Date: December 2, 2022

To: Professor Glenda Gray
President and CEO Medical Research Council

From: Professor Ames Dhai
Chair Bioethics Advisory Panel (Medical Research Council)

ADvisory: Consent for Health Research for Adolescents

Problem Statement:

When adolescents are involved in health research, protection from research harm needs to be weighed against inclusion in research, which may bring benefit. This balance between protection and inclusion is often fraught with indecision. In many countries, adolescents 12-17 years of age are often seen as a vulnerable population needing protection from risks of research involvement. Vulnerability mainly stems from a reduced ability of younger children to make reasoned choices, the lower social status of children and the power imbalance that renders children susceptible to adult coercion.

In most countries there is insufficient understanding of adolescent health and well-being, and inadequate local research to fully inform program and policy responses, including those related to adolescent rights and responsibilities. This is more pronounced in low- and middle-income countries (LMICs), which are home to 90 per cent of the world’s adolescents, and where research into issues of adolescent health and well-being – including sexual and reproductive health and HIV, nutrition, psychological well-being, injuries, social protection, child marriage, education and the transition to the labor force is particularly vital.

Some barriers to conducting research with adolescents include misunderstandings of adolescents’ cognitive abilities and capacity to provide informed consent; an overzealous valuing of protection over inclusion; institutional self-protection including from RECs; attitudes about adolescents as not holding equal rights to adults and legal barriers. As a result, adolescents risk exclusion from research that may benefit them individually and collectively. In South Africa conflicts between consent norms in the law (s71 of the NHA) versus ethics guidelines (DOH 2015) have placed stakeholders in a dilemma. The ongoing conundrum regarding consent for adolescent research has resulted in some research ethics committees (RECs) complying rigidly with section 71 of the NHA. This underscores that ethical review could be evolving to be more compliance-based at the expense of ethical reflection which necessitates real world and contextually relevant issues to be considered.


RATIONALE:

**National Health Act 61 of 2003**

Research involving minors (anyone under 16 years of age) is governed by section 71 of the National Health Act. Section 71(2) provides that therapeutic research may only be conducted if it complies with prescribed conditions (“in such manner and on such conditions as may be prescribed”); is in the best interests of the minor; if the parent or guardian of the child consents to the research, and where a minor is capable of understanding, with such minor’s consent. In other words, mandatory consent of the parents or guardians of a minor is required, and where the child has the ability to understand, he or she consents (not assent) along with his or her parents or guardian.

In the case of non-therapeutic research, section 71(3) requires that: relevant prescribed conditions must be met (“in such manner and on such conditions as may be prescribed”); the Minister must consent to the minor’s participation; the parent or guardian of the minor must consent; and where the minor is capable of understanding, that such minor must consent to participation. The Minister may withhold consent in the following instances:

- where the research objective may be achieved if conducted on an adult;
- where it is not likely to significantly improve scientific understanding of the minor’s health condition or significantly benefit such minor;
- where the consent from either minor, guardian or parent are contrary to public policy;
- where the research poses a significant risk to the minor’s health; or
- there is some risk to the minor’s health or well-being and the potential benefit of the research does not significantly outweigh that risk.

It is important to note that the requirement “in such manner and on such conditions as may be prescribed” refers to prescribed regulations in this regard.

**Regulations relating to Research with Human Participants**

Section 71 of the NHA is complemented by the 2014 Regulations relating to Research with Human Participants.3

Regulation (2014) section 4.1 states that research with minors should only take place when adults are not appropriate participants for the research; where the research poses no more than a minimal risk to the minor, or that where the research poses more than a minimal risk, that it has a direct benefit to the minor; or where the research poses more than minimal risk and has no direct benefit to the minor, that it may contribute to generalisable knowledge of the relevant health condition being studied and pose no more than a minor increase over minimal risk.

Regulation (2014) section 7 relating to Ministerial consent for non-therapeutic research with minors stipulates that non-therapeutic research involving minors must have ministerial consent or delegated authority. It also states the process to be followed to obtain ministerial consent. No reference, however, is made to clarify the other requirements set out in section 71(3) of the NHA.

The distinction between therapeutic and non-therapeutic research involving minors in the NHA and Regulations is peculiar, as research cannot always be clearly delineated as either therapeutic or non-therapeutic, and all research studies are a mix of interventions or procedures with some that have potential individual benefit and others that do not. This distinction requires RECs to carefully consider the risk-benefit ratio of interventions/ procedures to assess if risk-benefit ratios are met. It is noteworthy that the South African Law Reform Commission (SALRC) recognised that when parents or guardians are involved in certain types of therapeutic or nontherapeutic research, this might not always be in the best interest of children. For example, where a study involves abuse, and where the parent or guardian is the perpetrator, it is unlikely that he or she would give consent for the child to participate in such research. The SALRC recommended that consideration be given to allowing for the participation of children in non-therapeutic research without parental or guardian consent and making provision for the research ethics committee overseeing the study to waive

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parental or a guardian’s consent. While this recommendation is welcomed, it is still somewhat restrictive in that it applies to non-therapeutic research only. Nevertheless, it is a start in the direction towards legal reform in this context.

Regulation (2014) section 2 is of importance for two reasons: it establishes the 2015 Department of Health Guidelines on Ethics in Health Research as the mandatory minimum benchmark for health research, which recognises the legal force of the Guidelines. Section 2 furthermore provides that health research must be undertaken with “appropriate consent processes”. This phrase does little to guide researchers on how to address the varying consent approaches for minors’ participation in research in both the NHA, regulations and the 2015 Guidelines on Ethics in Health Research. However, it may be inferred that a broader approach than mandatory parental consent could be appropriate.

**Children’s Act 38 of 2005 and Choice on the Termination of Pregnancy Act 92 of 1996**

The regulation of minors’ consent in health research in the NHA stands in contrast to the recognition of the evolving capacities of minors in other contexts, such as the medical treatment (Children’s Act 38 of 2005; section 129); surgical operations (Children’s Act, section 129); access to contraceptives (Children’s Act, section 134); HIV-testing (Children’s Act, section 130); male circumcision (Children’s Act, section 12) and the termination of pregnancy (Choice on the Termination of Pregnancy Act 92 of 1996, section 5).

The Children’s Act explicitly recognises a child’s maturity and mental capacity, for example, in the case of surgical procedures, by providing that a child over the age of 12 may consent to surgical operations if he/she (i) has “sufficient maturity and has the mental capacity to understand the benefits, risks, social and other implications of the surgical operation”; and (ii) is assisted by a parent or guardian (section 129(3)). The Children’s Act 38 of 2005 hence recognises the participatory rights of children in certain instances, in terms of which they may participate in certain decisions affecting them. Furthermore, section 10 of the Children’s Act provides that children have a right to participate in an appropriate way in matters that affect them. Children, similar to adults, are Bill of Rights-holders whose moral equality with adults should be recognised. Exercising participatory rights by nature requires autonomy, which refers to those entitlements that allow persons the freedom of involvement in matters affecting them. Assessing an individual minor’s maturity level for the purpose of acknowledging the minor’s participatory rights is not a “one-size-fits-all” approach, but requires an individualised, context-specific exercise. In all contexts it is important to recognize that an individual’s social identity and personality is moulded by critical factors e.g. in certain traditional African contexts it may be moulded by community relationships. Such contextual factors should be identified through close engagement with community stakeholders.

The Choice on Termination of Pregnancy Act presents an anomaly with regard to female minors’ consent to the termination of pregnancy, which may constitute a medical or surgical procedure, depending on the case on hand. The Act permits a female of any age to independently consent on the termination of her pregnancy during the first twelve weeks. It does not specify the need for evidence in support of her maturity or mental capacity to understand the risks, social or other implications of the procedure.

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Research involving minors is not regulated by the Children’s Act, nor is it mentioned in the Choice on Termination of Pregnancy Act. However, these Acts suggest that the law recognizes several instances where children can consent on their own to health-related interventions.

The 2015 Department of Health Guidelines on Ethics in Health Research

The Guidelines deviate from the NHA's mandatory parental or legal guardian consent requirement by introducing a discretion when RECs consider the participation of minors in specific types of research. The Guidelines also state in par 3.2.2.1 that minors should participate in research only where their participation is scientifically indispensable to the research; i.e., the research objectives cannot be achieved by using adult participants. The research should investigate a problem of relevance to minors. Where the research is not of particular relevance to children or may be done involving adults only, research with minors should not be approved.

Minors should participate in research only where such research poses acceptable risks of harm, which means that it should be approved only if the research is not contrary to the minors' best interests; the research places the minors at no more than minimal or negligible risk of harm or the research involves greater than minimal risk of harm but provides the prospect of direct benefit to the minor or the research; if it involves greater than minimal risk of harm and no prospect of direct benefit to the minor, but has a high probability of providing significant generalisable knowledge.

In terms of Par 3.2.2, minors are in principle unable to choose independently whether to participate in research or not and a parent or guardian must give permission for the minor to choose. However, the Guidelines permit minors to independently consent to research participation in specific instances, where for reasons of sensitivity (for example, relating to sexual activity or substance abuse) it may be ethically justifiable and appropriate for mature minors (e.g., 16 years and older) to consent to research participation independently and without parental assistance. The Guidelines recommend that generally minimal risk research is suitable for independent consent by minors. A justification may be the need to recruit sufficient numbers of minors who may not otherwise participate if their parents are privy to the sensitive nature of the research.

The Guidelines recommend the following approach in justifying minors' independent consent: where prior engagement with participating community role players has taken place and is evidenced, the PI can request and should justify explicitly why REC approval of a waiver of the parental (or substitute) permission requirement is necessary. RECs that approve may grant a waiver of the requirement of written parental permission and must document the process carefully.

Legal status of the 2015 Guidelines vis-à-vis the National Health Act and Regulations

The question that arises is how to resolve the conflicting provisions relating to minors' consent in health research in the various statutes, regulations and the Ethical Guidelines discussed above. Alternatively, which legal instrument should prevail in order to guide RECs in reviewing research ethics applications involving minors in health research?

The 2014 Regulations relating to Research with Human Participants (section 2) has endorsed the 2015 Department of Health’s Ethics in Research Guidelines as the minimum legal standard or benchmark for research with human participants. One of the requirements in section 71 of the NHA that must be complied with, refers to prescribed regulations ("in such manner and on such conditions as may be prescribed"), which are the 2014 Regulations relating to Research with Human Participants. Hence, it is inferred that section 71 of the NHA, the 2014 Regulations and the 2015 Ethical Guidelines are all legally binding on the same level.

These provisions are not aligned, therefore the question arises as to how to resolve this legal impasse. The law of statutory interpretation may assist in providing some direction. Normally, where there is a conflict between legislation at different levels i.e. national and provincial legislation that a court cannot resolve, national legislation will trump provincial legislation. Where there is conflict between legislation at the same level (as is the case here) they should

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10 A provincial act can prevail only if that law has been approved by the National Council of Provinces. In determining the prevailing statute, the conditions in section 146(2) of the Constitution should be met for national legislation to prevail
be read together in a manner that is aligned with the Constitution and its values. If not possible, an interpretation closest to giving effect to the Bill of Rights should be preferred.

The Constitution of the Republic of South Africa

Following the enactment of the Constitution of the Republic of South Africa, 1996, the focus has turned from a once mechanical reiteration of legislator’s intention to one that is guided by the Constitution as an objective, normative legal framework. The Constitutional court’s judgment in S v Makwanyane emphasises the need to use the constitutional values in the interpretation process. The preamble to the Constitution refers to promoting a society based on democratic values, social justice and fundamental human rights which need to be protected by courts when legislation is interpreted.

Section 39(1) of the Constitution directs that “[w]hen interpreting the Bill of Rights, a court, tribunal or forum- (a) must promote the values that underlie an open and democratic society based on human dignity, equality and freedom; (b) must consider international law; and (c) may consider foreign law.” Section 39(2) refers pertinently to the interpretation of legislation and states that “[w]hen interpreting any legislation [...] every court, tribunal or forum must promote the spirit, purport and objects of the Bill of Rights”. In other words, an interpretation of the NHA, regulations and the Children’s Act should strive to advance the constitutional values of among others, human dignity, equality and freedom. Interpretation must not give effect to a meaning that would stultify the operation of the Constitution or the attainment of its aims. Context is very important in the interpretative process. Therefore, having a broader range of consent approaches gives effect to the constitution.

The recognition of minors’ evolving capacities promotes their self-determination and evolving autonomy and dignity as right-holders, which is closely aligned with the Bill of Rights and the constitutional values of human dignity, equality and the advancement of human rights and freedoms. This is also reflected in the context-specific approach for minors’ self-consent when criteria can be reached as espoused in the DoH Guidelines.

The Constitution protects children in section 28 with the directive that ‘the child’s best interests are of paramount importance in every matter concerning the child’ (our emphasis). In addition, children are afforded all of the rights conferred on ‘everyone’ in the Constitution. Rights relevant to children include the right to equality before the law and to equal protection and benefit of the law (section 9), as well as the prohibition of unfair discrimination by the state and private entities, for example on the ground of age. Similar to adults, the right to self-determination and autonomy will derive from other rights, such as the right to dignity (section 10), privacy (section 14); freedom of religion (section 15), expression and association (section 16), and very importantly, the right to bodily and psychological integrity, which includes, among others, ‘the right to security in and control over their body’ (sections 12(2)(b)). Parental control over children will, where a child has not yet reached the sufficient maturity to make independent decisions, constitute a justified limitation of children’s exercise of these rights. However, where such maturity and competencies exist, it will be increasingly difficult to use parental control as a justifiable limitation of a child’s autonomy. Section 9 of the Children’s Act reiterates section 28(2) of the Constitution. Although what is in the best interests of the child is not specifically defined by legislation, the Children’s Act does provide a list of factors to be taken into account when making such a determination. Perhaps the most important of these factors for determining whether it is in the best interests of the child to consent to research include: (1) the child’s age, maturity and stage of development; gender, background; and other relevant characteristics of the child; (2) the child’s physical and emotional security and their intellectual, emotional, social and cultural development; (3) the capacity of the parents; (4) any other care-giver or person to provide for the needs of the child including emotional and intellectual needs.

over provincial legislation. Section 150 states that a court should use a reasonable interpretation of the legislation that avoids a conflict.

11 Carmichele v Minister of Safety and Security 2001 4 SA 938 (CC) paras 54-55 58.
12 S v Makwanyane 1995 (3) SA 391 (CC) para 262.
13 See also ss 7, 36 and 39 of the Constitution.
16 Aktiebolaget Hassle v Triomed (Pty) Ltd 2003 1 SA 155 (SCA) para 1.
Section 39(1)(b) of the Constitution mandates the courts, when interpreting the Bill of Rights, to consider international law. International law, in accordance with section 231(4), includes international agreements that have been enacted into law in national legislation or a self-executing provision of an agreement that has been approved by parliament, unless inconsistent with the Constitution or an Act of Parliament. Furthermore, section 233 of the Constitution determines that “when interpreting any legislation, every court must prefer any reasonable interpretation of the legislation that is consistent with international law over any alternative interpretation that is inconsistent with international law”. One specific agreement that is critically important for the discussion on minors’ consent is the UN Convention on the Rights of the Child, the world’s most ratified treaty, which became the first legally binding international convention to affirm human rights for all children. South Africa signed the Convention in 1993 and ratified it on the 16th June 1995.

Furthermore, the Children’s Act and the 2015 DoH Guidelines were passed and introduced after the enactment of the NHA, which strengthens the assumption that these by implication may override the NHA with regard to issues pertaining to children and consent. In fact, the DoH Guidelines constitute the most recent development relating to children’s consent in health research that is not regulated in the Children’s Act, which is concerned with children’s consent to medical treatment, surgery, contraceptives, HIV-testing and circumcision respectively. The Children’s Act recognises the evolving capacities and maturity of children, however the DoH Guidelines go one step further by acknowledging specific instances and types of research in which REC’s may approve a waiver of parental or parental substitute’s permission and permit minors to self-consent to research participation, provided criteria can be met.

**International considerations**

Globally, there are more than a billion adolescents. Adolescence is a critical period of cognitive, emotional, physical and sexual development with consequences across the life course of the individual and a strong influence on whether the next generation has a healthy start to life. The significance of this period of rapid development has gained prominence in the international arena including the Sustainable Development Goals resulting in a greater focus on adolescents as both recipients of interventions to improve their well-being and as decision-makers and implementation partners in their own lives. However, international consensus as to the age of consent for participation in research is lacking. Nevertheless, the concept of a mature minor, i.e., an adolescent who demonstrates the capacity to understand and make reasonable decisions about their own well-being, is recognised in many legal systems.

For the purposes of this Advisory, the following documents were considered:

- UN Convention on the Rights of the Child
- WHO Guidance on Ethical considerations in planning and reviewing Research Studies on sexual and reproductive health in adults
- United Nations Children’s Fund: Ethical Research Involving Children
- United Nations Children’s Fund: Innocenti Research Briefs 1, 3 and 4

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17 Adopted and opened for signature, ratification and accession by General Assembly resolution 44/25 of 20 November 1989 entry into force 2 September 1990.
• Council for International Organisations of Medical Sciences (CIOMS) Ethical Guidelines for Health-related Research involving Humans\textsuperscript{24}
• World Medical Association Declaration of Helsinki\textsuperscript{25}
• Our future: A Lancet commission on adolescent health and well-being\textsuperscript{26}

Main themes emerging from these documents were:

a) Children are persons in their own right and are worthy and capable of recognition, respect and voice in research. They have a right to have a say and to be heard, including in the context of well-planned, ethical research;

b) Involvement of children in any kind of research should take place in partnership with caring, skilled adults who need to provide appropriate support and guidance, in order to help them formulate their views and participate in a safe and meaningful way;

c) It is essential that research is focused on understanding and improving adolescents’ lives and circumstances;

d) Engagement with the well-attested ethical principles of respect, benefit and justice during research is necessary;

e) Dialogue and a more reflexive approach should be promoted when attending to complex ethical issues that can emerge with research involving adolescents;

f) Ethical regulatory mechanisms and review processes may be experienced as supportive or restricting, but they do not ensure ethical practice, and cannot replace researchers’ contingent ethics in the field; and

g) Although much emphasis is placed on informed consent, it is an essential but imperfect mechanism to protect adolescents from research harm.

Any policy document should, at the outset take into consideration that adolescents are no longer children, but they are not yet adults and that they are unique beings with human rights, developmental needs and tremendous potential. Hence, respect for persons and their evolving capacity to make informed decisions should be key. To this end, the UNCRC is the central starting point. It is the first and most complete international instrument to assert the full range of rights of all children. It gives recognition to children as rights holders & draws attention to their protection and provision rights. It affirms obligations to consider the best interests of the child and to consider their evolving capacities to make sound decisions and participate in promoting their own welfare. Article 12 mandates that state parties are to assure to the child who is capable of forming his or her own views, the right to express those views freely in all matters affecting the child, with the views of the child being given due weight in accordance with the age and maturity of the child. While it does not refer specifically to research, its articles are elastic enough to address most aspects of children’s lives, including participation in research. This is particularly so when read in conjunction with the UN Committee on the Rights of the Child General Comments. South Africa’s Children’s Act and Choice on Termination of Pregnancy Act draw from principles in the UNCRC. However, it seems that this was not the case when it comes to the National Health Act’s stipulations on research involving minors.

Evolving capacities resulting in ability to provide truly informed consent has been directly informed by research on neurodevelopment and cognition during adolescence coupled with previous life experiences. It has been found that from age 12 adolescents have decision-making competence and 14-year-olds are as capable as adults in understanding multiple viewpoints and considering conflicting information and their ability to make decisions about research participation is similar to that of adults\textsuperscript{27}.


The WHO guidelines state that while the UNCRC makes it a requirement that children have their voices heard, this does not mean they have full autonomy, and therefore this does not give children the right to control all decisions irrespective of their implications either for themselves or others. Given that decision-making capacity is still considered to be evolving, only a child’s parent or legal guardian may legally provide consent for the child to participate in research. Legally, children can only assent to research participation until they are old enough to provide legally valid consent. In these cases, both the authorization and consent of the parents and the child’s assent or agreement must be obtained. It highlights that therapeutic and research contexts are distinct from each other and involve different risks. It cautions that informed consent requirements for both should not be confused. Importantly, it does however, allow for waiver of parent / guardian consent where it may not be permissible to solicit their consent, for example where they are untraceable or for reasons of sensitivity. In such cases, waivers may be granted by RECs or where the law does not permit this, the researcher may apply to court which is generally regarded as the upper guardian of the child. Similarly, CIOMS guidelines require parental consent but allow parental waiver under some circumstances. The Declaration of Helsinki lays down the requirement for permission from a legally authorised representative. These three international guidance documents are restrictive. It must be remembered that adolescents are best sources of information about their own lives and they may have priorities at odds with their family and community of origin and should have the right to make important decisions affecting their own lives. Parents are not always best positioned to consent for adolescents.

SYNTHESIS

Inevitably, harm may result if research to include all relevant adolescents necessary to achieve the objectives of the study is not undertaken. Vulnerable adolescents end up becoming even more vulnerable. Researchers have a responsibility to ensure that adolescents are not harmed by being declined participation in research and that risks are sufficiently minimized and sufficiently outweighed. In addition, the long-term and/or greater good for adolescents as social groups must be attended to. Researchers should be equipped with knowledge and skills and have a responsibility to ensure that adolescents as a group and as individuals are included in research pertinent to their needs.

While it is critically important to acknowledge parents in gate-keeping roles for protecting adolescents from potential harm, it is also necessary to recognise that parents may use power against adolescents and may not always have their best interests in mind. It is equally important to respect adolescent’s reasons for not wanting parental involvement thereby respecting their rights in line with their evolving capacity to consent.

RECOMMENDATIONS:

1. The National Health Act be amended to take into consideration the UNCRC’s provisos on the rights of children and their evolving capacities to make informed decisions, and to permit a broader range of consent approaches under justifiable conditions. This would also be in line with the recommendations of the SALRC, even though the latter is restricted to non-therapeutic research.

2. The SAMRC should take the lead in initiating amendments to the National Health Act, and a formal request for this change should be sent to the Minister of Health from the President and CEO of the SAMRC. (see Appendix 1 for proposed change)

3. While awaiting the change in law - an individualised, case by case basis approach is necessary and should be considered by the SAMRC REC:
   a) RECs are urged to consider Regulation 2 of the 2014 Human Subjects Regulations when making decisions about consent approaches for adolescent research where, for cogent and justifiable reasons, researchers request a waiver of parental consent. This does not mean that the REC review should be lax, but rather that ethics principles and in particular, the justice principle are reflected on and that no adolescent is unfairly discriminated against in research.
   b) RECs should share their approaches with each other to support networking around this issue.
   c) Researchers carefully consider whether the study meets criteria in ethics guidelines (DOH 2015) for parental waiver, and spell this out clearly in protocols so that RECs can make their assessment.
d) Where relevant, an added layer of protection for the adolescent would be that of consulting with relevant communities when considering adolescent consent for research.

Thank you for considering the recommendations in this Advisory.

Sincerely

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Professor A Dhai
Chairperson Bioethics Advisory Panel

[Signature]

8/15/2023
Appendix 1

Current Act

71. (1) Notwithstanding anything to the contrary in any other law, research or experimentation on a living person may only be conducted:
(a) in the prescribed manner; and
(b) with the written consent of the person after he or she has been informed of the objects of the research or experimentation and any possible positive or negative consequences on his or her health.

(2) Where research or experimentation is to be conducted on a minor for a therapeutic purpose, the research or experimentation may only be conducted:
(a) if it is in the best interests of the minor;
(b) in such manner and on such conditions as may be prescribed;
(c) with the consent of the parent or guardian of the child; and
(d) if the minor is capable of understanding, with the consent of the minor.

Proposed Amendment

71(2) Where research or experimentation is to be conducted on a minor, the research or experimentation may only be conducted:
(a) if it is in the best interests of the minor;
(b) in such manner and on such conditions as may be prescribed;
(c) with the consent of the minor, provided that the minor has sufficient maturity and mental capacity to be able to provide consent, and
(d) with the consent of the parent or guardian where the minor lacks sufficient maturity and mental capacity to be able to provide consent.