person (child) less than 18 years (s 137 Children's Act 38 0f 2005).
i. Neonate: Means a newborn child, including an infant less than a month old.
j. Orphan: Means a child who has no surviving parent caring for him or her.
k. Parent: Includes an adoptive parent.
l. Therapeutic research: entails research that includes interventions that may hold out the prospect of direct health-related benefit for the participant.
m. Non-Therapeutic research: This is where interventions do not hold out the prospect of direct health-related benefit for the child participant, but the results of such research may contribute significantly to generalizable knowledge about the participant's

condition.

4. Responsibilities

- RECs should take special care when deliberating research involving vulnerable populations;
- To ensure optimal protection of the "vulnerable" research participant the REC may ask for additional protective measures to ensure the safety of these participants.
- Strategies for recruiting these participants, inclusion and exclusion criteria, the informed consent process, the informed consent document, coercion versus willingness to participate and confidentiality etc. needs to be set out in detail in the research proposal.
- The REC must ensure that certain groups or communities are not over-researched merely because they are easily accessible, while the research can be carried out in a less vulnerable population.
- For community research the REC must ensure that the planned research is relevant and appropriate to the specific community's needs.
- The researcher must have adequate procedures in place to ensure that the possible participants have the capacity to understand and give informed consent or assent.

5. Categories of Vulnerable Groups

Contextual Circumstances

- very poor socio-economic conditions;
- low levels of formal education and literacy; and
- restricted access to health care services.
- political minorities

Personal Circumstances

- minors (children less than 18 years);
- orphans without guardians;
- pregnant women;
- adults with incapacity to consent;
- persons in dependent relationships;
- patients highly dependent on medical care;

- persons with physical disabilities;
- prisoners; and
- collectivities i.e. informal communities, commercial or social groups.

a. Research involving minors

Research with children must comply with ethical guidelines and the Children's Act 38 of 2005, as they are legally incapable to independently choose whether to participate in research or not: **a parent or a guardian** must give permission for the minor to take part in research (see templates for Parental/Guardian PICDs at www.up.ac.za/healthethics). The minor needs to give **assent (**see template for Assent ICD at www.up.ac.za/healthethics).

Note: A minor mother may not give consent for her child to take part in research. Her guardian must assist her in this situation.

The 'best interests of the child' is paramount in the decisions that affect the child. Risks against benefit need to be assessed and deliberated. Children's privacy and especially their genetic information as well as their confidentiality need to be protected. This must be stated in the informed consent document.

Note: When a child turns 18 years of age during a research study, they need to be re-consented as adults.

Children should participate in research only where such research poses acceptable risks of harm. That is, research involving minors should be approved only if:

- The research, including observational research, is not contrary to the best interest of the minor;
- The research, including observational research, places the minor at no more than minimal risk of harm (i.e. the 'everyday risks standard' which means the risk of harm is commensurate with daily life in a stable society or routine medical, dental, educational or psychological tests or examinations – referred to as 'negligible risk' in some guidelines); or

- The research, including observational research, involves greater than minimal risk of harm, with no prospect of direct benefit to the minor, but has a high probability of providing significant generalisable knowledge. The degree of risk of harm should be justified by the risk-knowledge ratio.
- Greater than minimal risk of harm should represent no more than a minor increase over minimal risk.
- Where appropriate, the minor will assent to participation.

Research involving children must be reviewed appropriately. Section 71(3)(a)(ii) of the National Health Act distinguishes research with children as 'therapeutic' and 'non-therapeutic' research. The intention is to ensure RECs give due consideration to the degree of risk of harm posed by a proposal and the likelihood of benefit to the child-participant.

Therapeutic research entails research that includes interventions that may hold out the prospect of direct health-related benefit for the participant. Non-therapeutic research entails research that includes interventions that will not hold out the prospect of direct health-related benefit for the participant but may produce results that contribute to generalisable knowledge.

According to Section 71(3)(a)(ii) of the National Health Act 'non-therapeutic' health research with minors, may only be conducted when the following four criteria are met: (i) in such manner and on such conditions as may be prescribed; (ii) with the consent of the Minister; (iii) with the consent of the parent or guardian of the minor; and (iv) if the minor is capable of understanding, the consent of the minor.

The Minister may delegate authority, in terms of s 92(a), to any person in the employ of the state, a council, board or committee established in terms of the Act to give this consent. The Minister has delegated authority to provide Ministerial Consent for 'non-therapeutic' health research with minors to RECs that have been found to be compliant with the audit and have achieved full registration with the NHREC. For this a Ministerial consent form – Form A- should be completed by the researcher, for applying for approval from the REC, as empowered by the Minister of Health. This form is available at www.up.ac.za/healthethics.

- Adequate provision should be made for obtaining assent from children and consent from their

parents or legal guardians. Templates for these forms are available at www.up.ac.za/healthethics

- Where parents and legal guardians are not available, the REC shall be guided by applicable laws and guidelines, as well as the merits of the study and expert opinion on legal and technical points concerning the proposed study.

b. Research involving orphans without guardians

Research planned with these vulnerable minors as participants is problematic, as no parental or legally appropriate parental substitutes are available.

As it is important to do research on these children regarding their psychosocial, economic and educational requirements, it is generally acceptable to do research that involves no more than minimal risk of harm.

Where research involve a minor increase over minimal risk of harm it needs to be justified why it would be unjustifiable to exclude these children from research on the basis of their legal status.

"According to the Department of Health's guideline (2015) the following parental substitutes should be considered in descending order, before the child can give assent:

i. If no parent, then guardian: either court-appointed OR as indicated by the parent in a Will (s 27 Children's Act);
ii. If no guardian, then foster parent (per order of Children's Court) (Note that social workers should request that the authority to give permission should be included expressly in the court order authorising foster care);
iii. If no foster parent (per ii. above), then caregiver (s 1 Children's Act: defined as '…any person other than a parent or guardian, who factually cares for a child and includes – a) a foster parent; b) a person who cares for the child with the implied or express consent of a parent or guardian of the child; c) a person who cares for the child whilst the child is in temporary safe care; d) the person at the head of a child and youth care centre where a child has been placed;

e) the person at the head of a shelter; f) a child and youth care worker who cares for a child who is without appropriate family care in the community; and g) the child at the head of a child headed household'); and

iv. If minor is caregiver in child-headed household and no supervisory adult (s 137 Children's Act), then trusted adult nominated by minor, including but not limited to social worker, community worker or teacher."

c. Research involving women

Women should not be excluded in research as this can lead to a lack of data regarding their health. If they are excluded it needs to be justified in the light of the specific research question to be investigated.

Additional health concerns arise during pregnancy, including the need to avoid unnecessary risk to the foetus.

Consequently, researchers and RECs should exercise extra caution when women participants are or may become pregnant. Exclusion of women from research may be justifiable

a) to protect the health of the foetus; and

b) if exclusion is scientifically supportable.

In clinical medicine trials the Participant Information Consent Document should be specific in regard to possible pregnancy and risks to the fetus.

d. Adults incapable to give informed consent

Proxy decision makers are not permitted for adult persons who lack capacity unless the proxy is a court-appointed curator. Neither the National Health Act 61 of 2003 nor the Mental Health Care Act 17 of 2002 makes provision for proxy decision makers for research purposes, but they provide clear lists of proxy decision makers for treatment purposes.

Since it would be unethical to exclude a category of persons from research participation without adequate justification, arguably, an ethical argument can be made for using the statutory treatment proxies to provide permission for participation in research that complies with the stipulations set out below. However, RECs must be careful not to confuse the distinction between treatment and

research. In unusual circumstances, e.g. major incident research (see 3.4.1), it may be ethically permissible to permit proxy consent also in a situation where no statutory proxy is available but the risk of harm to knowledge ratio justifies it.

Minimum conditions for research involving incapacitated adults

Research involving incapacitated adults should be approved only if

i. The research, including observational research, is not contrary to the best interest of the individual;

ii. The research, including observational research, places the incapacitated adult at no more than minimal risk (i.e. the 'everyday risk standard' which means the risk is commensurate with 'daily life or routine medical, dental or psychological examinations and in social or education settings activities' – referred to as 'negligible risk' in some guidelines); or

iii. The research involves greater than minimal risk but provides the prospect of direct benefit for the incapacitated adult. The degree of risk must be justified by the potential benefit; or

iv. The research, including observational research, involves greater than minimal risk, with no prospect of direct benefit to the incapacitated adult, but has a high probability of providing generalizable knowledge; i.e. the risk should be justified by the risk-knowledge ratio;

v. Greater than minimal risk must represent no more than a minor increase over minimal risk;

vi. The legally appropriate person (treatment proxies as stipulated in NHA s 7 or s 27(1)(a) of the Mental Health Care Act 17 of 2002) gives permission for the person to participate; and

vii. Where appropriate, the person will assent to participation. Note that the incapacitated person's refusal or resistance to participate, as indicated by words or behaviour, takes precedence over permission by a proxy.

The National Health Act specifies the sequence of legally appropriate treatment proxies as spouse or partner; parent; grandparent; adult child; brother or sister. The Mental Health Care Act provides, in no particular sequence, that legally appropriate proxies are spouse; next of kin; partner; associate (defined as 'a person with a substantial or material interest in the well-being of a mental health care user or a person who is in substantial contact with the user'); and parent or guardian

5.5 Persons in dependent relationships

This class of persons includes persons in junior or subordinate positions in hierarchically structured groups and may include relationships between older persons and their care-givers; persons with chronic conditions or disabilities and their care-givers; persons with life threatening illnesses; patients and health care professionals; wards of state and guardians; students and teachers (including university teachers); employees and employers, including farm workers, members of the uniformed services and hospital staff and their respective employers.

Particular attention should be given to ensuring that participants are adequately informed and can choose voluntarily whether to participate in research.

5.6 Prisoners

The chief reason to consider prisoners as a vulnerable class of persons is the potential effect of incarceration on the voluntariness of the decision to participate in research. Neither coercion (direct threat of negative sanction) nor undue influence is acceptable in the informed consent process. Researchers should pay attention to whether their intended participants are awaiting trial prisoners or convicted prisoners. Quite obviously, different ethical issues arise for the former group who remain innocent until proven guilty, notwithstanding being incarcerated. The recruitment strategy design must pay careful attention to how coercion and undue influence will be avoided. Similarly, persons administering questionnaires or conducting interviews must be conscious of environmental factors that may influence voluntariness.

Studies on prisoners should only be conducted on prisoners if the researcher satisfies HREC that the research cannot be carried out equally well on non-prisoners and the research question cannot be answered with non-prisoners. The purpose of the research must be to obtain knowledge relevant to the health needs of prisoners.

5.7 Collectivities i.e. informal communities, commercial or social groups

Community Research

HREC must ensure that, particularly with regard to research involving communities, those communities' traditions and values are accounted for decision-making. This applies particularly with regard to obtaining consent to participate in research. However, permission given by a community's leader does not absolve the researcher from also obtaining the fully informed

consent of each individual participant.

References

1. U.S. Department of Health and Human Services (USDHHS). (1979). Belmont Report.

2. Council for International Organisations of Medical Sciences(CIOMS). (2016). International ethical guidelines for biomedical research involving human subjects.

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4. Ethics in Health Research: Principles, Processes and Structures 2nd Edition, Department of Health, Republic of South Africa,2015.

5. Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa, 2006.

6. Human Sciences Research Council Act, Act 17 of 2008.

7. National Health Act 61 0f2003.

8. South African Constitution, 1996 (Chapter 2 – Bill of Rights)

9. South African Medical Research Council Human Research Ethics Committee (2018) Standard Operating Procedures.

10. Stellenbosch University (2018) Standard Operating Procedures Research Ethics

Committee: Human Research (Humanities).

11. Human Sciences Research Council Research Ethics Committee SOP (July 2019)